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[효능·효과] • **성인** 1. 류마티스 관절염 2. 건선성 관절염 3. 축성 척추관절염 (강직성 척추염, 방사선학적으로 확인되지 않는 축성 척추관절염) 4. 성인 크론병(18세 이상) 5. 건선 6. 궤양성대장염 7. 베체트 장염 8. 화농성 한선염 • **소아** 1. 소아 크론병 (6세~17세) 2. 소아 특발성 관절염 (다관절형 소아 특발성 관절염, 골부착부위염 관련 관절염) 3. 소아 판상 건선 **[용법·용량]** • **성인 (18세 이상)** 1. 류마티스 관절염: 40mg 2주에 1회 피하주사. 반응 감소 시 40mg 매주 또는 80mg 2주에 1회. 2. 건선성 관절염, 강직성 척추염 및 방사선학적으로 강직성 척추염이 확인되지 않는 중증 축성 척추관절염: 40mg 2주에 1회. 3. 성인 크론병: (유도) 첫 주 80mg, 2주 후 40mg 또는 첫 주 160mg, 2주 후 80mg. (유지) 40mg 2주에 1회. 반응 감소 시 40mg 매주 또는 80mg 2주에 1회. 4. 건선: (유도) 첫 주 80mg. (유지) 40mg 2주에 1회. 반응 감소 시 40mg 매주 또는 80mg 2주에 1회. 5. 궤양성 대장염: (유도) 첫 주 160mg, 2주 후 80mg. (유지) 40mg 2주에 1회. 반응 감소 시 40mg 매주 또는 80mg 2주에 1회. 6. 베체트 장염: 첫 주 160mg, 2주 후 80mg, 첫 투여 4주 후 40mg 2주에 1회. 7. 화농성 한선염: 첫 주 160mg, 2주 후 80mg, 첫 투여 4주 후 40mg 매주 또는 80mg 2주에 1회, 치료 중단 시 40mg 매주 또는 80mg 2주에 1회로 재투여. • **소아** 1. 소아 크론병 (6세~17세) (40kg 이상) 성인과 동일. 2. 소아 특발성 관절염 (다관절형 소아 특발성 관절염, 골부착부위염 관련 관절염) (30kg 이상) 40mg 2주에 1회. 3. 소아 판상 건선 (30kg 이상) 처음 2회 매주 40mg, 이후 40mg 2주에 1회. **[사용상의 주의사항]** 이 약은 휴미라주40밀리그램(아달리무맙, 유전자재조합)을 대조약으로 한 동등생물의약품이다. • **금기** 1.아달리무맙 또는 이 약의 성분에 과민증인 환자 2. 활동성 결핵 또는 패혈증, 기회감염과 같은 다른 중증 감염이 있는 환자 (경고항 참조) 3. 중등도 내지 중증의 심부전 (NYHA class III/IV) 환자 **[포장단위]** 프리필드시린지(0.8mL), 프리필드펜주(0.8mL) x 1개 / Box **[사용기간]** 제조일로부터 36개월 **[저장방법]** 밀봉용기, 냉장(2~8℃)보관, 차광보관 **[수입자, 제조의뢰자]** 삼성바이오에피스(주), 인천광역시 연수구 첨단대로 107 **[제조자]** Biogen(Denmark) Manufacturing ApS (원료의약품), 삼성바이오로직스주식회사, 대한민국, 인천광역시 연수구 송도바이오대로 300 (송도동, 삼성바이오로직스) (원료의약품) **[판매자]** ㈜유한양행, 서울특별시 동작구 노량진로 74 (대방동), 전화: 080-024-1188 **[개정연월일]** 프리필드시린지: 2021.07.20 프리필드펜: 2021.07.20 ※ 자세한 허가사항은 식약처 의약품통합정보시스템 홈페이지(https://nedrug.mfds.go.kr/)를 참조하여 주시기 바랍니다. 요약 허가사항에 반영되지 않은 허가 변경이 상기일자 이후에 있을 수도 있습니다.

1. 의약품 안전나라 의약품통합정보시스템(http://nedrug.mfds.go.kr/index)

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YUHAN

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2021년 4월 1일, 1일 1회 복용하는

젤잔즈 XR 11 mg 보험급여 인정[1,2]

(고시 제2021-101호)

FIRST MOVER 젤잔즈[3-8,*]

*RA (2014년 4월 국내 허가), UC 및 PsA (2018년 9월 국내 허가)
치료를 위한 국내 최초의 경구용 JAK 억제제

Monotherapy : RA 환자 대상 단독요법의 6년까지 지속된 젤잔즈 5mg의 효과[9a,†]
젤잔즈 XR 11 mg QD + MTX 병용요법 대비 24주까지 젤잔즈 XR 11 mg QD 단독요법의 비열등성[10b,‡] 확인

Oral administration : RA 치료에 있어 새로운 패러다임을 제공한 국내 최초의 경구용 JAK 억제제 젤잔즈,[3-8,11,12,*]
그리고 1일 1회 복용하는 젤잔즈 XR 11 mg의 보험급여 확대(2021년 4월)[1,2]

Various indications : RA, PsA, UC 치료에 젤잔즈 5mg의 효과 입증[13c-15e,#] 및 국내 허가[3]

Extensive clinical trials : DMARD-IR, MTX-IR, TNFi-IR RA 환자군에서 젤잔즈 5mg 단독 및 MTX 병용요법의 효과[9a,†,16f-20j,§],
9.5년 장기연장연구에서 젤잔즈 5mg의 일관된 안전성 프로파일 확인[21k]

Real-world experiences : 전 세계적으로 208,549명 이상의 환자[22,¶], 240,907 patient-years의 경험 축적[23,$] 및
미국 registry에서 허가 후 5년간 젤잔즈의 안전성 프로파일 확인[24l,††]

† ACR20/50/70 (American College of Rheumatology 20/50/70% improvement criteria) response rates were sustained up to month 72 for patients receiving tofacitinib 5 mg and 10 mg twice daily as monotherapy. At month 1, ACR20/50/70 response rates were 76.8%, 53.1% and 32.1%, respectively, with tofacitinib 5 mg twice daily monotherapy and 75.1%, 52.4% and 34.1%, respectively, with tofacitinib 10 mg twice daily monotherapy. Corresponding observed rates at month 72 were 84.9%, 68.7% and 42.4% with tofacitinib 5 mg twice daily and 84.6%, 56.4% and 35.9% with tofacitinib 10 mg twice daily.[9]

‡ The LSM (least squares mean) change from week 24 to week 48 in DAS28-4[ESR] (Disease Activity Score in 28 joints, erythrocyte sedimentation rate; primary efficacy endpoint) was greater (ie, increased disease activity) with tofacitinib monotherapy versus tofacitinib plus methotrexate, yet the difference between treatment groups of 0.30 (95% CI [confidence interval] 0.12–0.48) demonstrated that tofacitinib monotherapy after methotrexate withdrawal was non-inferior to continued tofacitinib plus methotrexate.[10]

* RA (2014년 4월 국내 허가), UC 및 PsA (2018년 9월 국내 허가) 치료를 위한 국내 최초의 경구용 JAK 억제제

· At month 3, a higher percentage of patients in the tofacitinib groups than in the placebo groups met the criteria for an ACR 20 response (59.8% in the 5-mg tofacitinib group and 65.7% in the 10-mg tofacitinib group vs. 26.7% in the combined placebo groups, P<0.001 for both comparisons). The reductions from baseline in HAQ-DI (Health Assessment Questionnaire–Disability Index) scores were greater in the 5-mg and 10-mg tofacitinib groups than in the placebo groups (−0.50 and −0.57 points, respectively, vs. −0.19 points; P<0.001).[13]
· ACR20 response rates at month 3 were 50% in the 5-mg tofacitinib group and 61% in the 10-mg tofacitinib group, as compared with 33% in the placebo group (P = 0.01 for the comparison of the 5-mg dose with placebo; P<0.001 for the comparison of the 10-mg dose with placebo); the rate was 52% in the adalimumab group. The mean change in the HAQ-DI score was −0.35 in the 5-mg tofacitinib group and −0.40 in the 10-mg tofacitinib group, as compared with −0.18 in the placebo group (P = 0.006 for the comparison of the 5-mg dose with placebo; P<0.001 for the comparison of the 10-mg dose with placebo); the score change was −0.38 in the adalimumab group.[14]
· In the OCTAVE Induction 1 trial, remission at 8 weeks occurred in 18.5% of the patients in the tofacitinib group versus 8.2% in the placebo group (P = 0.007); in the OCTAVE Induction 2 trial, remission occurred in 16.6% versus 3.6% (P<0.001). In the OCTAVE Sustain trial, remission at 52 weeks occurred in 34.3% of the patients in the 5-mg tofacitinib group and 40.6% in the 10-mg tofacitinib group versus 11.1% in the placebo group (P<0.001 for both comparisons with placebo).[15]

§ · At 6 months, ACR50 response was attained in 147 (38%) of 384 patients with tofacitinib monotherapy, 173 (46%) of 376 patients with tofacitinib and methotrexate, and 169 (44%) of 386 patients with adalimumab and methotrexate. Non-inferiority was declared for tofacitinib and methotrexate versus adalimumab and methotrexate (difference 2% [98.34% CI-6 to 11]) but not for tofacitinib monotherapy versus either adalimumab and methotrexate (−6 [−14 to 3]) or tofacitinib and methotrexate (−8 [−16 to 1]).[16]
· At month 6, ACR 20 response rates were higher among patients receiving 5 mg or 10 mg of tofacitinib (51.5% and 52.6%, respectively) and among those receiving adalimumab (47.2%) than among those receiving placebo (28.3%) (P<0.001 for all comparisons). There were also greater reductions in the HAQ-DI score at month 3 and higher percentages of patients with a DAS28-4(ESR) below 2.6 at month 6 in the active-treatment groups than in the placebo group.[17]
· At month 6, response rates according to the American College of Rheumatology 20% improvement criteria for tofacitinib at 5 mg and 10 mg twice daily were higher than those for placebo (51.5% and 61.8%, respectively, versus 25.3%; both P<0.0001). At month 6, least squares mean (LSM) changes in total modified Sharp/van der Heijde score for tofacitinib at 5 mg and 10 mg twice daily were 0.12 and 0.06, respectively, versus 0.47 for placebo (P=0.0792 and P≤0.05, respectively). At month 3, LSM changes in the Health Assessment Questionnaire disability index score for tofacitinib at 5 mg and 10 mg twice daily were −0.40 (significance not declared due to step-down procedure) and −0.54 (P<0.0001), respectively, versus −0.15 for placebo. At month 6, rates of remission (defined as a value <2.6 for the 4-variable Disease Activity Score in 28 joints using the erythrocyte sedimentation rate) for tofacitinib at 5 mg and 10 mg twice daily were 7.2% (significance not declared due to step-down procedure) and 16.0% (P<0.0001), respectively, versus 1.6% for placebo.[18]
· Mean treatment differences for ACR20 response rates (month 6) for the 5-mg and 10-mg tofacitinib groups compared with the combined placebo groups were 21.2% (95% CI, 12.2% to 30.3%; P<0.001) and 25.8% (CI, 16.8% to 34.8%; P<0.001), respectively. The HAQ-DI scores (month 3) and DAS28-4(ESR) less than 2.6 response rates (month 6) were also superior in the tofacitinib groups versus placebo.[19]
· At month 3, ACR20 response rates were 41.7% (55 of 132 [95% CI vs placebo 6.06–28.41]; p=0.0024) for tofacitinib 5 mg twice a day and 48.1% (64 of 133; [12.45–34.92]; p<0.0001) for tofacitinib 10 mg twice a day versus 24.4% (32 of 131) for placebo. Improvements from baseline in HAQ-DI were −0.43 ([−0.36 to −0.15]; p<0.0001) for 5 mg twice a day and −0.46 ([−0.38 to −0.17]; p<0.0001) for 10 mg twice a day tofacitinib versus −0.18 for placebo; DAS28<2.6 rates were 6.7% (eight of 119; [0–10.10]; p=0.0496) for 5 mg twice a day tofacitinib and 8.8% (11 of 125 [1.66–12.60]; p=0.0105) for 10 mg twice a day tofacitinib versus 1.7% (two of 120) for placebo.[20]

¶ 2019년 4월 기준[22]

$ RA 및 UC 환자 대상 젤잔즈 및 젤잔즈 XR, 2019년 11월 기준[23]

†† Patients with RA initiating tofacitinib had similar incidence of MACE, SIEs, malignancies, and death versus bDMARD initiators over 5 years. Incidence of VTEs was similar in both cohorts.[24]

[Study design] a. Data were pooled from open-label LTE (long-term extension) studies (ORAL Sequel (NCT00413699; ongoing; data collected 14 January 2016) and NCT00661661) involving 4967 patients who participated in qualifying index studies. Efficacy outcomes included ACR 20/50/70 rates, change from baseline in DAS28-4(ESR), Clinical Disease Activity Index (CDAI) and Health Assessment Questionnaire-Disability Index and DAS28-4(ESR) and CDAI low disease activity and remission. Safety was evaluated over 96 months. 4967 patients were treated.[9] b. ORAL Shift was a phase 3b/4 non-inferiority trial in patients aged at least 18 years with moderate-to-severe rheumatoid arthritis and an inadequate response to methotrexate done in 109 centres across 16 countries. After 24 weeks of open-label tofacitinib modified-release 11 mg once daily plus methotrexate, patients who achieved LDA (low disease activity; clinical disease activity index [CDAI] ≤10) were randomly assigned 1:1 via an automated web-based response system to receive tofacitinib plus placebo (tofacitinib monotherapy; ie, masked methotrexate withdrawal) or continue tofacitinib plus methotrexate for 24 weeks in a double-blind manner. The primary endpoint was the least squares mean change from week 24 to week 48 in disease activity score in 28 joints with four variables, including erythrocyte sedimentation rate (DAS28-4[ESR]). The primary analysis was done in all patients who received at least one dose of study treatment in both phases, and safety was assessed in all patients who received at least one dose of study treatment since enrolment. Noninferiority of tofacitinib monotherapy versus tofacitinib plus methotrexate was declared if the upper bound of the 95% CI for the difference in change in DAS28-4(ESR) between treatment groups was less than 0.6. Safety was assessed in both phases. Between Sept 1, 2016, and Nov 1, 2017, 694 patients were enrolled in the open-label phase and 623 received study treatment for 24 weeks.[10] c. In this phase 3, double-blind, placebo-controlled, parallel-group, 6-month study, 611 patients were randomly assigned, in a 4:4:1:1 ratio, to 5 mg of tofacitinib twice daily, 10 mg of tofacitinib twice daily, placebo for 3 months followed by 5 mg of tofacitinib twice daily, or placebo for 3 months followed by 10 mg of tofacitinib twice daily. The primary end points, assessed at month 3, were the percentage of patients with at least a ACR 20, the change from baseline in HAQ-DI scores (which range from 0 to 3, with higher scores indicating greater disability), and the percentage of patients with a DAS28-4(ESR) of less than 2.6 (with scores ranging from 0 to 9.4 and higher scores indicating more disease activity).[13] d. In this 12-month, double-blind, active-controlled and placebo-controlled, phase 3 trial, we randomly assigned patients in a 2:2:2:1:1 ratio to receive one of the following regimens: tofacitinib at a 5-mg dose taken orally twice daily (107 patients), tofacitinib at a 10-mg dose taken orally twice daily (104), adalimumab at a 40-mg dose administered subcutaneously once every 2 weeks (106), placebo with a blinded switch to the 5-mg tofacitinib dose at 3 months (52), or placebo with a blinded switch to the 10-mg tofacitinib dose at 3 months (53). Placebo groups were pooled for analyses up to month 3. Primary end points were the proportion of patients who had an ACR20 response (≥20% improvement from baseline in the number of tender and swollen joints and at least three of five other important domains) at month 3 and the change from baseline in the HAQ-DI score (scores range from 0 to 3, with higher scores indicating greater disability) at month 3.[14] e. The investigators conducted three phase 3, randomized, double-blind, placebo-controlled trials of tofacitinib therapy in adults with ulcerative colitis. In the OCTAVE Induction 1 and 2 trials, 598 and 541 patients, respectively, who had moderately to severely active ulcerative colitis despite previous conventional therapy or therapy with a tumor necrosis factor antagonist were randomly assigned to receive induction therapy with tofacitinib (10 mg twice daily) or placebo for 8 weeks. The primary end point was remission at 8 weeks. In the OCTAVE Sustain trial, 593 patients who had a clinical response to induction therapy were randomly assigned to receive maintenance therapy with tofacitinib (either 5 mg or 10 mg twice daily) or placebo for 52 weeks. The primary end point was remission at 52 weeks.[15] f. ORAL Strategy was a 1 year, double-blind, phase 3b/4, head-to-head, non-inferiority, randomised controlled trial in patients aged 18 years or older with active rheumatoid arthritis despite methotrexate therapy. Patients were randomly assigned (1:1:1) to receive oral tofacitinib (5 mg twice daily) monotherapy, oral tofacitinib (5 mg twice daily) plus methotrexate, or subcutaneous adalimumab (40 mg every other week) plus methotrexate at 194 centres in 25 countries. Eligible patients received live zoster vaccine at investigators' discretion. The primary endpoint was the proportion of patients who attained an ACR50 at month 6 in the full analysis set (patients who were randomly assigned to a group and received at least one dose of the study treatment). Non-inferiority between groups was shown if the lower bound of the 98.34% CI of the difference between comparators was larger than −13.0%. 1146 patients received treatment (384 had tofacitinib monotherapy; 376 had tofacitinib and methotrexate; and 386 had adalimumab and methotrexate).[16] g. In this 12-month, phase 3 trial, 717 patients who were receiving stable doses of methotrexate were randomly assigned to 5 mg of tofacitinib twice daily, 10 mg of tofacitinib twice daily, 40 mg of adalimumab once every 2 weeks, or placebo. At month 3, patients in the placebo group who did not have a 20% reduction from baseline in the number of swollen and tender joints were switched in a blinded fashion to either 5 mg or 10 mg of tofacitinib twice daily; at month 6, all patients still receiving placebo were switched to tofacitinib in a blinded fashion. The three primary outcome measures were a 20% improvement at month 6 in the ACR 20; the change from baseline to month 3 in the score on the HAQ-DI (which ranges from 0 to 3, with higher scores indicating greater disability); and the percentage of patients at month 6 who had DAS28-4[ESR] of less than 2.6 (with scores ranging from 0 to 9.4 and higher scores indicating greater disease activity).[17] h. In this double-blind, parallel-group, placebo-controlled study, patients receiving background MTX (methotrexate) were randomized 4:4:1:1 to tofacitinib at 5 mg twice daily, tofacitinib at 10 mg twice daily, placebo to tofacitinib at 5 mg twice daily, and placebo to tofacitinib at 10 mg twice daily. At month 3, nonresponder placebo-treated patients were advanced in a blinded manner to receive tofacitinib as indicated above; remaining placebo-treated patients were advanced at 6 months. Four primary efficacy end points were all analyzed in a step-down procedure.[18] i. This study was 1-year, doubleblind, randomized trial, performed 114 centers in 19 countries. 792 patients with active RA despite nonbiologic DMARD therapy were included. Patients were randomly assigned 4:4:1:1 to oral tofacitinib, 5 mg or 10 mg twice daily, or placebo advanced to tofacitinib, 5 mg or 10 mg twice daily. Primary end points were 20% improvement in ACR20 criteria; DAS28-4(ESR) of less than 2.6; DAS28-4(ESR)-defined remission, change in HAQ-DI score, and safety assessments.[19] j. We did a 6-month, double-blind, parallel-group phase 3 study at 82 centres in 13 countries, including North America, Europe, and Latin America. 399 patients aged 18 years or older with moderate-to-severe rheumatoid arthritis and inadequate response to tumour necrosis factor inhibitors (TNFi) were randomly assigned in a 2:2:1:1 ratio with an automated internet or telephone system to receive twice a day treatment with: tofacitinib 5 mg (n=133); tofacitinib 10 mg (n=134); or placebo (n=132), all with methotrexate. At month 3, patients given placebo advanced to either tofacitinib 5 mg twice a day (n=66) or 10 mg twice a day (n=66). Primary endpoints included ACR20 response rate, mean change from baseline in HAQ-DI, and rates of disease activity score (DAS)28-4(ESR) less than 2.6 (referred to as DAS28<2.6), all at month 3. The full analysis set for the primary analysis included all randomised patients who received at least one dose of study medication and had at least one post-baseline assessment.[20] k. Eligible patients had previously completed a phase 1, 2, or 3 qualifying index study of tofacitinib and received open-label tofacitinib 5 mg or 10 mg BID (twice daily). Stable background therapy, including csDMARDs (conventional synthetic disease-modifying antirheumatic drugs), was continued; adjustments to tofacitinib or background therapy were permitted at investigators' discretion. Assignment to dose groups (5 mg or 10 mg BID) was based on patients' average total daily dose. The primary objective was to determine the long-term safety and tolerability of tofacitinib 5 mg and 10 mg BID; the key secondary objective was to evaluate the long-term persistence of efficacy. Between February 5, 2007, and November 30, 2016, 4481 patients were enrolled. Total tofacitinib exposure was 16,291 patient-years. Safety data are reported up to month 114 for all tofacitinib; efficacy data are reported up to month 96 for tofacitinib 5 mg BID and month 72 for 10 mg BID (with low patient numbers limiting interpretation beyond these time points).[21] l. IRs (incidence rates; number of first events/100 patient-years) of major adverse cardiovascular events (MACE), serious infection events (SIEs), herpes zoster (HZ), malignancies, and death were estimated among tofacitinib and bDMARD (biological disease-modifying antirheumatic drug) initiators, regardless of dose/schedule, between November 6, 2012 (US Food and Drug Administration tofacitinib approval), and July 31, 2018 (follow-up through January 31, 2019). Propensity score (PS) methods were used to control for nonrandom prescribing practices. Hazard ratios (HRs) were calculated to compare rates using multivariable-adjusted Cox regression. Different risk windows were used for acute (MACE, SIEs, HZ, and venous thromboembolic events [VTEs]) and long-term (malignancy and death) events. VTEs were assessed descriptively. For MACE, SIEs, and HZ, 1999 (3152.1 patient-years) and 8358 (12 869.4 years) tofacitinib and bDMARD initiators were included, respectively; for malignancy/death, 1999 (4505.6 patient-years) and 6354 (16 670.8 patient-years) initiators were included, respectively.[24]

References 1. 젤잔즈XR 제품설명서(최초품목허가일: 2020.12.07). 2. 보건복지부 고시 제2021-101호. 3. 젤잔즈 제품설명서(개정년월일: 2021.05.08). 4. 식품의약품안전처. 올루미언트 제품정보. Available at https://nedrug.mfds.go.kr/pbp/CCBBB01/getItemDetail?itemSeq=201708280. Accessed May 2021. 5. 식품의약품안전처. 스마이랍 제품정보. Available at https://nedrug.mfds.go.kr/pbp/CCBBB01/getItemDetail?itemSeq=202000404. Accessed May 2021. 6. 식품의약품안전처. 린버크 서방정 제품정보. Available at https://nedrug.mfds.go.kr/pbp/CCBBB01/getItemDetail?itemSeq=202004222. Accessed May 2021. 7. 식품의약품안전처. 의약품 수입품목 허가사항 변경허가-젤잔즈정(2018.09.20). 8. Malemud CJ. The role of the JAK/STAT signal pathway in rheumatoid arthritis. Ther Adv Musculoskelet Dis. 2018;10(5-6):117-127. 9. Fleischmann R, et al. Safety and maintenance of response for tofacitinib monotherapy and combination therapy in rheumatoid arthritis: an analysis of pooled data from open-label long-term extension studies. RMD Open. 2017;3:e000491. 10. Cohen SB, et al. Methotrexate withdrawal in patients with rheumatoid arthritis who achieve low disease activity with tofacitinib modified-release 11 mg once daily plus methotrexate (ORAL Shift): a randomised, phase 3b/4, non-inferiority trial. Lancet Rheumatol. 2019;1:e23-34. 11. Iwata S, et al. Progress in understanding the safety and efficacy of Janus kinase inhibitors for treatment of rheumatoid arthritis. Expert Rev Clin Immunol. 2016;12(10):1047-1057. 12. Tanaka Y. The JAK inhibitors: do they bring a paradigm shift for the management of rheumatic diseases? Rheumatology (Oxford). 2019;58(Suppl 1):i1-i3. 13. Fleischmann R, et al. Placebo-Controlled Trial of Tofacitinib Monotherapy in Rheumatoid Arthritis. N Engl J Med. 2012;367(6):495-507. 14. Mease P, et al. Tofacitinib or Adalimumab versus Placebo for Psoriatic Arthritis. N Engl J Med. 2017;377:1537-1550. 15. Sandborn WJ, et al. Tofacitinib as Induction and Maintenance Therapy for Ulcerative Colitis. N Engl J Med. 2017;376:1723-1736. 16. Fleischmann R, et al. Efficacy and safety of tofacitinib monotherapy, tofacitinib with methotrexate, and adalimumab with methotrexate in patients with rheumatoid arthritis (ORAL Strategy): a phase 3b/4, double-blind, head-to-head, randomized controlled trial. Lancet. 2017;390(10093):457-468. 17. van Vollenhoven RF, et al. Tofacitinib or Adalimumab versus Placebo in Rheumatoid Arthritis. N Engl J Med. 2012;367(6):508-519. 18. van der Heijde D et al. Tofacitinib (CP-690,550) in Patients With Rheumatoid Arthritis Receiving Methotrexate. Arthritis Rheum. 2013;65(3):559-570. 19. Kremer J et al. Tofacitinib in Combination With Nonbiologic Disease-Modifying Antirheumatic Drugs in Patients With Active Rheumatoid Arthritis. Ann Intern Med. 2013;159(4):253-261. 20. Burmester GR, et al. Tofacitinib (CP-690,550) in combination with methotrexate in patients with active rheumatoid arthritis with an inadequate response to tumour necrosis factor inhibitors: a randomised phase 3 trial. Lancet. 2013;381(9865):451-460. 21. Wollenhaupt J, et al. Safety and efficacy of tofacitinib for up to 9.5 years in the treatment of rheumatoid arthritis: final results of a global, open-label, long-term extension study. Arthritis Res Ther. 2019;21(1):89. 22. Cohen SB, et al. Methotrexate withdrawal in patients with rheumatoid arthritis who achieve low disease activity with tofacitinib modified-release 11 mg once daily plus methotrexate (ORAL Shift): a randomised, phase 3b/4, non-inferiority trial. Lancet Rheumatol. 2019;1:e23-34. 23. Data on file, Pfizer. 24. Kremer JM, et al. Postapproval Comparative Safety Study of Tofacitinib and Biological Disease-Modifying Antirheumatic Drugs: 5-Year Results from a United States-Based Rheumatoid Arthritis Registry. ACR Open Rheumatology. 2021;3(3):173-184.

Abbreviations. RA, rheumatoid arthritis; PsA, psoriatic arthritis; UC, ulcerative colitis; JAK, Janus kinase; MTX, methotrexate; XR, extended-release; IR, inadequate response

[주요 안전성 정보[1,3]] 젤잔즈 투여 환자에서 중대한 감염, 악성 종양, 정맥혈전색전증이 보고되었습니다. 한국 화이자는 국내에서 허가 받지 않은 용법, 용량으로 젤잔즈를 투여하는 것을 권장하지 않습니다.

[제품요약정보] 젤잔즈정 5 mg 전문의약품 [원료약품 분량] 1정(206.00 mg) 중 토파시티닙시트르산염(토파시티닙으로서 5 mg) (별규) 8.078 mg [성상] 흰색의 원형 필름코팅정제 [효능·효과] 1. 류마티스 관절염: 메토트렉세이트에 적절히 반응하지 않거나 내약성이 없는 성인의 중등증 내지 중증의 활동성 류마티스관절염의 치료. 이 약은 단독투여 또는 메토트렉세이트나 다른 비생물학적 류마티스제제(DMARDs)와 병용투여 할 수 있다. 이 약은 생물학적 항류마티스제제 또는 아자티오프린 및 사이클로스포린과 같은 강력한 면역억제제와 함께 사용해서는 안 된다. 2. 건선성 관절염: 이전 항류마티스제제(DMARDs)에 적절히 반응하지 않거나, 내약성이 없는 성인의 활동성 건선성 관절염의 치료. 이 약은 메토트렉세이트나 다른 비생물학적 항류마티스제제 (DMARDs)와 병용투여 한다. 건선성 관절염 환자에 대한 이 약 단독요법의 유효성은 연구되지 않았다. 이 약을 생물학적 항류마티스제제 또는 아자티오프린 및 사이클로스포린과 같은 강력한 면역억제제와 함께 사용해서는 안 된다. 3.궤양성 대장염: 코르티코스테로이드, 아자티오프린, 6-메르캅토푸린(6-MP)을 포함한 통상적인 치료제 또는 생물학적 제제에 적절히 반응하지 않거나, 반응이 소실되거나 또는 내약성이 없는 성 인의 중등도-중증 활동성 궤양성 대장염의 치료. 이 약을 생물학적 제제나 아자티오프린 및 사이클로스포린과 같은 강력한 면역억제제와 함께 사용해서는 안된다. [용법·용량] 1. 투여시 주의사항 1) 절대림프구수(ALC)가 500 cells/㎣ 미만, 절대호중구수(ANC) 1,000 cells/㎣ 미만, 또는 헤모글로빈 수치 9 g/dL 미만인 환자에게는 이 약의 투여를 시작하지 않는다. 2) 이 약의 투여 전, 투여 중 및 투여 후 결핵을 포함한 감염에 대해 면밀히 모니터링해야 하며, 중대한 감염이 발생한 환자는 감염이 조절될 때까지 이 약의 투여를 중단해야 한다. 3) 림프구 감소, 호중구 감소 및 빈혈의 조절을 위해 일시적으로 이 약의 투여를 중단하는 것이 필요할 수 있다. 4) 이 약은 음식물 섭취와 상관없이 경구 투여할 수 있다. 2. 류마티스 관절염 및 건선성 관절염의 권장용량: 이 약의 권장용량은 1회 5 mg, 1일 2회 투여이다. 다음의 환자에서 이 약의 용량은 1일 1회, 1회 5 mg으로 감량해야 한다: 강력한 CYP3A4 억제제(예. 케토코나졸)를 투여 중인 환자, 중등도의 CYP3A4 억제제 및 강력한 CYP2C19 억제제(예. 플루코나졸)를 투여 중인 환자, 중등증 또는 중증의 신장애 환자, 중등증의 간장애 환자. 림프구 감소, 호중구 감소 및 빈혈의 조절을 위해 일시적으로 이 약의 투여를 중단하는 것이 필요할 수 있다. 3. 궤양성 대장염의 권장용량: 1회 10 mg 1일 2회로 최소 8주 동안 투여 후, 치료 반응에 따라 5 mg 또는 10 mg을 1일 2회 투여한다. 유지용량으로 최소 유효용량을 사용한다. 이 약 1회 10 mg을 1일 2회로 16주 동안 투여한 후에도 적절한 치료적 유익성을 보이지 않으면 투여를 중단한다. 다음의 환자에서 이 약 1회 10 mg을 1일 2회로 투여 중인 경우 1회 5 mg 1일 2회로 또는 이 약 1회 5 mg 1일 2회로 투여 중인 경우 1일 1회 5 mg으로 감량해야 한다: 강력한 CYP3A4 억제제(예. 케토코나졸)를 투여 중인 환자, 중등도의 CYP3A4 억제제 및 강력한 CYP2C19 억제제(예. 플루코나졸)를 투여 중인 환 자, 중등증 또는 중증의 신장애 환자, 중등증의 간장애 환자. 절대림프구수(ALC) 500 cells/㎣ 미만인 환자에서 이 약의 투여를 중단한다. 절대호중구수(ANC) 500-1,000 cells/㎣인 환자에서 이 약 1회 10 mg을 1일 2회 투여한 경우 1회 5 mg 1일 2회로 감량한다. 절대호중구수(ANC)가 1,000 cells/㎣ 초과가 되면, 임상적 반응에 따라 이 약 1회 10 mg 1일 2회로 다시 증량한다. 기존에 이 약 1회 5 mg을 1일 2회로 투여한 경우 투여를 잠정 중단한다. 절대호중구 수(ANC)가 1,000 cells/㎣ 초과가 되면, 이 약 1회 5 mg 1일 2회로 다시 투여한다. 절대호중구수(ANC) 500 cells/mm3 미만인 환자에서 이 약의 투여를 중단한다. 헤모글로빈 수치가 2 g/dL 초과의 감소 또는 8.0 g/dL 미만인 환자에서는 헤모글로빈 수치가 정상이 될 때까지 투여 잠정 중단할 수 있다. [사용상의 주의사항] 1. 경고 : 1) 중대한 감염: 이 약을 투여하는 환자들은 입원 또는 사망으로 이어질 수 있는 중대한 감염이 나타날 위험이 높다. 이러한 감 염이 나타난 대부분의 환자들은 메토트렉세이트 혹은 코르티코스테로이드 같은 면역억제제를 병용 투여하고 있었다. 중대한 감염이 나타난 경우, 감염이 조절될 때까지 이 약의 투여를 중단해야 한다. 보고된 감염은 다음을 포함한다: 폐질환 혹은 폐 이외의 질환이 있는 활성결핵. 환자들은 이 약을 투여하기 전 및 투여 중에 잠복결핵검사를 받아야 한다. 잠복결핵의 치료는 이 약 투여 전에 선행되어야 한다. 효모균증 및 간질성 형질세포폐렴을 포함한 침습적 진균감염. 침습적 진균감염 환자는 국소보다는 전신으로 확산되는 질환으로 나타난다. 기회 감염성 병원체에 기인한 세균성, 바이러스성(헤르페스 바이러스 포함) 및 기타 감염 만성 또는 재발성 감염환자는 이 약의 투여를 시작하기 전 치료의 위험성 및 유익성에 대해 주의 깊게 고려해야 한다. 이 약 투여 중 또는 투여 이후 환자들은 감염 징후 및 증상의 발현을 주의 깊게 관찰해야 하며, 치료 시작 전 잠복 결핵에 음성반응을 보인 환자에서 결핵 발현 가능성 에 대하여도 주의 깊은 관찰이 필요하다. 2) 악성종양: 이 약을 투여한 환자들에게서 림프종 및 기타 악성 종양이 관찰되었다. 이 약과 면역억제제를 병용투여받은 신장이식 환자에서 엡스테인-바 바이러스(Epstein Barr Virus)와 관련이 있는 이식 후 림프세포 증식성 질환이 증가하는 것으로 관찰되었다. 3) 정맥혈전색전증: 임상시험 및 시판 후 보고의 이 약을 투여한 환자들에게서 정맥혈전색전증이 관찰되었다. 적어도 1개 이상의 심혈관계 위험 요인이 있는 만 50 세 이상의 류마티스관절염 환자를 대상으로 진행중인 한 건의 대규모, 무작위배정, 허가 후 안전성감시(PASS) 연구에서 환자들은 토파시티닙 5 mg 1일 2회, 토파시티닙 10 mg 1일 2 회또는 TNF 억제제를 투여받았다. TNF 억제제에 비해 토파시티닙을 투여받은 환자들에서 폐색전증(PE)의 용량 의존적 증가가 관찰되었다. 이러한 폐색전증 사례들은 대부분 중증이었고, 일부에서 사망을 초래했다. 이 연구에서 토파시티닙 투여군의 폐색전증 사례는 다른 토파시티닙 임상시험들에 비해 더 빈번하게 보고되었다. 이 연구의 세 개 투여군 모두에서 심부정맥혈전증 사례가 관찰되었다. 환자들에 대해 투여시작 전과 투여 중 주기적으로 정맥혈전색전증 위험요인을 평가한다. 위험 요인이 있는 환자는 이 약을 주의하여 사용한다. 정맥혈전색전증의 징후 및 증상이 있는 환자는 긴급히 평가한다. 용법·용량 또는 효능·효과에 관계없이, 정맥혈전색전증이 의심되면 이 약을 중단한다. 2. 다음 환자에는 투여하지 말 것 : 1) 이 약 또는 이 약의 구성성분에 과민증이 있는 환자 2) 중대한 감염(예. 패혈증) 또는 국소 감염을 포함한 활성 감염이 있는 환자 3) 활동성 결핵이 있는 환자 4) 중증 간장애 환자 5) 절대호중구수(ANC) 500 cells/㎣ 미만인 환자 6) 절대림프구수(ALC) 500 cells/㎣ 미만인 환자 7) 헤모글로빈 수치 8 g/dL 미만인 환자 8) 임부 또는 임신가능성이 있는 여성 9) 이 약은 유당을 함유하고 있으므로 갈락토오스 불내성(galactose intolerance), Lapp 유당분해효소 결핍증(Lapp lactase deficiency)또는 포도당-갈락토오스흡수장애(glucose-galactose malabsorption) 등의 유전 적인 문제가 있는 환자에게는 투여하면 안 된다. 3. 다음 환자에는 신중히 투여할 것 1) 감염이 의심되는 환자 2) 결핵 병력이 있는 환자 3) 면역력이 약화된 환자 4) 고령자 5) 당뇨병 환자 6)위장관 게실환자(위장관 천공가능성이 있다.) 7) 호중구수 또는 림프구수 감소 환자, 헤모글로빈 수치 감소 환자 8) 경증 또는 중등도의 간 장애 환자 9) 신장애 환자 10) 간질성폐렴 병력이 있는 환자 4. 이상반응 1) 이상반응 : 기관계 및 CIOMS 빈도 분류에 따른 이상반응으로 폐렴, 인플루엔자, 대상포진, 요로감염, 부비동염, 기관지염, 코인두염, 인두염, 빈혈, 고지혈증, 두통, 고혈압, 기침, 복통, 구토, 설사, 구역, 위염, 소화불량, 발진, 관절통, 발열, 말초부종, 피로, 감마 글루타밀 전달효소 증가, 혈중 콜레스테롤 증가, 체중증가, 혈중 크레아틴 인산활성효소 증가가 흔하게 보고되었다. 2) 류마티스 관절염에 대한 임상시험: (상기도 감염, 코인두염 및 요로감염을 포함한) 전반적인 감염, (폐렴, 대상포진, 요로감염, 연조직염, 위장염, 게실염을 포함한) 중대한 감염, 결핵, 기회 감염, 바이러스 재활성화, 정맥혈전색전증 (비흑색종피부암(non-melanoma skin cancer) 제외한) 악성 종양, 간 효소 상승, 림프구 수 및 호중구 수 감소, 용량-관련 지질 및 혈청크레아티닌 증가가 보고되었다. 3) 건선성 관절염에 대한 임상시험: 이 약을 투여받은 활동성 건선성 관절염 환자에서 관찰된 안전성 프로파일은 류마티스 관절염환자에서 관찰된 안전성 프로파일과 유사하였다. 5. 일반적 주의: 이 약은 류마티스 관절염의 치료에 사용시, 류마티스전문의 또는 류마티스 관절염 치료에 전문 지식이 있는 의사에 의해 투여가 시작되고 모니터링 되어야한다. 제품설명서 개정년월일: 2021.05.08

[제품요약정보] 젤잔즈 XR 서방정 11 mg 전문의약품 [원료약품 분량] 1정(225.400 mg) 중 토파시티닙시트르산염(토파시티닙으로서 11 mg) (별규) 17.771 mg [성상] 분홍색의 한쪽 옆면에 구멍이 있는 타원형 정제 [효능효과] 메토트렉세이트에 적절히 반응하지 않거나 내약성이 없는 성인의 중등증 내지 중증의 활동성 류마티스 관절염의 치료. 이 약은 단독투여 또는 메토트렉세이트나 다른 비생물학적 항류마티스제제(DMARDs)와 병용투여 할 수 있다. 이 약은 생물학적 항류마티스제제 또는 아자티오프린 및 사이클로스포린과 같은 강력한 면역억제제와 함께 사용해서는 안된다. [용법용량] 정확한 용량 투여를 위해, 이 약은 통째로 삼켜야 하며, 으깨거나 쪼개거나 씹어서는 안된다. 1. 투여시 주의사항 1)~4) : 5mg과 상동. 5) 젤잔즈정과 젤잔즈 XR 서방정의 상호전환 : 젤잔즈정 5 mg 을 1 일 2 회 투여하는 환자는 젤잔즈정 5 mg 을 마지막으로 복용한 다음날부터 젤잔즈 XR 서방정 11 mg 1 일 1 회 용법으로 전환할 수 있다. 젤잔즈 XR 서방정 11 mg 을 1 일 1 회 투여하는 환자는 젤잔즈 XR 서방정 11 mg 을 마지막으로 복용한 다음날부터 젤잔즈정 5 mg 을 1 일 2 회 용법으로 전환할 수 있다. 젤잔즈 XR 서방정 11 mg 1일 1회는 젤잔즈정 5 mg 을 1일 2 회 투여와 약동학적 동등성이 입증되었다. 2. 류마티스 관절염의 권장용량 : 이 약의 권장용량은 1일 1회 11 mg 투여이다. CYP2C19 및/또는 CYP3A4 억제제를 투여중인 환자, 중등도 및 중증 신장애 환자, 중등도 간장애 환자에서는 젤잔즈정 5mg 1일 1회 투여로 감량하는 것이 권장된다. [사용상의 주의사항] 1. 경고 : 5mg과 상동. 2. 다음 환자에는 투여하지 말 것 : 유당 관련 내용 제외하고 5mg과 상동3. 다음 환자에는 신중히 투여할 것 : 5mg과 상동. 4. 이상반응 1) 이상반응 : 5mg과 상동. 2) 류마티스 관절염에 대한 임상시험: 5mg과 상동. 5. 일반적 주의: 1)~12) : 5mg과 상동. 13) 젤잔즈XR 서방정에만 해당되는 사항(1) 다른 비변형제제와 마찬가지로, 중증의(병리적 또는 의인성) 위장관 협착이 있는 환자에게 젤잔즈 XR 서방정을 투여 시 주의해야 한다. 협착이 있는 환자들에서 다른 비변형서방제형 약물의 소화과정 중, 폐쇄성 증상이 드물게 보고되었다. (2) 정제 껍질 젤잔즈 XR 서방정을 투여한 환자는 비활성 정제껍질이 변 또는 인공항문을 통해 배설되는 것을 발견할 수 있다. 정제 껍질이 발견되더라도, 이 약의 활성성분은 이미 흡수되었다는 것을 환자에게 알려야 한다. (3) 젤잔즈 XR 서방정은 소르비톨을 함유하고 있다. 소르비톨(또는 과당)을 함유한 제품을 병용 투여하거나 소르비톨(또는 과당)을 섭취하는 경우, 상가적인 영향에 대해 고려해야 한다.: 설명서개정년월일: 2020.12.07 * 제품에 대한 자세한 정보는 최신의 제품설명서를 참고하시기 바라며, 홈페이지(www.pfizer.co.kr)를 통해 확인하실 수 있습니다. 제품 의학정보 문의: Website: www.pfizermedicalinformation.co.kr / Tel: 080-210-2114/E-mail: mis.korea@pfizer.com

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2013

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주사부위 통증 감소

구연산을 제거한 제형으로 투여량이
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성인 환자들의 경우, 주사 직후 주사부위
통증이 84%나 감소하였으며(중앙값 기준)
결과적으로 복약 순응도 향상에 도움이 됩니다.[2,3,†]

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20 mg/0.2 mL의
프리필드 시린지 형태로
바이알이 없어 투여가 용이합니다.[1]

2019

*휴미라®는 1회에 한하여 최대 14일간 차광 조건 하에서 최대 25˚C의 온도에서 보관이 가능합니다. 냉장조건을 벗어난 제품은 다시 냉장보관해서는 안됩니다.[1]
†어떤 특성(조성, 용량, 및/또는 바늘 크기)이 통증 감소에 가장 큰 역할을 하는지는 아직 밝혀지지 않았습니다. 다른 연구자들의 보고를 통해, 구연산 기반의 완충액이 주사부위 통증의 주요 원인인 것으로 확인된 바 있습니다.[2,3]

Study description[2]

18세 이상의 류마티스관절염을 진단받은 환자 64명과 61 명을 각각 평가한 2가지 시험에 대한 통합 분석을 실시한 결과에 근거함. 두 시험에서 모두 휴미라® 40 mg/0.8 mL를 사용 중이며 주사부위 통증 평균을 최소 3 cm (0 – 10 cm의 시각통증척도[VAS] 사용)로 평가한 환자 또는 바이오의약품(생물학적 제제) 투여 경험이 없는 상태에서 휴미라® 40 mg/0.8 mL 투여를 시작한 환자들이 등록됨. 환자들을 무작위 배정하여 휴미라® 40 mg/0.8 mL 또는 휴미라® 40 mg/0.4 mL를 1회 투여한 다음, 이후에는 용량을 서로 바꾸어 1회 투여하였음. 일차 평가변수는 0 – 10 cm VAS로 측정한 주사 직후의 주사 부위 통증이었음.[2]

References

1. HUMIRA® 제품설명서(개정연월일: 2020년 6월 15일) 2. Nash P, Vanhoof J, Hall S, *et al.* Randomized Crossover Comparison of Injection Site Pain with 40 mg/0.4 or 0.8 mL Formulations of Adalimumab in Patients with Rheumatoid Arthritis. *Rheumatol Ther.* 2016;3(2):257-270. doi: 10.1007/s40744-016-0041-3 3. Gely C, Marín L, Gordillo J, *et al.* Impact of pain associated with the subcutaneous administration of adalimumab. *Gastroenterol Hepatol.* 2020;43(1):9-13. doi:10.1016/j.gastrohep.2019.06.008

[제품명] 휴미라펜주 40mg/0.4ml, 휴미라프리필드시린지주 40mg/0.4ml, 휴미라프리필드시린지주 20mg/0.2ml (아달리무맙, 유전자재조합) [효능・효과] 성인 1. 류마티스관절염: 메토트렉세이트를 포함한 DMARDs(disease-modifying anti-rheumatic drugs)에 대한 반응이 적절하지 않은 성인의 중등도에서 중증의 활동성 류마티스 관절염의 치료. 이전에 메토트렉세이트로 치료받지 않은 성인의 중증의 활동성 및 진행성 류마티스 관절염의 치료. 이 약은 단독투여 또는 메토트렉세이트나 다른 DMARDs와 병용 투여할 수 있다. 메토트렉세이트에 내약성이 없거나 지속적인 병용투여가 부적절한 경우에는 단독 투여한다. 이 약과 메토트렉세이트와의 병용투여는 관절손상 진행속도를 감소시키고 (X-선측정 결과) 신체활동기능을 향상시킨다. **2. 건선성 관절염:** 이전에 DMARDs(disease-modifying anti-rheumatic drugs)에 대한 반응이 적절하지 않은 성인의 활동성 및 진행성 건선성 관절염의 치료. 이 약은 다발성, 대칭성 아형을 지닌 환자의 말초 관절손상 진행속도를 감소시키고(X-선측정 결과), 신체활동기능을 향상시킨다. **3. 축성 척추관절염:** (1) 강직성 척추염: 기존 치료에 대한 반응이 적절하지 않은 성인의 중증의 강직성 척추염의 치료, (2)방사선학적으로 강직성 척추염이 확인되지 않는 중증 축성 척추관절염: 방사선학적 검사에서 강직성 척추염이 확인되지 않으나, 상승된 CRP 수치 및/또는 MRI상 객관적인 염증의 징후를 보이는 중증 축성 척추관절염의 치료. 이 약은 비스테로이드성 항염증제(NSAIDs) 약물에 대한 반응이 적절하지 않거나, 불내성인 환자에 사용한다. **4. 성인 크론병(만 18세 이상):** 코르티코스테로이드제나 면역억제제 등의 치료에 반응을 나타내지 않거나, 내약성이 없는 경우 또는 이러한 치료방법이 금기인 중등도에서 중증의 활성 크론병의 치료. 유도 요법의 경우 이 약은 코르티코스테로이드제와 병용투여한다. 코르티코스테로이드제에 내약성이 없거나, 지속적인 병용투여가 부적절한 경우 단독투여할 수 있다. **5. 건선:** 전신치료 또는 광선요법이 필요한 성인의 중등도에서 중증의 만성 판상 건선의 치료. **6. 궤양성 대장염:** 코르티코스테로이드 및 6-MP(6-mercaptopurine) 또는 AZA(azathioprine)를 포함한 통상적인 치료에 대해 반응이 적절하지 않거나 내약성이 없는 경우 또는 이러한 치료방법이 금기인 성인의 중등도에서 중증의 활성 궤양성 대장염의 치료. **7. 베체트 장염:** 스테로이드 또는 면역억제제 등의 통상적인 치료에도 적절한 반응이 나타나지 않는 베체트 장염의 치료. **8. 화농성 한선염:** 기존의 전신 요법에 적절한 반응을 나타내지 않는 중등도에서 중증의 활성 화농성 한선염의 치료. **9. 포도막염:** 코르티코스테로이드에 적절한 반응을 나타내지 않은 성인의 비-감염성 중간 포도막염, 후포도막염 및 전체포도막염의 치료. **소아 1. 소아 크론병(만 6~만 17세):** 일차 영양요법, 코르티코스테로이드, 면역조절제 등의 치료에 적절한 반응을 나타내지 않거나, 내약성이 없는 경우 또는 이러한 치료방법이 금기인 소아 환자의 중등도에서 중증의 활성 크론병의 치료. **2. 소아 특발성 관절염:** (1) 다관절형 소아 특발성 관절염: 하나 이상의 DMARDs(disease-modifying anti-rheumatic drugs)에 대해 부적절한 반응을 보인 만 2세 이상의 소아 및 청소년에서 활성 다관절형 소아 특발성 관절염의 치료. (2) 골부착부위염 관련 관절염: 기존 치료에 적절한 반응을 나타내지 않거나 내약성이 없는 만 6세 이상 어린이 및 청소년의 활성 골부착부위염 관련 관절염의 치료. **3. 소아 판상 건선:** 국소 치료 및 광선요법에 적절한 반응을 나타내지 않거나 해당 치료가 부적절한 만 4세 이상의 어린이 및 청소년의 중증 만성 판상 건선의 치료. **[용법・용량]** 환자가 자가 주사하는 것이 적절하며 필요시 치료 추적이 가능하다고 의사가 판단하는 경우, 환자는 주사방법에 대한 교육을 받은 후 이 약을 자가 주사할 수 있다. 80 mg의 투여는 하루에 40 mg을 2 번 주사한다. 160 mg의 투여는 하루에 40 mg을 4 번 주사하거나, 이틀에 걸쳐 40 mg을 2 번씩 주사할 수 있다. **성인 1. 류마티스 관절염:** 성인 류마티스 관절염 환자에 대한 이 약의 권장 용량은 아달리무맙 40 mg을 2주에 1회 피하 주사한다. 이 약을 투여하는 동안 메토트렉세이트의 병용투여를 유지한다. 글루코코르티코이드, 살리실산염, 비스테로이드성항염증제(NSAIDs), 진통제, 다른 DMARDs의 병용투여를 유지할 수 있다. 단독요법의 경우 이 약에 대한 반응이 감소한 환자는 40 mg 매주 투여 또는 80mg 격주 투여로 증량하면 유용한 효과를 얻을 수 있다. **2. 건선성 관절염, 강직성 척추염 및 방사선학적으로 강직성 척추염이 확인되지 않는 중증 축성 척추관절염:** 건선성 관절염, 강직성 척추염 및 방사선학적으로 강직성 척추염이 확인되지 않는 중증 축성 척추관절염 환자에 대한 이 약의 권장 용량은 아달리무맙 40 mg을 2주에 1회 피하 주사한다. 상기 효능효과에 대해 임상적인 반응은 보통 치료 12주 이내에 나타나며, 이 기간 내에 반응을 나타내지 않는 환자의 경우에는 투여 지속여부를 신중히 재고한다. **3. 성인 크론병:** 성인 중등도에서 중증 크론병에 대한 이 약의 권장 용량은 첫 주에 아달리무맙 80 mg을 투여하고 첫 투여 후 2주 후에 40 mg을 투여한다. 빠른 효과를 얻어야 할 필요가 있는 경우에는, 유도 요법동안 이상 반응에 대한 위험성이 증가한다는 것을 알리고, 첫 주에 160 mg을 투여하고 첫 투여 후 2주 후에 80 mg을 투여할 수 있다. 유도요법의 경우 이 약은 코르티코스테로이드제와 병용 투여한다. 코르티코스테로이드제에 내약성이 없거나, 지속적인 병용투여가 부적절한 경우 단독 투여할 수 있다. 유도 요법 후, 아달리무맙 40 mg을 2주에 1회 피하 주사한다. 만약 투여를 중지하고 재발의 증상과 징후가 나타나면 이 약을 재투여 할 수 있다. 8주 이상의 투여 중지 후 재투여에 대한 경험은 거의 없다. 유지 요법 동안 임상 지침에 따라 코르티코스테로이드제의 투여를 서서히 줄일 수 있다. 이 약에 대한 반응이 감소한 환자는 40 mg 매주 투여 또는 80mg 격주 투여로 증량하면 유용한 효과를 얻을 수 있다. 4주까지 반응을 보이지 않는 환자의 경우 12주까지 투여하여 반응을 나타낼 수 있다. 이 기간 내에 반응을 나타내지 않는 환자의 경우에는 투여 지속여부를 신중히 재고한다. **4. 건선:** 성인에 대한 이 약의 권장 용량은 첫 회에 아달리무맙 80 mg을 피하로 투여하고, 이어서 첫 투여 후 1주일 후에 40 mg을 격주로 투여한다. 16주 이내에 반응을 나타내지 않는 환자의 경우에는 투여 지속여부를 신중히 재고한다. 충분한 반응이 나타나지 않는 환자는 40mg 매주 투여 또는 80mg 격주 투여로 증량하여 유용한 효과를 얻을 수 있다. 증량 후 충분한 반응이 나타나지 않는 환자의 경우에는 이 약의 지속적 40mg 매주 투여 또는 80mg 격주 투여의 유용성과 위험성을 신중히 재고한다. **5. 궤양성 대장염:** 성인 중등도에서 중증의 궤양성 대장염에 대한 이 약의 권장 용량은 아달리무맙 160 mg을 투여하고 첫 투여 2주 후에 80 mg을 투여하는 것이다. 유도 요법 후 40 mg을 격주로 피하 주사한다. 유지 요법 동안 임상 지침에 따라 코르티코스테로이드제의 투여를 서서히 줄일 수 있다. 이 약에 대한 반응이 감소한 환자 중 일부는 40 mg 매주 투여 또는 80mg 격주 투여로 증량하여 유용한 효과를 얻을 수 있다. 지금까지 나온 데이터에 따르면 임상 반응은 대체로 투여 2~8주 이내에 도달한다. 이 기간 내에 반응을 보이지 않은 환자의 경우 투여 지속여부를 신중히 재고한다. **6. 베체트 장염:** 성인에 대한 이 약의 권장 용량은 첫 회에 160 mg을 피하로 투여하고 이어서 첫 투여 2주 후에 80 mg을 투여한다. 첫 투여 4주 후부터는 40 mg을 격주로 투여한다. 12주 이내에 반응을 나타내지 않는 환자의 경우에는 투여 지속 여부를 신중히 재고한다. **7. 화농성 한선염:** 이 약의 권장용량은 첫 회에 160 mg을 피하로 투여하고, 이어서 첫 투여 2주 후에 80 mg을 투여한다. 첫 투여 4주 후부터는 40 mg을 매주 투여 또는 80mg을 격주 투여한다. 필요 시 이 약의 치료 기간 동안 항생제를 계속 투여할 수 있다. 12주 이내에 반응을 나타내지 않는 환자의 경우에는 투여 지속 여부를 신중히 재고한다. 치료를 중단해야 하는 경우, 40 mg 매주 투여 또는 80mg 격주 투여로 재투여할 수 있다. **8. 포도막염:** 성인에 대한 이 약의 권장 용량은 첫 회 80 mg 투여하고 이어서 첫 투여 1주 후부터 40 mg을 격주로 투여한다. 이 약은 단독 또는 코르티코스테로이드 또는 면역억제제 (생물학적 면역억제제 제외)와 병용하여 사용할 수 있다. 코르티코스테로이드는 임상 경험에 따라 양을 줄일 수 있다. **소아 1. 소아 크론병:** 만 6세 이상의 소아 크론병 환자에서 이 약의 권장 투여 용량은 체중을 기반으로 한다. 이 약은 피하 투여한다.

체중(kg)	유도 용량	유지 용량
40kg 미만	• 첫 주에 40mg 투여하고 첫 투여 후 2주 후에 20mg 투여 • 빠른 효과를 얻어야 할 필요가 있는 경우에는, 고용량의 유도요법 동안 이상사례에 대한 위험성이 증가한다는 것을 알리고 아래 용량을 투여할 수 있다. - 첫 주에 80mg 투여하고, 첫 투여 후 2주 후에 40mg 투여	20mg 격주 투여
40kg 이상	• 첫 주에 80mg 투여하고 첫 투여 후 2주 후에 40mg 투여 • 빠른 효과를 얻어야 할 필요가 있는 경우에는, 고용량의 유도요법 동안 이상사례에 대한 위험성이 증가한다는 것을 알리고 아래 용량을 투여할 수 있다. - 첫 주에 160mg 투여하고, 첫 투여 후 2주 후에 80mg 투여	40mg 격주 투여

충분한 반응이 나타나지 않는 환자의 경우 증량하여 유용한 효과를 얻을 수 있다. • 40 kg 미만: 20mg 매주 투여 • 40 kg 이상: 40mg 매주 투여 또는 80mg 격주 투여. 12주까지 반응을 나타내지 않는 환자의 경우에는 투여 지속 여부를 신중히 재고한다. **2. 소아 특발성 관절염:** (1) 다관절형 소아 특발성 관절염: 이 약은 만 2세 미만 소아 또는 체중 10kg 미만 환자를 대상으로 연구된 바 없다. 이 약의 권장 투여 용량은 체중을 기반으로 한다. 이 약은 메토트렉세이트와 병용하여 투여한다. 메토트렉세이트에 내약성이 없거나 메토트렉세이트와 함께 지속적으로 투여하는 것이 부적절할 경우에는 이 약을 단독요법으로 투여할 수 있다.

체중 (kg)	용량
10kg 이상 30kg 미만	20mg 격주 투여
30kg 이상	40mg 격주 투여

지금까지 나온 데이터에 따르면 임상 반응은 대체로 투여 12주 이내에 도달한다. 이 기간 내에 반응을 보이지 않은 환자의 경우 투여 지속여부를 신중히 재고한다. (2) 골부착부위염 관련 관절염: 만 6세 이상의 골부착부위염 관련 관절염 환자에 대한 이 약의 권장 투여 용량은 체중을 기반으로 한다.

체중 (kg)	용량
15kg 이상 30kg 미만	20mg 격주 투여
30kg 이상	40mg 격주 투여

이 약은 만 6세 미만의 골부착부위염 관련 관절염 환자를 대상으로 연구된 바 없다. **3. 소아 판상 건선:** 소아 판상 건선에 대한 이 약의 권장 투여 용량은 체중을 기반으로 한다. 16주 이후에도 반응을 나타내지 않는 환자의 경우에는 투여 지속여부를 신중히 재고한다.

체중 (kg)	용량
15kg 이상 30kg 미만	20mg을 처음 2회는 매주 피하주사하고, 이후에는 격주 투여
30kg 이상	40mg을 처음 2회는 매주 피하주사하고, 이후에는 격주 투여

만약 이 약으로 다시 치료할 경우, 위에서 제시한 용량과 치료기간을 따라야 한다. 소아 판상 건선으로 만 4세 미만의 어린이에게 이 약을 사용한 적은 없다. **[주요 사용상의 주의사항] 1. 경고** 1) 감염: 이 약의 투여 전, 투여 동안 및 투여 후 결핵을 포함한 감염에 대해 면밀히 모니터링해야 한다. ① 심각한 감염 ② 결핵 ③ 기타 기회감염 2) 악성종양과 림프증식성 질환 3) B형 간염 재활성화 4) 신경학적 반응 **2. 다음 환자에는 투여하지 말 것** 1) 이 약 또는 이 약의 성분에 과민증인 환자 2) 활동성 결핵 또는 패혈증, 기회감염과 같은 다른 중증 감염이 있는 환자 3) 중등도 내지 중증의 심부전(NYHA class III/IV) 환자 **[제조원] 제조의뢰자: AbbVie Deutschland GmbH & Co. KG,** Knollstrasse 67061 Ludwigshafen, 독일 **[수입판매원] 한국애브비(주),** 서울특별시 강남구 영동대로 421 삼탄빌딩 6층, 전화: (02) 3429-9300, www.abbvie.co.kr **[공동판매원] 한국에자이(주),** 서울특별시 강남구 봉은사로 86길 6 빌딩 레베쌍트 10층, 전화: (02) 3451-5500, 전송: (02) 3451-5599 **[개정년월일]** 2020년 6월 15일
※의약품 부작용 신고를 생활화합시다(1644-6223, www.drugsafe.or.kr) ※ 자세한 제품정보는 제품설명서를 참조해 주십시오.

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BELIEF IN RELIEF

Cosentyx® secukinumab

Here with you

코센틱스®는 AS로 고통받고 있는 환자들에게 RELIEF, 그 이상의 가치를 제공합니다[1-6]

FAST & LONG LASTING RELIEF[3,6]

* The proportions of patients achieving ASDAS-CRP inactive disease were 25.8% and 16.8% at week 52 and 25.0% and 18.4% at week 156 with secukinumab 300 and 150 mg, respectively.

† Cosentyx® Patient Numbers From Launch Until October 2020. This numbers included patients with PsO, PsA, and AS.

Study design[1]: 4-year results from the MEASURE 1 study; Patients opting to enroll had completed 2 years' treatment in the MEASURE 1 core study with s.c secukinumab 150 or 75mg every 4weeks , following IV loading to Week 4, or placebo treatment to week 16/24. Up-titration from secukinumab 75-150mg q4week was permitted following a protocol amendment. Efficacy is reported for patients originally randomized to secukinumab. Radiographic changes were assessed using the mSASSS and changes in MRI measures of inflammation using the Berlin scoring method. Safety and tolerability were evaluated. Among 274 extension study participants, 89.7% (78/87) and 93.0% (93/100) originally randomized to secukinumab 150 and 75 mg, respectively, completed 208 weeks.

Study design[2]: 3-year long-term end of study results; Randomized, double blinded, parallel group, placebo-controlled phase 3 study. A total of 226 patients were randomized to IV secukinumab 10 mg/kg (baseline, weeks 2 and 4) followed by s.c. secukinumab 300 mg (IV-300 mg) or 150 mg (IV-150 mg) every 4 weeks, or a matched placebo. Patients in the placebo group were re-randomized to s.c. secukinumab at a dose of 300 or 150 mg at week 16. Analysis at week 156 included patients initially randomized to secukinumab and those who switched from placebo to secukinumab at week 16 (any secukinumab 300 or 150 mg). Outcome measures at week 156 included ASAS 20/40, BASDAI, ASAS PR, ASAS 5/6, and ASDAS-CRP inactive disease.

Study design[3]: After the 2-year MEASURE 1 trial, 274 patients receiving s.c. secukinumab 150 or 75 mg (following IV loading or initial placebo treatment to 16/24 weeks) every 4 weeks were invited to enter the 3-year extension study. Dose escalation from 75 to 150 mg (approved dose) was allowed at or after week 156 based on the judgement of the treating physician. Assessments at week 260 (5 years) included ASAS 20/40 and other efficacy outcomes. Data are presented as observed. Safety assessment included all patients who received ≥1 dose of study treatment.

Study design[4]: Randomized, double blinded, parallel group, placebo-controlled phase 3 study. A total of 226 patients were randomized to IV secukinumab 10 mg/kg (baseline, weeks 2 and 4) followed by s.c secukinumab 300 mg (IV-300 mg) or 150 mg (IV-150 mg) every 4 weeks, or a matched placebo. Patients in the placebo group were re-randomized to s.c. secukinumab at a dose of 300 or 150 mg at week 16. The primary endpoint was ASAS20 response rate at week 16 in the IV-300 mg or IV-150 mg versus placebo. Other endpoints assessed through week 52 included improvements in ASAS40, ASAS 5/6, BASDAI, and ASAS PR, as well as the change from baseline in hsCRP levels.

AS, ankylosing spondylitis; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score-C-Reactive Protein; PsO, psoriasis; PsA, psoriatic arthritis; s.c., subcutaneous; IV, intravenous; mSASSS, modified Stoke Ankylosing Spondylitis Spinal Score; MRI, magnetic resonance imaging; ASAS20, Assessment of SpondyloArthritis international Society criteria for 20% improvement; ASAS40, Assessment of SpondyloArthritis international Society criteria for 40% improvement; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; ASAS PR, Assessment of SpondyloArthritis international Society partial remission; ASAS, Assessment in SpondyloArthritis international Society; hsCRP, high-sensitivity C-reactive protein

References 1. Braun J, et al. Rheumatology (Oxford). 2018. doi: 10.1093/rheumatology/key375 **2.** Pavelka K, et al. ACR Open Rheumatol. 2020 Feb;2:119-127. **3.** Baraliakos X, et al. RMD Open. 2019 Sep 3;5:e001005. **4.** Data on file. COSENTYX® access. Novartis Pharmaceuticals Corp; October 2020. **5.** Marzo-Ortega H, et al. Arthritis Rheumatol. 2020; 72 (suppl 10). **6.** Pavelka K, et al. Arthritis Res Ther. 2017 Dec 22;19(1):285.

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Product Information

처방하시기 전 QR 코드 또는 식품의약품안전처 의약품통합정보시스템(https://nedrug.mfds.go.kr)을 통해 상세 제품정보를 참조하시기 바랍니다.

코센틱스센소레디펜 (세쿠키누맙,유전자재조합)

‡65세 이상 RA 환자의 경우 동반질환 및 감염 위험이 높아질 수 있으므로 치료에 주의를 요합니다. † 오렌시아는 연령에 관계없이 remission rate, EULAR 반응율,DAS28-ESR 감소율이 모두 비슷하게 나타났습니다.[1] * 오렌시아는 65세 이상 RA 환자에서 효과 부족으로 인한 치료 중단 및 안전성 문제로 인한 치료 중단이 낮았으며 이로 인한 높은 persistence를 확인하였습니다.[2]
RA, rheumatoid arthritis; DAS28, 28-joint disease activity score; ESR, erythrocyte sedimentation rate

오렌시아®주 250mg(아바타셉트)

[효능 · 효과] 1. 성인 류마티스 관절염: 중등증-중증의 활동성 류마티스 관절염을 가진 성인 환자 2. 소아 특발성 관절염: 중등증-중증의 활동성 류마티스 관절염을 가진 6세 이상의 소아 환자 **[용법 · 용량]** 1. 성인 류마티스 관절염: 오렌시아®는 표1에 제시한 체중 범위별 투여량을 참고하여 30분간 정맥 내 주입으로 투여해야 합니다. 첫 투여 이후에, 오렌시아®는 첫 주입 이후 2주 및 4주 후, 그리고 그 이후에는 매 4주마다 투여해야 합니다. 오렌시아®는 단독치료제로 사용하거나 또는 TNF길항제를 제외한 DMARDs와 병용으로 투여할 수 있습니다. 소아 특발성 관절염 환자에는, 각 환자의 체중을 기준으로 계산 용량을 사용합니다. 2. 소아 특발성 관절염: 75kg 미만의 체중인 6 내지 17세의 소아 특발성 관절염 환자에의 오렌시아®의 권장용량은 매 투여시 환자의 체중을 기초로 10mg/kg을 투여합니다. 75kg 이상의 체중인 소아 환자에게는 성인의 권장 용량을 따라 오렌시아®를 투여해야하며, 최고 1000mg을 초과하지 않습니다. 오렌시아®는 30분간의 정맥 주입으로 투여해야 합니다. 첫 투여 이후에, 오렌시아®는 첫 투여후 2주 및 4주 후에 투여하고 그 이후 매 4주마다 투여합니다. 오렌시아®는 단독요법 또는 메토트렉세이트(MTX)와 병용하여 사용할 수 있습니다. **[사용상의 주의사항]** 다음 환자에는 투여하지 말 것: 이 약은 주성분(아바타셉트)이나 또는 이외의 구성 성분에 과민반응을 나타내는 것으로 알려진 환자에게 투여해서는 안 됩니다. *최신 제품정보는 (주)한국BMS제약 홈페이지(bms.com/kr) 또는 식약처 홈페이지 의약품정보란에서 확인하실 수 있습니다. **[제조회사]** BMS Company **[판매회사]** 한국BMS제약

표1. 정맥 투여 시 오렌시아® 주 250mg(아바타셉트)의 용량

환자 체중	용량	바이알 개수[a]
< 60kg	500mg	2
60 내지 100kg	750mg	3
> 100kg	1g	4

[a] 각 바이알에는 아바타셉트 250mg이 들어있다.

오렌시아® 서브큐 프리필드시린지 125mg(아바타셉트)

[효능 · 효과] 성인 류마티스 관절염: 중등증에서 중증의 활동성 류마티스 관절염을 가진 성인 환자. **[용법 · 용량]** 성인 류마티스 관절염: 아바타셉트는 단독치료제로 사용하거나 또는 TNF 저해제를 제외한 DMARDs와 병용으로 투여할 수 있습니다. 1. 피하 투여 요법: 이 약은 일주일에 한 번 피하 투여용으로만 사용해야 합니다. 이 약은 오렌시아® 주 250mg(아바타셉트) 정맥 부하 용량 투여 없이 시작할 수 있습니다. 의사가 필요하다고 판단하는 경우, 정맥 부하 용량 투여로 치료를 시작하는 환자는 표 1의 체중에 따른 분류에 따라 한 번의 정맥 주입으로 시작하여야 합니다. 정맥 투여 후 하루 이내에 이 약의 첫 피하 투여를 실시해야 합니다. 오렌시아® 정맥 투여를 받고 있던 환자가 피하 투여로 변경하는 경우에는 다음에 계획된 정맥 투여 용량 대신에 첫 피하 투여 용량을 적용합니다. 2. 정맥 투여 요법: 부하 용량으로서 오렌시아® 주 250mg(아바타셉트)을 이용한 정맥 투여는 표 1에 제시한 체중 범위별 투여량을 참고하여 30분간 정맥 내 주입으로 투여해야 합니다. **[사용상의 주의사항]** 다음 환자에는 투여하지 말 것: 이 약은 주성분(아바타셉트)이나 또는 이외의 구성성분에 과민반응을 나타내는 것으로 알려진 환자에게 투여해서는 안 됩니다. *최신 제품정보는 (주)한국BMS제약 홈페이지(bms.com/kr) 또는 식약처 홈페이지 의약품정보란에서 확인하실 수 있습니다. **[제조회사]** BMS Company **[판매회사]** 한국BMS제약

References 1. Lahaye C, et al. Rheumatology (Oxford) 2016;55:874-84. **2** Ebina K et al. PLoS One. 2019 May 8;14(5):e0216624 7.
3. Harigai M, et al. Mod Rheumatol 2016;26:491-498. 4. Zhang J, et al. Ann Rheum Dis. 2016;75(10):1813–8.

Bristol Myers Squibb™ 서울시 강남구 테헤란로 504 해성1빌딩 12층, 02-3404-1300, bms.com/kr

ORENCIA® (abatacept)

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Prograf® Tacrolimus

국내에서 수행된 MTX에 반응하지 않는
75명의 RA환자를 대상으로 한 4상 임상시험에서

TAC 병용은 LEF 병용에 비해 **비열등한 DAS28 개선 효과**를 보였으며, **양호한 내약성**을 나타냈습니다.[1]

- 24주 시점에서 **DAS28 score**를 보았을 때 TAC+MTX 군은 LEF+MTX군에 비해 **비열등 하였습니다.**[1]
  mean difference of DAS28: −0.1812, 95% CI: −0.8073, 0.4450
- TAC+MTX 군의 경우 37명 중 18명,
  LET+MTX 군의 경우 38명 중 27명에서
  이상사례가 보고되었습니다.[2]

LOVE Prograf®

[study information]
A 24-week multi-center, double-blind, randomized, non-inferiority study in 75 rheumatoid arthritis(RA) patients with inadequate response to methotrexate (MTX) to investigate the efficacy and safety of tacrolimus(TAC) versus leflunomide(LEF) when combined with MTX in RA patients. Initial add-on dose: 1 capsule/day (TAC 1.5 mg/day) or LEF (10 mg/day) for 4 weeks(If tolerable, doses were then increased to 2 capsules/day until the end of the study).

[Reference] 1. Shin, K, et al. Efficacy and safety of add-on tacrolimus versus leflunomide in rheumatoid arthritis patients with inadequate response to methotrexate. Int J Rheum Dis. 2019 Jun;22(6):1115-1122. 2. Shin, K, et al. Efficacy and safety of add-on tacrolimus versus leflunomide in rheumatoid arthritis patients with inadequate response to methotrexate. Int J Rheum Dis. 2019 Jun;22(6):1115-1122. Supplementary Table 2.

* 보다 자세한 안전성 정보는 제품 설명서를 참고해 주십시오.(제품설명서 작성일: 프로그랍 캡슐 2020.05.14)

▶ 프로그랍 제품설명서

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Help her move forward with the relentless protection of **Prolia**®[1-2]

Reference 1. Camacho PM, *et al. Endocr Pract.* 2016;22(Suppl 4):1-421. **2.** Bone HG, *et al. Lancet Diabetes Endocrinol.* 2017;5(7):513-523.

PROLIA® Product Information [제품명] 프롤리아프리필드시린지(데노수맙) **[효능·효과]** 1. 폐경 후 여성 골다공증 환자의 치료 2. 남성 골다공증 환자의 골밀도 증가를 위한 치료 3. 글루코코르티코이드 유발성 골다공증의 치료 4. 안드로겐 차단요법을 받고 있는 비전이성 전립선암 환자의 골 소실 치료 5. 아로마타제 저해제 보조요법을 받고 있는 여성 유방암 환자의 골 소실 치료 **[용법·용량]** 이 약은 보건의료 전문가에 의해 투여되어야 한다. 이 약 1시린지(데노수맙 60mg)을 매 6개월마다 상완, 허벅지 위쪽 또는 복부에 피하 주사한다. 모든 환자는 칼슘 1000mg과 비타민D 400IU 이상을 매일 복용해야 한다. 정기 투여일에 이 약을 투여하지 못했을 경우, 가능한 빨리 투여한다. 그 후, 마지막 투여일자로부터 매 6개월마다 투여한다. **[경고]** 턱뼈 괴사가 보고되었다. **[다음 환자에게는 투여하지 말 것]** 1. 저칼슘혈증이 있는 환자는 이 약의 투여를 시작하기 전에 저칼슘혈증을 치료해야 한다. 2. 임부 3. 과민반응 **[약물유해반응]** 폐경 후 골다공증 환자에서 보고된 가장 흔한(≥5%이며 위약군보다 흔한) 약물이상반응은 등 통증, 팔다리 통증, 근골격통, 고콜레스테롤혈증 및 방광염. 남성 골다공증 환자에서 보고된 가장 흔한(≥5%이며 위약군보다 흔한) 약물이상반응은 등 통증, 관절통, 비인두염. 글루코코르티코이드 유발성 골다공증 환자에서 보고된 가장 흔한(≥3%이며 활성대조군보다 흔한) 약물이상반응은 등 통증, 고혈압, 기관지염 및 두통. 안드로겐 차단요법을 받고 있는 전립선암 환자 또는 아로마타제 저해제 보조요법을 받고 있는 유방암 환자의 골 소실에 대하여 보고된 가장 흔한(10%) 약물이상반응은 관절통, 등 통증. **[임반적 주의]** 이 약 투여 중 엑스지바주를 투여하면 안 된다. 과민반응, 저칼슘혈증 및 무기질 대사, 턱뼈 괴사, 비정형 전자하부 및 골간 대퇴골 골절, 이 약의 치료 중단 후 다발성 척추 골절, 심각한 감염, 피부 유해사례, 골격근 통증, 골 교체 억제의 가능성이 있으므로 환자를 모니터링하고 필요시 치료 중단 등의 의학적 조치를 고려한다. **[직용상의 주의]** 우발적으로 주사침에 찔리는 것을 최소화하기 위하여, 이 약에는 녹색의 보호대가 장착되어 있다. 투여하기 전에 주사침 압쪽으로 녹색 보호대를 밀어서는 안된다. **[보관 및 취급상의 주의사항]** 동결을 피하여 차광, 냉장 (2-8°C) 보관. **[수입판매원]** 암젠코리아유한회사 (서울특별시 중구 을지로5길 19, 20층 (수하동, FERRUM TOWER)). **※제품을 처방하시기 전 상세 제품설명서를 참고하여주시기 바랍니다.**

AMGEN®

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KR-03518-PRO-2019-Oct

보건의료전문가용

2021년 2월부터
벤리스타의 보험 급여가 적용됩니다[1]

구분	세부인정기준 및 방법
[142] Belimumab 주사제 [품명] 벤리스타주 120 밀리그램, 벤리스타주 400 밀리그램	허가사항 범위 내에서 아래와 같은 기준으로 투여 시 요양급여를 인정하며, 동 인정기준 이외에는 약값 전액을 환자가 부담토록 함. **가. 투여대상** 1) 표준요법(코르티코스테로이드, 항말라리아약, 면역억제제 단독 또는 병용투여)으로 3개월 이상 치료 중인 자가항체 양성인 활동성 전신홍반루푸스 만 18세 이상 성인 환자로서 다음 가), 나), 다) 조건을 모두 만족하는 경우 **가) SELENA-SLEDAI※ 10 이상　나) 항dsDNA 항체 양성　다) 낮은 보체(C3 또는 C4)** 2) 중증의 활성 중추신경계 전신홍반루푸스, 중증의 활성 루푸스 신염 환자에는 인정하지 아니함 **나. 투여방법** 1) **최초 투약 후 24주째 평가**를 통하여 SELENA-SLEDAI가 4이상 감소한 경우 추가 6개월간의 사용을 인정함 2) **최초 투약 후 12개월째 평가**를 통하여 첫 24주째의 평가 결과가 유지되면 추가 6개월간의 사용을 인정함 **(최대 18개월)**

벤리스타 약가 정보[2]

	120 mg	400 mg
보험코드	650002901	650002891
상한금액	**182,696 원**	**608,988 원**
환자 부담금(상한액)*	18,270 원	60,899 원

*기관 또는 계통 침범을 동반한 전신홍반루푸스 (KCD 코드: M32.1) 로 확진 받은 환자는 산정특례 대상자로 경감된 부담금을 지불하게 됩니다. 산정특례란 희귀난치성질환자로 확진 받은 환자가 등록절차에 따라 건강보험공단에 신청한 경우, 약제에 대한 본인 부담률을 10%로 경감하는 제도입니다.

※SELENA-SLEDAI: a Safety of Estrogen in Lupus National Assessment-Systemic Lupus Erythematosus Disease Activity Index

Reference 1. 보건복지부 공고 제 2020-915호

Abbreviated Prescribing Information Version 08

벤리스타주 120 밀리그램, 400 밀리그램(벨리무맙) [단클론항체, 유전자재조합] [수입의약품] [전문의약품]

■ 원료약품 원료약품 및 그 분량 : 이 약 1바이알(120mg/바이알) 중 주성분 벨리무맙 (별규) 120mg, 이 약 1바이알(400mg/바이알) 중 주성분 벨리무맙 (별규) 400mg ■ 효능 · 효과 : 표준요법으로 치료중인 자가 항체 양성인 활동성 전신홍반루푸스 성인 환자의 치료 ■ 용법 · 용량 : 권장 용량은 10 mg/kg이며 초기 3회 투여는 2주 간격으로 투여하고 그 이후에는 4주 간격으로 투여한다. 정맥 내 연속주입용으로 조제, 최적하고 1시간에 걸쳐 투여한다. 주입 반응 및 과민 반응을 예방하기 위한 전처치를 고려해야 한다. 이 약 투여 6개월 후에도 질환 조절에 개선이 없는 경우, 이 약의 투여 중단을 고려해야 한다. ■ 사용상의 주의사항 주의사항 1, 경고 1) 감염: 이 약을 포함한 면역억제제를 투여 받은 환자들에서 심각하고 때로는 치명적일 수 있는 감염이 보고되고 있다. 활동성 감염이 있는 환자들에서는 이 약 치료를 개시하지 않도록 한다. 환자에게 중대한 감염이 나타난 경우에는 감염이 통제될 때까지 이 약의 투여를 중단하도록 한다. 신속한 평가와 적절한 치료가 이루어지기 위하여, 감염을 암시하는 특정 증상이 나타날 때에는 즉시 의료 전문가에게 연락하도록 환자들을 지도한다. 2. 다음 환자에게는 투여하지 말 것. 이 약의 성분에 대하여 아나필락시스의 기왕력이 있는 환자 3. 다음 환자에는 신중히 투여할 것 1) 이 약은 다음 환자군에서 연구된 적이 없으며, 치료의 이득과 위험을 고려하여 투여 결정을 해야 한다. · 중증의 활성 중추신경계 전신홍반루푸스 · 중증의 활성 루프스 신염 · HIV · B형 또는 C형 간염의 병력 또는 최근 감염 · 저감마글로불린혈증(IgG <400 mg/dl) 또는 IgA 결핍(IgA<10mg/dl) · 주요 장기 이식 또는 조혈모세포골수 이식 또는 신장 이식의 병력 2) 우울증 및 자살생각: 정맥 내 주입 임상시험과 피하주사 임상시험에서 정신질환(우울증, 자살생각, 자살행동)이 이 약 투여군에서 더 자주 보고되었다. 이 약 10 mg/kg 투여군과 이 약 1 mg/kg 투여군에서 각각 한 건의 자살이 보고되었다(이상사례 항 참조). 의사는 이 약 투여 전 환자의 기왕력과 현재 정신건강 상태를 고려하여 우울증 및 자살의 위험성을 평가하여야 하며, 치료기간 동안 환자의 상태를 모니터링해야 한다. 의사는 환자(및 적절한 경우 보호자)에게 환자의 새롭거나 악화된 정신과적 증상에 대하여 의료인에게 알리도록 해야 한다. 이러한 증상이 발현된 환자에 대해서는 이 약을 지속적으로 투여하는 것에 대해 위험성과 유익성을 주의깊게 평가해야 한다. 4. 약물이상반응 1) 임상시험 경험 ○이상사례 요약표: 이 약 10 mg/kg을 투여했을 때 발생한 이상사례를 MedDRA 기관계 분류 및 발생 빈도에 따라 정리하였다. 매우 흔함 ≥ 1/10, 흔함 ≥ 1/100에서 (1/10, 흔하지 않음 ≥ 1/10000에서 (1/100. 각각의 빈도 군에서, 중대함이 높은 순서로 나타내었다. · 감염: 매우 흔함- 세균 감염(예, 기관지염, 방광염), 흔함- 바이러스성 위장염, 인두염, 코인두염/ 혈액 및 림프계 장애: 흔함- 백혈구 감소증/ 면역계 장애: 흔함- 과민 반응*, 흔하지 않음- 아나필락시스 반응, 혈관 부종/ 정신 질환: 흔함- 우울증, 불면증, 흔하지 않음- 자살생각, 자살행동/ 신경계 장애: 흔함- 편두통/ 위장 장애: 매우 흔함- 설사, 오심/ 피부 및 피하 조직 장애: 흔하지 않음-두드러기, 발진/ 근골격 및 결합조직 장애: 흔함- 사지통/ 전신 장애 및 투여 부위 상태: 흔함- 주입 관련 전신 반응*, 발열, [* '과민반응' 은 아나필락시스를 포함하는 용어의 통칭이며, 저혈압, 혈관부종, 두드러기 또는 기타 발진, 소양증 및 호흡곤란 등을 포함하는 다양한 증상으로 발현될 수 있다. '주입 관련 반응' 은 용어의 통칭이며 서맥, 근육통, 두통, 발진, 두드러기, 발열, 저혈압, 고혈압, 어지러움 및 관절통 등의 다양한 증상으로 발현될 수 있다. 징후 및 증상이 중복되기 때문에, 과민 반응과 주입 반응을 모든 사례에서 구별할 수는 없다.] 2) 사망: 임상시험기간 동안 위약보다 이 약 투여군에서 더 많은 사망이 보고되었다. 사망의 뚜렷한 주요원인은 없었으며, 감염, 심혈관계 질환, 자살과 같은 원인들을 포함하였다. 3) 심각한 감염: 성인에서의 사망률 및 특정관심 이상사례를 평가하기 위한 무작위(1:1), 이중 눈가림, 위약 대조, 52주, 시판 후 안전성 연구(BEL115467) 결과, 이 약 10mg/kg 정맥투여 군 3.7%와 위약 투여군 4.1%에서 심각한 감염이 발생하였다. 사망을 초래한 감염은 이 약 투여군의 0.45%(9/2002) 및 위약 투여군의 0.15%(3/2001)에서 발생하였으며, 모든 원인으로 인한 사망률은 이 약 투여군 0.50%(10/2002), 위약 투여군 0.40%(8/2001)이었다. 4) 진행성 다초점 백질뇌병증(Progressive Multifocal Leucoencephalopathy, PML) 5) 악성 종양: 다른 면역 조절제와 마찬가지로 이 약의 작용기전은 악성 종양의 진행에 대한 위험성을 증가시킬 수 있다. 6) 아나필락시스를 포함한 과민반응 7) 주입 반응 8) 우울증 9) 면역원성 5. 일반적 주의 1) 예방접종: 임상적 안전성이 확립되어 있지 않으므로, 생백신을 이 약과 동시 투여하거나 이 약 투여 전 30일 이내에 투여해서는 안 된다. 생백신을 투여 받은 환자에서 이 약 투여 환자로의 감염의 이차 전이 또는 새로운 예방접종에 대한 이 약의 영향에 관한 이용 가능한 자료는 없다. 이 약의 작용기전으로 인해 이 약은 예방접종의 반응을 간섭할 수 있다. 그러나, 23가 폐렴구균 백신에 대한 반응성을 평가한 소규모 연구에서, 다른 혈청형들에 대한 전반적인 면역 반응은 예방접종할 때 벨리무맙을 투여받고 있지 않던 전신홍반루푸스 환자와 벨리무맙을 투여받고 있던 전신홍반루푸스 환자에서 유사했다. 제한된 자료에서 이 약은 이 약 투여 전의 예방접종에 대한 항이 면역 반응을 유지하는 능력에는 유의한 영향을 미치지 않는 것으로 나타났다. 2) 다른 생물학적 제제 요법 또는 정맥 내 투여용 시클로포스파미드의 병용: B-세포 표적 치료를 포함한 다른 생물학적 제제 요법 또는 정맥 내 투여용 시클로포스파미드와 이 약의 병용은 연구되지 않았다. 따라서, 이 약과 생물학적 제제 요법 또는 정맥 내 투여용 시클로포스파미드와의 병용은 권장되지 않는다. 3) 이 약이 운전 또는 기계 조작에 미치는 영향을 조사한 시험은 없다. 이 약의 약물학적 특성상 부정적인 영향은 없을 것으로 예상된다. 판단, 운동 또는 인지 기능을 요하는 일을 수행하는 환자의 능력을 고려해야 할 때, 환자의 임상적 상태 및 이 약의 안전성 프로파일을 주지해야 한다. 6. 임부 및 수유부에 대한 투여 1) 임부: 임부에서 이 약을 사용한 자료는 제한적이다. 임부를 대상으로 이 약을 사용하여 실시한 적절하고, 잘 통제된 임상 시험은 없다. 이 약을 포함하여 면역글로불린G(IgG) 항체는 태반을 통과할 수 있다. 동물 생식발생독성시험 이 사람에서의 반응을 항상 예측할 수는 없기 때문에, 임신 기간 동안 이 약은 잠재적 유익성이 태아에 대한 잠재적 위험성을 상회하는 경우에만 투여해야 한다. 임신의 가능성이 있는 여성은 이 약의 투여 기간 및 최종 투여 후 최소 4개월 동안 적절한 피임을 시행해야 한다 2) 수유부: 수유 중 이 약 사용에 대한 안전성은 확립되지 않았다. 이 약이 모유로 분비되는지 또는 섭취 후 전신으로 흡수되는지 여부는 알려져 있지 않다. 수유부에서 이 약의 치료에 대한 결정은 유아에 대한 모유 수유의 중요성, 수유부에 대한 약물의 중요성, 및 벨리무맙 또는 모체의 기저 상태에 의한 수유 중인 소아에 대한 잠재적 유해 영향을 고려하여 결정되어야 한다. ■ 최종허가변경일: 2020.04.10 ■ 이 개정일자 이후 변경된 내용 및 제품 정보 전문은 kr.gsk.com에서 확인하실 수 있습니다. ■ GSK 제품 사용 중 발생한 이상사례(부작용)는 080-901-4100 또는 kr-medical.drug-safety@gsk.com으로 보고해 주시기 바랍니다.

Abbreviated Safety Information

1. 경고 1) 감염: 이 약을 포함한 면역억제제를 투여 받은 환자들에서 심각하고 때로는 치명적일 수 있는 감염이 보고되고 있다. 활동성 감염이 있는 환자들에서는 이 약 치료를 개시하지 않도록 한다. 환자에게 중대한 감염이 나타난 경우에는 감염이 통제될 때까지 이 약의 투여를 중단하도록 한다. 신속한 평가와 적절한 치료가 이루어지기 위하여, 감염을 암시하는 특정 증상이 나타날 때에는 즉시 의료 전문가에게 연락하도록 환자들을 지도한다. 2. 다음 환자에게는 투여하지 말 것. 이 약의 성분에 대하여 아나필락시스의 기왕력이 있는 환자 3. 다음 환자에는 신중히 투여할 것 1) 이 약은 다음 환자군에서 연구된 적이 없으며, 치료의 이득과 위험을 고려하여 투여 결정을 해야 한다. · 중증의 활성 중추신경계 전신홍반루푸스 · 중증의 활성 루프스 신염 · HIV · B형 또는 C형 간염의 병력 또는 최근 감염 · 저감마글로불린혈증(IgG <400 mg/dl) 또는 IgA 결핍(IgA<10mg/dl) · 주요 장기 이식 또는 조혈모세포골수 이식 또는 신장 이식의 병력 2) 우울증 및 자살생각: 정맥 내 주입 임상시험과 피하주사 임상시험에서 정신질환(우울증, 자살생각, 자살행동)이 이 약 투여군에서 더 자주 보고되었다. 이 약 10 mg/kg 투여군과 이 약 1 mg/kg 투여군에서 각각 한 건의 자살이 보고되었다(이상사례 항 참조). 의사는 이 약 투여 전 환자의 기왕력과 현재 정신건강 상태를 고려하여 우울증 및 자살의 위험성을 평가하여야 하며, 치료기간 동안 환자의 상태를 모니터링해야 한다. 의사는 환자(및 적절한 경우 보호자)에게 환자의 새롭거나 악화된 정신과적 증상에 대하여 의료인에게 알리도록 해야 한다. 이러한 증상이 발현된 환자에 대해서는 이 약을 지속적으로 투여하는 것에 대해 위험성과 유익성을 주의깊게 평가해야 한다. 4. 약물이상반응 1) 임상시험 경험 ○이상사례 요약표: 이 약 10 mg/kg을 투여했을 때 발생한 이상사례를 MedDRA 기관계 분류 및 발생 빈도에 따라 정리하였다. 매우 흔함 ≥ 1/10, 흔함 ≥ 1/100에서 (1/10, 흔하지 않음 ≥ 1/10000에서 (1/100. 각각의 빈도 군에서, 중대함이 높은 순서로 나타내었다. · 감염: 매우 흔함- 세균 감염(예, 기관지염, 방광염), 흔함- 바이러스성 위장염, 인두염, 코인두염/ 혈액 및 림프계 장애: 흔함- 백혈구 감소증/ 면역계 장애: 흔함- 과민 반응*, 흔하지 않음- 아나필락시스 반응, 혈관 부종/ 정신 질환: 흔함- 우울증, 불면증, 흔하지 않음- 자살생각, 자살행동/ 신경계 장애: 흔함- 편두통/ 위장 장애: 매우 흔함- 설사, 오심/ 피부 및 피하 조직 장애: 흔하지 않음-두드러기, 발진/ 근골격 및 결합조직 장애: 흔함- 사지통/ 전신 장애 및 투여 부위 상태: 흔함- 주입 관련 전신 반응*, 발열, [* '과민반응' 은 아나필락시스를 포함하는 용어의 통칭이며, 저혈압, 혈관부종, 두드러기 또는 기타 발진, 소양증 및 호흡곤란 등을 포함하는 다양한 증상으로 발현될 수 있다. '주입 관련 반응' 은 용어의 통칭이며 서맥, 근육통, 두통, 발진, 두드러기, 발열, 저혈압, 고혈압, 어지러움 및 관절통 등의 다양한 증상으로 발현될 수 있다. 징후 및 증상이 중복되기 때문에, 과민 반응과 주입 반응을 모든 사례에서 구별할 수는 없다.] 2) 사망: 임상시험기간 동안 위약보다 이 약 투여군에서 더 많은 사망이 보고되었다. 사망의 뚜렷한 주요원인은 없었으며, 감염, 심혈관계 질환, 자살과 같은 원인들을 포함하였다. 3) 심각한 감염: 성인에서의 사망률 및 특정관심 이상사례를 평가하기 위한 무작위(1:1), 이중 눈가림, 위약 대조, 52주, 시판 후 안전성 연구(BEL115467) 결과, 이 약 10mg/kg 정맥투여 군 3.7%와 위약 투여군 4.1%에서 심각한 감염이 발생하였다. 사망을 초래한 감염은 이 약 투여군의 0.45%(9/2002) 및 위약 투여군의 0.15%(3/2001)에서 발생하였으며, 모든 원인으로 인한 사망률은 이 약 투여군 0.50%(10/2002), 위약 투여군 0.40%(8/2001)이었다. 4) 진행성 다초점 백질뇌병증(Progressive Multifocal Leucoencephalopathy, PML) 5) 악성 종양: 다른 면역 조절제와 마찬가지로 이 약의 작용기전은 악성 종양의 진행에 대한 위험성을 증가시킬 수 있다. 6) 아나필락시스를 포함한 과민반응 7) 주입 반응 8) 우울증 9) 면역원성

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- 방사선학적 평가를 통해 단독요법, DMARDs 병용요법에서 관절손상 억제효과를 확인하였습니다.[2-3]
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Reference. 1. ADACTA study. Lancet. 2013 May 4;381(9877):1541-50 2. REACTION study. Mod Rheumatol. 2011;21(2):122-33 3. ACT-RAY study. Ann Rheum Dis. 2013;72:43-50 4. STREAM study. Ann Rheum Dis. 2009;68:1580-4 5. MUSASHI study. Arthritis Care Res (Hoboken). 2014 Mar;66(3):344-54 6. Arthritis Research&Therapy. 2011;13:R141

[제품요약정보] 악템라®주, 악템라® 피하주사 162mg [전문의약품] **■주성분** 토실리주맙(Tocilizumab) • IV : 80mg/4ml, 200mg/10ml, 400mg/20ml • SC(PFS/AI) : 162mg/0.9ml **■효능·효과** [류마티스 관절염(성인)]: 메토트렉세이트(MTX)를 포함한 이전에 한 가지 이상의 DMARDs (Disease-Modifying anti Rheumatic Drug)에 대한 반응이 적절하지 않거나 불내성인 성인의 중등도 내지 중증의 활동성 류마티스 관절염의 치료, 메토트렉세이트와의 병용투여 시 관절손상 진행속도의 감소(X-선 측정결과)와 신체 기능의 향상 [전신형 소아 특발성 관절염]: 비스테로이드성 소염진통제(NSAID) 및 전신성 코르티코스테로이드(Corticosteroid)에 대한 반응이 적절하지 않은 2세 이상의 전신형 소아 특발성 환자의 치료 [다관절형 소아 특발성 관절염]: 메토트렉세이트(MTX)에 대한 반응이 적절하지 않은 2세 이상의 다관절형 소아 특발성 환자의 치료 **■용법·용량** [IV] [류마티스 관절염(성인)] • 이 약은 단독 투여 또는 메토트렉세이트나 다른 DMARD와 병용 투여할 수 있다. 메토트렉세이트에 내약성이 없거나 지속적인 병용 투여가 부적절한 경우에는 단독 투여할 수 있다. • 성인의 활동성 류마티스 관절염에 대해, kg(몸무게)당 8 mg을 4주 1회 정맥 투여하며, 100 kg 이상의 환자에 대해서는 정맥 투여 시 800 mg을 초과해서는 안 된다. • 간 효소의 상승, 호중구감소증 및 혈소판감소증 등의 실험실적 검사치 이상이 발생한 경우 용량 조절이 권장된다. • 투여 시 생리식염 주사액으로서 최종 100 mL가 되도록 희석하고, 1시간 이상 점적정주 한다. [전신형 소아 특발성 관절염(2세이상)] • 이 약은 메토트렉세이트와 병용 투여한다. 메토트렉세이트에 내약성이 없거나 지속적인 병용 투여가 부적절한 경우에는 단독 투여할 수 있다. • 몸무게 30kg미만 : 전신형 소아 특발성 관절염에 대해, kg(몸무게)당 12mg을 2주 1회 정맥 투여한다. • 몸무게 30kg이상 : 전신형 소아 특발성 관절염에 대해, kg(몸무게)당 8mg을 2주 1회 정맥 투여한다. • 100 kg 이상의 환자에 대해서는 정맥 투여 시 800 mg을 초과해서는 안 된다. • 간 효소의 상승, 호중구감소증 및 혈소판감소증 등의 실험실적 검사치 이상이 발생한 경우 용량 조절이 권장된다. • 투여 시 생리식염 주사액으로서 최종 100 mL(몸무게가 30kg 미만인 경우 50mL)가 되도록 희석하고, 1시간 이상 점적정주 한다. [다관절형 소아 특발성 관절염(2세이상)] • 이 약은 메토트렉세이트와 병용 투여한다. 메토트렉세이트에 내약성이 없거나 지속적인 병용 투여가 부적절한 경우에는 단독 투여할 수 있다. • 몸무게 30kg미만 : 다관절형 소아 특발성 관절염에 대해, kg(몸무게)당 10mg을 4주 1회 정맥 투여한다. • 몸무게 30kg이상 : 다관절형 소아 특발성 관절염에 대해, kg(몸무게)당 8mg을 4주 1회 정맥 투여한다. • 100 kg 이상의 환자에 대해서는 정맥 투여 시 800 mg을 초과해서는 안 된다. • 간 효소의 상승, 호중구감소증 및 혈소판감소증 등의 실험실적 검사치 이상이 발생한 경우 용량 조절이 권장된다. • 투여 시 생리식염 주사액으로서 최종 100 mL가 되도록 희석하고, 1시간 이상 점적정주 한다. • 4주 간격으로 '악템라주(토실리주맙)(유전자재조합)'를 정맥 투여받고 있던 환자가 이 약으로 변경하고자 할 경우에는 다음에 계획된 정맥 투여 일정부터 이 약 162 mg을 2주 간격으로 피하 투여한다. **■주요 사용상의 주의사항** [다음 환자에는 투여하지 말 것] 1) 심각한 감염증이 있는 환자(감염증이 악화될 우려가 있다) 2) 활동성 결핵 환자(증세를 악화시킬 우려가 있다) 3) 이 약 및 이 약의 성분에 과민증 환자 [다음 환자에는 신중히 투여할 것] 1) 감염 합병증이 있는 환자 또는 감염증이 의심되는 환자 2) 결핵의 기간염자(특히 결핵의 과거 병력이 있는 환자 및 흉부 X선상 결핵 치유 소견이 있는 환자) 3) 감염 감수성 증가 상태에 있는 환자 4) 간질성 폐렴의 기왕력이 있는 환자 5) 위장 궤양이나 장관 게실이 있는 환자 6) 백혈구 감소, 호중구 감소, 혈소판 감소가 있는 환자 7) 활동성 간 질환이나 간 장애가 있는 환자

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1. Schwartzman, Sergio, and G. James Morgan."Does route of administration affect the outcome of TNF antagonist therapy?." Arthritis research & therapy 6.2 (2004): S19.

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연구이사	신기철 (서울의대)		
정보이사	김근태 (고신의대)		
의료정책이사	백한주 (가천의대)		
법제윤리이사	박용범(연세의대)		
무임소이사	공현식 (서울의대)	김현아 (한림의대)	엄완식 (한양류마엄완식내과)
	이상일 (경상의대)	이은봉 (서울의대)	차훈석 (성균관의대)
이　　사	강태영 (강태영내과)	김건우 (대구파티마병원)	김성규 (대구가톨릭의대)
	김성수 (울산의대)	김성호 (인제의대)	김종민 (울산의대)
	김진석 (제주의대)	김해림 (건국의대)	남언정 (경북의대)
	서창희 (아주의대)	안종균 (연세의대)	이규훈 (한양의대)
	임승재 (성균관의대)	주지현 (가톨릭의대)	
감　　사	이성원 (동아의대)	서영일 (한림의대)	

대한류마티스학회 위원회 명단

총무위원회

이사	이창근 (울산의대)		
위원	방소영 (한양의대)	허진욱 (을지의대)	김재훈 (고려의대)
	오지선 (서울아산병원)	송　란 (경희의대)	

재무위원회

이사	김완욱 (가톨릭의대)		
위원	김혜림 (건국의대)	서영일 (한림의대)	천윤홍 (경상의대)
	최성재 (고려의대)	한승우 (경북의대)	

간행위원회

이사	이영호 (고려의대)		
간사	조수경 (한양의대)		
위원	김성규 (대구가톨릭의대)	김태종 (전남의대)	박민찬 (연세의대)
	박진균 (서울의대)	안종균 (연세의대)	안중경 (성균관의대)
	이승근 (부산의대)	임두호 (울산의대)	주영빈 (한양의대)

학술위원회

이사	성윤경 (한양의대)		
간사	안중경 (성균관의대)		
위원	공현식 (서울의대)	곽승기 (가톨릭의대)	김기조 (가톨릭의대)
	김성규 (대구가톨릭의대)	김용길 (울산의대)	김진현 (충남의대)
	김현아 (아주의대)	박진균 (서울의대)	송정식 (연세의대)
	이연아 (경희의대)	전찬홍 (순천향의대)	조수경 (한양의대)

국제위원회

이사	심승철 (충남의대)		
간사	이지연 (가톨릭의대)		
위원	곽승기 (가톨릭의대)	권성렬 (인하의대)	유인설 (충남의대)
	이은영 (서울의대)	이재준 (성균관의대)	정상윤 (차의대)
	최찬범 (한양의대)		

보험위원회

이사	윤보영 (인제의대)	홍승재 (경희의대)	
간사	김현숙 (순천향의대)	유종진 (한림의대)	
위원	강태영 (강태영내과)	민홍기 (건국의대)	박민찬 (연세의대)
	서영일 (한림의대)	손일웅 (조은손병원)	이주하 (가톨릭의대)
	이주현 (인제의대)	정영옥 (류마앤정내과)	최성재 (고려의대)
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	최찬범 (한양의대)	하유정 (서울의대)	

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이사	이명수 (원광의대)		
간사	허진욱 (을지의대)		
위원	강은하 (서울의대)	구본산 (인제의대)	김상현 (계명의대)
	김윤성 (조선의대)	김현숙 (순천향의대)	김현옥 (경상의대)
	박경수 (가톨릭의대)	박동진 (전남의대)	배영덕 (류마내과)
	이승근 (부산의대)	임미진 (인하의대)	정재현 (고려의대)
	채지영 (분당제생병원)		

교육수련위원회

이사	윤종현 (가톨릭의대)		
간사	이주하 (가톨릭의대)	이창훈 (원광의대)	
위원	김근태 (고신의대)	김상현 (계명의대)	김재훈 (고려의대)
	성윤경 (한양의대)	송 란 (경희의대)	엄완식 (한양류마엄완식내과)
	이상원 (연세의대)	이윤종 (서울의대)	천윤홍 (경상의대)
	최상태 (중앙의대)		

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이사	신기철 (서울의대)		
간사	한승우 (경북의대)		
위원	고정희 (가톨릭의대)	구본산 (인제의대)	김진현 (충남의대)
	김태종 (전남의대)	김해림 (건국의대)	김현아 (아주의대)
	문수진 (가톨릭의대)	박동진 (전남의대)	오지선 (서울아산병원)
	이상엽 (동아의대)	이상진 (경북의대)	이재준 (성균관의대)
	이화정 (대구가톨릭의대)	주지현 (가톨릭의대)	최인아 (충북의대)
	하유정 (서울의대)	홍석찬 (울산의대)	

정보위원회

이사	김근태 (고신의대)		
간사	채지영 (분당제생병원)		
위원	고혁재 (가톨릭의대)	김성수 (울산의대)	문기원 (강원의대)
	박성훈 (대구가톨릭의대)	손창남 (계명의대)	이상엽 (동아의대)
	이상원 (연세의대)	장성혜 (순천향의대)	정상윤 (차의대)
	정주양 (아주의대)	정종혁 (원광의대)	최윤정 (전북의대)

의료정책위원회

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간사	이은봉 (서울의대)	최병용 (서울의료원)	
위원	강은하 (서울의대)	김건우 (대구파티마병원)	김형진 (성균관의대)
	문기원 (강원의대)	박은정 (국립의료원)	서미령 (가천의대)
	엄완식 (한양류마엄완식내과)	윤종현 (가톨릭의대)	이광훈 (동국의대)
	이명수 (원광의대)	이성원 (동아의대)	이승원 (한양류마티스내과)
	이지수 (이화의대)	홍승재 (경희의대)	

법제윤리위원회

이사	박용범 (연세의대)		
간사	최상태 (중앙의대)		
위원	박희진 (가톨릭관동의대)	방소영 (한양의대)	이광훈 (동국의대)
	이창훈 (원광의대)	정재현 (고려의대)	정주양 (아주의대)
	표정윤 (연세의대)		

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	Yun-Woo Lee (Withus Medical Clinic)	Choong-Ki Lee (Yeungnam Univ.)
	Duke Whan Chung (Kyung Hee Univ.)	Young Kil Choi (Kangnam CHA Hosp.)
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Director of Academic Affairs	Yoon-Kyoung Sung (Hanyang Univ.)	
Director of International Cooperation	Seung Cheol Shim (Chungnam Nat'l Univ.)	
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Director of Health Policy Affairs	Han Joo Baek (Gachon Univ.)	
Director of Legislation & Ethics	Young-Beom Park (Yonsei Univ.)	
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	Wan Sik Uhm (Uhm's Hanyang Rheumatism Clinic)	Sang-Il Lee (Gyeongsang Nat'l Univ.)
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	Seong-Ho Kim (Inje Univ.)	Jong-Min Kim (Univ. of Ulsan)
	Jin Seok Kim (Jeju Nat'l Univ.)	Hae-Rim Kim (Konkuk Univ.)
	Eon Jeong Nam (Kyungpook Nat'l Univ.)	Chang-Hee Suh (Ajou Univ.)
	Jong Gyun Ahn (Yonsei Univ.)	Kyu Hoon Lee (Hanyang Univ.)
	Seung-Jae Lim (Sungkyunkwan Univ.)	Ji Hyeon Ju (The Catholic Univ. of Korea)
Auditor	Sung Won Lee (Dong-A Univ.)	Young-Il Seo (Hallym Univ.)

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	Ran Song (Kyung Hee Univ.)	

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	Ki-Jo Kim (The Catholic Univ. of Korea)	Seong-Kyu Kim (Daegu Catholic Univ.)
	Yong-Gil Kim (Univ. of Ulsan)	Jinhyun Kim (Chungnam Nat'l Univ.)
	Hyoun-Ah Kim (Ajou Univ.)	Jin Kyun Park (Seoul Nat'l Univ.)
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Executive Secretary	Ji Yeon Lee (The Catholic Univ. of Korea)	
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	Min-Chan Park (Yonsei Univ.)	Young-Il Seo (Hallym Univ.)
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	Jung Ran Choi (Pohang St. Mary's Hospital)	Ji-Young Choi (Sungae Hospital)
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	Hyun-Sook Kim (Soonchunhyang Univ.)	Hyun-Ok Kim (Gyeongsang Nat'l Univ.)
	Kyung-Su Park (The Catholic Univ. of Korea)	Dong-Jin Park (Chonnam Nat'l Univ.)
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	Jae Hoon Kim (Korea Univ.)	Yoon-Kyoung Sung (Hanyang Univ.)
	Ran Song (Kyung Hee Univ.)	Wan Sik Uhm (Uhm's Hanyang Rheumatism Clinic)
	Sang-Won Lee (Yonsei Univ.)	Yun Jong Lee (Seoul Nat'l Univ.)
	Yun Hong Cheon (Gyeongsang Nat'l Univ.)	Sang Tae Choi (Chung-Ang Univ.)

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Executive Secretary	Seung Woo Han (Kyungpook Nat'l Univ.)	
Member	Jung-Hee Koh (The Catholic Univ. of Korea)	Bon San Koo (Inje Univ.)
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	Hae-Rim Kim (Konkuk Univ.)	Hyoun-Ah Kim (Ajou Univ.)
	Su-Jin Moon (The Catholic Univ. of Korea)	Dong-Jin Park (Chonnam Nat'l Univ.)
	Ji Seon Oh (Asan Medical Center)	Sang Yeob Lee (Dong-A Univ.)

Research Committee

Member	Sang Jin Lee (Kyungpook Nat'l Univ.)	Jaejoon Lee (Sungkyunkwan Univ.)
	Hwajeong Lee (Daegu Catholic Univ.)	Ji Hyeon Ju (The Catholic Univ. of Korea)
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	Seokchan Hong (Univ. of Ulsan)	

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	Sang-Won Lee (Yonsei Univ.)	Sung Hae Chang (Soonchunhyang Univ.)
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	Eun-Jung Park (National Medical Center)	Mi Ryoung Seo (Gachon Univ.)
	Wan Sik Uhm (Uhm's Hanyang Rheumatism Clinic)	Chong-Hyeon Yoon (The Catholic Univ. of Korea)
	Kwanghoon Lee (Dongguk Univ.)	Myeung Su Lee (Wonkwang Univ.)
	Sung Won Lee (Dong-A Univ.)	Seung-Won Lee (Hanyang Clinic)
	Jisoo Lee (Ewha Womans Univ.)	Seung-Jae Hong (Kyung Hee Univ.)

Legislation and Ethics Committee

Director	Yong-Beom Park (Yonsei Univ.)	
Executive Secretary	Sang Tae Choi (Chung-Ang Univ.)	
Member	Heejin Park (Catholic Kwandong Univ.)	So-Young Bang (Hanyang Univ.)
	Kwanghoon Lee (Dongguk Univ.)	Chang Hoon Lee (Wonkwang Univ.)
	Jae Hyun Jung (Korea Univ.)	Ju-Yang Jung (Ajou Univ.)
	Jung Yoon Pyo (Yonsei Univ.)	

DAY 1. | October 21(Thu)

Time	Room A Grand Ballroom – Hanra A & B,3F	Room B Grand Ballroom - Baekdu A & B, 5F	Room C Grand Ballroom - Hanra C, 3F	Room D Shilla Room, 3F
08:00-09:00	-			
09:00-10:00	Registration			Musculoskeletal US Workshop I (Advanced Course)
10:00-12:00	Year in Review (Clinical)	Year in Review (Basic) Recent Advances of T Cell Immunology in Autoimmunity		
12:00-13:00	Luncheon Symposium I Pfizer Korea	Luncheon Symposium II CELLTRION PHARM CELLTRION	Luncheon Symposium III abbvie Eisai Korea Inc.	
13:00-13:10	Opening Remark & Welcome Address			
13:10-14:00	Presidential Plenary Session			
14:00-16:00	International Free Paper Session (Clinical)	Basic Research Workshop for Rheumatologists		Musculoskeletal US Workshop II (Basic Course)
16:00-16:30	Coffee Break			
16:30-18:30	International Free Paper Session (Basic)	Clinical Research Workshop for Rheumatologists	Editorial Committee Workshop	
19:00-20:00	KCR 40th Anniversary Ceremony			

DAY 2. | October 22(Fri)

Time	Room A Grand Ballroom – Hanra A & B,3F	Room B Grand Ballroom - Baekdu A & B, 5F	Room C Grand Ballroom - Hanra C, 3F
08:00-09:00	**Breakfast Symposium I** abbvie	**Breakfast Symposium II** JW Pharmaceutical	**Breakfast Symposium III** Pfizer Korea
09:00-10:00	**Keynote Lecture** The Future of Rheumatology : A Message from the ACR President on the Occasion of the 40th Anniversary of the Korean College of Rheumatology		
10:00-10:30	Coffee Break		
10:30-12:00	**International Symposium** "State-of-the-art" in Systemic Lupus Erythematosus	**Free Paper Session** Sjögren's Syndrome, Systemic Sclerosis, Inflammatory Myopathies, and Miscellaneous	**Free Paper Session** Epidemiology & Health Services Research
12:00-13:00	**Luncheon Symposium IV** Lilly	**Luncheon Symposium V** Bristol Myers Squibb	**Luncheon Symposium VI** YUHAN SAMSUNG BIOEPIS
13:00-14:30	**International Symposium** Update of Fibromyalgia	**KCR-JCR Joint Symposium** Precision Medicine in Rheumatology	**Free Paper Session** Spondyloarthritis
14:30-15:30	Poster Viewing and Coffee Break		
15:30-17:00	**International Symposium** Initiation or Flare of Inflammation in RA : Functions of Fibroblast	**Free Paper Session** Vasculitis and Metabolic Bone Disease	**Medical Humanities Symposium** COVID-19 and Inequality
17:00-17:30	Academic Awards		
17:30-18:00	General Assembly		

DAY 3. | October 23(Sat)

Time	Room A Grand Ballroom – Hanra A & B,3F	Room B Grand Ballroom - Baekdu A & B, 5F	Room C Grand Ballroom - Hanra C, 3F
08:00-09:00	**Breakfast Symposium IV** YUHAN SAMSUNG BIOEPIS	**Breakfast Symposium V** astellas	**Breakfast Symposium VI** Lilly
09:00-10:00	**Keynote Lecture** EULAR participates in KCR's 40th–anniversary celebrations		
10:00-10:30	Coffee Break		
10:30-12:00	**International Symposium** Osteoporosis Update	**Free Paper Session** Rheumatoid Arthritis Clinical Research	**Free Paper Session** Osteoarthritis, Orthopedics, and Osteoporosis
12:00-13:00	**Luncheon Symposium VII** NOVARTIS	**Luncheon Symposium VIII** gsk	**Luncheon Symposium IX** AMGEN
13:00-14:30	**International Symposium** Gout : Comorbidity Matters and Optimal Management Strategies	**KCR-ARA-NZRA Joint Symposium** Digital Healthcare in Rheumatology	**Free Paper Session** Systemic Lupus Erythematosus
14:30-15:30	Poster Viewing and Coffee Break		
15:30-17:00	**International Symposium** Targeted Therapy of Spondyloarthritis	**Free Paper Session** Rheumatoid Arthritis Basic Research	**Visiting Scholarship Symposium**
17:00-17:30	Presentation Awards Session		
17:30-18:00	Closing Remark		

K Korean E English

10:00-12:00 [Symposium] Year in Review (Clinical) — Room A — K

Chairs	Bin Yoo *(Univ. of Ulsan, Korea)* Sang-Heon Lee *(Konkuk Univ., Korea)*
10:00-10:30	**Rheumatoid arthritis** Min-Chan Park *(Yonsei Univ., Korea)*
10:30-11:00	**Spondyloarthropathies** Eun Young Lee *(Seoul Nat'l Univ., Korea)*
11:00-11:30	**Crystal arthropathies** Seokchan Hong *(Univ. of Ulsan, Korea)*
11:30-12:00	**Osteoarthritis** Sang Hyon Kim *(Keimyung Univ., Korea)*

10:00-12:00 [Symposium] Year in Review (Basic) : Recent Advances of T Cell Immunology in Autoimmunity — Room B — K

Chairs	Sung-Hwan Park *(The Catholic Univ. of Korea, Korea)* Young Mo Kang *(Kyungpook Nat'l Univ., Korea)*
10:00-10:30	**Diversity of helper and regulatory T cells** Yun Kyung Lee *(Soonchunhyang Univ., Korea)*
10:30-11:00	**Microbiome and T cell interaction in autoimmunity** Sung Hwan Park *(The Catholic Univ. of Korea, Korea)*
11:00-11:30	**Lipid metabolic control of T cell immunity** Yeonseok Chung *(Seoul Nat'l Univ., Korea)*
11:30-12:00	**Innate immune cells in autoimmune diseases** Yong-Wook Park *(Chonnam Nat'l Univ., Korea)*

09:00-12:00 [Workshop] Musculoskeletal US Workshop I -Advanced Course Practical Applications of Musculoskeletal Ultrasound in Rheumatology Clinic — Room D — K

Chair	Chong-Hyeon Yoon *(The Catholic Univ. of Korea, Korea)*
09:00-09:45	**Therapeutic musculoskeletal ultrasound applications** Ran Song *(Kyung Hee Univ., Korea)*
09:45-10:30	**Sono-guided extra-articular injection** Chang Hoon Lee *(Wonkwang Univ., Korea)*
10:30-11:15	**Salivary gland ultrasound in Sjögren's syndrome: Where do we stand?** Kyung-Ann Lee *(Soonchunhyang Univ., Korea)*
11:15-12:00	**Assessing rheumatoid arthritis disease activity with ultrasound** Jooha Lee *(The Catholic Univ. of Korea, Korea)*

12:00-13:00 | [Luncheon Symposium I - Pfizer] | Room A (E)

Practical Review of RA Treatment Option

Chair	Eun-Bong Lee *(Seoul Nat'l Univ., Korea)*
12:00-12:40	**Tofacitinib in RA** **: Exploring the efficacy and safety profile in real-world experience** Roy Fleischmann *(Univ. of Texas Southwestern Medical Center, USA)*

12:00-13:00 | [Luncheon Symposium II - Celltrion] | Room B (E)

New Treatment Option in Rheumatic Disease

Chair	Sang-Hoon Lee *(Kyung Hee Univ., Korea)*
12:00-12:40	**Benefits of switching from IV to SC infliximab: European cases** Martin Perry *(NHS Greater Glasgow and Clyde, United Kingdom)*

12:00-13:00 | [Luncheon Symposium III - Abbvie & Eisai] | Room C (K)

Management of Patients with Rheumatic Diseases during the COVID-19 Pandemic

Chair	Jung Soo Song *(Chung-Ang Univ., Korea)*
12:00-12:40	**Solving the puzzle: A pragmatic approach to anti TNF therapy during the COVID-19 pandemic** Jin Kyun Park *(Seoul Nat'l Univ., Korea)*

13:10-14:00 | [Special Lecture] | Room A, B, C (K)

Presidential Plenary Session

Chairs	Gwan Gyu Song *(Korea Univ., Korea)* Tae-Hwan Kim *(Hanyang Univ., Korea)*
13:10-13:35	**Presidential lecture** Gwan Gyu Song *(Korea Univ., Korea)*
13:35-14:00	**My memory about KCR** Soo Kon Lee *(Bundang Cha Hosp., Korea)*

14:00-16:00 [Free Paper Session] Room A

International Free Paper Session (Clinical)

E

Chairs Chang Keun Lee *(Univ. of Ulsan, Korea)*
Myeung Su Lee *(Wonkwang Univ., Korea)*

IO-01	**The course of rheumatoid arthritis-associated interstitial lung disease, focusing on lung physiology and disease activity : A prospective observational study of the Korean rheumatoid arthritis-associated interstitial lung disease (KORAIL) cohort** Sung Hae Chang *(Soonchunhyang Univ., Korea)*
IO-02	**Withdrawn**
IO-03	**Relationship between the risk of new onset diabetes mellitus and exposure to individual antirheumatic drugs in patients with rheumatoid arthritis: A nationwide population study** So Hye Nam *(Uijeongbu Eulji Medical Center, Korea)*
IO-04	**Changes in healthcare costs before and after the diagnosis of systemic lupus erythematosus in Korea** Hyoungyoung Kim *(Hanyang Univ., Korea)*
IO-05	**Achieving LLDAS-50 is associated with less organ damage and better quality of life during 5-year follow-up in patients with systemic lupus erythematosus** Ji-Hyoun Kang *(Chonnam Nat'l Univ., Korea)*
IO-06	**The impact of smoking status on radiographic progression in patients with ankylosing spondylitis during anti-TNF treatment** Bora Nam *(Hanyang Univ., Korea)*
IO-07	**Longitudinal analysis of symptom-based clustering in patients with primary Sjögren's syndrome : A prospective cohort study with a 5-year follow-up period** Jooha Lee *(The Catholic Univ. of Korea, Korea)*
IO-08	**Metabolic obesity and the risk of knee osteoarthritis progression in elderly community residents : A 3-year longitudinal cohort study** Dong Jin Go *(Hallym Univ., Korea)*
IO-09	**A randomized, double-blind, placebo-controlled trial of ramosetron, a 5-hydroxytryptamine 3 receptor antagonist for treating refractory fibromyalgia** Dong-Jin Park *(Chonnam Nat'l Univ., Korea)*

14:00-16:00 [Workshop] Basic Research Workshop for Rheumatologist

Room B (K)

Chairs	Jungsik Song *(Yonsei Univ., Korea)* Kichul Shin *(Seoul Nat'l Univ., Korea)*
14:00-14:30	**Osteoclast in rheumatoid arthritis** Hae-Rim Kim *(Konkuk Univ., Korea)*
14:30-15:00	**Experimental methods of osteoclast differentiation** Hong Ki Min *(Konkuk Univ., Korea)*
15:00-15:30	**Neuroimmune interactions in chronic pain** Seog Bae Oh *(Seoul Nat'l Univ., Korea)*
15:30-16:00	**An animal model for studying the neuro-immune mechanism of chronic pain** Hyoung Woo Kim *(Seoul Nat'l Univ., Korea)*

13:30-16:30 [Workshop] Musculoskeletal US Workshop II - Basic Course Basics of Musculoskeletal Ultrasound

Room D (K)

Chair	Hyun-Sook Kim *(Soonchunhyang Univ., Korea)*
13:30-14:15	**Standard scan of musculoskeletal ultrasound - Hand and wrist** Jae Hoon Kim *(Korea Univ., Korea)*
14:15-15:00	**Standard scan of musculoskeletal ultrasound - Elbow and shoulder** Yun Sung Kim *(Chosun Univ., Korea)*
15:00-15:45	**Standard scan of musculoskeletal ultrasound - Knee** Hyun-Ok Kim *(Gyeongsang Nat'l Univ., Korea)*
15:45-16:30	**Standard scan of musculoskeletal ultrasound – Ankle and foot** In Ah Choi *(Chungbuk Nat'l Univ., Korea)*

16:30-18:30 [Free Paper Session] Room A

International Free Paper Session (Basic)

E

Chairs Dae Hyun Yoo *(Hanyang Univ., Korea)*
Wan-Uk Kim *(The Catholic Univ. of Korea, Korea)*

IO-10	**Lipidome profile predictive of disease evolution and activity in rheumatoid arthritis** Jung Hee Koh *(The Catholic Univ. of Korea, Korea)*
IO-11	**Anti-TNF- α antibody modified gold nanorods as optical imaging nanoprobes for early diagnosis of rheumatoid arthritis** Chin Hee Mun *(Yonsei Univ., Korea)*
IO-12	**DJ-1 control Th17/Treg imbalance, inflammatory response of fibroblast-like synoviocytes, and osteoclastogenesis of rheumatoid arthritis** Hong Ki Min *(Konkuk Univ., Korea)*
IO-13	**Citrullination inhibits histone-induced chemokine-mediated inflammatory responses** Eunju Lee *(Yonsei Univ., Korea)*
IO-14	**Baricitinib attenuates autoimmune phenotype and podocyte injury in a murine model of systemic lupus erythematosus** Youngjae Park *(The Catholic Univ. of Korea, Korea)*
IO-15	**Circulating and renal fibrocytes are associated with interstitial fibrosis in lupus nephritis** Seokchan Hong *(Univ. of Ulsan, Korea)*
IO-16	**Renin-Angiotensin system is involved in the differentiation of osteoclasts and osteoblasts in spondyloarthritis** Min-joo Ahn *(Chungnam Univ., Korea)*
IO-17	**Desiccating stress triggers conjunctival monocyte to macrophage cascade – Implications for Sjögren's syndrome keratoconjunctivitis** Jehan Alam *(Baylor College of Medicine, USA)*
IO-18	**Defective efferocytosis in Sjögren's syndrome is mediated by dysfunctional Mer tyrosine kinase receptor** Richard Witas *(Univ. of Florida, USA)*

16:30-18:30 [Workshop] Room B

Clinical Research Workshop for Rheumatologists : Practical 'Hands-on' Statistical Analysis

Chairs	Kyung-Su Park *(The Catholic Univ. of Korea, Korea)* Hae-Rim Kim *(Konkuk Univ., Korea)*
16:30-17:00	**Cross-sectional data analysis** Ji Seon Oh *(Asan Medical Center, Korea)*
17:00-17:30	**Survival analysis for beginners** Jung Hee Koh *(The Catholic Univ. of Korea, Korea)*
17:30-18:00	**Statistical analysis for longitudinal data in cohort studies** Jun Won Park *(Seoul Nat'l Univ., Korea)*
18:00-18:30	**Issues of healthcare data de-identification in Korea** Kwang-il Kim *(Seoul Nat'l Univ., Korea)*

16:30-18:30 [Workshop] Room C

Editorial Committee Workshop

Chairs	Jae-Bum Jun *(Hanyang Univ., Korea)* Young Ho Lee *(Korea Univ., Korea)*
16:30-17:00	**How can the journal be added in SCIE from ESCI** Sun Huh *(Hallym Univ., Korea)*
17:00-17:30	**Writing peer reviews with clarity and politeness** Yunhee Whang *(Compecs Inc., Korea)*
17:30-18:00	**How to avoid an accidental plagiarism: Paraphrasing** Kwangil Oh *(Editage, Korea)*
18:00-18:30	**Common errors by Korean authors** Kwangil Oh *(Editage, Korea)*

K Korean E English

08:00-09:00 [Breakfast Symposium I - Abbvie] Room A

Management of Rheumatoid Arthritis

K

Chair	Hoon-Suk Cha *(Sungkyunkwan Univ., Korea)*
08:00-08:40	**Striving for remission with JAK inhibition in the management of rheumatoid arthritis** Yune-Jung Park *(The Catholic Univ. of Korea, Korea)*

08:00-09:00 [Breakfast Symposium II - JW Pharmaceutical] Room B

IL-6R Inhibition : Transforming People's Lives, for a Future on their Term

K

Chair	Sang-Heon Lee *(Konkuk Univ., Korea)*
08:00-08:40	**Tocilizumab- an effective treatment option for Still's disease** Yeon-Ah Lee *(Kyung Hee Univ., Korea)*

08:00-09:00 [Breakfast Symposium III - Pfizer] Room C

Practical Guideline on Rheumatic Disease Management under COVID-19

K

Chair	Han Joo Baek *(Gachon Univ., Korea)*
08:00-08:40	**Is an additional dose of COVID-19 vaccine needed for patients with rheumatic diseases?** Jin Kyun Park *(Seoul Nat'l Univ., Korea)*

09:00-10:00 [Keynote Lecture] Room A, B, C

Keynote Lecture of ACR

E

Chair	Gwan Gyu Song *(Korea Univ., Korea)*
09:00-10:00	**The future of rheumatology : A message from the ACR president on the occasion of the 40th anniversary of the Korean College of Rheumatology** David R Karp *(American College of Rheumatology, USA)*

10:30-12:00 [International Symposium] "State-of-the-art" in Systemic Lupus Erythematosus

Room A

E

Chairs	Sang-Cheol Bae *(Hanyang Univ., Korea)* Seung-Cheol Shim *(Chungnam Nat'l Univ., Korea)*
10:30-11:00	Recent advances in the treatment of lupus nephritis Frédéric Houssiau *(Univ. catholique de Louvain, Belgium)*
11:00-11:30	Molecular mimicry & genetic mechanisms implicate Epstein-Barr virus as the major environmental factor causing systemic lupus erythematosus John B. Harley *(Univ. of Cincinnati (Retired), USA)*
11:30-12:00	Clinical and multiomics studies of SLE towards precision medicine Sang-Cheol Bae *(Hanyang Univ., Korea)*

10:30-12:00 [Free Paper Session] Sjögren's Syndrome, Systemic Sclerosis, Inflammatory Myopathies, and Miscellaneous

Room B

K

Chairs	Jinseok Kim *(Jeju Nat'l Univ., Korea)* Eun-Bong Lee *(Seoul Nat'l Univ., Korea)*
O-01	Glandular and extra-glandular manifestations and effects of hypergammaglobulinemia in primary Sjögren's syndrome : Result from KISS cohort study Jung Hee Koh *(The Catholic Univ. of Korea, Korea)*
O-02	Validity and reliability of the breath-holding test in systemic sclerosis Jina Yeo *(Gachon Univ., Korea)*
O-03	Scleroderma-like nailfold capillaroscopic abnormalities are common in patients with idiopathic inflammatory myopathies and associated with interstitial lung diseases Sang-Wan Chung *(Kyung Hee Univ., Korea)*
O-04	Different features of interleukin-37 and interleukin-18 as disease activity markers of adult-onset still's disease Seoung Wan Nam *(Wonju Severance Christian Hosp., Korea)*
O-05	Elevated expression of the TLR2 and TLR7 and their correlation with disease activity and clinical manifestations in adult-onset Still's disease Hyoun-ah Kim *(Ajou Univ., Korea)*
O-06	CCL2 is a useful serum marker for monitoring disease activity in patients with adult-onset Still's disease Ju-Yang Jung *(Ajou Univ., Korea)*
O-07	Change of serum IgG4 level during immunosuppressive therapy as a predictor of relapse in IgG4-related disease Su Jin Choi *(Univ. of Ulsan, Korea)*
O-08	Tocilizumab in adult patients with secondary haemophagocytic lymphohistiocytosis Ju Yeon Kim *(Seoul Nat'l Univ., Korea)*

10:30-12:00 [Free Paper Session] Epidemiology & Health Services Research

Room C (K E)

Chairs	Yun Jong Lee *(Seoul Nat'l Univ., Korea)* Seong-Ho Kim *(Inje Univ., Korea)*
O-09	Risk of malignancy in Korean patients with rheumatoid arthritis treated with JAK inhibitors : A nationwide population-based study Yeo-Jin Song *(Hanyang Univ., Korea)*
O-10	Factors for starting JAK inhibitors in patients with rheumatoid arthritis Yeo-Jin Song *(Hanyang Univ., Korea)*
O-11	Effect of sarcopenia on comorbidities of rheumatoid arthritis : Results of a nationwide cross-sectional health examination Ju Ho Lee *(Seoul Nat'l Univ., Korea)*
O-12	Withdrawn
O-13	Hypouricemia is a risk factor for periodontitis : Data from the Korean national health and nutrition survey (KNHANES) 2016-2018 Seung-Geun Lee *(Pusan Nat'l Univ., Korea)*
O-14	Clinical and demographic characteristics of patients with rheumatic diseases who underwent COVID-19 Eugenia Aronova *(V.A. Nasonova Research Institute of Rheumatology, Russian Federation)*
O-15	Prognostic implication of baseline sarcopenia for length of hospital stay and survival in patients with Coronavirus disease 2019 Ji-Won Kim *(Daegu Catholic Univ., Korea)*
O-16	Effect of hydroxychloroquine pre-exposure on infection with SARSCoV- 2 in rheumatic disease patients : A population-based cohort study Sangtae Choi *(Chung-Ang Univ., Korea)*

12:00-13:00 [Luncheon Symposium IV - Lilly] Exploring Baricitinib Experience in Treating RA

Room A (K)

Chair	Wan-Uk Kim *(The Catholic Univ. of Korea, Korea)*
12:00-12:40	Going beyond : Long-term treatment results with Baricitinib in RA Sang Hyon Kim *(Keimyung Univ., Korea)*

12:00-13:00 [Luncheon Symposium V - BMS Pharmaceutical] Real World Perspectives of Patient Care in Rheumatoid Arthritis

Room B (K)

Chair	Jung-Yoon Choe *(Catholic Univ. of Daegu, Korea)*
12:00-12:20	Improving patient outcomes of rheumatoid arthritis with interstitial lung disease patients Eun Young Lee *(Seoul Nat'l Univ., Korea)*
12:20-12:40	Insight from real world: Treatment considerations of rheumatoid arthritis in an aging society Yun-Hong Cheon *(Gyeongsang Nat'l Univ., Korea)*

12:00-13:00 [Luncheon Symposium VI - Yuhan] Room C

What`s the Meaning of Adalimumab Biosimilar to Treat Rheumatoid Disease Patients?

E

Chair	Dae Hyun Yoo *(Hanyang Univ., Korea)*
12:00-12:40	**The position of the 1st adalimumab biosimilar in Europe** Ulf Müller-Ladner *(Justus Liebig Univ. Giessen, Germany)*

13:00-14:30 [International Symposium] Room A

Update of Fibromyalgia

E

Chairs	Shin-Seok Lee *(Chonnam Nat'l Univ., Korea)* Geun Tae Kim *(Kosin Univ., Korea)*
13:00-13:30	**Diagnosis of fibromyalgia** Ji Hyun Lee *(Maryknoll Hosp., Korea)*
13:30-14:00	**Medical and non-medical treatment of fibromyalgia** Yeon-Ah Lee *(Kyung Hee Univ., Korea)*
14:00-14:30	**Cognitive-behavior therapy for fibromyalgia-focusing on acceptance-commitment therapeutic approach** Seonyoung Lee *(Seoul Acceptance-Commitment Therapy Center, Korea)*

13:00-14:30 [Symposium] Room B

KCR-JCR Joint Symposium - Precision Medicine in Rheumatology

E

Chairs	Tae-Hwan Kim *(Hanyang Univ., Korea)* Yoshiya Tanaka *(Univ. of Occupational and Environmental Health, Japan)*
13:00-13:30	**Big data analysis of autoimmune diseases** Yukinori Okada *(Osaka Univ., Japan)*
13:30-14:00	**Pathological pathways revealed by functional genome analysis of immune-mediated diseases** Keishi Fujio *(The Univ. of Tokyo, Japan)*
14:00-14:30	**Optimal selection of targeted therapeutics using genetics and transcriptomics in rheumatoid arthritis** Hye-Soon Lee *(Hanyang Univ., Korea)*

13:00-14:30 [Free Paper Session] Spondyloarthritis

Room C K

Chairs	Han Joo Baek *(Gachon Univ., Korea)* Young Il Seo *(Hallym Univ., Korea)*
O-17	**Well-controlled C-reactive protein level during the first 3 months is associated with slowing radiologic progression in patients with ankylosing spondylitis: 18-year real world evidence** Bon San Koo *(Inje Univ., Korea)*
O-18	**Computed tomography-based assessment of radiographic progression in spine and sacroiliac joints after pregnancy in women with ankylosing spondylitis** Kyung-Ann Lee *(Soonchunhyang Univ., Korea)*
O-19	**The occurrence of acute anterior uveitis in patients initiating TNF-α inhibitor for ankylosing spondylitis : An analysis of Korean nationwide claims data** Soo Min Ahn *(Univ. of Ulsan, Korea)*
O-20	**A cluster analysis in patients with axial spondyloarthritis using TNFi based on clinical characteristics** Seulkee Lee *(Sungkyunkwan Univ., Korea)*
O-21	**Radiographic facet joint damage of the cervical spine in patients with ankylosing spondylitis and its impact on functional status: A longitudinal analysis in relation to the damage of vertebral body** Tae-Han Lee *(Keimyung Univ., Korea)*
O-22	**Clinical features of patients with active ankylosing spondylitis who did not respond to adalimumab but responded to Ixekizumab: A post-hoc analysis** Hyeun Seung Roh *(Eli Lilly and Company, Korea)*
O-23	**PDGF-BB as a novel therapeutic target in pathological bone formation of AS** Sungsin Jo *(Hanyang Univ., Korea)*
O-24	**Multicenter study for the prevalence and fracture risk of osteoporosis in patients with ankylosing spondylitis** Ji-Won Kim *(Ajou Univ., Korea)*

15:30-17:00 [International Symposium] Initiation or Flare of Inflammation in RA : Functions of Fibroblast

Room A E

Chairs	Sang-Il Lee *(Gyeongsang Nat'l Univ., Korea)* Seungwoo Han *(Kyungpook Nat'l Univ., Korea)*
15:30-16:00	**RNA identification of prime cells predicting rheumatoid arthritis flares** Dana E. Orange *(Rockefeller Univ., USA)*
16:00-16:30	**Inflammation or damage : Fibroblasts decide** Christopher D. Buckley *(Univ. of Oxford, United Kingdom)*
16:30-17:00	**Mitochondrial STAT3 attenuates rheumatoid arthritis by regulation of synovial fibroblast autophagy** Mila Cho *(The Catholic Univ. of Korea, Korea)*

15:30-17:00 [Free Paper Session] Vasculitis and Metabolic Bone Disease — Room B (K)

Chairs	Soo Kon Lee *(Bundang Cha Hosp., Korea)* Sung-Soo Kim *(Univ. of Ulsan, Korea)*
O-25	Vascular uptake on 18F-FDG PET/CT during the clinically inactive state of Takayasu arteritis is associated with a higher risk of relapse Oh Chan Kwon *(Yonsei Univ., Korea)*
O-26	Surgical outcomes after operative procedures in patients with Behcet's disease Youjin Jung *(Seoul Nat'l Univ., Korea)*
O-27	Clinical characteristics and radiographic outcome of vascular Behcet's disease involving aorta and its major branches Seulkee Lee *(Sungkyunkwan Univ., Korea)*
O-28	Soluble immune checkpoint molecules in patients with antineutrophil cytoplasmic antibody-associated vasculitis Jung Yoon Pyo *(Yonsei Univ., Korea)*
O-29	Ncoa6 is a novel regulator of NLRP3 inflammasome and gouty arthritis Kang-Gu Lee *(The Catholic Univ. of Korea, Korea)*
O-30	Increased risk of cardiovascular events and death in the initial phase after discontinuation of febuxostat or allopurinol : Another story of the CARES trial Byeongzu Ghang *(Jeju Nat'l Univ., Korea)*
O-31	The appropriate starting dose of urate lowering treatment Joondon Lee *(Jeju Nat'l Univ., Korea)*
O-32	Catch-up growth of infants born to mothers with autoimmune rheumatic disorders Hye Yeon Choi *(The Catholic Univ. of Korea, Korea)*

15:00-17:00 [Symposium] 필수과목 교육 프로그램 Medical humanities Symposium - COVID-19 and Inequality — Room C (K)

Chairs	Choong-Ki Lee *(Yeungnam Univ., Korea)* Yong-Beom Park *(Yonsei Univ., Korea)*
15:00-16:00	Justice and fairness in the era of COVID-19 Seon-Wook Kim *(Soongsil Univ., Korea)*
16:00-17:00	Ethics of vaccine refusal Cheul Kang *(Univ. of Seoul, Korea)*

K Korean E English

08:00-09:00 [Breakfast Symposium IV - Yuhan] Room A

The Treatment Companion of Rheumatoid Disease Patients

K

Chair	Yong-Beom Park *(Yonsei Univ., Korea)*
08:00-08:40	**RA/AS treatment journey with biosimilars** Chan-Bum Choi *(Hanyang Univ., Korea)*

08:00-09:00 [Breakfast Symposium V - Astellas] Room B

Lupus Nephritis

E

Chair	Seung-Cheol Shim *(Chungnam Nat'l Univ., Korea)*
08:00-08:40	**Calcineurin inhibitors in systemic lupus erythematosus : A revisit** Chi-Chiu Mok *(Tuen Mun Hosp., Hong Kong)*

08:00-09:00 [Breakfast Symposium VI - Lilly] Room C

Up-to-date Treatment of SpA

K

Chair	Shin-Seok Lee *(Chonnam Nat'l Univ., Korea)*
08:00-08:40	**Ixekizumab : New treatment option for patients with axial SpA** Sang-Hoon Lee *(Kyung Hee Univ., Korea)*

09:00-10:00 [Keynote Lecture] Room A, B, C

EULAR Participates in KCR's 40th-anniversary Celebrations

E

Chair	Tae-Hwan Kim *(Hanyang Univ., Korea)*
09:00-10:00	**EULAR strategy, collaborations and activities in the COVID-19 era** Annamaria Iagnocco *(Univ. of Turin, Italy)*

10:30-12:00 [International Symposium] Osteoporosis Update — Room A (E)

Chairs	**Won Park** *(Inha Univ., Korea)* **Jun-ki Min** *(The Catholic Univ. of Korea, Korea)*
10:30-11:00	**Osteoporosis update. Clinical update** Peter Ebeling *(Monash Univ., Australia)*
11:00-11:30	**New insights into the osteocyte** Lynda F. Bonewald *(Indiana Univ., USA)*
11:30-12:00	**Novel approach for evaluating bone mineral density of hips based on Sobel gradient-based map of radiographs utilizing convolutional neural network** Jonghun Yoon *(Hanyang Univ. ERICA, Korea)*

10:30-12:00 [Free Paper Session] Rheumatoid Arthritis Clinical Research — Room B (K)

Chairs	**Jung-Yoon Choe** *(Catholic Univ. of Daegu, Korea)* **Hye-Soon Lee** *(Hanyang Univ., Korea)*
O-33	**Incident and recurrent herpes zoster for first-line bDMARDs and tsDMARD users in seropositive rheumatoid arthritis patients : A nationwide cohort study** Seogsong Jeong *(Seoul Nat'l Univ., Korea)*
O-34	**Safety of JAK inhibitor in patients with rheumatoid arthritis who developed reactivation of herpes zoster after receiving JAK inhibitor** Wonho Choi *(Asan Medical Center, Korea)*
O-35	**Comparison between non-TNF-targeted treatment and use of a second anti-TNF inhibitor for rheumatoid arthritis patients showing an insufficient response to the first anti-TNF inhibitor** Dong-Jin Park *(Chonnam Nat'l Univ., Korea)*
O-36	**Comparison of efficacy and drug retention between JAK inhibitors in rheumatoid arthritis : From the nationwide KOrean college of rheumatology BIOlogics (KOBIO) registry** Ju-Yang Jung *(Ajou Univ., Korea)*
O-37	**Association of first, second, and third-line bDMARDs and tsDMARD with drug survival among seropositive rheumatoid arthritis patients: Cohort study in a real world setting** Seulggie Choi *(Seoul Nat'l Univ., Korea)*
O-38	**The effects of biologic DMARDs on hemoglobin and disease activity index in rheumatoid arthritis patients** Hwajeong Lee *(Daegu Catholic Univ., Korea)*
O-39	**Time-integrated cumulative parameters predictive of radiographic progression of rheumatoid arthritis: Real-world data from a prospective single-center cohort** Youngjae Park *(The Catholic Univ. of Korea, Korea)*
O-40	**Drug survival of biologics depending on shared epitope in Korean patients with rheumatoid arthritis** Howook Jeon *(The Catholic Univ. of Korea, Korea)*

10:30-12:00 [Free Paper Session] Room C

Osteoarthritis, Orthopedics, and Osteoporosis

K

Chairs	Sung Won Lee *(Dong-A Univ., Korea)* Hyun Sik Gong *(Seoul Nat'l Univ., Korea)*
O-41	**The functional role of DKK1 in mineralization of osteoblast differentiation** Hyosun Park *(Hanyang Univ., Korea)*
O-42	**Status of glucocorticoid-induced osteoporosis preventive care in Korea : A nationwide population-based retrospective cohort study using the Korean national health insurance service database** Seung-Geun Lee *(Pusan Nat'l Univ., Korea)*
O-43	**Muscle exercise mitigate the negative influence of low socioeconomic status on muscle strength** Hanna Lee *(Gyeongsang Nat'l Univ., Korea)*
O-44	**Withdrawn**
O-45	**Skeletal muscle atrophy and its relationship with osteoarthritis** Ju-Ryoung Kim *(Hallym Univ., Korea)*
O-46	**Female reproductive factors and risk of joint replacement arthroplasty of the knee and hip due to osteoarthritis in postmenopausal women : A nationwide cohort study of 1.36 million women** Yeonghee Eun *(Sungkyunkwan Univ., Korea)*
O-47	**The association of index-to-ring finger ratio with trapeziometacarpal joint osteoarthritis in a Korean elderly population** Ji Sup Hwang *(Seoul Nat'l Univ., Korea)*
O-48	**Folate deficiency is associated with increased radiographic severity of osteoarthritis in the knee joints, but not in the hand joints** Sung-Eun Choi *(Chonnam Nat'l Univ., Korea)*

12:00-13:00 [Luncheon Symposium VII - Novartis] Room A

Reimagining AS Management

E

Chair	Eun Young Lee *(Seoul Nat'l Univ., Korea)*
12:00-12:40	**IL-17 pathway : A voyage towards understanding its role in AS** Xenofon Baraliakos *(Rheumazentrum Ruhrgebiet, Germany)*

12:00-13:00 [Luncheon Symposium VIII - GSK] Benlysta

Room B K

Chair	Sang-Cheol Bae *(Hanyang Univ., Korea)*
12:00-12:40	**Benlysta : Shaping new SLE treatment paradigm in Korea** Seung-Ki Kwok *(The Catholic Univ. of Korea, Korea)*

12:00-13:00 [Luncheon Symposium IX - Amgen] Prolia, Osteoporosis

Room C E

Chair	Seung-Jae Hong *(Kyung Hee Univ., Korea)*
12:00-12:40	**Breaking myths, not bones** Peter Ebeling *(Monash Univ., Australia)*

13:00-14:30 [International Symposium] Gout : Comorbidity Matters and Optimal Management Strategies

Room A E

Chairs	Hyun Ah Kim *(Hallym Univ., Korea)* Jung-Soo Song *(Chung-Ang Univ., Korea)*
13:00-13:30	**Epidemiologic study for gout and comorbidities in Korea** Ki Won Moon *(Kangwon Nat'l Univ., Korea)*
13:30-14:00	**Cardiovascular risk of urate-lowering therapy in gout** Tuhina Neogi *(Boston Univ., USA)*
14:00-14:30	**What's new in gout management** Nicola Dalbeth *(Univ. of Auckland, New Zealand)*

13:00-14:30 [Symposium] KCR-ARA-NZRA Joint Symposium - Digital Healthcare in Rheumatology

Room B E

Chairs	Sang-Heon Lee *(Konkuk Univ., Korea)* Catherine Hill *(The Queen Elizabeth and Royal Adelaide Hosp., Australia)*
13:00-13:30	**Digital health and rheumatoid arthritis – Current state, future horizons** Rebecca Grainger *(Univ. of Otago, New Zealand)*
13:30-14:00	**Background and application of MyRA in the digital healthcare in rheumatology** Catherine Hill *(The Queen Elizabeth and Royal Adelaide Hosp., Australia)*
14:00-14:30	**Application of ICT in the clinical practice of Korea** Ji Hyeon Ju *(The Catholic Univ. of Korea, Korea)*

13:00-14:30 [Free Paper Session] Systemic Lupus Erythematosus

Room C K

Chairs	Shin-Seok Lee *(Chonnam Nat'l Univ., Korea)* Chang-Hee Suh *(Ajou Univ., Korea)*
O-49	**A high genetic risk burden is associated with diverse clinical manifestation in systemic lupus erythematosus** Young-Chang Kwon *(Hanyang Univ., Korea)*
O-50	**Clinical and genetic risk factors associated with the presence of lupus nephritis** Jung-min Shin *(Hanyang Univ., Korea)*
O-51	**Risk of bloodstream infection in patients with systemic lupus erythematosus exposed to prolonged moderate to high dose glucocorticoids** Mi Hyeon Kim *(Seoul Nat'l Univ., Korea)*
O-52	**Depression is associated with frailty in systemic lupus erythematosus patients : Multicenter retrospective analysis using systemic lupus erythematosus international collaborating clinics-frailty index** Eunyoung Lee *(Uijeongbu Eulji Medical Center, Korea)*
O-53	**Discovery of urine biomarkers of lupus nephritis via quantitative and comparative proteome analysis** Oh Chan Kwon *(Yonsei Univ., Korea)*
O-54	**Increased expression of NRP-1 in systemic lupus erythematosus and its correlation with disease activity** Yunjung Choi *(Jeonbuk Nat'l Univ., Korea)*
O-55	**A novel spleen tyrosine kinase inhibitor SKI-O-703 attenuates lupus and rheumatoid arthritis in murine models** Somi Cho *(Hanyang Univ., Korea)*
O-56	**Efficacy and safety of belimumab in Korean patients with systemic lupus erythematosus : Subgroup analysis of a phase 3, randomized, placebo-controlled trial** Sang-Bae Yoo *(GlaxoSmithKline, Korea)*

15:30-17:00 [International Symposium] Targeted Therapy of Spondyloarthritis

Room A E

Chairs	Hoon-Suk Cha *(Sungkyunkwan Univ., Korea)* Eun Young Lee *(Seoul Nat'l Univ., Korea)*
15:30-16:00	**Polygenic risk scores and the practice of rheumatology** Matthew Brown *(King's College London, United Kingdom)*
16:00-16:30	**Proper assessment and evaluation for treatment** Tae-Jong Kim *(Chonnam Nat'l Univ., Korea)*
16:30-17:00	**Translational researches for new target treatment** Dennis McGonagle *(Univ. of Leeds, United Kingdom)*

15:30-17:00 [Free Paper Session] Rheumatoid Arthritis Basic Research

Room B (K)

Chairs	Ho-Youn Kim *(The Catholic Univ. of Korea, Korea)* Seong Wook Kang *(Chungnam Nat'l Univ., Korea)*
O-57	Soluble immune checkpoint molecules in patients with rheumatoid arthritis and their association with autoantibodies Jung Yoon Pyo *(Yonsei Univ., Korea)*
O-58	Several certain substances within MSCs secretome can restrain IL-2-mediated NK cells activity Eunhee Ko *(Yonsei Univ., Korea)*
O-59	Reduced levels of reactive oxygen species in peripheral blood mononuclear cells supresses inflammatory response of fibroblast-like synoviocytes in rheumatoid arthritis patients Ha-Reum Lee *(Chungnam Nat'l Univ., Korea)*
O-60	Interleukin (IL)-18 binding protein regulates IL-17 induced osteoclastogenesis and type 17 helper T cell / regulatory T cell imbalance in rheumatoid arthritis Hong Ki Min *(Konkuk Univ., Korea)*
O-61	Therapeutic potential of a novel Bifidobacterium strain identified through microbiome profiling of rheumatoid arthritis patients with different rheumatoid factor levels Joo Yeon Jhun *(The Catholic Univ. of Korea, Korea)*
O-62	Identification of osteoclast suppression by Kynurenine through the AHR pathway So Yeon Kim *(Hanyang Univ., Korea)*
O-63	Secretome of adipose-derived mesenchymal stem cells shift macrophage polarization toward M2b/c subtype Taejun Yoon *(Yonsei Univ., Korea)*
O-64	Etanercept improve cognitive dysfunction through the suppression of peripheral inflammation and neuroinflammation in a mouse model of rheumatoid arthritis Yun Hong Cheon *(Gyongsang-Nat'l Univ., Korea)*

15:30-17:00 [Symposium] Visiting Scholarship Symposium

Room C (K)

Chairs	Yeong-Wook Song *(Seoul Nat'l Univ., Korea)* Won Tae Chung *(Dong-A Univ., Korea)*
15:30-15:50	IL-12 driven cytolytic CD4+ T cell program in SLE Sungsoo Jung *(Soonchunhyang Univ., Korea)*
15:50-16:10	Using claims databases for rheumatology research questions Soo-Kyung Cho *(Hanyang Univ., Korea)*
16:10-16:30	Periodontal inflammation and microbiome in individuals at serologically increased risk of rheumatoid arthritis Hyoun-Ah Kim *(Ajou Univ., Korea)*
16:30-16:50	Conventional radiography in clinical study of RA Yune-Jung Park *(The Catholic Univ. of Korea, Korea)*

No.	Title	Presenter
	RA-pathogenesis and animal model & Cytokines and mediators	
P-001	Dasatinib prevents joint destruction through regulation of T cell differentiation and attenuation of osteoclastogenesis in collagen-induced arthritis model	Hong Ki Min *(Konkuk Univ. Medical Center, Korea)*
P-002	PLAG as a regimen to prevent the development of interstitial lung disease in autoimmune arthritis model	Doo-Ho Lim *(Univ. of Ulsan College of Medicine, Ulsan Univ. Hosp., Ulsan, Korea)*
P-003	Soluble CD27 as a biomarker of rheumatoid arthritis	Su-Jin Yoo *(Chungnam Nat'l Univ. , Korea)*
P-004	Identification of differentially expressed genes contributing to immune reaction in 232 patients with rheumatoid arthritis	Jae Hyun Jung *(Korea Univ. College of Medicine, Korea)*
P-005	Withdrawn	-
P-006	Lactobacillus sakei suppresses collagen-induced arthritis and modulates the differentiation of T helper 17 cells and regulatory B cells	Joo Yeon Jhun *(The Catholic Univ. of Korea, Korea)*
P-007	EC-18 ameliorates autoimmune arthritis by suppressing inflammatory cytokines and osteoclastogenesis	Jin-Sil Park *(The Catholic Univ. of Korea, Korea)*
P-008	Resveratrol loaded chitosan nanoparticles attenuates severity of collagen induced arthritis in animal model : Role of NF-jB and STAT3 signaling pathway	Deepika Singh *(Rama Univ., Kanpur, India)*

No.	Title	Presenter
	RA-clinical aspects	
P-009	Which cardiovascular disease risk calculator best reflects the subclinical atherosclerosis of coronary artery in rheumatoid arthritis patients? : Pilot study	Se Hee Kim *(Konkuk Univ. Medical Center, Korea)*
P-010	Withdrawn	-
P-011	Modification of auto-antibody profiles in rheumatoid arthritis : Data from a Malaysian 10-year follow-up study	Abdul Ahmad Siti Aisyah *(Allergy and Immunology Research Center, Institute for Medical Research, Ministry of Health Malaysia, Malaysia)*
P-012	Incidence rate and characteristics of herpes zoster in patients including Japanese with moderate-to-severe rheumatoid arthritis: Update from baricitinib clinical studies	Hyeun Seung Roh *(Eli Lilly and Company, Korea)*
P-013	Machine learning based prediction model for responses of bDMARDs in patients with rheumatoid arthritis and ankylosing spondylitis	Seulkee Lee *(Samsung Medical Center, Sungkyunkwan Univ. School of Medicine, Korea)*
P-014	Lactobacillus sakei suppresses collagen-induced arthritis and modulates the differentiation of T helper 17 cells and regulatory B cells	Min Wook So *(Pusan Nat'l Univ. Yangsan Hosp., Korea)*
P-015	The value of the simplified RAMRIS-5 in RA patients using 3T MRI	Recep Sade *(Ataturk Univ., Turkey)*
P-016	Muscle mass and function in patients with rheumatoid arthritis	Ju-Yang Jung *(Ajou Univ. School of Medicine, Korea)*
P-017	Disassociation between intensity of morning stiffness and various disease activity indices in Korean patients with rheumatoid arthritis	Mi Hyeon Kim *(Seoul Nat'l Univ. Hosp., Korea)*
P-018	Sustained remission in patients with rheumatoid arthritis treated with targeted therapy: Results from the KOBIO registry	Jung Hee Koh *(Bucheon St. Mary's Hosp., College of Medicine, The Catholic Univ. of Korea, Korea)*

No.	Title	Presenter
	RA-treatment	
P-019	Significant factors predicting the trend of disease activity in rheumatoid arthritis patients treated with biologics: Trajectory-based clustering approaches for KOBIO registry	Bon San Koo *(Inje Univ. Seoul Paik Hosp., Inje Univ. College of Medicine, Korea)*
P-020	Revealing a portrait of a patient with refractory arthritis	Eugenia Aronova *(V.A. Nasonova Research Institute of Rheumatology, Russian Federation)*
P-021	Infectious complications as reason for discontinuations of biologics	Eugenia Aronova *(V.A. Nasonova Research Institute of Rheumatology, Russian Federation)*
P-022	Immunological remission and prognosis of anti-TNF α treatment response among diagnostic biomarkers in rheumatoid arthritis	Bogdan Ion Gavrila *(Univ. of Medicine and Pharmacy „Carol Davila", Internal Medicine and Rheumatology Department, Romania)*
P-023	A study of factors affecting long-term persistence of rituximab in patients with RA : Results from the Korean rheumatology biologics registry	Ji-Won Kim *(Ajou Univ. School of Medicine, Korea)*
P-024	Switching from TNFα inhibitor to tacrolimus as maintenance therapy in rheumatoid arthritis after achieving low disease activity with TNFα inhibitors and methotrexate : 24-week result from a non-randomized, active-controlled trial	Jung Hee Koh *(Bucheon St.Mary's Hosp., The Catholic Univ. of Korea, Korea)*
P-025	Radiographic progression of structural joint damage over 5 years of baricitinib treatment in patients with rheumatoid arthritis : Results from RA-BEYOND	Hyeun Seung Roh *(Eli Lilly and Company, Korea)*
P-026	Signal detection of adverse drug reactions of biologic and target synthetic DMARDs used in rheumatoid arthritis patients on real-world data in South Korea	Seong-ji Park *(Konyang Univ. Hosp., Korea)*
P-027	Immunological remission and prognosis of anti-TNF α treatment response among diagnostic biomarkers in rheumatoid arthritis	Claudia Ciofu *(Univ. of Medicine and Pharmacy „ Carol Davila", Internal Medicine and Rheumatology Department, Romania)*
P-028	Flare after switching from intravenous tocilizumab to subcutaneous formulation in patients with rheumatoid arthritis	Soo Min Ahn *(Asan Medical Center, Korea)*
P-029	Therapeutic outcomes of patients with rheumatoid arthritis based on DAS-28 at different clinical settings of Pakistan	Mudassar Iqbal Arain *(Faculty of Pharmacy Univ. of Sindh Jamshoro, Pakistan)*
P-030	Long-term safety of a single infusion of human umbilical cord blood-derived mesenchymal stem cell therapy in rheumatoid arthritis : The 5-year follow-up of the phase I clinical trial	Min Jung Kim *(Seoul Metropolitan Government–Seoul Nat'l Univ. Boramae Medical Center, Korea)*
P-031	Risk of herpes zoster infection in Korean patients with rheumatoid arthritis treated with JAK inhibitors	Yeo-Jin Song *(Hanyang Univ. Hosp. for Rheumatic Diseases, Korea)*
P-032	Treatment response to the second JAK inhibitor in patients with rheumatoid arthritis	Wonho Choi *(Asan Medical Center, Korea)*
P-033	Withdrawn	-
P-034	Withdrawn	-

No.	Title	Presenter
	RA-treatment	
P-035	Real-world comparative effectiveness of tofacitinib versus tumor necrosis factor inhibitor in patients with rheumatoid arthritis: A prospective observational study	Soo-Kyung Cho *(Hanyang Univ. Hosp. for Rheumatic Diseases, Korea)*
P-036	Construction of numerous classifiers to prognosis rheumatoid arthritis in patients by data mining approach	Manvendra Singh *(HMFA-MIET, AKTU, India)*
P-037	Comparison of retention rate and efficacy between tocilizumab monotherapy and MTX combination therapy from KOBIO registry	Howook Jeon *(Uijeongbu St. Mary's Hosp., College of Medicine, The Catholic Univ. of Korea, Korea)*
P-038	Quality assessment of health care of rheumatoid arthritis in Korea based on multicenter medical record reviews	Mi Ryoung Seo *(Gil Medical Center, Gachon University College of Medicine, Korea)*
P-039	Clinical efficacy of cevidoplenib (SKI-O-703), a selective SYK inhibitor, in early rheumatoid arthritis patients in phase II a clinical trial	Taeyoung Yoon *(Oscotec Inc, Korea)*

No.	Title	Presenter
	SLE-clinical aspects, APS	
P-040	Myocardial involvement with pericarditis presenting as decompensated congestive cardiac failure at lupus onset	Choon Seong NG *(Hosp. Pulau Pinang, Malaysia)*
P-041	Outcome of transient proteinuria in systemic lupus erythematosus	Young Eun Kim *(Asan Medical Center, Univ. of Ulsan College of Medicine, Korea)*
P-042	Risk of bleeding-related complications after kidney biopsy in patients with systemic lupus erythematosus	Eunsong Kang *(Asan Medical Center, Korea)*
P-043	Radiological imaging findings and outcome of stroke in patients with systemic lupus erythematosus	Recep Sade *(Ataturk Univ., Turkey)*
P-044	Magnetic resonance imaging in the assessment of shoulder involvement in systemic lupus erythematosus	Berhan Pirimoglu *(Ataturk Univ. School of Medicine, Turkey)*
P-045	Adjusted global antiphospholipid syndrome score (aGAPSS) based nomogram for predicting avascular necrosis in SLE	Sai Kumar Dunga *(Jawaharlal institute of postgraduate medical education and research, India)*
P-046	Clinicopathological correlation at baseline and its impact on one year renal outcome in lupus nephritis	Aishwarya Gopal *(Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), India)*
P-047	Clinical significance of frailty to cumulative organ damage and quality of life in patients with systemic lupus erythematosus: A 5-year longitudinal cohort study	Ji-Hyoun Kang *(Chonnam Nat'l Univ. Hosp., Korea)*
P-048	The correlations among renal SLEDAI with pro-inflammatory biomarkers and serum urea to creatinne ratio in SLE patients	Komang Amijaya *(Faculty of Medicine, Nursing and Public Health, Univ. Gadjah Mada, Yogyakarta, Indonesia)*
P-049	Distinct clinical characteristics of initial onset macrophage activation syndrome in systemic lupus erythematosus	Joa Kim *(Chosun Univ. Hosp., Gwangju, Korea)*
P-050	A clinical and histopathological characteristics and one year responses in lupus nephritis : Prospective cohort study	Dae Jin Park *(Hanyang Univ. Seoul Hosp., Korea)*
P-051	A case report of sqamous cell carcinoma arising within a lesion of discoid lupus erythematosus	Mahabaleshwar Mamadapur *(MMC CHENNAI, India)*

No.	Title	Presenter
	SLE-clinical aspects, APS	
P-052	A rare case of simultaneous subarachnoid hemorrhage and superficial vein thrombosis in systemic lupus erythematosus without anti-phospholipid antibody syndrome	*Chong Hyuk Chung (Wonkwang Univ. Hosp., Korea)*
P-053	The relationship among serum albumin with disease severity level of systemic lupus erythematosus (SLE) patients in Dr. Sardjito central hospital Yogyakarta	*Purbosari Lisnaedy (Clinical Pathology Fellowship, Indonesia)*

No.	Title	Presenter
	SLE-pathogenesis and animal model	
P-054	HLA profiling in Malay female patients with systemic lupus erythematosus	Malarvili Selvaraja *(UCSI Univ., Malaysia)*
P-055	Serum and saliva S100A8 are potential biomarkers for patients with systemic lupus erythematosus	Ji-Won Kim *(Ajou Univ. School of Medicine, Korea)*
P-056	CTLA-4 gene polymorphisms promotor-1661A/G with risk of systemic lupus erythematosus: Update metaanalysis	Bastomy Eka Rezkita *(Sebelas Maret Univ., Indonesia)*

No.	Title	Presenter
	SLE-treatment	
P-057	Clinical response of tacrolimus treatment for patients with lupus nephritis	Ji-Won Kim *(Ajou Univ. School of Medicine, Korea)*
P-058	A case of successful treatment of hemophagocytic lymphohistiocytosis with ruxolitinib in the patient with systemic lupus erythematosus	Ji In Jung *(Seoul Nat'l Univ. Hosp., Korea)*

No.	Title	Presenter
	Spondyloarthropathies and psoriatic arthritis	
P-059	Expanded IL-22+ group 3 innate lymphoid cells and role of oxidized LDL-C in the pathogenesis of axial spondyloarthritis with dyslipidaemia	Hong Ki Min *(Konkuk Univ. Medical Center, Korea)*
P-060	Biologic retention rate and efficacy in patients with cluster-based phenotypes of ankylosing spondylitis: data from a Korean biologics registry	Hong Ki Min *(Konkuk Univ. Medical Center, Korea)*
P-061	Retention rate and effectiveness of secukinumab vs TNF inhibitor in ankylosing spondylitis patients with prior TNF inhibitor exposure	Hong Ki Min *(Konkuk Univ. Medical Center, Korea)*
P-062	Clinical efficacy of alternative TNF inhibitor and secukinumab between primary non-responder and secondary non-responder of prior TNF inhibitor in ankylosing spondylitis	Hong Ki Min *(Konkuk Univ. Medical Center, Korea)*
P-063	Effectiveness and drug retention of biologic disease-modifying antirheumatic drugs in Korean patients with late-onset ankylosing spondylitis	Se Hee Kim *(Konkuk Univ. Hosp., Korea)*
P-064	Development of machine learning model to predict radiographic progression in patients with ankylosing spondylitis	Bon San Koo *(Inje Univ. Seoul Paik Hosp., Inje Univ. College of Medicine, Korea)*
P-065	Body mass composition, adipokines, disease factors and their relationship in determining atherosclerotic cardiovascular risk in spondyloarthritis	Chengappa Kavadichanda *(JIPMER, India)*
P-066	Signal detection of adverse drug reactions of biologic DMARDs used in ankylosing spondylitis patients on real-world data in South Korea	Seong-ji Park *(Konyang Univ. Hosp., Korea)*

No.	Title	Presenter
	Spondyloarthropathies and psoriatic arthritis	
P-067	Correlation of whole spinal inflammatory activity on MRI with radiographic progression and systemic inflammatory burden in axial spondyloarthritis	Jung Gon Kim *(Division of Rheumatology, Seoul St. Mary's Hosp., College of Medicine, Korea)*
P-068	ERAP1/ERAP2 and IL23R gene variations and the risk of developing ankylosing spondylitis in multi-ethnic Malaysian population with different HLA-B*27 allele subtypes	Chun-Lai Too *(Ministry of Health Malaysia, Malaysia)*
P-069	Clinical features and drug survival of tumor necrosis factor inhibitor in elderly patients with ankylosing spondylitis: Results from the nationwide KOrean college of rheumatology BIOlogics (KOBIO) registry	Ji-Won Kim *(Ajou Univ. School of Medicine, Korea)*
P-070	Achievement of low disease activity according to BASDAI with Ixekizumab in patients with axial spondyloarthritis: 16-week results from the COAST trials	Hyeun Seung Roh *(Eli Lilly and Company, Korea)*
P-071	Evaluation of spinal radiographic progression in patients with radiographic axial spondyloarthritis receiving Ixekizumab therapy over 2 Years	Hyeun Seung Roh *(Eli Lilly and Company, Korea)*
P-072	Efficacy and safety of Ixekizumab versus adalimumab (SPIRIT-H2H) with and without concomitant conventional synthetic disease-modifying antirheumatic drugs (DMARD) in biologic DMARD-naïve patients with psoriatic arthritis: 52-week results	Hyeun Seung Roh *(Eli Lilly and Company, Korea)*
P-073	Challenges of referral, diagnosis and management of axial spondyloarthritis	Khalid Alnaqbi *(Tawam Hosp., United Arab Emirates)*
P-074	Spinal mobility impairment among patients with axial spondyloarthritis stratified by HLA-B*27 status	Alias Haziqah-Itqan *(Ministry of Health Malaysia, Malaysia)*
P-075	Comparison of comorbidity profiles between HLA-B*27 positive and HLA-B*27 negative patients with axial spondyloarthritis	Mohd Rashid Nur-Aida-Sabrina *(Ministry of Health Malaysia, Malaysia)*
P-076	Incidence and risk of overall infections in patients with ankylosing spondylitis receiving biologic therapies: A real-world prospective observational study using KOBIO registry	Kyung Min Ko *(International St. Mary's Hosp., Catholic Kwandong Univ., Incheon, Korea)*
P-077	Elevated WNT16 expression induced cell senescence of osteoblasts in ankylosing spondylitis	Sungsin Jo *(Hanyang Univ. Institute for Rheumatology Research, Korea)*
P-078	Clinical and genetic factors associated with severe radiographic damage in ankylosing spondylitis	Bora Nam *(Hanyang Univ. Hosp. for Rheumatic Diseases, Korea)*
P-079	Age-stratified trend of spinal radiographic damage progression in patients with ankylosing spondylitis	Tae-Han Lee *(Keimyung Univ. Dongsan Hosp., Korea)*

No.	Title	Presenter
	Behcet's disease & Vasculitis	
P-080	Aortic valve surgery in patients with Takayasu's arteritis: A nationwide analysis of 1,197 patients during a 9-year period	Sung Soo Ahn *(Yongin Severance Hosp., Yonsei Univ. College of Medicine, Korea)*
P-081	Incidence, prevalence, and risk of stroke in patients with Takayasu arteritis: A nationwide population-based study in South Korea	Sung Soo Ahn *(Yongin Severance Hosp., Yonsei Univ. College of Medicine, Korea)*
P-082	The relationship of brain plaques with radiological severity after COVID-19 as a cause of vasculitis	Gökhan Polat *(Atatürk Univ., Turkey)*

No.	Title	Presenter
	Behcet's disease & Vasculitis	
P-083	Pulmonary involvement evaluation with high resolution computed tomography in aortic arch syndrome patients	*Recep Sade (Ataturk Univ., School of Medicine, Turkey)*
P-084	Chest MRI findings of Behcet's disease	*Fatih Alper (Atatürk Univ., Turkey)*
P-085	Withdrawn	-
P-086	Novel mortality-predicting index at diagnosis can effectively predict all- cause mortality in patients with antineutrophil cytoplasmic antibody-associated vasculitis	*Hyunsue Do (Severance Hosp., Yonsei Univ. College of Medicine, Korea)*
P-087	Three cases of Takayasu's arteritis with Crohn's disease in young female patients	*Hye-Jin Jeong (Keimyung Univ. Dongsan Hosp., Korea)*
P-088	Risk of ocular comorbidities and blindness among patients with Behçet's disease : A nationwide population-based cohort study in Korea	*Se Rim Choi (Seoul Nat'l Univ. Hosp., Korea)*

No.	Title	Presenter
	Metabolic and crystal arthropathies	
P-089	Development of a plain radiographic scoring system for new bone formation in gout	Chang-Nam Son *(Keimyung Univ. School of Medicine, Korea)*
P-090	The association between hyperuricemia and oral health : A cross sectional study using KNHANES data	Junyong Park *(Dong-A Univ. Hosp., Korea)*
P-091	Patient perspectives and preferences regarding gout and gout management : Impact on adherence	Min Kyung Chung *(Ewha Womans Univ. College of Medicine, Seoul, Korea)*
P-092	The impact of gout on the risk of dementia according to age group : A nationwide population-based cohort study	Jihyoun Kim *(Chungbuk Nat'l Univ. Hosp., Korea)*
P-093	Reliability and quality of Korean youtube videos for patient education regarding gout	Bon San Koo *(Inje Univ. Seoul Paik Hosp., Inje Univ. College of Medicine, Korea)*
P-094	Diagnostic value of ultrasound versus dual-energy computed tomography in patients with gouty acute gouty arthritis	Recep Sade *(Atatürk Univ., Turkey)*
P-095	Gout as an independent risk factor for major adverse cardiac events	Byeongzu Ghang *(Jeju Nat'l Univ. School of Medicine, Korea)*
P-096	Gender differences in associations between the serum level of uric acid and metabolic disorders in Russian overweight patients	Ivan Pchelin *(Saint Petersburg State Univ., Russian Federation)*
P-097	Association between female reproductive factors and gout : A nationwide population-based cohort study of 1 million postmenopausal women	Yeonghee Eun *(Samsung Medical Center, Sungkyunkwan Univ. School of Medicine, Korea)*
P-098	The risk of hyperuricemia associated with metabolic syndrome and smoking is more pronounced in women than in men	In Young Kim *(Nat'l Police Hosp., Korea)*
P-099	Cardiovascular risk associated with treatment of allopurinol and benzbromaronein patients with gout	Yeonghee Eun *(Samsung Medical Center, Sungkyunkwan Univ. School of Medicine, Korea)*
P-100	Altered risk of gout according to change of metabolic syndrome status in young male	Yeonghee Eun *(Samsung Medical Center, Sungkyunkwan Univ. School of Medicine, Korea)*

No.	Title	Presenter
	Pediatric rheumatology	
P-101	Childhood SLE with isolated mycobacterium tuberculous spinal epidural abscess: A case report and review of unusual presentations	Prayong Vachvanichsanong *(Prince of Songkla Univ., Thailand)*
P-102	Clinical outcomes of juvenile idiopathic arthritis and predictors of joint damage	Anu Balakrishnan *(Sanjay Gandhi Postgraduate Institute of Medical Sciences, India)*
P-103	Systemic juvenile idiopathic arthritis flare after ChAdOx1 nCoV-19 vaccine	Sanket Shah *(Assistant Professor, India)*
P-104	Idiopathic intracranial hypertension (IIH) with papilledema developed in juvenile idiopathic arthritis (JIA) during the biologic therapy	Hyoung Suk Park *(Myongji Hosp., Korea)*

No.	Title	Presenter
	Idiopathic inflammatory myositis and muscle biology	
P-105	Reevaluation of the prognostic significance of oropharyngeal dysphagia in idiopathic inflammatory myopathies	Jung Gon Kim *(Division of Rheumatology, Seoul St. Mary's Hosp., Korea)*
P-106	Timed function tests as measures of disease activity and functional outcome in inflammatory myositis	Sai Kumar Dunga *(Jawaharlal institute of postgraduate medical education and research, India)*
P-107	Inverse and ulcerative Gottron's: Sinister sign in case of dermatomyositis	Jui Shah *(Junior doctor, India)*
P-108	Anti-synthetase syndrome masquerading as COVID-19	Rajat Kharbanda *(Sanjay Gandhi Post Graduate Institute of medical Sciences, India)*
P-109	Systematic review of mycobacterial infections in patients with idiopathic inflammatory myopathies	Saloni Haldule *(Byramjee Jeejeebhoy Government Medical College and Sassoon General Hosp., Pune, India)*
P-110	Successful treatment of calcinosis universalis with infliximab in juvenile dermatomyositis	Chong Hyuk Chung *(Wonkwang Univ. Hosp., Korea)*

No.	Title	Presenter
	Sjögren's syndrome	
P-111	Ultrasonographic characteristics of major salivary glands in anti-centromere antibody-positive primary Sjögren's syndrome: A retrospective case-control study	Hong Ki Min *(Konkuk Univ. Medical Center, Korea)*
P-112	Sjögren's syndrome initially diagnosed with tubulointerstitial nephritis and thymoma	Yoon Ji Tak *(Soonchunhyang Univ. Seoul Hosp., Korea)*
P-113	Autoimmune hepatic involvement in patients with Sjögren's syndrome in Korea: An analysis of single-center, retrospective data	Youngjae Park *(Seoul St. Mary's Hosp., The Catholic Univ. of Korea, Korea)*
P-114	Acute renal failure as the initial presentation of Sjögren's syndrome	Upendra Rathore *(Sanjay Gandhi Postgraduate Institute Of Medical Sciences, Lucknow, India)*
P-115	Disease-specific antigen presentation on MHC class II can be inhibited by small molecules in Sjögren's syndrome	Shivai Gupta *(Univ. of Florida, USA)*
P-116	Increased syndecan-1 expression in the salivary gland of NOD mouse, a model for primary Sjögren's syndrome	Eun Joo Lee *(Daegu Fatima Hosp., Korea)*

No.	Title	Presenter
	Systemic sclerosis and Raynaud's phenomenon	
P-117	Macrovascular dysfunction and its clinical implication in systemic sclerosis	Devender Bairwa *(Jawaharlal Postgraduate Institute of Medical Education & Research, Pondicherry, India)*
P-118	Low trabecular bone score is associated with high C-reactive protein levels in systemic sclerosis	Kyung-Ann Lee *(Soonchunhyang Univ. Seoul Hosp., Korea)*
P-119	A refractory case of juvenile systemic sclerosis with myocardial dysfunction	Archan Sil *(Post Graduate Institute of Medical Education and Research, Chandigarh, India)*
P-120	Establishment of a humanized animal model for systemic sclerosis by injection of human peripheral blood leukocytes from patients with systemic sclerosis	Youngjae Park *(Seoul St. Mary's Hosp., The Catholic Univ. of Korea, Korea)*
P-121	Butyrate ameliorates skin and lung fibrosis in bleomycin-induced fibrotic mouse models	Ok-Yi Jeong *(College of Medicine, Gyeongsang Nat'l Univ., Korea)*
P-122	Development of digital ulcers on fingertips of patient with systemic sclerosis after capillary glucometer monitoring	Yunjung Choi *(Jeonbuk Nat'l Univ. School of Medicine, Korea)*
P-123	Significance of antineutrophil cytoplasmic antibody positivity in patients with systemic sclerosis: A single-centre pilot study in Korea	Jangwoo Ha *(Severance Hosp., Korea)*
P-124	Withdrawn	-

No.	Title	Presenter
	Miscellaneous rheumatic and inflammatory diseases	
P-125	Impact of hospitalization on clinical outcomes in patients with connective tissue disease associated interstitial lung disease (CTD-ILD)- A single center observational study	Navneet Kaur *(Montefiore Medical Center / Albert Einstein College of Medicine, USA)*
P-126	Risk of hepatitis B virus reactivation according to the timing of starting anti-viral agents in patients receving biologics	Soo Min Ahn *(Asan Medical Center, Korea)*
P-127	Macrophage activation syndrome in rheumatic disease: Clinical characteristics and prognosis of 20 patients	Joo hyang Chun *(Kangdong Kyung Hee Univ. Hosp., Korea)*
P-128	Involvement of white matter fiber tracts in patients with seropositive inflammatory arthritis in magnetic resonance diffusion tensor tractography	Ahmet Yalcin *(Ataturk Univ., Faculty of Medicine, Turkey)*
P-129	Combined pulmonary fibrosis and emphysema syndrome in interstitial pneumonia with autoimmune features : A case report and literature review	Yukai Wang *(Shantou Central Hosp., China)*
P-130	Performance of the 2019 ACR/EULAR classification criteria for IgG4-related disease in Seoul St. Mary's hospital cohort	Sunhee Jang *(Seoul St. Mary's Hosp., Korea)*
P-131	A case with immunoglobulin G4 related hypertrophic pachymeningitis mimicking brain tumor	Hyo-Jin Choi *(Gachon Univ. Gil Medical Center, Korea)*
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Osteoporosis and metabolic bone diseases

Osteoarthritis and biology of bone and joint

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KCR 2021

41st Korean College of
Rheumatology Annual Scientific Meeting
and the 15th International Symposium

October 21(Thu) - 23(Sat), 2021
Seoul Dragon City, Seoul, Korea

DAY 01

PROGRAM

October 21(Thu)

Symposium

Year in Review (Clinical)

JRD Journal of Rheumatic Diseases
Vol. 28, Suppl. 1, October, 2021

Rheumatoid arthritis

Min-Chan Park
Yonsei Univ., Korea

Rheumatoid arthritis (RA) is one of the common autoimmune inflammatory diseases and large volumes of studies on novel etiological mechanisms and outcomes are being reported. In particular, patients with RA receive various immune response-based medications for a prolonged period of time for the treatment of diseases, and various researches on novel therapeutics are being actively conducted.

The impact of COVID-19, which began a global epidemic in early 2020, raises questions about the influence of viral infection on outcomes of RA, whether the strategy of arthritis treatment should be changed, and how to manage the course of the disease. As these clinical interests have risen, recent research trends have also been greatly affected.

In this review, the research trends and the results of important studies that have been mainly dealt with in the clinical field of RA over the past year will be addressed. Particular interests in the issues on the course and treatment of autoimmune diseases under the COVID-19 pandemic with a focus on RA will be addressed, and the recently published 2021 American College of Rheumatology guideline for the treatment of RA will be introduced.

Several other topics of high clinical interest, such as the concepts of pre-RA evolving to clinical RA and the safety of commonly used biologics will also be explored.

Spondyloarthropathies

Eun Young Lee
Seoul Nat'l Univ

Spondyloarthritis (SpA) is a chronic inflammatory disease mainly involving the axial skeleton associated with significant pain and disability. Previously, the diagnosis of ankylosing spondylitis required evident bony abnormalities on plain radiographs of the sacroiliac joints. Recently, new classification criteria released in 2009, identified relatively early stage patients who were under the age of 45, with back pain for more than 3 months evene in the absence of radiographic sacroiliitis. Those group of patients can be classified as axSpA based on a positive magnetic resonance imaging or HLA-B27 positivity and specific clinical features. This subgroup was labeled non-radiographic (nr)-axSpA. Compared with those identified by the New York criteria, nr-axSpA patients contained a larger percentage of women and demonstrated less structural damage. However, their clinical manifestations and response to biologics were similar to radiographic axSpA. TNF inhibitors are widely used to treat axSpA patients who are refractory to NSAIDs treatment. TNF inhibitors showed rapid clinical responses and improved quality of life of active axSpA patients but failed to prevent actual ankylosis. Recent discovery of the interleukin (IL) IL-23/IL-17 pathway revealed another molecules involved in the pathophysiology of axSpA. Antibodies directed toward IL-17A demonstrated effective treatment responses in axSpA which were similar to those observed with anti-TNF agents. The agents that block IL-23 were not effective in axSpA in contrast to the effect of psoriasis or psoriatic arthritis. New agents with dual inhibition of the IL-17A and F isoforms and some oral small molecule agents that target the Jak-STAT pathway, have also shown efficacy in axSpA.

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Crystal arthropathies

Seokchan Hong
Univ. of Ulsan, Korea

Crystal arthropathies are a group of acute and chronic inflammatory disorders characterized by the deposition of crystals, including monosodium urate crystals, in the joints and/or soft tissues. This group of disorders includes gouty arthritis and calcium pyrophosphate crystal deposition (CPPD) disease. These disorders are not only characterized by acute or chronic inflammatory arthritis, but are also associated with a variety of systemic cardiovascular and metabolic diseases. Hyperuricemia is linked to an increased risk of development of cardiovascular and chronic kidney disease as well as gouty arthritis. However, it is unclear whether elevated serum urate levels have a causative role in the pathogenesis and progression of these various cardiovascular and metabolic diseases. Thus, recent researches have investigated the detection and role of urate crystals on the vascular and renal systems. In addition, ACR provides a new guidance for the management of gout in 2020. This presentation will summarize recent advances in the diagnosis and management of crystal arthropathies.

Osteoarthritis

Sang Hyon Kim
Keimyung Univ., Korea

It is well-known that numerous factors contribute to the development of osteoarthritis (OA). Given that an increased prevalence of cardiovascular disease is found in OA, recent research on modifiable risk factors for OA have investigated the influence of cardiometabolic risk factors on risk of OA (1).

Concerning the treatments, no current drug is able to modify the progression of OA and prevent long-term disability. Therefore, outcomes for patients with OA are usually suboptimal. Although OA was previously regarded as a degenerative disorder resulting from cartilage damage, growing evidence suggests that it results from the failure of the joint organ with a heterogeneous involvement of the whole joint structures, including cartilage damage, subchondral bone remodeling, and synovial inflammation (2). In addition, advances in the understanding of OA pathophysiology have enabled the identification of a variety of potential therapeutic targets involved in the structural progression of OA (3). Therefore, emerging therapies include those targeting inflammation mechanisms, cellular senescence, cartilage metabolism, subchondral bone remodeling, and the peripheral nociceptive pathways (3, 4).

This narrative review aims to summarize the risk factors and recent developments of agents for the treatment of OA.

References

1. Gill D, Karhunen V, Malik R, Dichgans M, Sofat N. Cardiometabolic traits mediating the effect of education on osteoarthritis risk: a Mendelian randomization study. Osteoarthritis Cartilage. 2021;29(3):365-71.
2. Loeser RF, Goldring SR, Scanzello CR, Goldring MB. Osteoarthritis: a disease of the joint as an organ. Arthritis Rheum. 2012;64(6):1697-707.
3. Latourte A, Kloppenburg M, Richette P. Emerging pharmaceutical therapies for osteoarthritis. Nat Rev Rheumatol. 2020;16(12):673-88.
4. Cai X, Yuan S, Zeng Y, Wang C, Yu N, Ding C. New Trends in Pharmacological Treatments for Osteoarthritis. Front Pharmacol. 2021;12:645842.

Symposium

Year in Review (Basic) : Recent Advances of T Cell Immunology in Autoimmunity

Journal of Rheumatic Diseases
Vol. 28, Suppl. 1, October, 2021

Diversity of helper and regulatory T cells

Yun Kyung Lee
Soonchunhyang Institute of Medi-Bioscience, Soonchunhyang University, Korea

CD4+ T cells are a principle component of the adaptive immune system that is required for the efficient elimination of foreign antigens, however dysregulated CD4+ T cell responses may result in autoimmune and chronic inflammatory diseases. The differentiation of CD4+ T cells is directed by cytokines elicited by pathogen-driven innate immune responses. Therefore, the coordinated innate and adaptive immune responses provide an efficient system for host protection. Recently, our understanding how CD4+ T cells differentiate into T helper subsets and regulatory T cells has expanded. This lecture will give an overview of diversity of helper and regulatory CD4+ T cells.

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Microbiome and T cell interaction in autoimmunity

Sung Hwan Park
The Catholic Univ. of Korea, Korea

Increasing evidence shows that altered gut microbiome composition influences a wide spectrum of rheumatic diseases, including SpA, PsA, SLE, Sjogren syndrome and RA. Intestinal dysbiosis is a feature of several inflammatory rheumatic disorders. The immune system is essential for maintaining a delicate balance between eliminating pathogens and maintaining tolerance to self-tissues to avoid autoimmunity. Both innate and adaptive immunity are influenced by gut microbiota, locally in the gut as well as systemically

The mucosal microbiota has great potential to interact with the host, both in a positive and in a negative man¬ner, owing to host–microorganism proximity over a large surface area in the gut. Both the innate and adaptive immune systems can respond to microbiota.

Many autoimmune diseases arise from an imbalance between pathogenic effector T cells and regulatory T (Treg) cells. Recent interest has emerged in understanding how cross-talk between gut microbiota and the host immune system promotes autoimmune development by controlling the differentiation and plasticity of T helper and Treg cells.

However, it is not clear how gut microbiome contributes to autoimmunity, and initial triggers for microbiome-host interactions leading to systemic autoimmune responses remain unknown.

Mechanism leads to autoimmunity is suggested molecular mimicry and dual TCRs in the recognition of commensal bacteria by T-cell receptor (TCR). Several studies have demonstrated, as a result of the cross-reactive nature of TCRs, that autoreactive T cells can recognize both a self-antigen and a gut commensal-antigen. Recognition of a microbial antigen is able to activate autoreactive T cells, which in turn migrate to the tissue where their cognate self-antigen is expressed and elicit autoimmune diabetes, autoimmune uveitis, and lupus. Another mechanism involves autoreactive T cells that are able to recognize gut commensal-antigens through expression of a secondary TCR in addition to self-antigen recognizing TCR and differentiate into T helper type 17 (Th17) cells. These T cells differentiate into Th17cells through TCR recognition of segmented filamentous bacteria(SFB), then traffic to the lung where they mediate lung pathology.

Research into the mechanisms whereby ‘therapeutically’ altered microorganisms could modulate autoimmune diseases and restoring intestinal homeostasis by altered microbiota is an attractive therapeutic strategy to combat autoimmune rheumatic diseases

Lipid Metabolic Control of T Cell Immunity

Yeonseok Chung
Seoul Nat'l Univ., Korea

Upon antigenic stimulation, naïve T cells are activated and differentiate into diverse effector subsets with non-redundant functions in host defense. Depending in the types of cytokine signals, activated T cells differentiate into Th1, Th2, Th17, follicular helper T (Tfh), and regulatory T (Treg) cells that express distinct lineage programs. In addition, each effector Th subset exerts non-redundant role in host defense as well as in the pathogenesis of immune disorders. Of note, epidemiological studies showed that patients with systemic autoimmune diseases exhibit a higher incidence of cardiovascular diseases. Conversely, hyperlipidemia has been known to accelerate autoimmune diseases in humans and animal models. Nevertheless, how imbalanced lipid metabolism impacts the immune system and immune disorders remains poorly understood. Our previous studies have demonstrated that hyperlipidemia stimulates dendritic cells to promotes autoimmune Th17 and Tfh cell responses in vivo. Our unpublished preliminary studies demonstrate that dysregulated lipid metabolic pathways significantly impact the differentiation of effector T cells in a cell-intrinsic manner. Moreover, lipid metabolism is shown to be associated with autoimmunity and cancer in vivo. Thus, we propose that lipid metabolism is a critical factor in the differentiation and function of T cells as well as in the pathogenesis of immune disorders. Targeting lipid metabolic pathway may pave the development of novel therapeutics for immune disorders.

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Innate Immune Cells in Autoimmune Diseases

Yong-Wook Park
Chonnam Nat'l Univ., Korea

Natural killer (NK) cells, natural killer T (NKT) cells, and mucosal-associated invariant T (MAIT) cells are immune cells that possess innate immune function. NK cells are large granular lymphocytes derived from pluripotent hematopoietic stem cells (HSCs). NK cells principally contribute to innate immunity and adaptive immune responses by killing target cells directly, or indirectly by promptly producing a variety of cytokines and chemokines. Furthermore, NK cells exposed to IL-2 kill K562 cells more efficiently, which is referred to as lymphokine activated killer (LAK) activity. Due to these effector functions, NK cells play a significant role in host defense against malignancies and certain viruses, and they may also be important in the regulation of autoimmunity. NKT cells are a distinct subset of T cells that express invariant Vα24-Jα18 T cell receptor (TCR) chain paired with Vβ11 TCR chain. TCR αβ pairs can recognize self or foreign glycolipids such as α-galactosylceramide (α-GalCer) presented by CD1d, a major histocompatibility complex (MHC) class I-like molecule as cognate antigen. NKT cells play a bridging role between innate and adaptive immune cells, including dendritic cells, monocytes, NK cells, T cells, and B cells by rapidly producing large amounts of Th1 and Th2 cytokines such as interferon-γ (IFN-γ) and interleukin-4 (IL-4). NKT cells play either protective or harmful role in a broad range of diseases, including autoimmunity, cancer, infection, sepsis, and ischemia/reperfusion-related tissue injury. MAIT cells are a relatively newly recognized T cell subset that expresses a conserved invariant TCR α-chain (Vα7.2-Jα33) paired with a limited set of Vβ chains. MAIT cells recognize bacteria-derived riboflavin (vitamin B2) metabolites presented by the MHC class 1b-like related protein (MR1). Upon antigen recognition, MAIT cells rapidly produce proinflammatory cytokines, such as IFN-γ, TNF-α, and IL-17, in an innate-like manner. MAIT cells maintain an activated phenotype throughout the course of an infection, secrete inflammatory cytokines, and have the potential to directly kill infected cells; thus, playing an important role in controlling the host response and mucosal immunity. MAIT cells have been known to be associated with infectious diseases and autoimmune disorders. In our previous studies, we examined the level and function of innate immune cells in patients with systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), adult-onset Still's disease (AOSD) and gouty arthritis (GA), and determined the clinical relevance of innate immune cells. Circulating NK, NKT, and MAIT cell levels were reduced in SLE patients and these cell deficiencies were correlated with disease activity. Cytotoxicity and LAK activity of NK cells and proliferative capacity of HSCs were reduced in SLE patients. Furthermore, the differentiation of HSCs into NK cells was found to be defective. NKT cell proliferation was impaired in SLE patients, and cytokine production by NKT cells in response to α-GalCer was diminished. This poor responsiveness to α-GalCer was found to be due to NKT cell dysfunction. IFN-γ production in MAIT cells was impaired in SLE patients, which was due to an intrinsic defect in the Ca2+/calcineurin/NFAT1 signaling pathway. α-GalCer-stimulated NKT cells had a regulatory effect on osteoclastogenesis and a protective effect against inflammatory bone destruction. However, these effects of α-GalCer were diminished in RA patients, which was related to NKT cell dysfunction. These findings provide important information for those searching for novel therapeutic strategies to prevent bone destruction in RA. NKT cells were numerically and functionally deficient in AOSD patients. In addition, NK cell dysfunction was related to NKT cell deficiency. These abnormalities contribute to innate immune dysfunction in AOSD. Circulating MAIT cells were activated and numerically deficient in GA patients. In addition, MAIT cells had the potential to migrate to inflamed tissues and induce osteoclastogenesis. These findings provide an important role of MAIT cells in the pathogenesis of inflammation and bone destruction in GA patients. Collectively, these abnormalities of the innate immune cells possibly contribute to immune system dysregulation in autoimmune diseases.

Luncheon Symposium I - Pfizer

Practical Review of RA Treatment Option

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Tofacitinib in RA: Exploring the Efficacy and Safety Profile in the Real-World

Roy Fleischmann
Univ. of Texas Southwestern Medical Center, USA

With respect to how to use tofacitinib, the 2021 ACR guideline for the treatment of RA is quite clear that a targeted synthetic disease modifying anti-rheumatic drug (tsDMARD), such as tofacitinib, should be used in patients who have failed or are intolerant to methotrexate (MTX). In a MTX incomplete responder (IR), the guideline currently suggests that a biologic disease modifying anti-rheumatic drug (bDMARD) or a tsDMARD is recommended over triple therapy. If a patient is started on a bDMARD or tsDMARD and fails to respond adequately, then the patient should be changed to a medication with a different mechanism of action (MOA). The guidelines further states that if the patient reaches the goal of treatment on combination of a bDMARD or a tsDMARD with MTX and it is desired to reduce therapy, MTX should be tapered first.

The guideline also discusses safety. In a patient with heart failure, a tsDMARD or a non-TNF bDMARD should be used rather than a TNFi. There is a statement about the use of a tsDMARD is the face of an SIE which is problematic. The guideline states that the tsDMARD should not be restarted for a period of 1 year. There is no supporting evidence of this, and multiple reports have suggested that the tsDMARD should be started after the SIE resolves.

The 2019 EULAR recommendations also state that a tsDMARD or a bDMARD should be started in the a MTX-IR or a csDMARD-IR. The difference from the ACR guideline is that EULAR suggests that if the first MOA fails, then a switch to another molecule in that class or to different MOA is reasonable.

With respect to “real world” data, a study from Australia showed that the efficacy of tofacitinib is similar to bDMARDs and there is more use of tofacitinib as monotherapy compared to bDMARDs. Another study compared the efficacy of tofacitinib to tocilizumab, either as monotherapy or in combination with MTX in both bDMARD naïve and IR patients. The authors found that tofacitinib is more effective than tocilizumab in the bDMARD naïve population with equal efficacy in the bDMARD-IR population. A study from Canada showed that the persistence of tofacitinib was 62.7% and 49.6% after 1 and 2 years of treatment, respectively with better persistence in the bDMARD naïve patients vs those who failed multiple bDMARDs prior to tofacitinib.

An interesting analysis showed that in a “real world” population of patients with RA, the risk of MACE, SIEs, malignancies, death and VTE was similar in patients who initiated tofacitinib versus those who initiated a bDMARD. This analysis was in the general RA population and not limited to those patients who were older with a cardiovascular risk.

COVID-19 is a great importance to rheumatologists. A seminal study concluded that SARS-CoV-2 vaccines are immunogenic in patients receiving immunosuppression although the response is impaired compared with healthy individuals. B-cell depletion following RTX impairs serological responses, but T-cell responses are preserved in this group.

The ACR has published recommendations for COVID-19 vaccination. In brief, the consensus is that all patients should be vaccinated as there is an increased risk and worse outcomes with COVID in the immunosuppressed population and, if possible, vaccination should occur prior to the start of an immunosuppressant. If the patient is on MTX, MTX should be held for 1 week before vaccination. There is a controversial recommendation that tsDMARDs should be held for one week after vaccination.

Finally, a report from the Global Rheumatology Alliance stated that there is a higher risk of hospitalization, use of oxygen or ventilation and death with a tsDMARD in patients diagnosed with COVID-19 while on a tsDMARD. However, very importantly, these risks were seen almost universally in those patients in whom the tsDMARD was discontinued rather than continued in whom these risks were minimal.

Luncheon Symposium II – Celltrion

New Treatment Option in Rheumatic Disease

Journal of Rheumatic Diseases
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Benefits of switching from IV to SC infliximab: European cases

Martin Perry
NHS Greater Glasgow and Clyde, United Kingdom

1. Introduction and brief note on the RCT's (CT-P13 SC 3.5 RA Study Part 2, Meta-analysis of CT-P13 SC Pivotal Data) showing equivalent efficacy and safety with comparable pharmacokinetic profiles in both patient groups receiving CT-P13 and originator infliximab
2. What are the current advantages of switching to S/C therapy?
   - Patient preference
   - Capacity in hospitals
   - Covid -19 risk
   - Consistent serum drug levels
3. Recent gastroenterology advances: Royal Liverpool Hospital UK switch data and successful outcomes
4. Rheumatology Case 1: speakers patient 1
5. Rheumatology Case 2: speakers patient 2
6. Summary and lessons learned

Luncheon Symposium III - Abbvie & Eisai

Management of Patients with Rheumatic Diseases during the COVID-19 Pandemic

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Solving the puzzle : A pragmatic approach to anti TNF therapy during the COVID-19 pandemic

Jin Kyun Park
Seoul Nat'l Univ., Korea

Biological DMARDs including tumor necrosis factor inhibitor (TNFi) have dramatically improved the outcome of major rheumatic diseases. In treatment of ankylosing spondylitis (AS) TNFi remains the first line treatment after NSAID failure. Interleukin (IL)-17 inhibitors such as secukinumab or ixekizumab are considered as alternatives after TNFi failure. The choice of biological DMARDs can be further influenced by the existing comorbidities such as uveitis and inflammatory bowel disease. For example, TNFi monoclonal antibodies such as adalimumab and infliximab improve the uveitis severity and recurrence, whereas etanercept does not. This highlights the importance of drug choice even within the same drug class. In severe Behcet disease including Neurobehcet and refractory uveitis, TNFi proves to be quite safe and effective.

In the midst of the Covid-19 pandemic, the use of immunosuppressant in patients with rheumatic diseases should be cautious, since the underlying immune dysfunction and immunosuppressive therapy render them more susceptible to a severe Covid-19 infection. Vaccination against Covid-19 is highly recommended. Since TNFi suppress preferentially the innate immunity (and the adaptive immune response to a less extent), it might be safe to continue TNFi during the Covid-19 infection. It is possible that TNFi even neutralizes the released TNF during the hyperinflammatory syndrome/cytokine storm of a severe Covid-19 disease. Strikingly, TNFi does not negatively affect the vaccine response to the different Covid-19 vaccines. Therefore, TNFi can be safely continued during the Covid-19 pandemics.

Special Lecture
- Presidential Plenary Session

JRD Journal of Rheumatic Diseases
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Presidential lecture

Gwan Gyu Song
Korea Univ., Korea

2021 marks the 40th anniversary of KCR, since its establishment in 1981. We have overcome countless challenges and made some truly meaningful strides over the past 40 years. We are determined to continue this tradition, staying ready and nimble for what lies ahead.

In the spirit of celebrating four decades of commitment and devotion, I hope this gathering serves as a chance to cherish our history, while keeping our eyes on the horizon.

The Presidential Plenary Session is a new addition to KCR 2021. It is my honor to give a presidential lecture in the KCR Annual Scientific Meeting. Prevention and treatment of rheumatic diseases are part of KCR's purposes. I would like to share my own perspectives on the progress in the management of rheumatoid arthritis over the past 30 years during which I was a member of KCR.

My memory about KCR

Soo Kon Lee
Bundang Cha Hosp., Korea

"이기적인 경쟁은 우리를 불행하게 만들고 선의의 경쟁은 성장과 발전을 초래하나 사랑이 있는 경쟁은 행복을 더 해준다. 학문과 사회를 위해 더 많은 도움을 주도록 경쟁하라!" – 김형석 저 "백년을 살아보니" 126 쪽 (Denstory)-

1900년대 초 미국에서는 정형외과 의사들이 관절염 환자를 진료하고 있었다. 이 당시 유럽에서는 1925년 의학수문학회(medical hydrology)에서 Jan van Breemen (1874-1961 Netherlands)이 International Committee on Rheumatism을 창립하였다. 이 모임에 참석했던 미국 Mayo clinic의 Louis B Wilson (1866-1943, Mayo Clinic USA)이 1928년 American Committee for the Control of Rheumatism 지회를 설립하고 이를 모태로 American Association for the Study and Control of Rheumatism을 1934년 결성하였으며 곧 이어 1937년 American Rheumatism Association으로 개명하였다. Mayo clinic을 중심으로 Philip Hench(1896-1965 Mayo Clinic USA) 가 1928년부터 류마티스학 수련을 시작하였고 제자들이 Harvard Medical School, Columbia University 그리고 New York University 등에서 류마티스학을 연구하고 수련교육을 실시하며 세가 확장되었다. 결과적으로 1971년 Rheumatology Subspecialty Board가 만들어 졌고 1985년 American College of Rheumatology로 개명하여 오늘에 이르고 있다.

50년 늦게 시작한 우리나라의 역사도 비슷해 보인다. 우리나라에서 1980년 대까지 관절염의 진료는 정형외과 의사들에 의해 이루어 졌고 1981년 정형외과 한문식 교수를 초대회장으로 대한류마티스학회가 창립되었다. 곧 이어 내과 전문의들이 류마티스학회에 참여하기 시작하였다. 1985년 김호연 교수가 미국에서 연수 후 귀국하였고 연이어 서울대학의 최성재, 한양대학의 김성윤, 서울대 이윤우 교수 등이 해외 연수를 바치고 귀국하여 1세대를 형성하였고 류마티스학의 전도사 역할을 시작하였다. 1989년 교원병연구회를 결성하여 내과의사들 중심의 학술 활동을 하던 중 1992년 대한내과학회에서 분과전문의 제도를 도입하면서 류마티스를 전공하는 내과의사가 많아 지게 되어 내과전문의가 중심이 된 오늘의 대한류마티스학회에 이르게 되었다. 2000년 의약분업이 이루어 지기 전까지 병원에서 입원환자의 약을 처방하던 시기에는 류마티스학의 인기가 높았었다. 의약분업이 이루어 진 후 병원처방이 없어 지면서 류마티스의 병원내 위상이 많이 감소하였지만 류마티스관절염의 임상에 항TNF 제제들이 도입되면서 류마티스학회는 제2의 전성기를 맞이하게 되었다. 그동안 학회는 이사장제도를 도입하였고 류마티스학연구재단을 설립하였으며 여류사랑캠페인, 관절염1,23 캠페인등 사회적 활동도 활발히 하였다. 1996년 APLAR를 성공적으로 개최하고 KJCMR도 지속적으로 개최함으로써 동아시아권에서의 입지를 확보하여 오고 있다.

그러나 우리나라 류마티스학의 수준은 국제적 기준에 비추어 볼 때 초등의 단계라고 보아야 할 것이다. 특별히 기초과학자의 저변 확대가 필요하다. 이들을 통해 신약을 개발하도록 해야 할 것이다. 이를 위해 학회는 류마티스 기초과학 인재양성에 노력을 기울여야 한다. 류마티스연구재단을 통한 기금마련을이 주요한 아젠다로 삼아 주기 바란다. 류마티스학회 기금교수를 선발하여 급여와 연구비를 충분한 기간 동안 전폭적으로 지원하는 제도를 만들어 시행하면 좋겠다.

Free Paper Session

International Free Paper Session (Clinical)

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The course of rheumatoid arthritis-associated interstitial lung disease, focusing on lung physiology and disease activity: A prospective observational study of the Korean rheumatoid arthritis-associated interstitial lung disease (KORAIL) cohort

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Background

Interstitial lung disease (ILD) is a severe extra-articular manifestation of rheumatoid arthritis (RA). We assessed the natural course of lung physiology and the relationship between arthritis activity and pulmonary physiology in patients with RA-ILD.

Methods

We analyzed data from the prospective observational Korean Rheumatoid Arthritis ILD (KORAIL) cohort. RA disease activity was annually evaluated using disease activity score (DAS) 28, pulmonary function tests (PFT), and chest CT scans. Progression was defined as a ≥10% forced vital capacity (FVC) decline, or a 5–10% FVC decline plus a ≥15% DLco decline.

Results

Our analyses included 143 patients with PFT measurements during a 2-year follow-up (2.1± 0.3 years). The annual FVC change was −39 ml/year (95% CI, −63 to −15 mL/year). Each year, ~10% of patients showed a ≥10% decline of the percent of predicted FVC compared to the previous year (17/141, 12.1% in 1st year, 17/120,14.2% in 2nd year). Progression occurred in ~40% of patients annually, and 55.2% over two years. FVC decreased significantly faster within 2 years post-diagnosis (−57.1 mL/year) compared to ≥5 years post-diagnosis (32.1 mL/year) (p=0.02). Patients who maintained moderate-to-severe disease activity consistently showed the lowest FVC and most profound annual FVC decline (−113 mL/year, −206 ~−21 mL/year). Progression and annual FVC decline were observed in all patients irrespective of disease activity although most profound in patients with worsening disease activity.

Conclusions

In RA-ILD, ~50% of patients experienced progression over two years, and the annual FVC decline was more rapid in early-stage disease. Worsening RA disease activity was associated with rapid ILD deterioration but controlling RA disease activity was insufficient to slow ILD progression.

Keywords

Rheumatoid arthritis, interstitial lung disease, lung function test

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IO-03

Relationship between the risk of new onset diabetes mellitus and exposure to individual antirheumatic drugs in patients with rheumatoid arthritis: A nationwide population study

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Background

We aimed to investigate the effect of individual disease-modifying antirheumatic drugs (DMARDs) on the development of diabetes mellitus (DM) in patients with rheumatoid arthritis (RA).

Methods

We conducted a nested case-control study on a cohort of 69,779 DM-naïve adult patients (≥ 18 years old) with RA from the Korean Health Insurance Review and Assessment Service claims data from 2011 to 2019. Patients with DM were identified and individually matched to randomly selected controls (1:4 matched). DMARDs use was measured for one year prior to the event or index date and stratified by duration of exposure. The association between the use of each DMARD and the risk of DM was estimated using conditional logistic regression.

Results

3,772 (5.4%) patients were newly diagnosed with DM (mean age, 62.3 ± 10.9 years; 77.6% women), and the risk of DM depended on the type of DMARD and the duration of exposure. In a multivariable-adjusted analysis, exposure to conventional DMARDs for less than 90 days per year was associated with an increased risk of DM compared with no use. However, when the duration of exposure exceeded 270 days per year, hydroxychloroquine (HCQ; adjusted OR, 0.76; 95% CI, 0.69-0.84; p <0.001) and methotrexate (MTX; adjusted OR, 0.81; 95% CI, 0.74-0.89; p <0.001) were associated with a significant decrease in the risk of DM, and tacrolimus (adjusted OR, 1.27; 95% CI, 1.07-1.51; p = 0.006) was associated with an increased risk. Among the biologic DMARDs, non- TNF inhibitors were associated with a significant decrease in the risk of DM when the duration of exposure exceeded 270 days per year (adjusted OR, 0.52; 95% CI, 0.29-0.93; p = 0.026).

Conclusions

This study suggested that long-term use of HCQ, MTX, or non-TNF inhibitors for periods longer than 270 days per year was associated with a reduction in the incidence of DM.

Keywords

Diabetes, Rheumatoid arthritis, Disease-modifying antirheumatic drug

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Changes in healthcare costs before and after the diagnosis of systemic lupus erythematosus in Korea

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Background

We aimed to investigate the differences in direct healthcare costs between Korean patients with systemic lupus erythematosus (SLE) and subjects without SLE and to identify the changes in direct healthcare costs before and after the diagnosis of SLE.

Methods

Incident patients with SLE and matched controls by age, sex, and calendar year were identified between 2008 and 2018 using the Korean National Health Insurance Service databases. We compared the mean annual direct healthcare costs in the index year between patients with SLE and subjects without SLE (matched 1:4). Changes in mean annual direct healthcare costs per patient for 5 years before and after the diagnosis of SLE were also estimated.

Results

A total of 11,375 incident patients with SLE and 45,500 subjects without SLE were selected. In the first year after the diagnosis, mean direct healthcare costs per patient of SLE and controls were $5,694 and $736, respectively. In patients with SLE, blood test costs ($1,454, 25.5%) and medication costs ($1,101, 19.3%) represented the major direct cost categories and followed by in-patient costs ($1,000, 17.6%). Outpatient fee for physician services ($483, 8.5%) and imaging test ($335, 5.9%) were important further direct cost components. Mean direct healthcare costs of SLE patients in 5 years before SLE diagnosis was 1.8 times higher than controls, while they increased to 3.7 times ($2,565 vs. $695) 1 year before the diagnosis. Total direct healthcare costs peaked at $5,694 during the first year after SLE diagnosis and abruptly dropped to $2,578 in the second year, while they persist during 5 years after the diagnosis (Fig. 1).

Conclusions

Patients with SLE had significantly high direct healthcare costs compared to their matched controls. SLE patients incurred the highest direct healthcare costs during 1 year after the diagnosis, and they remained high during 5 years after diagnosis.

Keywords

Systemic Lupus Erythematosus, Healthcare costs, Diagnosis

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IO-05

Achieving LLDAS-50 is associated with less organ damage and better quality of life during 5-year follow-up in patients with systemic lupus erythematosus

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Background

A lupus low disease activity state (LLDAS) is a pragmatic, realistic treatment goal, since remission in systemic lupus erythematosus (SLE) is extremely rare and usually temporary. Because patients who have a longer LLDAS should have better clinical outcomes, we investigated the effect of achieving LLDAS for more than 50% of the follow-up period, the so-called LLDAS-50, on disease activity, damage, and quality of life in our Korean SLE cohort during a 5-year follow-up period.

Methods

We evaluated 199 SLE patients from the Korean Lupus Network (KORNET) registry. Demographics, clinical manifestations, laboratory findings, disease activity, organ damage, and quality of life were assessed at enrollment, and then annually for 5 consecutive years. We divided the patients into two groups according to whether LLDAS-50 was achieved (LLDAS-50 and non-LLDAS-50 groups). Univariate and multivariate analyses were used to assess the association between LLDAS-50 and clinical outcomes in SLE patients.

Results

Of the 199 patients, 140 (70.4%) were assigned to the LLDAS-50 group and 59 (29.6%) to the non-LLDAS-50 group. The LLDAS-50 group was less likely to have a malar rash (p=0.031), serositis (p=0.025), and anti-nRNP (p=0.005), anti-nucleosome (p=0.048), and anti-histone (p=0.002) antibodies. The mean PGA and Systemic Lupus Erythematosus Disease Activity Index during follow-up were significantly lower in the LLDAS-50 group (both p<0.001). During follow-up, the SF-36 Mental Component Summary (MCS) scores improved significantly, and the SLICC damage index (SDI) scores increased less in the LLDAS-50 group (both p=0.006). In the multivariate analysis, LLDAS-50 was significantly associated with the SF-36 MCS (OR = 1.061, 95% CI: 1.019–1.105, p=0.004) and SDI (OR = 0.682, 95% CI: 0.518–0.898, p=0.006) after adjustment.

Conclusions

Attaining LLDAS-50 was associated with less organ damage and a better quality of life during the 5-year follow-up.

Keywords

LLDAS-50, organ damage, qulity of life

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The impact of smoking status on radiographic progression in patients with ankylosing spondylitis during Anti-TNF treatment

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Background

Tumor necrosis factor inhibitors (anti-TNFs) have revolutionized Ankylosing spondylitis (AS) treatment. In real world settings, patients may stay in the anti-TNF treatment only if the disease is controlled adequately. However, radiographic damage can still progress during anti-TNF treatment. This study aimed to investigate factors associated with radiographic progression during anti-TNF treatment with a focus on smoking status which is known as one of poor prognostic factors for AS.

Methods

We conducted a retrospective cohort study of AS patients who began the first-line anti-TNF between 2001 and 2018 according to availability of smoking data. All enrolled patients were observed until the time of their last visit, discontinuation of anti-TNF, or December 2019. Radiographic damage was assessed using the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). For the patients who have more than 2 full sets of spine radiographs during follow up duration, mSASSS progression rate (unit/year) was calculated by using baseline mSASSS, the last mSASSS, and the duration between them. Univariable and multivariable logistic regression analyses were performed to identify associated factors of mSASSS progression rate > 1 unit/year.

Results

Among 573 AS patients, 235 (41.0%) patients were never smokers, 80 (14.0%) ex-smokers and 258 (45.0%) current smokers at initiation of anti-TNF treatment. Ex- and current smokers had higher mSASSS progression rate than that of never smokers (never smoker 0.12 [0.00-0.71], ex-smoker 0.58 [0.00-1.48], and current smoker 0.55 [0.00-1.45] unit/year, P<0.001). After adjusting clinical factors, current smoking (adjusted odds ratio [OR] 1.69, 95% CI 1.01-2.82, P=0.047) and increased baseline mSASSS (adjusted OR 1.03, 95% CI 1.01-1.04, P<0.001) were associated with mSASSS progression rate > 1 unit/year.

Conclusions

Current smoking was associated with significant radiographic progression during anti-TNF treatment.

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IO-07

Longitudinal analysis of symptom-based clustering in patients with primary Sjogren's syndrome: a prospective cohort study with a 5-year follow-up period

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Background

Sjogren's syndrome (SS) is a heterogenous disease with various phenotypes. We aimed to provide a relevant subclassification based on symptom-based clustering for patients with primary (p) SS.

Methods

Data from patients in a prospective pSS cohort in Korea were analysed. Latent class analysis (LCA) was performed using patient reported outcomes, including pain, fatigue, dryness, and anxiety/depression. Clinical and laboratory differences between the classes were analysed. Latent transition analysis (LTA) was applied to the longitudinal data (annually for up to 5 years) to assess temporal stability of the classifications.

Results

LCA identified three classes among 341 patients with pSS (i.e., 'high symptom burden', 'dryness dominant', 'low symptom burden'). Each group had distinct laboratory and clinical phenotypes. LTA revealed that class membership remained stable over time. Baseline class predicted future salivary gland function and damage accrual represented by a Sjogren's syndrome disease damage index.

Conclusions

Symptom-based clustering of heterogenous patients with primary Sjogren's syndrome provided a relevant classification supported by temporal stability over time and distinct phenotypes between the classes. This clustering strategy may provide more homogenous groups of pSS patients for novel treatment development and predict future phenotypic evolvement.

Keywords

cluster analysis, latent class analysis, Sjogren's syndrome

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Metabolic obesity and the risk of knee osteoarthritis progression in elderly community residents: A 3-year longitudinal cohort study

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Background
Metabolic syndrome is a major health problem worldwide associated with obesity, thus drawing attention to its relation to osteoarthritis (OA). However, it is still uncertain whether metabolic syndrome or body fat distribution is associated with knee OA. The aim of this longitudinal study was to elucidate the association between metabolic obesity and adverse structural changes of knee OA assessed by magnetic resonance imaging (MRI).

Methods
Participants were recruited from the Hallym Aging Study cohort in Korea. Knee MRI scans, along with dual-energy X-ray absorptiometry (DEXA), were assessed in 226 participants at baseline and after 3 years. The structural progression in tibiofemoral joint was evaluated using the Whole-Organ MRI Score (WORMS) for cartilage morphology and bone marrow lesion (BML). Logistic regression with generalized estimating equation (GEE) was performed for associations of metabolic risk factors with worsening of WORMS scores at the subregional level.

Results
Metabolic syndrome and each of its components were not associated with cartilage loss or increase of BML. In the medial compartment, fat mass in women was associated with cartilage loss, but the statistical significance disappeared after adjusting for BMI. In women with metabolic syndrome, obesity (BMI $\geq$25) was a significant risk factor for cartilage loss and increase of BML; however, the interaction effects of metabolic syndrome on the association between obesity and knee OA progression were not significant.

Conclusions
In this study, metabolic effects of obesity on deterioration of knee OA were not demonstrated. Further large-scale studies are required to prove the causal relationship between metabolic obesity and knee OA.

Keywords
osteoarthritis, metabolic obesity, fat mass

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IO-09

A randomized, double-blind, placebo-controlled trial of ramosetron, a 5-hydroxytryptamine 3 receptor antagonist for treating refractory fibromyalgia

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Background

This study evaluated the efficacy and safety of ramosetron for pain relief in adult patients with fibromyalgia (FM) refractory to conventional treatment.

Methods

This prospective, double-blind, placebo-controlled trial randomly assigned 80 patients with FM to receive placebo (n = 40) or ramosetron (n = 40) 0.3 mg/day intravenously for 5 days. The primary outcome was the reduction in pain intensity at the end of treatment, measured with a visual analogue scale (VAS). Secondary outcomes were the scores on the patient global impression of change (PGIC), FM Impact Questionnaire, Beck Depression Inventory (BDI), Multi-Dimensional Health Assessment Questionnaire (MDHAQ), EuroQol-5 Dimension (EQ-5D), and State-Trait Anxiety Inventory (STAI) on days 5 (end of treatment), 7, 10, and 28. Safety was monitored throughout.

Results

At the end of the treatment period, 0.3 mg ramosetron resulted in a significantly greater reduction of VAS pain scores than placebo (1.18 ± 1.60 vs. 0.54 ± 1.59, $p<0.05$). Furthermore, the 0.3 mg ramosetron group showed significant ($p<0.05$) improvements in the BDI (4.42 ± 5.18 vs. 1.33 ± 4.87) and MDHAQ pain scale (0.37 ± 0.74 vs. 0.04 ± 0.52) scores. However, the improvements in VAS pain and BDI scores did not last until day 28. The safety and tolerability of 0.3 mg ramosetron was good; gastrointestinal tract symptoms, such as constipation, were the most frequently reported adverse events.

Conclusions

Intravenous ramosetron safely and effectively reduced pain intensity in FM patients showing an inadequate response to standard treatment.

Keywords

ramosetron, fibromyalgia, treatment

Workshop

Basic Research Workshop for Rheumatologist

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Osteoclasts in rheumatoid arthritis

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Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease characterized by active synovitis and subsequent joint destruction. Among the various pathologic events occurring in the affected joints, bone destruction is the most clinically relevant feature in RA because it is related to functional impairment, the progression of joint damage and joint disability among patients with RA.

Osteoclasts, which are implicated in the development of bony erosion in RA, are specialized bone-resorbing cells. They are multinucleated giant cells derived monocyte lineage which are originated from hematopoietic stem cells. In RA, osteoclasts are locally differentiated from tissue macrophages or blood and synovial fluid monocytes by inflammatory mediators such as TNF-alpha, IL-17 and RANKL. After differentiation, they take the initiative in invasion of the peri-articular bone at the pannus which is inflammatory synovial tissue interfaces the bone.

The mechanism of osteoclast activation and differentiation in RA has been intensively studied because the blockage of osteoclast produces a new therapeutic option for prevention of joint destruction in RA.

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Experimental methods of osteoclast differentiation

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1. Cell preparation

Osteoclast precursor cells are hematopoietic stem cells (HSCs) and monocyte – macrophage lineage cells. We can obtain osteoclast precursor cells via three ways: 1) human cells, 2) animal cells, 3) cell line. The HSCs usually reside in bone marrow, therefore, extracting HSCs are not usually feasible in human. Therefore, peripheral blood (PB) are usually used as osteoclast precursor cells of human. Ficoll paque method can divide PB into three layer, and among them white layer contains peripheral blood mononuclear cells (PBMCs). After extracting PBMCs, CD14+ magnetic beads are used to isolate monocytes from PBMCs.

In animal models, osteoclast precursor cells are usually obtained from bone marrow of long bones (femur, tibia et al.). After sacrificing animal, long bones are isolated and chopped into small pieces. Then, 25G syringe are used to flush the bone marrow cells from the chopped bones. Amount of PB in small animals (such as mice, rat) are small, therefore isolating monocytes from PB is almost impossible.

The last source of osteoclast precursor cells are by using cell lines such as RAW264.7, and THP-1 cells. RAW264.7 is macrophage cell line, therefore, it could be directly differentiated into osteoclast via stimulation of M-CSF and RANKL. THP-1 is monocyte cell line which was obtained from acute myeloid leukemia patient. Therefore, pre-stimulation with M-CSF for 2-3 days are required to form osteoclast precursor state.

2. Cytokine stimulation

Most important osteoclast stimulating cytokines are macrophage colony-stimulating factor (M-CSF) and receptor activator of nuclear factor kappa-B ligand (RANKL). Both cytokines are primarily produced by adjacent osteoblast, however, nowadays recombinant M-CSF and RANKL are commercially on sale. M-CSF is essential for not only forming osteoclast precursor state, but also on osteoclast maturation and differentiation. After forming osteoclast precursor, then RANKL is required. In specific experimental circumstance, other pro-inflammatory cytokines such as IL-17A, IL-22, TNF-a could use as osteoclastogenesis inducing factors. The exact concentration of M-CSF, RANKL, and pro-inflammatory cytokines should be determined by each experiment environments.

3. Osteoclast differentiation evaluation

Several methods are used to evaluate the amount of osteoclastogenesis. First of all, tartrate resistant acid phosphatase (TRAP) staining is widely used to count the osteoclast. After staining against TRAP, TRAP positive multinucleated cells are the mature osteoclasts. For analyzing function of osteoclast, we can use pit area assay. Using dentine plate, osteoclast can dissolve bone of the plate. Quantifying dissolved area can measure the functional capacity of osteoclasts. Expression levels of osteoclast associated genes can be measured by real-time quantitative polymerase chain reaction. Widely used osteoclast associated genes are cathepsin K, TRAP, NFATc1, RANK, OC-STAMP. However, dominant gene expression can be differed from the different stage of osteoclast (osteoclast precursor, mononuclear osteoclast, multinucleated osteoclast et al.). Therefore, selecting genes should be determined by the experimenter.

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Neuroimmune interactions in chronic pain

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Intractable chronic pain such as neuropathic pain frequently manifests features of neuro-inflammatory disease which involve activation of neuroglial cells such as microglia and astrocytes in the central nervous system (CNS), and inflammatory/immune cells in the peripheral nervous system (PNS). While it is well documented how neuro-glia crosstalks in the spinal dorsal horn contribute to the mechanisms of central sensitization following peripheral nerve injury, functional significance of peripheral neuroimmune interactions remains elusive. My lab has been studying response and functional role of peripheral immune cell in the context of peripheral nerve injury and neuropathic pain from adult mice. In this talk, I will discuss role of natural killer (NK) cells, one of cytotoxic immune cells, in the context of peripheral nerve injury. Our recent work reveals that cytotoxic NK cells infiltrate into the sciatic nerve by extravasation following nerve injury, and NK cells degenerate injured afferents and reduce incidence of long-term pain hypersensitivity. This neuro-immune mechanism of selective NK cell-mediated degeneration of damaged sensory axons provides a therapeutic potential of modulating NK cell function to resolve peripheral neuropathy and chronic pain through the clearance of partially damaged nerves.

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An animal model for studying the neuro-immune mechanism of chronic pain

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Seoul Nat'l Univ., Korea

Peripheral nerves can regenerate after nerve damage by their intrinsic properties and the interplay with immune cells in the peripheral nervous system. Nevertheless, painful symptoms usually persist for more extended periods, which makes them challenging to manage. The research from Prof. Oh's lab first suggested that the remaining damaged axons after nerve injury are the critical pain-provoking factor. Furthermore, enhancing the role of natural killer cells on selective degeneration of damaged axons could attenuate the development of chronic pain. These outstanding results have been obtained by utilizing appropriate research techniques in mice. In this lecture, I will introduce the in vitro technique to visually assess neuro-immune interaction and the novel peripheral nerve injury model (Partial Crush Injury; PCI) that reflects both regeneration and chronic pain. In addition, I will present behavioral assessment techniques of different types of sensory hypersensitivity in the PCI model.

Free Paper Session

International Free Paper Session (Basic)

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Lipidome profile predictive of disease evolution and activity in rheumatoid arthritis

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Background

A variety of lipid mediators are known to be crucial for the pathogenesis of rheumatoid arthritis (RA). To systematically define the lipidome underlying the dynamics of the disease evolution, activation, and resolution of rheumatoid arthritis (RA).

Methods

We performed untargeted lipidomics analysis of synovial fluids and sera from RA patients at different disease activity and clinical phases from pre-clinical phase to active phase and to sustained remission by mass spectrometry. Ultrasonography was performed for affected joints to define synovitis severity at the time of arthrocentesis. Disease activity of RA patients was determined based on disease activity score 28-ESR (DAS28-ESR). Patients with DAS28-ESR>3.2 underwent follow-up blood sampling at 6 months after treatment with anti-rheumatic drugs.

Results

The lipidome profile in RA joint fluid was severely perturbed; correlated with the extent of leukocytosis and the severity of synovitis on ultrasonography. The serum lipidome profile of active RA, albeit less prominent than the synovial lipidome, was also distinguishable from that of RA in the sustained remission phase, and from that of non-inflammatory osteoarthritis. Of note, the serum lipidome profile at the pre-clinical phase of RA closely mimicked that of active RA. Specifically, alterations in a set of lysophosphatidylcholine, phosphatidylcholine, ether-linked phosphatidylethanolamine, and sphingomyelin subclasses correlated with RA activity, reflecting treatment responses to anti-rheumatic drugs when monitored serially.

Conclusions

These results suggest that analysis of lipidome profiles is useful for identifying biomarker candidates that predict the evolution of pre-clinical to definitive RA, and will facilitate the assessment of disease activity and treatment outcomes.

Keywords

Rheumatoid arthritis, lipidomics, disease activity

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IO-11

Anti-TNF-α antibody modified gold nanorods as optical imaging nanoprobes for early diagnosis of rheumatoid arthritis

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Background

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disorder that presents synovial joint inflammation result in joint damage and loss of function. With recent advances in the control and prevention of RA, medical imaging plays an important role in early diagnosis. However, conventional RA diagnosis imaging methods have limitations of no or little difference from healthy and initial inflamed states without visible inflammatory symptom. We investigated the new imaging techniques as diagnosis and clinical management of RA using gold nanorods (GNRs) in collagen-induced arthritis (CIA) mice.

Methods

GNRs were modified protein G firstly and then protein G-GNRs was conjugated with anti-tumor necrosis factor-α (anti-TNF-α) antibody for targeting inflamed regions. To improve stability in physiological conditions, anti-TNF-α conjugated GNRs were functionalized with thiol-terminated methoxy-poly(ethylene glycol). CIA mice were injected intravenously with 100 μg of GNRs. Clinical activity in CIA mice, degree of inflammation, serum cytokine levels, and in vivo NIR absorbance images were evaluated.

Results

CIA mice treated with GNRs showed the near-infrared (NIR) absorbance optical images in early inflamed RA. Especially, anti-TNF-α conjugated GNRs showed the stronger signal in NIR absorbance optical images than anti-TNF-α unconjugated GNRs at 1 week after 2nd immunization without erythema and mild swelling in paws of CIA mice.

Conclusions

We showed the optical image of anti- TNF-α conjugated GNRs relevant to inflammatory status in CIA mice although invisible arthritic symptoms. These results suggests that anti- TNF-α conjugated GNRs could be an imaging contrast for early RA diagnosis.

This study was supported by a grant of the Korean Health Technology R&D Project, Ministry of Health & Welfare, Republic of Korea (HR14C0006).

Keywords

early diagnosis, rheumatoid arthritis, gold nanorods

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DJ-1 control Th17/Treg imbalance, inflammatory response of fibroblast-like synoviocytes, and osteoclastogenesis of rheumatoid arthritis

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Background

DJ-1 is known to suppress osteoclast differentiation, and osteoclast is the main effector cells in joint destruction of rheumatoid arthritis (RA). We aimed to evaluate the effect of DJ-1 on helper T cell differentiation, fibroblast-like synoviocyte (FLS) activation, and osteoclastogenesis of RA.

Methods

Serum and synovial fluid (SF) of patients with RA and OA were collected, and DJ-1 and H2O2 levels were measured by the enzyme-linked immunosorbent assay and ROS Assay Kit, respectively. Peripheral blood mononuclear cells (PBMCs) were cultured under type 17 helper T cell (Th17) polarisation conditions, then CD4+ T cell differentiation, pro-inflammatory cytokines, and soluble receptor activator of nuclear factor kappa-B ligand (RANKL) were measured. RA-FLS was stimulated with H2O2 50 μM and DJ-1 (10, 50, 100 ng/mL) was added to evaluate MMP-9, VEGF, TNF-α, and sRANKL production, and RANKL+ FLS was measured by flow cytometry. Furthermore, monocytes were cultured with RANKL or IL-17A with or without DJ-1, then tartrate-resistant acid phosphatase (TRAP) staining and real-time quantitative polymerase chain reaction of osteoclast-related genes were performed.

Results

DJ-1 levels of serum and SF of RA patients were significantly higher than those of OA patients. In T cell differentiation experiment, CD4+RANKL+ and CD4+IL-17A+ T cell decreased, whereas CD4+CD25highFoxp3+ T cell increased by DJ-1 administration with dose dependent manner. Also, IL-17A, TNF-α, and sRANKL levels of culture media decreased in DJ-1 added groups. DJ-1 lowered MMP-9, VEGF, TNF-α, and sRANKL levels in ROS stimulated RA-FLS culture media. RANKL+ FLS decreased in DJ-1 100 ng/mL. Both in RANKL and IL-17A stimulated osteoclast differentiation, DJ-1 decreased TRAP+ cell count dose dependently, and gene expression levels of TRAP, OC-sTAMP, ATP6v0d2, NFATc1, and cathepsin K were lowered in DJ-1 added condition.

Conclusions

In present study, DJ-1 regulated Th17/Treg imbalance, inflammatory cytokine production, FLS activation, and osteoclastogenesis. These could support the potential of DJ-1 as RA therapy.

Keywords

DJ-1, rheumatoid arthritis, helper T cell

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IO-13

Citrullination inhibits histone-induced chemokine-mediated inflammatory responses

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Background

Histones are cationic DNA-binding proteins released by cells during cell death process, such as NETosis[1]. In this study, we investigated the molecular process of histone-induced cytotoxicity in macrophages, which play essential roles in mediating inflammatory responses[2].

Methods

We used the human monocytic cell line THP-1[3]. We evaluated histone-induced gene expression through RNA-seq analysis of THP-1 cells treated with cytotoxic α1 domain of H2B. We also analyzed RNA-seq data of histone treated THP-1 cells when arginine in H2B-α1 was replaced with citrulline[4].

Results

H2B-α1 peptide treatment changed the gene expression pattern of THP-1 cells. Pathway analysis of 408 differentially expressed genes (DEGs) showed activation of the following pathways: interleukin-1 signalling, nuclear receptor signalling, chemokines, and toll-like receptors. Expression clustering of RNA-seq data revealed that gene expression change induced by native histone was alleviated when the histone was citrullinated.

Conclusions

Citrullination of positively charged arginine of cytotoxic H2B-α1 peptide decreases the histone-induced gene expression of THP-1 cells, which is mainly involved in the chemokine pathway.

Keywords

Histones, Citrullination, RNA-seq

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Baricitinib attenuates autoimmune phenotype and podocyte injury in a murine model of systemic lupus erythematosus

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Background

Baricitinib, a selective inhibitor for janus kinase (JAK) 1 and JAK2, is approved for use in rheumatoid arthritis. Systemic lupus erythematosus (SLE) is recently regarded as a potential candidate targeted by JAK inhibitors because of the relationship between its pathogenesis and JAK/signal transducer and activator of transcription (STAT) pathway-mediated cytokines such as type I interferons. The objective of this study was to determine whether baricitinib could effectively ameliorate SLE using a murine model

Methods

To investigate effects of baricitinib on various autoimmune features, especially renal involvements in SLE, eight-week-old MRL/lpr mice were used as a lupus-prone animal model and treated with baricitinib for eight weeks. Immortalized podocytes and primary podocytes and B cells isolated from C57BL/6 mice were used to determine the in vitro efficacy of baricitinib.

Results

Baricitinib remarkably suppressed lupus-like phenotypes of MRL/lpr mice, such as splenomegaly, lymphadenopathy, proteinuria, and systemic autoimmunity including circulating autoantibodies and pro-inflammatory cytokines. It also modulated immune cell populations and effectively ameliorated renal inflammation, leading to the recovery of the expression of structural proteins in podocytes. According to in vitro experiments, baricitinib treatment could mitigate B cell differentiation and restore disrupted cytoskeletal structures of podocytes under inflammatory stimulation by blocking the JAK/STAT pathway.

Conclusions

The present study demonstrated that baricitinib could effectively attenuate autoimmune features including renal inflammation of lupus-prone mice by suppressing aberrant B cell activation and podocyte abnormalities. Thus, baricitinib as a selective JAK inhibitor could be a promising therapeutic candidate in the treatment of SLE.

Keywords

Systemic lupus erythematosus, Baricitinib, Podocytes

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IO-15

Circulating and renal fibrocytes are associated with interstitial fibrosis in lupus nephritis

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Background
Fibrocytes, the extracellular matrix (ECM)-producing cells derived from bone marrow progenitors, contribute to organ fibrosis. We investigated the presence and characteristics of fibrocytes in the peripheral blood and kidney of patients with lupus nephritis (LN), and the association of the abundance of fibrocytes with renal tubular epithelial cells (RTECs) in LN fibrogenesis.

Methods
Fibrocytes were identified with type I collagen (col I), alpha-smooth muscle actin (α-SMA), CD34, and CD45 using flow cytometry and confocal imaging. The associations between the levels of fibrocytes and pathologic features of patients with LN were analyzed. The contribution of RTECs in the fibrocyte generation was determined using LN sera-treated HK-2 cells.

Results
Spindle-shaped fibrocytes (colI+α-SMA+CD34+CD45+ cells) were present in the peripheral blood and their abundance was especially high in LN patients with interstitial fibrosis compared with healthy control. Renal fibrocytes (colI+α-SMA+CD45+ cells) were found in the tubulointerstitium in patients with LN, and their numbers were significantly associated with the degrees of chronicity indices including interstitial fibrosis and renal dysfunction. Stimulation of peripheral blood mononuclear cells with supernatants from LN sera treated HK-2 cells led to a significant generation of fibrocytes, which was abrogated by the addition of IL-6 neutralizing antibody.

Conclusions
Fibrocytes were significantly increased in the blood and kidney tissue of patients with LN, especially those with interstitial fibrosis. Fibrocytes could be differentiated from blood cells, with an active contribution from RTECs. Our results show that fibrocytes can contribute to tubulointerstitial fibrosis and may serve as a novel therapeutic target for LN fibrogenesis.

Keywords
lupus nephritis, fibrocyte, renal tubular epithelial cell

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Renin-Angiotensin system is involved in the differentiation of osteoclasts and osteoblasts in spondyloarthritis

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Background

The renin angiotensin system (RAS) was classically viewed as an endocrine system that regulates blood pressure and electrolyte balance. The recently emerged concept of tissue RAS, combined with the discovery of new RAS components, provides a broader outlook on the physiologic and pathologic relevance on chronic inflammatory diseases. Spondyloarthritis (SpA) is a disease with chronic inflammation and abnormal bone formation. Herein, we sought to determine the role of RAS and its components in the pathogenesis of SpA.

Methods

SKG mice were injected with curdlan to make in vivo models of SpA. Osteoclasts (OCs) and osteoblasts (OBs) were differentiated in culture systems. Peripheral blood monocytes (PBMCs) and osteoprogenitor cells were collected from control subjects and axial SpA patients (axSpA). The effects of angiotensin II receptor blocker (ARB), angiotensin-converting enzyme inhibitor (ACEi), and various components of RAS were tested in in vivo, in vitro, and human samples.

Results

In vitro, OC and OB differentiation were promoted by angiotensin II and prohibited by ARB. Unexpectedly, ACEi promoted OC and OB differentiation. The promoting effect of angiotensin II disappeared when ACE2i, which inhibits the conversion of angiotensin II into angiotensin (1-7), was administered together. Inhibitors of neprilysin, an enzyme that converts angiotensin I to angiotensin (1-7), also blocked OC and OB differentiation. In vivo, ARB and ACEi did not significantly change the arthritis morphology score. However, colitis score was reduced by ARB while increased by ACEi. Erosion and new bone formation were reduced by ARB while aggravated by ACEi. In human samples, RAS was upregulated in the PBMC of axSpA compared with control subjects. ARB inhibited OB differentiation from osteoprogenitor cells in control subjects and axSpA.

Conclusions

RAS is involved in the differentiation of OCs and OBs in spondyloarthritis, and may serve as a novel therapeutic target.

Keywords

Renin-Angiotensin system, Osteoclast and osteoblast, Spondyloarthritis

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IO-17

Desiccating stress triggers conjunctival monocyte to macrophage cascade – Implications for Sjögren Syndrome keratoconjunctivitis

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Background

Lacrimal gland secretory dysfunction in Sjögren syndrome (SS) causes ocular surface desiccation that is associated with increased cytokine expression and number of antigen-presenting cells (APCs) in the conjunctiva. This study evaluated the hypothesis that desiccating stress (DS) alters the percentage and gene expression of myeloid cells in the conjunctiva.

Methods

DS was induced by suppression of tear secretion and exposure to drafty low humidity environment. Bone marrow chimeras and adoptive transfer were used to track DS-induced myeloid cell recruitment to the conjunctiva. Flow cytometry evaluated myeloid cell populations in conjunctivae obtained from non-stressed eyes and those exposed to DS for 5 days. NanoString immune arrays were performed on sorted cell populations

Results

DS significantly increased the recruitment of adoptively transferred MHCII positive and negative myeloid cells to the conjunctiva in a CCR2 dependent fashion. The percentage of resident conjunctival monocytes (Ly6C+CD64-) significantly decreased while CD64+MHCII+ macrophages increased over 5 days of DS ($P < 0.05$ for both). Comparison of gene expression between the MHCII- monocyte and MHCII+ populations in non-stressed conjunctiva revealed a >2 log2 fold increase in 95 genes and decrease in 46 genes. Upregulated genes are associated with antigen presentation, cytokine/chemokine, M1 macrophage and NLRP3 inflammasome pathways. DS increased innate inflammatory genes in monocytes and MHCII+ cells and increased M1 macrophage (Trem1, Ido1, Il12b, Stat5b) and decreased homeostasis (Mertk) and M2 macrophage (Arg1) genes in MHCII+cells.

Conclusions

There are myeloid cell populations in the conjunctiva with distinct phenotype and gene expression patterns. DS recruits myeloid cells from the blood and significantly changes their phenotype in the conjunctiva. Immature monocytes in the unstressed conjunctiva appear to cascade to MHCII+ macrophages during DS, suggesting that DS promotes maturation of monocytes to antigen presenting cells with increased expression of inflammatory genes that may contribute to keratoconjunctivitis sicca in SS.

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Defective efferocytosis in Sjögren's syndrome is mediated by dysfunctional Mer tyrosine kinase receptor

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Background

Objectives: Sjögren's syndrome (SjS) is a chronic autoimmune disease primarily involving the exocrine glands where the involvement of the innate immune system is largely uncharacterized. Mer signaling has been found to be protective in several autoimmune diseases but remains unstudied in SjS. Here, we investigated the role of Mer signaling in SjS.

Methods

Methods: Mer knockout (MerKO) mice were examined for SjS disease criteria. SjS-susceptible (SjSs) C57BL/6.NOD-Aec1Aec2 mice were assessed for defective Mer signaling outcomes, soluble Mer (sMer) levels, A disintegrin and metalloprotease 17 (ADAM17) activity, and Rac1 activation. In addition, SjS patient plasma samples were evaluated for sMer levels via ELISA, and sMer levels were correlated to disease manifestations.

Results

Results: MerKO mice developed submandibular gland (SMG) lymphocytic infiltrates, SMG apoptotic cells, autoantibodies, and reduced saliva flow. Mer signaling outcomes were observed to be diminished in SjSs mice as evidenced by reduced Rac1 activation in SjSs mouse macrophages in response to apoptotic cells and impaired efferocytosis. Increased sMer was also detected in SjSs mouse sera, coinciding with higher ADAM17 activity, the enzyme responsible for cleavage and inactivation of Mer. sMer levels were elevated in patient plasma and positively correlated with focus score, ocular staining scores, rheumatoid factor, and anti-Ro60 levels.

Conclusions

Conclusions: Our data indicate that Mer plays a protective role in SjS, similar to other autoimmune diseases. Furthermore, we suggest a series of events where enhanced TACE activity increases Mer inactivation, depresses Mer signaling, thus removing protection against the loss of self-tolerance and onset of autoimmune disease in SjSs mice.

Keywords

Sjögrens syndrome, Macrophage, Efferocytosis

Workshop

Clinical Research Workshop for Rheumatologists : Practical 'Hands-on' Statistical Analysis

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Cross-sectional data analysis

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Cross-sectional study, also known as cross-sectional analysis or transverse study, is a type of observational research method that analyzes data from a population at a specific point in time (or over a short period of time). This study type is mainly used to assess the prevalence of a disease, understand determinants of health, describe features of a population. The cross-sectional study contrasts with longitudinal studies such cohort studies in that exposures and outcomes are measured at the same time, making it relatively difficult to establish a causal relationships.

This research is usually conducted through data collection through questionnaires or interviews with participants, and the previously collected data can be utilized. An example of available data sources suitable for cross-sectional studies is the Korea National Health and Nutrition Examination Survey (KNHANES).

Cross-sectional study has advantages that it is usually inexpensive, quick and easy to conduct. Therefore, it is useful for generating hypotheses or establishing preliminary evidence for future research. It can also be the best way to determine the prevalence and can study the associations between multiple outcomes and exposures. However, cross-sectional studies have limitations in that the incidence rate cannot be evaluated, research on rare diseases is difficult, and it is difficult to make a causal inference.

Cross-sectional studies can be classified into descriptive or analytical. When cross-sectional data is used for analytical purposes of associations between exposures and outcomes, researchers and readers should be careful not to make causal inferences, unless the exposure may safely be assumed to be stable over time and not influenced by the outcome.

In this lecture, the characteristics, strengths and weaknesses, methodological issues, and some research cases of cross-sectional studies will be reviewed.

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Survival analysis for beginners

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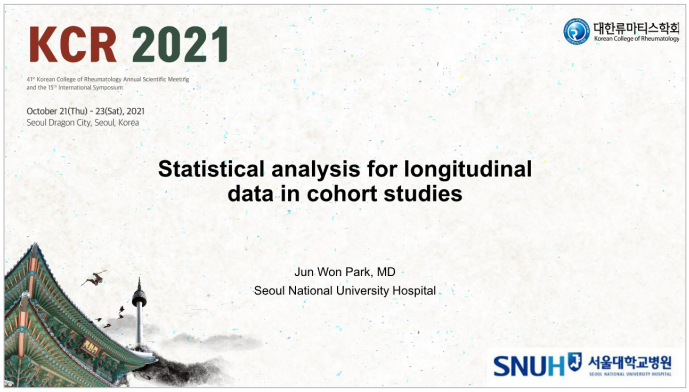
Survival analysis corresponds to a set of statistical approaches for data analysis where the outcome variable of interest is time until an event occurs. For example, when death is the event of interest, it estimates the survival time from the time an object begins to be observed to death. The objectives of survival analysis include the analysis of patterns of event times, the comparison of distributions of survival times in different groups of individuals, and examining whether and by how much some factors affect the risk of an event of interest. In this session, we demonstrate how to perform and visualize survival analyses using statistical packages.

The two most important measures when performing survival analysis are “time” and an “event”. Here, “time” is relative time, calculated as zero from the time researchers start observation. An “event” is an object to be analyzed through survival analysis, for example, death, admission, childbirth, and cessation of certain drugs. In the survival analysis, an event occurs only once, usually coded by 0 and 1. “Censoring” occurs if the event of interest has not been observed with the study time period.

A survival function calculates the probability that an event occurs or does not occur later than a given reference time. The estimation method of survival functions can be divided into the univariate and multivariate estimation. The Kaplan-Meier estimation method is a representative univariate estimation, nonparametric method of calculating the probability of an event occurring at each point, and estimates cumulative survival probabilities using the values generated by accumulating events at each point. The representative multivariate estimation of the survival function is the Cox proportional hazard model. This model is a combination of survival functions and covariates that affect the occurrence of events.

Statistical analysis for longitudinal data in cohort studies

Jun Won Park
Seoul Nat'l Univ



강의의 주요 목표

1. 고전적인 회귀분석의 전제 조건에 대해 이해한다
2. (Real world) longitudinal data 에 고전적인 통계분석을 적용하기 어려운 이유를 이해한다.
3. GEE 와 mixed model 의 차이를 파악한다

Index

1. Longitudinal data in real-world study
2. Generalized estimating equation (GEE) & Mixed model
3. A brief example

Longitudinal data

- 실제 임상 연구에서 가장 많이 수집하는 데이터 형태
  - ✓ 한 참가자에게서 **시간에 따른 반복적인** 데이터 수집
  - ✓ 전향적 / 후향적 코호트 연구

BSRBR
The British Society for Rheumatology Biologics Registers Rheumatoid Arthritis

RHEUMATOLOGY
Review
DANBIO—powerful research database and electronic patient record
Merete Lund Hetland[1,2]

Longitudinal data 를 이용한 연구의 강점

- 장기간의 추적관찰을 필요로 하는 연구에 적합
  - ✓ 장기간 스테로이드 사용에 따른 감염의 위험
  - ✓ 생물학적제제와 암 발생의 연관
  - ✓ TNFi 가 강직척추염의 방사선적 진행에 미치는 영향
  - ✓ 흡연 여부에 따른 질병 활성도의 시간에 따른 변화

클라이언트가 원하는 결과물

클라이언트가 받아 볼 결과물

1. Longitudinal data in real-world study

(Real world) Longitudinal data 의 문제점

- **자료 수집에서의 고려 사항**
  1. **Missing data**
  2. **균일하지 않은 측정 (추적관찰) 간격**
- 통계적인 관점에서 고려 사항
  1. Correlation
  2. Heterogeneous variability : Variance of response changes over time.

1. Longitudinal data in real-world study

Balanced vs. Unbalanced data

Balanced panel

Person Sl No	Year	Income	Age	Sex
1	2004	800	45	1
1	2005	900	46	1
1	2006	1000	47	1
2	2004	1500	29	2
2	2005	2000	30	2
2	2006	2500	31	2

Unbalanced Panel

Person Sl No	Year	Income	Age	Sex
1	2005	1750	32	1
1	2006	2500	33	1
2	2004	2000	40	2
2	2005	2500	41	2
2	2006	2800	42	2
3	2006	2500	28	2

Mistimed measurement
- Removed from rm-ANOVA

Online at https://mpra.ub.uni-muenchen.de/76869/

1. Longitudinal data in real-world study

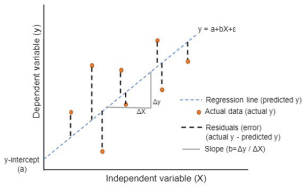
(Real world) Longitudinal data 의 문제점

- 자료 수집에서의 고려 사항
  1. Missing data
  2. 균일하지 않은 측정 (추적관찰) 간격
- **통계적인 관점에서 고려 사항**
  1. **Correlation among observations**
  2. **Heterogeneous variability : Variance of response changes over time.**

1. Longitudinal data in real-world study

고전적인 통계 분석 (Linear regression) 의 기본 전제

1. 선형성: 독립변수 (x) 와 종속변수 (y) 는 선형 관계에 있다.
2. 오차항의 정규성: 모든 독립변수의 값에서 종속변수는 정규분포를 이룬다.
3. 오차항의 독립성: 개별 잔차 (residual) 는 서로 독립이다.
4. 오차항의 등분산성: 모든 독립변수의 값에서 종속변수의 분산은 같다.



1. Longitudinal data in real-world study

(Real world) Longitudinal data 의 문제점

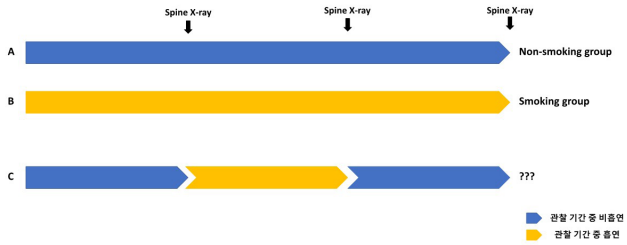
- **통계적인 관점에서 고려 사항**
  1. **Correlation among observations**
     - 각각의 관찰들이 (같은 사람에게서 측정한 것이기 때문에) 연관되어 있다
  2. **Heterogeneous variability : Variance of response changes over time.**
     - 오차가 시간에 따라 동일하지 않다.

각각의 관찰이 독립되어 있지 않고, 오차가 변동을 하기 때문에
t-test, ANOVA, linear regression 분석의 기본 전제를 위배한다

1. Longitudinal data in real-world study

Another problem…

- 흡연이 강직 척추염의 방사선적 진행에 미치는 영향



1. Longitudinal data in real-world study

Summary – Part 1

- Characteristics of real-world longitudinal data
  1. **Unbalanced data**
  2. **Within-subject correlation**
  3. **Time-dependent covariates**

2. GEE & Mixed model

Generalized Estimating Equation (GEE)

- Extension of generalized linear model
  - ✓ 'Generalized' : facilitate regression analysis on dependent variables that are **not normally distributed**
- Population-average or Marginal model
  - ✓ **Average response for observations sharing the same covariates** as a function of the covariates
- Able to consider within-subject correlation
  - ✓ Working matrix of correlation (Correlation structure)

2. GEE & Mixed model

Population average model

- Describe changes in the **population mean** given changes in covariates, **while accounting for 'within-neighborhood' non-independence of observations**
- Not dependent on joint distribution of observed data and random effects

$$\sum_{i=1}^{K} \frac{\partial \mu_i^\top}{\partial \beta} V_i^{-1}(Y_i - \mu_i) = 0.$$

$$V_i = \phi A_i^{1/2} R_i(\alpha) A_i^{1/2}$$

Working covariance matrix of Y_i

Working correlation matrix

2. GEE & Mixed model

Consideration in GEE analysis

1. Specify the link function
2. Distribution of the dependent variable
3. Correlation structure

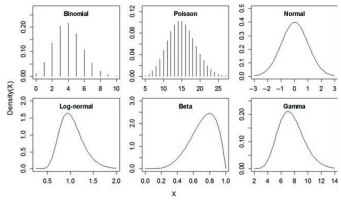
2. GEE & Mixed model

1. Link function

- Allow the dependent variable to be expressed parameter estimate (β)
  - ✓ GLM : Identify link (No transformation) $g(\mu_{ij}) = \mu_{ij}$ "Identity link"
  - ✓ Logistic regression: logit link $g(\mu_{ij}) = \log[\mu_{ij}/(1-\mu_{ij})]$ "Logit link"
  - ✓ Poisson regression : log link $g(\mu_{ij}) = \log(\mu_{ij})$ "Log link"

2. GEE & Mixed model

2. Distribution of the response variable



- **Binary data – binomial**
- **Counted response – Poisson (or negative binomial)**
- **Continuous – Normal or log-normal**

2. GEE & Mixed model

Correlation within response variable (correlation structure)

1. Independence (diagonal)

$$R(\alpha) = \begin{pmatrix} 1 & 0 & \cdots & 0 \\ 0 & 1 & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \cdots & 1 \end{pmatrix}$$

2. Exchangeable

$$R(\alpha) = \begin{pmatrix} 1 & \alpha & \cdots & \alpha \\ \alpha & 1 & \cdots & \alpha \\ \vdots & \vdots & \ddots & \vdots \\ \alpha & \alpha & \cdots & 1 \end{pmatrix}$$

3. Autoregression1 (ar1)

$$R(\alpha) = \begin{pmatrix} 1 & \alpha & \cdots & \alpha^{t-1} \\ \alpha & 1 & \cdots & \alpha^{t-2} \\ \vdots & \vdots & \ddots & \vdots \\ \alpha^{t-1} & \alpha^{t-2} & \cdots & 1 \end{pmatrix}$$

2. GEE & Mixed model

R : geeglm

```
geeglm(
  formula,
  family = gaussian,
  data = parent.frame(),
  weights,
  subset,
  na.action,
  start = NULL,
  etastart,
  mustart,
  offset,
  control = geese.control(...),
  method = "glm.fit",
  contrasts = NULL,
  id,
  waves = NULL,
  zcor = NULL,
  corstr = "independence",
  scale.fix = FALSE,
  scale.value = 1,
  std.err = "san.se",
  ...
)
```

Family	Default Link Function
binomial	(link = "logit")
gaussian	(link = "identity")
Gamma	(link = "inverse")
inverse.gaussian	(link = "1/mu^2")
poisson	(link = "log")
quasi	(link = "identity", variance = "constant")
quasibinomial	(link = "logit")
quasipoisson	(link = "log")

```
gee01 <- geeglm (Weight ~ Time + Cu , id =Pig, data = dietox,
                 family=gaussian,corstr="ex")
```

2. GEE & Mixed model

Mixed (effect) model

- Basic assumption
  - ✓ Individuals in the population are assumed to have their **'own' subject-specific** response trajectories

$$E(Y_{ij} \mid X_{ij}, \alpha_j) = g[\mu(X_{ij} \mid \beta) + U_{ij}(\alpha_j, X_{ij})]$$

Fixed effect

Random effect

Link function

Neighborhood random effect

Coefficient of fixed effect

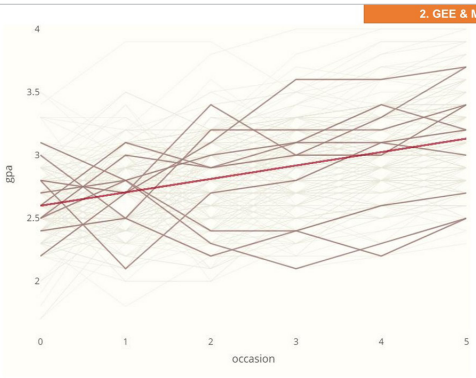
2. GEE & Mixed model

Mixed model in the longitudinal data

student	occas	gpa	job	sex	highgpa	admitted	year	ses
1	year 1 semester 1	2.3	2 hours	female	2.8	yes	1	1
1	year 1 semester 2	2.1	2 hours	female	2.8	yes	1	2
1	year 2 semester 1	3	2 hours	female	2.8	yes	2	1
1	year 2 semester 2	3	2 hours	female	2.8	yes	2	2
1	year 3 semester 1	3	2 hours	female	2.8	yes	3	1
1	year 3 semester 2	3.3	2 hours	female	2.8	yes	3	2
2	year 1 semester 1	2.2	2 hours	male	2.5	no	1	1
2	year 1 semester 2	2.5	3 hours	male	2.5	no	1	2
2	year 2 semester 1	2.6	2 hours	male	2.5	no	2	1
2	year 2 semester 2	2.6	2 hours	male	2.5	no	2	2

Question : 시간이 지날수록 GPA score 가 어떻게 변화하는가?

2. GEE & Mixed model



2. GEE & Mixed model

Mixed model in the longitudinal data

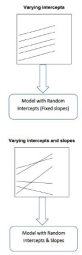
- Standard (linear) regression

$$\text{gpa} = b_{\text{intercept}} + b_{\text{occ}} \cdot \text{occasion} + \epsilon \qquad \epsilon \sim \mathcal{N}(0, \sigma)$$

- (Linear) mixed model : random effect in intercept and/or slope

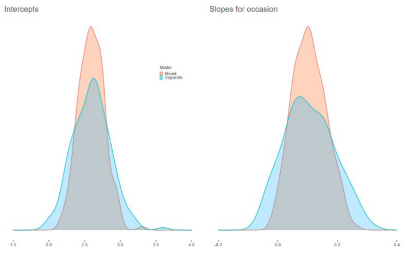
$$\text{gpa} = b_{\text{intercept}} + b_{\text{occ}} \cdot \text{occasion} + (\text{effect}_{\text{student}} + \epsilon) \qquad \text{effect}_{\text{student}} \sim \mathcal{N}(0, \tau)$$

$$\text{gpa} = b_{\text{int\_student}} + b_{\text{occ}} \cdot \text{occasion} + \epsilon \qquad b_{\text{int\_student}} \sim \mathcal{N}(b_{\text{intercept}}, \tau)$$



2. GEE & Mixed model

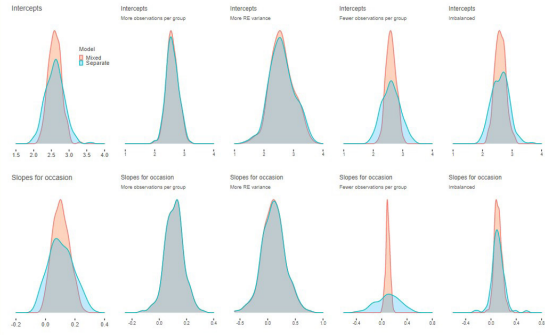
Regulating effect of mixed model



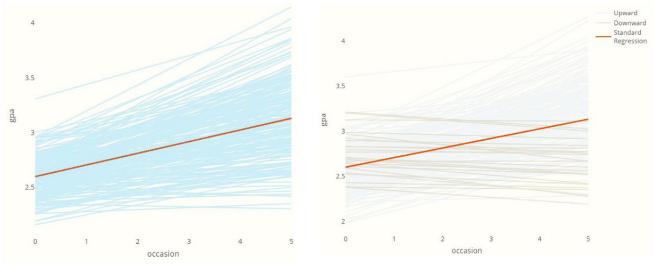
'Shrinkage' in the mixed model

- Cluster-specific effect (fixed effect) are shrunk toward the population-average effect as the imposed normal distribution for the random effects makes the extreme value less probable

2. GEE & Mixed model



2. GEE & Mixed model



2. GEE & Mixed model

R : lmer (linear), glmmTMB (generalized)

```
fm1 <- lmer(Reaction ~ Days + (Days | Subject), sleepstudy))
```

```
## Binomial model
data(cbpp, package="lme4")
(bovine <- glmmTMB(cbind(incidence, size-incidence) ~ period + (1|herd),
  family=binomial, data=cbpp))
```

```
lmer(formula, data = NULL, REML = TRUE, control = lmerControl(),
    start = NULL, verbose = 0L, subset, weights, na.action,
    offset, contrasts = NULL, devFunOnly = FALSE)
```

```
glmmTMB(
  formula,
  data = NULL,
  family = gaussian(),
  ziformula = ~0,
  dispformula = ~1,
  weights = NULL,
  offset = NULL,
  contrasts = NULL,
  na.action = na.fail,
  se = TRUE,
  verbose = FALSE,
  doFit = TRUE,
  control = glmmTMBControl(),
  REML = FALSE,
  start = NULL,
  map = NULL
)
```

2. GEE & Mixed model

Linear mixed model vs. non-linear mixed model

- In linear and log-linear mixed model, the regression coefficient can be interpreted as either coefficients of the conditional mean of Yij or as coefficients of the population average association of Y_{ij} and X_{ij} : E (Y_{ij} | X_{ij}).

$$E(Y_{ij} \mid X_{ij}, \alpha_j) = g[\mu(X \mid \alpha, \quad ,$$

- In the logistic regression model, the coefficients are **not equivalent** in the random-effects and population-average models.

$$L(Y_{ij} \mid X_{ij}) = \int_{-\infty}^{+\infty}\int_{-\infty}^{+\infty} P(Y_{ij} \mid X_{ij}, \alpha_{0j}, \alpha_{1j}) h(\alpha_{0j}, \alpha_{1j}) d\alpha_{0j}\, d\alpha_{1j}$$

The random effect model for the density is nonparametrically non-identifiable.

✓ Estimate of β depends on assumptions about the distribution of the random effects

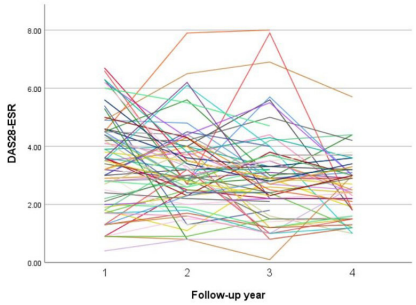
2. GEE & Mixed model

GEE vs. mixed model

	Mixed model	GEE
Focus of interest	Variance component + Regression coefficient	Regression coefficient
Parameter interpretation	Neighborhood (subject) specific	Population average
Linear (estimates equivalent)	Change in the mean outcome for a unit change in the associated neighborhood exposure, **keeping the random effect (neighborhood) fixed**	Change in the mean outcome for a unit change in the associated neighborhood exposure **across all of the neighborhoods observed**
Binary (estimates not equivalent)	The log(OR) of an outcome for a unit change in the associated neighborhood exposure, keeping the neighborhood fixed. Not identifiable in cross-sectional studies of neighborhoods without additional assumptions on random effects distribution.	The log(OR) of an outcome for a unit change in the in the associated neighborhood exposure across all of the neighborhoods observed
Assumptions	Correctly specified error distribution	No. neighborhoods sufficiently large for robust estimation of standard errors
Pitfalls	SE not robust to model misspecification	With small no. neighborhoods, SE biased

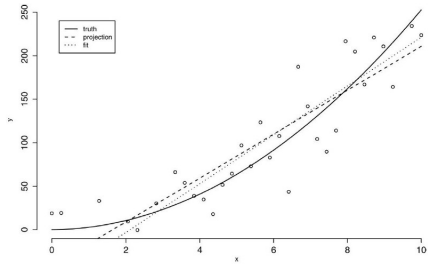
2. GEE & Mixed model

What's the aim of the investigation?



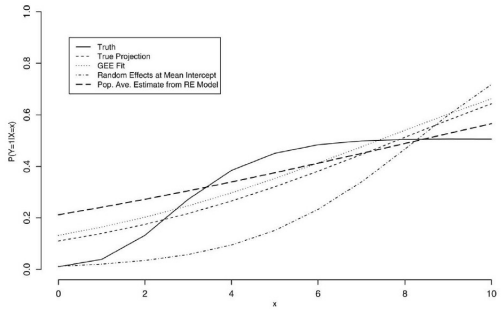
2. GEE & Mixed model

Regression model as projection



2. GEE & Mixed model

Regression model as projection



2. GEE & Mixed model

Summary

1. GEE 의 경우 집단 내에서 covariate 가 보이는 **평균적인 effect size** 를 계산하는 데 중점을 둔다면, mixed model 의 경우 **covariate 가 고정되어 있는 상태 (fixed effect) 에서 집단 내 구성원의 변동량 (random effect) 을 추정**하는 데 중점을 둔다.

2. Linear mixed model 에서 추정되는 coefficient 는 GEE 를 통해 추정된 coefficient 와 거의 동일하다.

3. Non-linear mixed model 와 GEE 에서 추정되는 coefficient 는 상당한 차이를 보일 수 있다.
   - Non-linear mixed model 의 경우 random effect 간 distribution 에 따른 fixed effect 의 변동이 심하다.

3. Brief example

Brief example

- 가설: bDMARD 를 사용하고 있는 RA 환자 중 tocilizumab 을 사용한 환자들은 다른 bDAMRD 를 이용하는 환자들에 비해 DAS28-based disease activity 가 더 낮다.
- DATA name : kcr
  - ✓ N=1017
  - ✓ 1년차~4년차 추적관찰 자료
- Outcome variables
  - ✓ DASE : DAS28-ESR score
  - ✓ DASE_REM : DAS28-remission
  - ✓ TCZ : tocilizumab 을 사용 시 1, 다른 bDMARD 0
  - ✓ FLW : follow-up year (numerical variable)

3. Brief example

Long-form data

NEW_ID	FLW	BMI	AGE_DX	TCZ	DASE
17	1	23.5	43.5	0	3.10
17	2	23.2	43.5	0	1.30
17	3	23.8	43.5	0	1.40
17	4	23.5	43.5	0	1.50
17	5	23.1	43.5	0	2.00
18	1	21.5	45.0	0	4.60
18	2	21.8	45.0	0	4.00
18	3	21.8	45.0	0	5.60
18	4	21.3	45.0	0	1.80
18	5	21.8	45.0	0	2.40
18	6	22.7	45.0	0	2.00
19	1	23.2	19.0	0	3.90
19	2	22.8	19.0	0	2.60
19	3	23.7	19.0	0	4.20
19	4	24.1	19.0	0	4.40
19	5	24.4	19.0	0	3.00
19	6	24.1	19.0	0	3.00
20	1	22.4	21.8	1	3.50
20	2	22.6	21.8	1	3.80
20	3	22.6	21.8	1	0.80
20	4	22.3	21.8	1	1.20
20	5	22.4	21.8	1	1.60
21	1	20.3	42.4	0	3.50
21	2	19.8	42.4	0	3.80

3. Brief example

Brief example

- R package
  - ✓ linear mixed model – lmer
  - ✓ GEE – geeglm
  - ✓ generalized mixed model – glmmTMB

3. Brief example

1. 시간에 따른 DAS28-ESR 의 경향

- 단순 회귀분석

```
# GLM
lm1 = lm(DASE ~ FLW, data=kcr)
summary(lm1)
```

```
Coefficients:
             Estimate Std. Error t value Pr(>|t|)
(Intercept)  3.02078    0.04983   60.63   <2e-16 ***
FLW         -0.00756    0.01646   -0.46     0.65
```

3. Brief example

1. 시간에 따른 DAS28-ESR 의 경향

- Linear mixed model : random effect (intercept, within-subject level)

```
lm1_me = lmer(DASE ~ FLW + (1 | NEW_ID), data=kcr)
summary(lm1_me)
```

```
Random effects:
 Groups   Name        Variance Std.Dev.
 NEW_ID   (Intercept) 1.05     1.02
 Residual             1.05     1.02
Number of obs: 2983, groups:  NEW_ID, 1017

Fixed effects:
            Estimate Std. Error t value
(Intercept)   3.2488     0.0540    60.1
FLW          -0.1283     0.0186    -6.9
```

- V(NEW_ID)/ (V(NEW_ID)+V(residual)
= 1.05 / 1.05+1.05 = 0.5
: Intra-class correlation

```
Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  3.02078    0.04983   60.63   <2e-16 ***
FLW         -0.00756    0.01646   -0.46     0.65
```

3. Brief example

1. 시간에 따른 DAS28-ESR 의 경향

- GEE : within-correlation structure = exchangeable

```
gee1 <- geeglm(DASE ~ FLW, data=kcr, id=NEW_ID,
family=gaussian, corstr="ex")
summary(gee1)
```

```
Coefficients:
            Estimate Std.err   Wald Pr(>|W|)
(Intercept)   3.2479  0.0598 2952.3  < 2e-16 ***
FLW          -0.1277  0.0213   36.1  1.9e-09 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation structure = exchangeable
Estimated Scale Parameters:

            Estimate Std.err
(Intercept)     2.08  0.0786
  Link = identity
```

```
Fixed effects:
            Estimate Std. Error t value
(Intercept)   3.2488     0.0540    60.1
FLW          -0.1283     0.0186    -6.9
```

3. Brief example

1. 시간에 따른 DAS28-ESR 의 경향

- Linear mixed model : random effect (intercept+FLW, within-subject level)

```
lm2 = lmer(DASE ~ FLW + (1+FLW | NEW_ID), data=kcr)
summary(lm2)
```

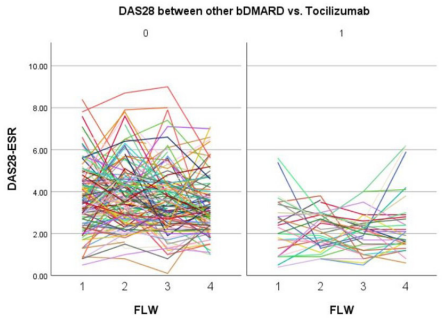
```
Random effects:
 Groups   Name        Variance Std.Dev. Corr
 NEW_ID   (Intercept) 1.908    1.381
          FLW         0.114    0.337   -0.68
 Residual             0.879    0.938
Number of obs: 2983, groups:  NEW_ID, 1017

Fixed effects:
            Estimate Std. Error t value
(Intercept)   3.2450     0.0595   54.58
FLW          -0.1260     0.0210   -6.01
```

```
Fixed effects:
            Estimate Std. Error t value
(Intercept)   3.2488     0.0540    60.1
FLW          -0.1283     0.0186    -6.9
```

3. Brief example

2. TCZ vs. other bDMARD



3. Brief example

2. TCZ vs. other bDMARD – main effect

- GEE : within-correlation structure = exchangeable
  - ✓ Covariate : FLW, TCZ (main effect)

```
g2 <- geeglm(DASE ~ FLW+TCZ, data=kcr, id=NEW_ID,
family=gaussian, corstr="exchangeable")
summary(g2)
```

```
Coefficients:
            Estimate Std.err   Wald Pr(>|W|)
(Intercept)   3.4916  0.0643 2946.6  < 2e-16 ***
FLW          -0.1261  0.0209   36.4  1.6e-09 ***
TCZ          -0.7781  0.0827   88.5  < 2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation structure = exchangeable
Estimated Scale Parameters:

            Estimate Std.err
(Intercept)     1.93  0.0764
  Link = identity
```

시점과 상관없이 TCZ 을 사용할 경우 다른 bDMARD 를 사용하는 환자에 비해 DAS28-ESR 이 0.78점 낮다

3. Brief example

2. TCZ vs. other bDMARD – main effect

- Linear mixed model : random effect (intercept, within-subject level)
  - ✓ Covariate : FLW, TCZ (main effect)

```
lm5 = lmer(DASE ~ FLW + TCZ + (1 | NEW_ID),
data=kcr)
summary(lm5)
```

```
Random effects:
 Groups   Name        Variance Std.Dev.
 NEW_ID   (Intercept) 0.926    0.962
 Residual             1.032    1.016
Number of obs: 2983, groups:  NEW_ID, 1017

Fixed effects:
            Estimate Std. Error t value
(Intercept)   3.4922     0.0569    61.4
FLW          -0.1270     0.0184    -6.9
TCZ          -0.7760     0.0686   -11.3

Correlation of Fixed Effects:
    (Intr) FLW
FLW -0.670
TCZ -0.380 -0.002
```

```
Coefficients:
            Estimate Std.err   Wald Pr(>|W|)
(Intercept)   3.4916  0.0643 2946.6  < 2e-16 ***
FLW          -0.1261  0.0209   36.4  1.6e-09 ***
TCZ          -0.7781  0.0827   88.5  < 2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation structure = exchangeable
Estimated Scale Parameters:

            Estimate Std.err
(Intercept)     1.93  0.0764
  Link = identity
```

3. Brief example

3. TCZ vs. other bDMARD – interaction with FLW

- GEE : within-correlation structure = exchangeable
  - ✓ Covariate : FLW*TCZ

```
g3 <- geeglm(DASE ~ FLW*factor(TCZ), data=kcr,
id=NEW_ID, family=gaussian, corstr="exchangeable")
summary(g3)
```

```
Coefficients:
                Estimate Std.err   Wald Pr(>|W|)
(Intercept)       3.5593  0.0691 2652.67  < 2e-16 ***
FLW              -0.1582  0.0239   43.93  3.4e-11 ***
factor(TCZ)1     -0.9991  0.1226   66.42  3.3e-16 ***
FLW:factor(TCZ)1  0.1044  0.0450    5.38     0.02 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation structure = exchangeable
Estimated Scale Parameters:

            Estimate Std.err
(Intercept)     1.93  0.0766
  Link = identity
```

- Change in DAS28-ESR (/year) in other bDMARD = -0.1582
- Change in DAS28-ESR in TCZ users = -0.1582 + 0.1044
- The interaction is statistically significant

3. Brief example

3. TCZ vs. other bDMARD – interaction with FLW

- Linear mixed model : random effect (intercept, within-subject level)
  - ✓ Covariate : FLW*factor(TCZ)

```
lm6 = lmer(DASE ~ FLW*TCZ + (1 | NEW_ID), data=kcr)
summary(lm6)
```

```
Random effects:
 Groups   Name        Variance Std.Dev.
 NEW_ID   (Intercept) 0.933    0.966
 Residual             1.027    1.013
Number of obs: 2983, groups:  NEW_ID, 1017

Fixed effects:
            Estimate Std. Error t value
(Intercept)   3.5619     0.0627   56.80
FLW          -0.1601     0.0222   -7.20
TCZ          -1.0032     0.1102   -9.10
FLW:TCZ       0.1075     0.0408    2.64

Correlation of Fixed Effects:
       (Intr) FLW    TCZ
FLW    -0.738
TCZ    -0.544  0.440
FLW:TCZ  0.421 -0.563 -0.783
```

```
Coefficients:
                Estimate Std.err   Wald Pr(>|W|)
(Intercept)       3.5593  0.0691 2652.67  < 2e-16 ***
FLW              -0.1582  0.0239   43.93  3.4e-11 ***
factor(TCZ)1     -0.9991  0.1226   66.42  3.3e-16 ***
FLW:factor(TCZ)1  0.1044  0.0450    5.38     0.02 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation structure = exchangeable
Estimated Scale Parameters:

            Estimate Std.err
(Intercept)     1.93  0.0766
  Link = identity
```

3. Brief example

4. TCZ vs. other bDMARD on achieving DAS28-remission

- GEE : within-correlation structure = exchangeable
  - ✓ Covariate : FLW*TCZ

```
g4 <- geeglm(DASE_REM ~ FLW*factor(TCZ), data=kcr,
id=NEW_ID, family=binomial("logit"),
corstr="exchangeable")
summary(g4)
```

```
Coefficients:
                Estimate Std.err   Wald Pr(>|W|)
(Intercept)      -1.0710  0.1041 105.89  < 2e-16 ***
FLW               0.1871  0.0369  25.72 3.9e-07 ***
factor(TCZ)1      1.3450  0.1817  54.82 1.3e-13 ***
FLW:factor(TCZ)1 -0.0890  0.0693   1.65       0.2
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation structure = exchangeable
Estimated Scale Parameters:

            Estimate Std.err
(Intercept)    0.989  0.0166
  Link = identity
```

- Logit link function 을 이용하였기 때문에 exp (beta) 값을 계산 = Odds ratio

```
exp(-0.0890) [1] 0.915
```

- extractOR 함수를 이용하면 편함

```
extractOR(g4, digit=3)
```

```
                    OR   lcl  ucl     p
(Intercept)      0.343 0.279 0.42 0.000
FLW              1.206 1.122 1.30 0.000
factor(TCZ)1     3.838 2.689 5.48 0.000
FLW:factor(TCZ)1 0.915 0.799 1.05 0.199
```

3. Brief example

4. TCZ vs. other bDMARD on achieving DAS28-remission

- glmmTMB : random effect (intercept, within-subject level)
  - ✓ Covariate : FLW*TCZ

```
lm7 = glmmTMB(DASE_REM ~ FLW*TCZ + (1 | NEW_ID),
data=kcr, family = binomial)
summary (lm7)
```

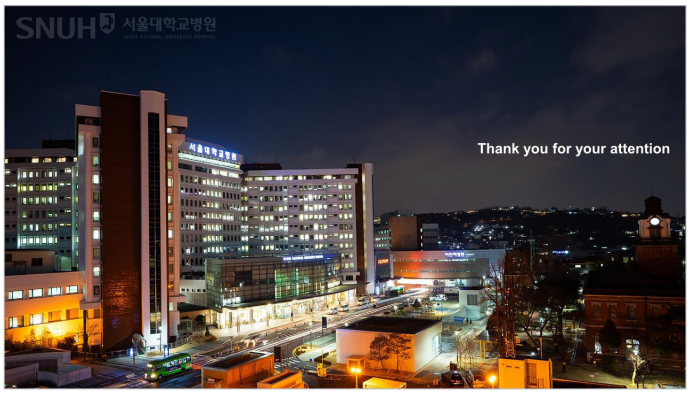
```
Random effects:

Conditional model:
 Groups Name        Variance Std.Dev.
 NEW_ID (Intercept) 4.08     2.02
Number of obs: 2983, groups:  NEW_ID, 1017

Conditional model:
            Estimate Std. Error z value Pr(>|z|)
(Intercept)  -1.8503     0.1794  -10.31  < 2e-16 ***
FLW           0.3145     0.0618    5.09  3.6e-07 ***
TCZ           2.3317     0.2996    7.78  7.1e-15 ***
FLW:TCZ      -0.1554     0.1093   -1.42     0.16

Coefficients:
                Estimate Std.err   Wald Pr(>|W|)
(Intercept)      -1.0710  0.1041 105.89  < 2e-16 ***
FLW               0.1871  0.0369  25.72 3.9e-07 ***
factor(TCZ)1      1.3450  0.1817  54.82 1.3e-13 ***
FLW:factor(TCZ)1 -0.0890  0.0693   1.65       0.2
```

Artist Vincent van Gogh
Year 1889
Catalogue F612 · JH1731
Medium Oil on canvas
Dimensions 73.7 cm × 92.1 cm (28.7 in × 36¼ in)
Location Museum of Modern Art, New York City



Journal of Rheumatic Diseases
Vol. 28, Suppl. 1, October, 2021

Issues of healthcare data de-identification in Korea

Kwang-il Kim
Seoul Nat'l Univ

Workshop

Editorial Committee Workshop

Journal of Rheumatic Diseases
Vol. 28, Suppl. 1, October, 2021

How can the journal be added in SCIE from ESCI

Sun Huh
Hallym Univ., Korea

Journal of Rheumatic Diseases has been searchable from the issues of 2018 in Web of Science Core Collection as an ESCI journal. ESCI journal means that it fulfilled the basic requirement as a scholarly journal. To be listed as an SCIE journal, four criteria will be evaluated. Those criteria are designed to select the most influential journals in a specific field. The first criterion is comparative citation analysis. The minimum level of the impact factor to be considered is at least the 2nd quartile at the corresponding JCR ranking. JCR ranking of 50% of the year 2019 in the rheumatology category corresponds to 3.244 as an impact factor. The second criterion is author citation analysis. However, it is nearly impossible to control the author's citation, for example, h-index. Journal of Rheumatic Diseases is still not an SCIE journal; therefore, it is impossible to select the manuscript from authors with high h-index. The third criterion is an editorial board citation analysis. It is possible to fulfill this criterion by recruiting or inviting researchers with a high h-index. What is the criterion of a high h-index. Although there was no presented one by the Clarivate, it is usually considered as 15. The fourth criterion is content significance. It usually means a uniqueness of the journal's scope or regional focus that can enrich the Web of Science database. The 2nd criterion is challenging. The 4th criterion is unique aims and scope. Therefore, the aims and scope should be differentiated from other SCIE journals in the same category. The 3rd criterion is easy to be resolved because the society members have a high h-index. Furthermore, it is possible to recruit foreign editorial board members with high h-index. The 1st criterion is the essential part out of 4 criteria. It is mandatory to add journals to PubMed Central/PubMed to increase the impact factor and total cites. Journal of Rheumatic Diseases can reapply to PubMed Central on April 3, 2022. The critical comments from the National Library of Medicine PubMed Central Applications Team should be reflected in the journal editing and publishing. Then, it will be able to be indexed in PubMed Central as well as PubMed. After that, the journal's impact factor will increase at least 5 times. The main comment was a variable article quality. Therefore, it is recommended to adopt the reporting guidelines, for example, STROBE for an observational study, CONSORT for randomized controlled study, PRISMA for systemic review and meta-analysis, or CARE for case report. Other issues were appropriate reference citation and the English grammar. Those issues can be overcome by meticulous editing and professional English proofreading. It will be hard work to add a journal to SCIE. However, after adding a journal to PubMed Central, it can be realized through the increase of impact factor.

Writing peer reviews with clarity and politeness

Yunhee Whang
Compecs Inc., Korea

Academic peer review in journal publication is a vitally important process wherein reviewers are invited to provide authors constructive insights into how to improve their work, enabling authors to learn how their scholarly peers assess their research. In order to facilitate this intricate collaboration, reviewers need to present their comments clearly and respectfully. Communicating successfully, however, can be particularly tough for non-native English speaking (NNES) reviewers because of the language barrier. While formal training in writing peer review reports is becoming a popular practice lately, practical language tips on writing with clarity and politeness are still not widely available. The goal of this presentation is to help NNES reviewers (and authors) improve clarity and achieve politeness in their writing.

By examining examples of effective and ineffective reviewer comments, this presentation offers some language tips and introduces various politeness strategies for writing compliments and mitigating criticisms. Writing with clarity is crucial for effective communication between reviewers and authors but challenging to both. Reviewers strive to write their comments clearly so that authors know exactly what the reviewers expect to be revised or clarified. Some tips that could help writers and reviewers improve clarity in their writing include the following: (1) understand information structure, (2) achieve cohesion, and (3) create emphasis appropriately. Effective politeness strategies include (1) avoid the second-person pronoun, (2) use conditionals, (3) present good news and bad news together, and (4) use hedging.

Effective communication between authors and reviewers is very important for improving the quality of a journal. In order to optimize effective communication, it is crucial for NNES reviewers to be clear and polite when writing comments. Offering regular training to reviewers can contribute to improving communication between authors and reviewers.

JRD Journal of Rheumatic Diseases
Vol. 28, Suppl. 1, October, 2021

How to avoid an accidental plagiarism: Paraphrasing

Kwangil Oh
Editage, Korea

Learning objectives:

This session will help you to learn types of plagiarism; how to avoid plagiarism; how plagiarism can be detected; and why citations are important.

Session outline:

The session will deal with how plagiarism is typically defined and how researchers commit plagiarism mistakenly. Learning the types of plagiarism will help you to think of whether your behavior leads to plagiarism in writing a manuscript. In many cases, accidental plagiarism is committed because of an author's ignorance on what is plagiarism. Copy-and-paste without citation will be a typical misbehavior. Through this session, I would like you to have time to reflect your habits in drafting a manuscript. An accidental plagiarism just can happen. This session will also provide practical advice for you to avoid accidental plagiarism with some basic tips for paraphrasing.

Common errors by Korean authors

Kwangil Oh
Editage, Korea

Learning objectives:

This session will help you to learn language mistakes made by Korean authors through actual cases.

Session outline:

Small language mistakes might not be such a great factor as a journal editor reject a manuscript without going through peer-reviewing if the manuscript had been written clearly enough to deliver the author's intended meanings to readers. Still, recurring language mistakes must be annoying to readers and would result in making a negative impression for journal editors and peer reviewers to have a prejudice to the author. Sometimes, editors and reviewers might doubt the author's research findings. This session will deal with language mistakes that journal editors and reviewers commonly consider important, and basic sentence structures and rules with actual cases by Korean authors.

KCR 2021

41st Korean College of
Rheumatology Annual Scientific Meeting
and the 15th International Symposium

October 21(Thu) - 23(Sat), 2021
Seoul Dragon City, Seoul, Korea

DAY 02

PROGRAM

October 22(Fri)

Breakfast Symposium I - Abbvie

Management of Rheumatoid Arthritis

Striving for remission with JAK inhibition in the management of rheumatoid arthritisLecture

Yune-Jung Park
The Catholic Univ. of Korea., Korea

Management of rheumatoid arthritis (RA) has improved over the past few decades resulting in increased rates of remission and better disease control. Remission or low disease activity (LDA) is the treatment target of RA and European Alliance of Associations for Rheumatology/American College of Rheumatology (EULAR/ACR) guidance recommends treatment should be aimed at reaching a target of sustained remission or LDA in every patient.

There is variability in the remission rates reported in the real world. Overall, remission rates are often below 30% in patients with moderate or severe RA, so there are significant unmet needs for effective treatments that lead to sustained clinical remission.

RA imparts a high burden on patients that extends far beyond the signs and symptoms of the disease whereas achieving remission not only can improve outcomes and reduce the burden of patients but also can reduce disease comorbidities and the number of physician visits. For example, achievement of remission in RA can reduce cardiovascular risk and rates of serious infection. Also, in patients with RA with poorly controlled disease, the risk of lymphoma or major orthopedic surgery incidence is increased.

EULAR treatment guidance places Janus kinase (JAK) inhibitors alongside biologic disease-modifying anti-rheumatic drugs (bDMARDs) after failure of conventional synthetic DMRADs (csDMARDs). There are many phase III clinical trials comparing JAK inhibitors to adalimumab (ADA) in patients with RA with an inadequate response to MTX. In ORAL Strategy, the percentages of patients achieving remission, by any definition, were similar for both tofacitinib (TOFA) + methotrexate (MTX) and ADA+MTX and were numerically lower for TOFA monotherapy. In RA-BEAM, BARI + MTX was superior to placebo (PBO)+MTX for ACR20 and BARI + MTX was superior to ADA+MTX for change in DAS28-CRP and ACR20 at week 12. However, no significant differences were observed between BARI+MTX and ADA+MTX for any remission endpoints at week 12, 24 and 52. In SELECT-COMPARE, upadacitinib (UPA) + MTX was superior to PBO + MTX for both primary endpoints at week 12, and UPA + MTX was superior to ADA + MTX for ACR50 and improvement in pain and the Health Assessment Questionnaire Disability Index (HAQ-DI) at week 12. Also, significantly higher percentages of patients achieved remission with UPA + MTX vs ADA + MTX, irrespective of remission definition, at 12, 26, and 48 weeks. Within three JAK inhibitor's individual head-to-head comparisons against ADA+MTX, UPA was the only JAK inhibitor to consistently demonstrate significantly higher rates of remission by all definitions across all time points. UPA is available for the patients with moderate to severe RA and will be the one of the better options for achieving remission.

Breakfast Symposium II - JW Pharmaceutical

IL-6R Inhibition : Transforming People's Lives, for a Future on their Term

JRD Journal of Rheumatic Diseases
Vol. 28, Suppl. 1, October, 2021

Tocilizumab- an effective treatment option for Still's disease

Yeon-Ah Lee
Kyung Hee Univ.

IL-6 has emerged as a pivotal pathway involved in immune regulation in health and dysregulation in various rheumatic diseases, since its discovery in 1973. Tocilizumab (Actemra/RoActemra®) is the first approved a humanized IL-6 receptor-inhibiting monoclonal antibody that binds to both the membrane-bound and soluble form of the IL-6 receptor. Tocilizumab intravenous and subcutaneous formulations are approved in the US and Europe for systemic juvenile idiopathic arthritis (sJIA) and polyarticular juvenile idiopathic arthritis (pJIA) in children two years of age and older. Tocilizumab is also approved for the treatment of adult-onset Still's disease (AOSD), Castleman's disease, and Takayasu arteritis in Japan in addition to the indications mentioned above.

sJIA is the rarest form of JIA and accounts for about 10 percent of JIA cases. sJIA may sometimes be referred to as pediatric Still's disease, which is named after the doctor who first reported it in children in the late 1800s. sJIA is characterized by inflammation in one or more joints, and a daily, spiking fever for at least two weeks, which may be accompanied by a skin rash. Other symptoms may include anemia, enlargement of the liver or spleen, and inflammation of the lining of the heart and/or lungs. When the disease develops after age 16, it's called AOSD. AOSD and sJIA are increasingly considered to be the same disease, with AOSD occurring in adulthood and sJIA in childhood. Still's disease has very heterogeneous spectrum, ranging from benign course to life-threatening complications, such as macrophage activation syndrome (MAS) requiring intensive immune modulation including biologics. In 2005, clinical trials of tocilizumab in patients with sJIA conducted in the UK and Japan provided proof of the efficacy of IL-6 inhibition in this severe pediatric condition. Two subsequent trials of tocilizumab in more than 150 children with sJIA confirmed extensive improvements in the signs and symptoms of disease following treatment with tocilizumab. In a double-blind RCT of 27 patients with AOSD refractory to treatment with glucocorticoids, an ACR50 response at week 4 was achieved in ~61% of patients treated with tocilizumab, compared with ~31% of placebo-treated patients, although the difference was not statistically significant. Tocilizumab group also had improvements in systemic symptoms and a decreased dose of glucocorticoids compared with the placebo group. Based on the data from this trial, tocilizumab was approved for the treatment of AOSD in Japan in 2019. The number of AOSD patients treated with tocilizumab has been increasing with clinical response ranging from 64 % to 100%. Substantial advances have been made in translating the biology of IL-6 to the treatment of patients with autoimmune diseases. Tocilizumab has shown benefit in patients with pediatric and adult Still's disease (sJIA and AOSD) and might also be beneficial in patients with other autoimmune diseases and even beyond.

KCR 2021 | October 21(Thu) - 23(Sat), 2021
Seoul Dragon City, Seoul, Korea

Breakfast Symposium III - Pfizer

Practical Guideline on Rheumatic Disease Management under COVID-19

Is an additional dose of COVID-19 vaccine needed for patients with rheumatic diseases?

Jin Kyun Park
Seoul Nat'l Univ

All available Covid-19 vaccines have markedly decreased the rate and the severity of the Covid-19 infection. Immunocompetent vaccinated individuals rarely developed breakthrough infections and these infections were infrequently severe and/or fatal. Although new rare but severe adverse events such as myocarditis, vaccine-induced thrombocytopenic thrombosis and anaphylaxis have been associated with the Covid-19 vaccines, the benefit clearly outweighs the risk of Covid-19 vaccines.

Since patients with autoimmune inflammatory rheumatic diseases (AIIRD) are at an increased risk for severe COVID-19 infection due to underlying immune dysfunction and treatment-associated immunosuppression, AIIRD patients should be prioritized for vaccination. However, due to the use of immunosuppressants such as methotrexate and rituximab, some patients with AIIRD do not mount a protective vaccine response after primary vaccination and they might not be fully protected against Covid-19. Indeed, the rise in antibody titers after the Covid-19 vaccination were dampened immunosuppressed individuals. To improve or increase the rate of complete immune protection, an additional dose (i.e. a third dose) can be given 4 weeks after the initial 2 doses as a part of "a primary 3-dose vaccination series". Since vaccine-induced immunity wanes over time, the CDC recommends that patients aged 60 years or older receive a booster dose 6 months after the primary vaccination. American College of Rheumatology recommends a third dose of Covid-19 mRNA vaccine for patients with AIIRD at least 28 days of the second dose. The additional dose can function as a compromise of a third dose and a booster dose.

As of now, there is no clinical evidence from clinical trials that shows a clear benefit of a booster in patients with AIIRD. Therefore, a booster dose should be given to patients with AIIRD after careful consideration.

Keynote Lecture

Keynote Lecture of ACR

JRD Journal of Rheumatic Diseases
Vol. 28, Suppl. 1, October, 2021

The future of rheumatology : A message from the ACR president on the occasion of the 40th anniversary of the Korean College of Rheumatology

David R. Karp
American College of Rheumatology, USA

It is my pleasure, as President of the American College of Rheumatology, convey our happiest wishes to you on this, the fortieth anniversary of the founding of the Korean College of Rheumatology. This is a very auspicious year for you. Your leadership, Chairman Kim, President Lee and your Board of Directors have all taken your professional society to the highest level. It is through our societies that the very highest standards of evidence-based patient care can happen. Through our Colleges, our members form a professional network of friends, colleagues, teachers and students that facilitates and promotes a culture of life-long learning and dedication to improving the lives of our patients. Your forty years of excellence as a professional organization is a testament to your strength and the commitment of Korean rheumatologists to their profession.

The rheumatology community is truly a global one. We have national rheumatology societies around the world as well as multi-national organizations including in Europe, Central and South America, Africa, and of course, in the Asia-Pacific regions. Along with the ACR, these organizations work with one another to promote the global exchange of knowledge at our annual meetings. These groups provide a forum for collaborations in research, education and advocacy for patient care. The most amazing example of international research collaboration is the Global Research Alliance or GRA, currently a section of the ACR. This project began in March 2020 and has harnessed the worldwide rheumatology community to study the effects of COVID-19 in patients with rheumatic diseases. Education and training have also become a global effort. Last year, the ACR launched three separate virtual learning programs for fellows in training as well as practicing rheumatologists that have been viewed by thousands of people around the globe. Lastly, the ACR Board of Directors has created the Global Engagement Special Committee. This committee is charged with facilitating the interaction between the ACR and rheumatologists around the world including collaboration on world-wide conferences and seminars, creating international research opportunities, and opening doors for multinational efforts to improve access to rheumatology care. As pandemic restrictions on international travel are relaxed in the future, we look forward to carrying out the plans of our Global Engagement Committee to interact more meaningfully and consistently with rheumatology colleagues around the world.

What does the future hold for the diagnosis and treatment of our patients? There are three themes to follow. The first is the use of registries and big data to both inform the diagnosis and treatment of patients based on national and international trends as well as 'targeted' research that can provide individualized care based on specific genomic, proteomic, and other patient characteristics including social determinants of health. Second, there are novel ways of classifying systemic autoimmune and inflammatory diseases that are based more on molecular pathophysiology and less on historical lessons so that we can develop more rational therapeutic strategies across disease categories. Lastly, it is time for rheumatology to move past describing and treating disease and move confidently to the era where we can accurately screen for diseases like rheumatoid arthritis and lupus and prevent them from happening entirely.

International Symposium

"State-of-the-art" in Systemic Lupus Erythematosus

JRD Journal of Rheumatic Diseases
Vol. 28, Suppl. 1, October, 2021

Recent advances in the treatment of lupus nephritis

Frédéric A. Houssiau
Univ. catholique de Louvain

The current treatment paradigm in lupus nephritis consists of an initial phase aimed at inducing remission and a subsequent remission maintenance phase. With this so-called sequential treatment approach, complete renal response is achieved in a disappointing proportion of 20–30% of the patients within 6–12 months, and 5–20% develop end-stage kidney disease within 10 years. Treat-to-target approaches are detained owing to uncertainty as to whether the target should be determined based on clinical, histopathological, or immunopathological features. Until reliable non-invasive biomarkers exist, tissue-based evaluation remains the gold standard, necessitating repeat kidney biopsies for treatment evaluation and therapeutic decision-making. In this viewpoint, we discuss the pros and cons of voclosporin and belimumab as add-on agents to standard therapy, the first drugs to be licenced for lupus nephritis after recent successful randomised phase III clinical trials. We also discuss the prospect of obinutuzumab and anifrolumab, also on top of standard immunosuppression, currently tested in phase III trials after initial auspicious signals. Undoubtably, the treatment landscape in lupus nephritis is changing, with combination treatment regimens challenging the sequential concept. Meanwhile, the enrichment of the treatment armamentarium shifts the need from lack of therapies to the challenge of how to select the right treatment for the right patient. This has to be addressed in biomarker surveys along with tissue-level mapping of inflammatory phenotypes, which will ultimately lead to person-centred therapeutic approaches. After many years of trial failures, we may now anticipate a heartening future for patients with lupus nephritis.

JRD Journal of Rheumatic Diseases
Vol. 28, Suppl. 1, October, 2021

Molecular mimicry & genetic mechanisms implicate Epstein-Barr virus as the major environmental factor causing systemic lupus erythematosus

John B. Harley
Univ. of Cincinnati (Retired), USA

The discovery that the major autoimmune epitope of Sm B/B' in systemic lupus erythematosus (SLE), PPPGMRPP, was immunologically cross-reactive with PPPGRRP of Epstein-Barr virus (EBV) nuclear antigen-1 (EBNA1), has led to many additional inquiries that have established a strong body of circumstantial evidence making the host response to EBV infection an attractive candidate for the original cause of the autoimmune abnormalities seen in SLE. Cross reactions between anti-EBNA1 antibodies are not only known for Sm B/B', but also for Sm D, 60 kd Ro, and C1q. In three of four of these examples, immunization with the EBNA1 epitope induces cross reacting autoantibodies in animals. The possibility that EBV is fundamentally important for the pathophysiology is reinforced by the association of the DNA sequences immunoprecipitated by anti-EBNA2 with SLE risk loci, which has been independently confirmed by work led by colleagues in Korea and has recently been extended to EBNA3C and EBNALP. All three transcription co-factors, EBNA2, EBNALP, and EBNA3C, are gene products encoded by EBV when the viral genome is expressing the Latency III program of gene expression, which is responsible for transforming B cells. Further, human transcription factors also concentrate at the SLE risk loci. The datasets that show this tendency also have a strong predilection to have been collected in EBV transformed B cells. These results also make the EBV transformed B cell a candidate for the site of mechanistic action for many SLE risk loci that alters the risk for developing SLE.

JRD Journal of Rheumatic Diseases
Vol. 28, Suppl. 1, October, 2021

Clinical and multiomics studies of SLE towards precision medicine

Sang-Cheol Bae
Hanyang Univ., Korea

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder characterized by diverse clinical manifestations with highly variable disease progression. Significant genetic contribution on the liability to SLE was well validated in twin studies and 44~66% of the phenotypic variance of SLE was explained by genetics factors.

For the last decade, large-scale, genome-wide association studies (GWAS) have efficiently scanned human disease genomes to identify the individual SLE loci in multiple ancestral populations, especially in Asian and European populations, bringing the SLE loci to ~180. The associations in majority of the SLE loci were accounted for by common variants with modest effect sizes that explained over 30% of heritability. A large fraction of genetic causes is still missing so that even more active collaborative works and challenging approaches are required to ensure a better detection power for genetic factors (including common low-risk variants and rare high-risk variants) and the epistatic interaction between causes. Along with the effort in the identification of SLE-associated loci, many research groups have actively investigated the potentially causal variants in the associated regions, SLE-relevant immune cell types and signal pathways based on GWAS results with other new omics data and public knowledge/omics databases using appropriate statistical methods.

Beyond SLE susceptibility, SLE is highly heterogeneous in terms of clinical manifestations, prognosis and treatment response including adverse events at an individual level.

This talk will briefly summarize recent advances in our understanding of epidemiologic, genetic, and multi-omics studies of SLE which have revolutionized the landscape of SLE and have brought us closer to precise and molecular diagnosis of the disease. In future, personalized immuno-monitoring & molecular profiling using advanced technology and integrative analysis with clinical data will be required for a more rational use of available treatments, improving patient selection for clinical trials, and the development of novel targeted drugs for precision medicine. In addition, SLE development prediction & prevention will be anticipated. For these approaches, a better coordination among patients, clinicians, clinical and basic scientists is required.

Free Paper Session

Sjögren's Syndrome, Systemic Sclerosis, Inflammatory Myopathies, and Miscellaneous

JRD Journal of Rheumatic Diseases
Vol. 28, Suppl. 1, October, 2021

Glandular and extra-glandular manifestations and effects of hypergammaglobulinemia in primary Sjogren's syndrome: Result from KISS cohort study

Jung Hee Koh[1], Youngjae Park[2], Jennifer Lee[2], Sung-Hwan Park[2], Seung-Ki Kwok[2]

[1] Division of Rheumatology, Department of Internal Medicine, Bucheon St.Mary's hospital, the Catholic university of Korea, Republic of Korea
[2] Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary's hospital, College of Medicine, The Catholic University of Korea, Republic of Korea

Background

Immunoglobulins produced by B cells and plasma cells reflect B-cell hyperactivity. To investigate whether the immunoglobulin level changes over time, and the persistent hypergammaglobulinemia is associated with subsequent glandular and extraglandular damage in patients with Sjogren's syndrome (SS).

Methods

A longitudinal study of primary SS patients in the Korean Initiative of SS cohort was conducted. Immunoglobulin level was measured at baseline and every year. Persistent hypergammaglobulinemia was defined as an increased median immunoglobulin G (IgG) ≥1600 mg/dL over 3 years. Salivary glandular damage was assessed by salivary flow impairment, lacrimal gland damage was assessed by ocular structural abnormalities, and extraglandular damage was determined by solid organ damage. The predictors of glandular and extraglandular damage in the 3-year follow-up were assessed using multivariate logistic regression.

Results

Of 388 patients with SS (median age, 54 years; 99% female), 50% had a high IgG at baseline. During the first two years, IgG level was decreased, and it was associated with baseline age and using hydroxychloroquine, methotrexate, and oral glucocorticoids (Figure 1). IgG levels were correlated with ESSDAI, physician's global assessment, salivary flow rate, white blood cell counts, and hemoglobin level, whereas it was not correlated with patient's reported outcome. Persistent hypergammaglobulinemia was associated with salivary flow impairment (OR, 1.862; 95% CI, 1.050–3.332), and solid organ damage (OR, 3.262; 95% CI, 1.212–8.776) after adjusting age and medication use. Patients who decreased IgG more than -80 mg/dL over 2 years showed less salivary flow impairment and solid organ damage.

Conclusions

IgG levels sightly decreased during the follow-up period and were associated with hydroxychloroquine, methotrexate, and oral glucocorticoid use. Persistent hypergammaglobulinemia was associated with salivary flow impairment and solid organ damage, and decreased IgG level was associated with less organ dysfunction.

Keywords

Immunoglobulin, Sjogren's syndrome, organ dysfunction

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O-02

Validity and reliability of the breath-holding test in systemic sclerosis

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Background

Pulmonary involvement is a major causes of death in systemic sclerosis (SSc). Six-minute-walk test (6MWT) is a standard outcome measure for exercise capacity in cardiopulmonary diseases. However, the results of 6MWT may not reflect real cardiopulmonary function of SSc patients in whom musculoskeletal system is frequently inflicted. This study aimed to evaluate the clinical utility of breath-holding test (BHT) in evaluating cardiopulmonary function in SSc patients.

Methods

Seventy-two patients with SSc were prospectively enrolled and underwent BHT and 6MWT with measurement of Borg dyspnea scale and Scleroderma Health Assessment Questionnaire (SHAQ). Data on pulmonary function test and echocardiography, were also collected. For BHT, participants were repeated three times, with 5-minute intervals. Validity was assessed based on the correlation between the highest value of the BHT time and clinical parameters. To assess the reliability of BHT, additional 32 patients with SSc were collected and underwent BHT twice with maximum 2-week interval.

Results

The BHT time showed a statistically significant correlation with Borg dyspnea scale (pre-test, $r = -0.336$, $p = 0.002$; post-test, $r = -0.252$, $p = 0.034$), DLCO (%, $r = 0.409$, $p < 0.001$) and FVC (liters, $r = 0.402$, $p < 0.001$). We also found a statistically significant correlation between BHT time and SHAQ score ($r = -0.451$, $p < 0.001$). However, EF and PASP showed no significant relationship with BHT time (EF, $r = -0.108$, $p = 0.374$; PASP, $r = -0.246$, $p = 0.054$). BHT showed high reliability ($r=0.897$; intraclass correlation coefficient (2, 1)=0.976, 95% CI=0.95-0.99). Bland-Altman plot also presented good agreement for repeated BHT in SSc.

Conclusions

The BHT, a simple and less time-consuming test, shows excellent reliability and significant correlation with Borg scale, SHAQ, and pulmonary parameters. Our results suggest that the BHT might be a useful surrogate marker of cardiopulmonary capacity in SSc patients.

Keywords

Breath-holding test, 6 minute walk test, Systemic sclerosis

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Scleroderma-like nailfold capillaroscopic abnormalities are common in patients with idiopathic inflammatory myopathies and associated with interstitial lung diseases

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Background

Nailfold videocapillaroscopy (NVC) allows non-invasive assessment of the microvascular abnormalities and may help in early recognition of connective tissue disease. NVC alterations are described in IIM, but available data are discordant. The aim of this study was to describe the NVC abnormalities of IIM and to investigate their association with organ involvement and immunological significance.

Methods

We analyzed 21 consecutive patients with IIM in a cross-sectional study. Clinical features, NVC findings and autoantibody profile by immunoprecipitation and ELISA were compared. NVC findings of 10 DM and 11 PM patients were analyzed. Capillary loss, enlarged or giant capillaries, microhemorrhages, disorganization of the vascular array and ramified capillaries were scored by a semiquantitative rating (0-3, respectively, total 0-18). The presence of MSA and MAA was assessed using the immunoblot .

Results

Among 21 patients with IIM, only 6 patients had Raynaud phenomenon, however, NVC abnormalities with scleroderma (SD)-like pattern were observed in almost IIM patients (18/21, 85.7%). Significant differences were observed between PM and DM with higher mean score of NVC changes (4.6 vs 8.6) and higher frequency of capillary loss (9/10, 90%), enlarged or giant capillary (5/10, 50%) and hemorrhage (7/10, 70%) in DM. Among 18 IIM patients with NVC changes, 13 patients had interstitial lung disease (ILD). Higher mean score of NVC changes was noted in IIM-ILD compared with IIM without ILD (7.18 vs.5.5). Autoantibodies were present in 11/21 patients (52.4%) and anti-Ro52 was the most frequently found. We could not determine NVC specific patterns associated with MSA and MAA subtypes due to limited series of patients.

Conclusions

Our study demonstrates the presence of SD-like microvascular changes detected by NVC in majority of patients with IIM irrespective of Raynaud's phenomenon. IIM-ILD was associated with NVC abnormalities, although further studies are needed to confirm our results and to establish the clinical significance of microangiopathy in IIM.

Keywords

nailfold capillaroscopy, idiopathic inflammatory myopathy, interstitial lung disease

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O-04

Different features of interleukin-37 and interleukin-18 as disease activity markers of adult-onset Still's disease

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Background

The aim of this study was to evaluate the usefulness of serum interleukin (IL)-37 and IL-18 as disease activity markers of adult-onset Still's disease (AOSD) and to compare their related clinical features.

Methods

Forty-five patients with a set of high and subsequent low disease activity status of AOSD were enrolled. Modified Pouchot (mPouchot) score and serologic disease activity markers including levels of IL-37 and IL-18 were compared between high and low disease activity status. The relationships between disease activity parameters and differences in levels of cytokines according to each disease manifestation were evaluated in high disease activity status.

Results

The mean age of study population was 47.1 (±14.0) years. The mean interval between high disease activity status and subsequent low disease activity status was 6.0 (±2.7) months. mPouchot score and all disease activity markers including IL-37 and IL-18 significantly declined after treatment. Though both cytokines positively correlated with mPouchot score, the two did not correlate with each other in high disease activity status. IL-18 positively correlated with ferritin, AST, and LDH while IL-37 correlated better with CRP. The expression level of IL-37 was related to leukocytosis while IL-18 was related to pleuritis, pneumonitis, abnormal LFT, and hyperferritinemia. In addition, patients in the IL-18 dominant group presented with higher LDH levels and required a higher mean corticosteroid dose.

Conclusions

IL-37 can be used as an efficient disease activity marker in AOSD patients. And, it has a distinctive role as disease activity marker and inflammatory modulator in AOSD patients.

Keywords

Adult-Onset Still's Disease, Interleukin-37, Interleukin-18

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Elevated expression of the TLR2 and TLR7 and their correlation with disease activity and clinical manifestations in adult-onset Still's disease

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Background

Adult-onset Still's disease (AOSD) is a rare systemic inflammatory disease manifesting with a typical skin rash, hepatosplenomegaly, persistent high fever, and leukocytosis. Toll-like receptors (TLRs) could potentially play roles in initial acute inflammation of AOSD. We investigated the potential role of several TLRs in adult-onset Still's disease (AOSD).

Methods

The study included 20 AOSD patients and 15 healthy controls (HCs). The TLR were quantified in peripheral blood using flow cytometry. We described the TLR expression pattern in skin lesions and lymph nodes (LNs) of patients with AOSD. TLR1, TLR2, TLR4, TLR7, and TLR9 expression was evaluated immunohistochemically.

Results

Significantly higher mean intensities of cells presenting TLR2 and TLR7 from whole blood were observed in patients with AOSD than in HCs. TLR2 intensities from whole cells correlated with systemic scores and levels of lactate dehydrogenase (LDH) and ferritin. The percentage of TLR2-positive inflammatory cells was higher in skin biopsy samples from AOSD patients than in those from HC ($p = 0.002$). TLR9-expressing positive inflammatory cells was higher in skin lesions from AOSD patients than in those from HCs ($p = 0.001$), eczema ($p = 0.041$), and psoriasis ($p = 0.001$) groups. The expression levels of TLR1, TLR4, TLR7, and TLR9 were higher in LN with AOSD than in those of T cell lymphoma and reactive lymphadenopathy.

Conclusions

Circulating TLR2 and TLR7-positive cells may contribute to the pathogenesis of AOSD. Furthermore, immunohistochemical staining for TLRs in skin lesions and LNs may aid in differentiating AOSD form other mimickers.

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O-06

CCL2 is a useful serum marker for monitoring disease activity in patients with adult-onset Still's disease

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Background

Adult-onset Still's disease (AOSD) is a systemic inflammatory disease resulting from activation of the innate immune system. Chemokine (C-C motif) ligand (CCL) 2 and CC chemokine receptor (CCR) 2, a CCR2 ligand, are chemoattractants.

Methods

This study measured the serum CCL2 and CCR2 concentrations by enzyme-linked immunosorbent assay and analyzed their associations with clinical activity in patients with AOSD.

Results

The serum CCL2 level was significantly increased in AOSD patients (476.41 ± 689.06 pg/mL) compared to rheumatoid arthritis (RA) patients (169.15 ± 118.71 pg/mL, $p = 0.007$) and healthy controls (HC) (135.14 ± 71.66 pg/mL, $p = 0.003$). The serum CCR2 level was also increased in AOSD patients compared to RA patients and HC, but the difference was not significant. The serum CCL2 level was correlated with the systemic score ($r = 0.539$, $p < 0.001$), leukocyte ($r = 0.316$, $p = 0.041$) and neutrophil ($r = 0.316$, $p = 0.041$) counts, and C-reactive protein ($r = 0.321$, $p = 0.044$), ferritin ($r = 0.607$, $p < 0.001$), lactate dehydrogenase ($r = 0.597$, $p < 0.001$), and albumin ($r = -0.428$, $p = 0.005$) levels. After disease resolution, the CCR2 level decreased significantly in patients with AOSD ($p = 0.029$).

Conclusions

CCL2 was elevated in the serum of patients with AOSD in association with disease activity, suggesting a role of CCL2 in the pathogenesis of AOSD.

Keywords

Adult onset Still's disease, CCL2, disease activity

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Change of serum IgG4 level during immunosuppressive therapy as a predictor of relapse in IgG4-related disease

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Background

IgG4-related disease (IgG4-RD) often recur even after a favourable response to immunosuppressive therapy. Serum IgG4 level is one of the diagnostic criteria for IgG4-RD, but their clinical implication for relapse has not yet been fully established. We investigated the predictors of relapse in IgG4-RD, focusing on the serum IgG4 level during immunosuppressive therapy.

Methods

We retrospectively recruited 57 patients with active IgG4-RD and elevated serum IgG4 level in a tertiary hospital between 2011. JAN and 2020. DEC. They were followed up for >6 months after initiation of immunosuppressive therapy. Clinical and laboratory findings, including serum IgG4 levels at baseline and 6 months, were reviewed and compared between relapsed (n = 16) and non-relapsed groups (n = 41). Multivariate Cox regression analysis was used to assess the predictors for relapse. We performed a Kaplan-Meier analysis with a log-rank test to evaluate the cumulative relapse rate for 2 years.

Results

Baseline serum IgG4 levels did not differ between relapsed and non-relapsed group (median, 343 vs. 288 mg/dL, p = 0.129). After 6 months, median serum IgG4 levels were higher in the relapsed group than in the non-relapsed group (176 [IQR, 96–215] vs. 84 [IQR, 47–187] mg/dL, p = 0.020). Serum IgG4 levels were normalized after 6 months in 6 (37.5%) relapsed and 27 (65.9%) non-relapsed patients. Normalized serum IgG4 levels and baseline central nervous system involvement were associated with the relapse, with hazard ratios of 0.243 (p = 0.011) and 16.850 (p = 0.018). In Kaplan-Meier analysis, the total cumulative relapse rate was 40.5% at 24 months (Figure 1). The cumulative relapse rate was lower in the normalized serum IgG4 group at 6 months than in the elevated serum IgG4 group at 6 months (p = 0.013).

Conclusions

Normalized serum IgG4 levels during immunosuppressive therapy predict favourable relapse-free outcome in IgG4-RD.

Keywords

Immunoglobulin G4-Related Disease, Serum IgG4, Recurrence

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O-08

Tocilizumab in adult patients with secondary haemophagocytic lymphohistiocytosis

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Background

Haemophagocytic lymphohistiocytosis (HLH) is a cytokine-driven inflammatory syndrome that leads to devastating multi-organ failure and substantial mortality. Although many studies have reported benefits of tocilizumab in severe forms of inflammatory disease, including HLH at the far end of the spectrum, but its effect remains uncertain [1-4]. In this study, we investigated the efficacy and safety of tocilizumab in secondary HLH (sHLH).

Methods

This retrospective study included patients aged ≥ 18 years and who fulfilled the HLH-2004 criteria for HLH. Included patients were classified into two groups according to the treatment regimen at baseline: tocilizumab (n = 8) versus all other treatments including HLH-2004 protocol (n = 34), chemotherapy (n = 7), glucocorticoid alone (n = 8), and other immunosuppressant (n = 5) (TCZ group vs. control group). The primary outcome was composite outcome (progression or death) at D56. Secondary endpoints included the treatment response at D14, 28, and 56, overall survival at D56, and adverse events within 56 days after the treatment.

Results

A total of 62 patients were analyzed. Baseline characteristics between the two groups were comparable. Until D56, 87.5% (7/8) in the TCZ group and 50% (25/50) in control group expired due to underlying HLH. At D14, 23 (42.6%) patients in control group showed complete or partial response, but no patients in the TCZ group achieved either response. At D56, composite outcome occurred in 87.5% and 56.0% of the TCZ and control group, respectively (P = 0.090) (Figure 1). This result was consistent even after adjusting for age, symptom duration, baseline renal and liver function and baseline fibrinogen level (adjusted OR 11.48 [95% CI 1.01-129.98]). More infectious complications occurred in the TCZ group (IRR 4.24 [95% CI 2.15-8.38]).

Conclusions

In patients with sHLH, tocilizumab was associated with poor outcome and more infectious complications compared to the conventional treatment.

Keywords

Haemophagocytic lymphohistiocytosis, Tocilizumab

Free Paper Session

Epidemiology & Health Services Research

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O-09

Risk of malignancy in Korean patients with rheumatoid arthritis treated with JAK inhibitors : A nationwide population-based study

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Background

In February 2021, the U.S. Food and Drug Administration warned about the increased risk of cancer in patients using tofacitinib. In this study, we aimed to determine the risk of malignancy in Korean patients with rheumatoid arthritis (RA) treated with Janus kinase inhibitors (JAKis) compared with tumor necrosis factor (TNF) inhibitors.

Methods

A retrospective cohort of patients with RA who started their first targeted therapy with JAKi or TNF inhibitor was established using the National Health Insurance Service database between 2015 and 2019, and those with a history of any malignancy in the past 5 years were excluded. They were followed from treatment initiation to the occurrence of malignancy, drug discontinuation with permissible gap of 12 weeks, death, or the end of the study in December 2019. Baseline features of patients were balanced through inverse probability of treatment weighting (IPTW) using propensity score. Cox proportional hazard model with considering death as competing risk was performed to estimate the hazard ratio (HR) for the risk of malignancy in patients who received JAKis compared with TNF inhibitors.

Results

A total of 4929 patients (1064 JAKi-treated and 3865 TNF inhibitor-treated patients) were included, and the observation periods were 1288.6 person-years (PYs) for JAKi users and 6823.8 PYs for TNF inhibitor users. The incidence rates of any malignancy were 0.54 per 100 PYs (95% confidence interval (CI) 0.26–1.14) in JAKi users and 0.85 per 100 PYs (95% CI 0.66–1.10) in TNF inhibitor users. In IPTW analysis with a balanced sample (4075 JAKi-treated and 5172 TNF inhibitor-treated patients), HR was 0.77 (95% CI 0.52–1.13) for all malignancies: 0.70 (95% CI 0.47–1.05) for solid malignancy and 2.95 (95% CI 0.56–15.52) for hematologic malignancy.

Conclusions

There was no increased risk of malignancy in patients with RA treated with JAKis compared with TNF

Keywords

malignancy, rheumatoid arthritis, Janus kinase inhibitor

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Factors for starting JAK inhibitors in patients with rheumatoid arthritis

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Background

The introduction of targeted therapy with Janus kinase inhibitors (JAKis) has led to significant changes in the guidelines for rheumatoid arthritis (RA) treatment. We aimed to identify factors for selecting JAKis in patients with RA who were refractory to conventional synthetic disease-modifying antirheumatic drugs (csDMARDs).

Methods

We selected biologic DMARD (bDMARD)-naïve RA patients between March 2017 and August 2020 from single-center prospective cohorts of RA patients receiving targeted therapy. They were divided into three groups: JAKi, tumor necrosis factor (TNF) inhibitor and non-TNF inhibitor. We performed multinomial logistic regression analysis to identify factors for starting JAKis.

Results

A total of 439 patients with RA were included in the study (mean age 53.1±14.1 years): 145, 205, and 89 patients in the JAKi, TNF inhibitor, and non-TNF inhibitor groups, respectively. In multinomial logistic regression analyses, the JAKi group was less likely to have chronic pulmonary disease compared with the TNF inhibitor group (odds ratio (OR) 0.07, 95% confidence interval (CI) 0.01–0.52) or the non-TNF inhibitor group (OR 0.05, 95% CI 0.01–0.36). Physicians' global assessment was higher in the JAKi group than the TNF inhibitor group (OR 1.89, 95% CI 1.51–2.36) or the non-TNF inhibitor group (OR 1.61, 95% CI 1.01–1.05). In terms of age, JAKi users were older than TNF inhibitor users (OR 1.03, 95% CI 1.01–1.05) but younger than non-TNF inhibitor users (OR 0.97, 95% CI 0.95–1.00). Disease duration of RA was longer in JAKi users than non-TNF inhibitor users (OR 1.05, 95% CI 1.01–1.09). In addition, patients with RA who have used tacrolimus were more likely to start JAKis than TNF inhibitors (OR 2.14, 95% CI 1.27–3.63).

Conclusions

Pulmonary comorbidities, physicians' global assessment, age, and medication history of tacrolimus were influencing factors for selecting JAKis when RA patients started targeted therapy.

Keywords

rheumatoid arthritis, Janus kinase inhibitor, biologic disease-modifying antirheumatic drugs

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O-11

Effect of sarcopenia on comorbidities of rheumatoid arthritis : Results of a nationwide cross-sectional health examination

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Background

To examine the effect of sarcopenia on comorbidities among patients with rheumatoid arthritis (RA).

Methods

We selected RA patients and age- and sex-matched non-RA controls at a 1:5 ratio from the 2008-2011 Korea National Health and Nutrition Examination Survey. Sarcopenia was defined based on appendicular skeletal muscle mass measured by dual energy X-ray assay. We assessed the association between sarcopenia and individual comorbidities among RA patient. To evaluate the interactive effect of RA and sarcopenia, we also compared three stratified subgroups (RA/sarcopenia, RA/non-sarcopenia, non-RA/sarcopenia) to the non-RA/non-sarcopenia subgroup regarding individual comorbidities. The weighted logistic regression analysis was performed to estimate the odds ratios (ORs) and 95% confidence intervals (CIs), adjusting for age, sex, and income.

Results

A total of 400 RA patients and 2,000 age- and sex-matched non-RA controls were included. Sarcopenia was observed in 20.5% of RA and 19.3% of non-RA group. Among RA patients, sarcopenia was associated with obesity (OR 2.61, 95% CI 1.42-4.83), diabetes (OR 2.07, 95% CI 0.99-4.33), dyslipidemia (OR 3.09, 95% CI 1.37-6.98), chronic obstructive pulmonary disease (OR 18.77, 95% CI 2.40-146.55), and hepatitis B infection (OR 8.69, 95%CI 1.15-65.58). The prevalence of these comorbidities, cardiovascular events (myocardial infarction/angina/stroke), and depression were significantly higher with the RA/sarcopenia subgroup but not with the other subgroups, compared to the non-RA/non-sarcopenia subgroup (Figure 1).

Conclusions

In this nation-wide cross-sectional study, sarcopenia was found to associate with cardiovascular, pulmonary, and infectious comorbidities among RA patients. These comorbidities together with depression were significantly more prevalent when RA and sarcopenia were co-present compared to when either RA or sarcopenia was present.

Keywords

rheumatoid arthritis, rheumatoid cachexia, sarcopenia

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Hypouricemia is a risk factor for periodontitis: Data from the Korean national health and nutrition survey (KNHANES) 2016-2018

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Background

Serum uric acid (SUA) levels above or below the normal range are known to be associated with various diseases. We aimed to investigate the relationship between SUA levels and the risk of periodontitis.

Methods

This cross-sectional study used data from the Korean National Health and Nutrition Survey 2016-2018 and analyzed 12,735 Korean adults aged ≥ 19 years who received oral examination. Hypouricemia was defined as SUA < 3 mg/dL in men and < 2 mg/dL in women and hyperuricemia was defined as ≥ 7 mg/dL in men and ≥ 6 mg/dL in women. Sampling weights were applied to represent the general Korean population with minimal bias, and weighted prevalence and weighted odds ratios (ORs) and 95% confidence intervals (CIs) of hypouricemia or hyperuricemia for periodontitis was calculated.

Results

Weighted mean age of study subjects was 51.2 years and 56.2% was female. Weighted prevalence of hypouricemia and hyperuricemia were 0.6% and 12.9%, respectively. The overall weighted periodontitis was 30.5%. Subjects with hypouricemia had a significantly higher age, fasting blood glucose levels and estimated glomerular filtration rate compared with those with normal SUA levels or hyperuricemia. The frequency of periodontitis in subjects with hypouricemia, normal range of SUA, and hyperuricemia were 51.1%, 30.3% and 30.6% respectively. In univariable logistic regression analyses, hypouricemia but not hyperuricemia was associated with the presence of periodontitis. Association between hypouricemia and periodontitis also remained significant in weighted multivariable logistic regression models (Table 1) and full-adjusted model revealed that adjusted OR of hypouricemia with periodontitis was 1.62 (95% CI=1.13-2.33, p=0.037). However, the relationship between hyperuricemia and periodontitis in multivariable logistic regression model was not significant.

Conclusions

Our data suggests that hypouricemia is associated with an increased risk of periodontitis, suggesting that anti-oxidant effect of uric acid may play a role in prevention of periodontitis.

Keywords

Hypouricemia, Hyperuricemia, Periodontitis

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O-14

Clinical and demographic characteristics of patients with rheumatic diseases who underwent COVID-19

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Background

To characterize the clinical and demographic indicators of patients with immunoinflammatory rheumatic diseases (IIRD) who underwent COVID-19, to assess the severity of the course and outcomes of infection in the study group, to identify patterns characteristic of patients with IIRD.

Methods

We studied the material of the Russian database (RIR/ARR-COVID-19), formed on the basis of reports from practicing rheumatologists, which included information about adults (over 18 years old) patients with background IIRD who underwent COVID-19.

Results

Data were obtained on 132 patients (100 women, 75%) aged 51.8±14.4 years, of which 29 (21.9%) were 65 years old and older. IIRZ activity was assessed in 122 patients, incl. high - in 19 (15.7%), moderate - in 43 (35.2%), low - in 43 (35.2%), remission - in 17 (13.9%). Monotherapy with sDMARDs or bDMARDs received 52 patients, combined therapy with sDMARDs in combination with bDMARDs or targeted DMARDs - 19 patients. 55 patients received oral glucocorticoids. The most frequent clinical manifestations of COVID-19 were fever (60.6%), cough (40.2%), anosmia (38.6%), shortness of breath (35.5%). In general, in the study group, a favorable outcome was observed in 113 patients (97.4%). When conducting a correlation analysis, the deterioration in the course of IIRD after suffering COVID-19 was associated with the male sex ($r = 0.22$, $P < 0.05$), a high level of C-reactive protein (>75 mg /l) ($r = 0.2$, $P < 0.05$) and high activity of IIRZ ($r = -0.3$, $P < 0.05$) at the time of development of COVID-19.

Conclusions

In the studied group, the course of COVID-19 was predominantly favorable, despite the presence of signs of clinical and laboratory activity of IIRZ and comorbid conditions. Serious complications were noted in 2.25% of cases. Further research in a larger cohort is needed to study in detail the characteristics of the course of COVID-19 in patients with IIRD.

Keywords

COVID-19, rheumatic disease, bDMARDs

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Prognostic implication of baseline sarcopenia for length of hospital stay and survival in patients with Coronavirus disease 2019

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Background

The impact of sarcopenia on clinical outcomes of coronavirus disease 2019 (COVID-19) is not clearly determined yet. We aimed to investigate the association between baseline sarcopenia and clinical outcomes in patients with COVID-19.

Methods

All hospitalized adult patients with COVID-19 who had baseline chest computed tomography (CT) scans at a Korean university hospital from February 2020 to May 2020 were included. The main outcome was time from hospital admission to discharge. Death was considered as a competing risk for discharge. Baseline skeletal muscle cross-sectional area at the level of the 12th thoracic vertebra was measured from chest CT scans. The lowest quartile of skeletal muscle index (skeletal muscle cross-sectional area divided by height-squared) was defined as sarcopenia.

Results

Of 121 patients (median age, 62 years; 44 men; 29 sarcopenic), 7 patients died and 86 patients were discharged during the 60-day follow-up. Patients with sarcopenia showed a longer time to discharge (median, 55 vs. 28 days; $p<0.001$) and a higher incidence of death (17.2% vs. 2.2%; $p=0.004$) than those without sarcopenia. Baseline sarcopenia was an independent predictor of delayed hospital discharge (adjusted hazard ratio [aHR], 0.47; 95% CI, 0.23-0.96), but was not independently associated with mortality in patients with COVID-19 (aHR, 3.80; 95% CI, 0.48-30.26). The association between baseline sarcopenia and delayed hospital discharge was consistent in subgroups stratified by age, sex, comorbidities, and severity of COVID-19.

Conclusions

Baseline sarcopenia was independently associated with prolonged hospital stay in patients with COVID-19. Sarcopenia could be a prognostic marker in COVID-19.

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O-16

Effect of hydroxychloroquine pre-exposure on infection with SARSCoV- 2 in rheumatic disease patients: a population-based cohort study

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Background

Early in vitro studies have suggested that hydroxychloroquine (HCQ) is a potentially useful drug against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections. This study was conducted to determine whether HCQ had a preventive effect on coronavirus disease 2019 (COVID-19) in rheumatic disease patients who were taking HCQ.

Methods

We conducted a population-based retrospective cohort study using the records of the Korean Health Insurance Review and Assessment (HIRA) claim records. The clinical data of patients with rheumatoid arthritis (RA) or systemic lupus erythematosus (SLE) who were tested for SARS-CoV-2 were investigated. We compared the attack rate of COVID-19 between those who underwent HCQ therapy within 14 days before the test for SARS-CoV-2 (HCQ users) and HCQ non-users. Data were analysed using logistic regression models, c2, and Student's t-tests.

Results

As of 15th May 2020, 2066 patients with RA or SLE were tested for COVID-19. Among them, 31.4% (649/2066) were treated with HCQ. Most HCQ users (93.7%, 608/649) were taking 200e400 mg/day recommended for the treatment of rheumatic diseases. The attack rate of COVID-19 in the HCQ users (2.3%, 15/649) did not differ from that in the HCQ non-users (2.2%, 31/1417) (p 0.86).

Conclusions

HCQ prophylactic use at a usual dose did not prevent COVID-19 in patients with rheumatic disease.

Keywords

COVID-19, Hydroxychloroquine, rheumatic disease

Luncheon Symposium IV – Lilly

Exploring Baricitinib Experience in Treating RA

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Going beyond : Long-term treatment results with Baricitinib in RA

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Rheumatoid arthritis (RA) is a chronic autoimmune disease that reults in progressive joint damage and multiple comorbidities that may lead to impaired physical function, diminished overall quality of life, and mortality. Long-term treatments that are safe and efficacious are needed to reduce disease symptoms, to prevent irreversible joint damage, and to reduce the burden of disease from comorbidities.

A revolution in the treatment of RA started more than 20 years ago with the introduction of biologic therapies. Novel small molecule JAK inhibitors that are orally administered have challenged the status-quo by providing evidence of superiority to first- (methotrexate, [MTX]) and second-line (adalimumab) standards-of-care through innovative head-to-head clinical trials.

Baricitinib, an oral, selective and reversible Janus kinase (JAK) 1 and 2 inhibitor approved for the treatment of adult patients with moderately to severely active RA, was the first JAK inhibitor to demonstrate superiority to MTX and adalimumab.

This lecture addresses the major clinical studies and long-term outcomes of baricitinib. Baricitinib has demonstrated efficacy and safety in populations that span the clinically relevant patient populations in RA, including patients who are inadequate response (IR) to MTX (RA-BEAM), conventional synthetic DMARDs (RA-BUILD) or biological DMARDs (RA-BEACON). Also, baricitinib showed maintenance of RA control in a single long-term extension (LTE) study (RA-BEYOND).

Efficacy of barcitinib starts to show as early as 1 week and the efficacy tends to maintain overall, including low disease activity (LDA) and remission over the long-term. In addition to its effectiveness as a DMARD, baricitinib has also demonstrated the ability to deliver rapid and robust outcomes in physical function and pain.

The baricitinib safety profile has been characterized with more than 13,000 patient-years of exposure. Baricitinib is well tolerated with treatment experience out to 8.4 years; incidence rates for safety topics of interest in DMARD therapy, including serious infections, major adverse cardiovascular event (MACE), venous thromboembolism (VTE), and malignancy are in-line with incidences observed in the overall RA population and have not increased over time.

Baricitinib may be an effective treatment option to consider for long-term treatment of early-stage and refractory rheumatoid arthritis.

Luncheon Symposium V - BMS Pharmaceutical

Real World Perspectives of Patient Care in Rheumatoid Arthritis

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Improving patient outcomes of rheumatoid arthritis with interstitial lung disease patients

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Rheumatoid arthritis (RA) affects respiratory system including airway, parenchyma, pleura or vasculature (1). Among RA-related lung diseases, interstitial lung disease (ILD) is the most common lung disease contributing to the morbidity and mortality in RA patients (2). Clinical characteristics associated with occurrence of ILD in RA are higher rheumatoid factor and anti-citrullinated protein antibody (ACPA) titers in our study. Airway diseases such as bronchiectasis are also prevalent. Previous studies have shown clear association between RA and lung disease in epidemiological aspects. Increasing number of recent articles dealing with ILD of RA patients reflects growing interest of rheumatologists on this field (3-7).

Lung diseases were usually recognized as one of extra-articular manifestations of RA. However, there are some perspectives that lung plays active role in pathogenesis of RA. For example, autoimmune response with emergence of ACPAs was observed in bronchiectasis patients (8). Relationship between bronchiectasis and RA can be a model of tolerance breakdown induced by chronic bacterial infection. Interstitial lung disease is also regarded as a process of autoimmune reaction because RA patients with ILD have higher titer and broader repertoire of ACPAs than those without ILD (9). As respiratory system is exposed to several environmental agonists such as smoking and microbes, lung can be a first site of inflammation igniting autoimmune reaction. Smoking, a well-known environmental risk factor of RA, increased concentration of peptidylarginine deiminase (PAD) which citrullinates arginine in the lungs (10). Therefore, the lung might be most active site of citrullination and no more innocent victim in pathogenesis of RA.

Therapeutics for RA should be considered as another variable in patients with lung disease. Most generally used disease-modifying antirheumatic drugs (DMARDs), methotrexate (MTX), is suspicious for causal agent of lung disease. According to recent meta-analysis of randomized controlled trials, MTX increased the risk of lung disease significantly compared to other DMARDs and biologic agents (11). But the amount of risk increase was very small (10%) and the scope of lung diseases in this meta-analysis included all adverse respiratory events including infection. On the other hand, results from the other two meta-analysis dealing with risk of lung disease contributed by MTX and leflunomide, showed no increased risk of lung disease in MTX users (6, 12). Although those meta-analysis using randomized controlled trials compass large number of patients, the results have to be interpreted with caution because most clinical trials excluded ILD patients at enrollment. For biologic agents in RA, serious ILD events were reported in anti-tumor necrosis factor (TNF) and they are not commonly used in patients with preexisting ILD or other lung diseases (13). Tocilizumab which is blocking IL-6, tends to be used in RA-ILD patients more

frequently than anti-TNF drugs. However, acute exacerbations of ILD was also reported in tocilizumab users (7). CTLA4 Ig or rituximab treatment might be an option for RA-ILD patients, but there is not enough evidence. As ILD exacerbation may result in fatal event in RA patients, choice of medication and appearance of respiratory events should be tracked thoroughly by both patient and physician.

Diagnosis in early stage is very important to remove definite aggravating factors of RA related lung disease and several genetic and biologic markers are under investigation. Our study showed that older age at the time of the ILD diagnosis and usual interstitial pneumonia (UIP) subtype on high-res¬olution computed tomography were associated with mortality of RA-ILD patients (14). For biomarkers, MMP-7, IP-10/CXCL10, pulmonary and activation-regulated chemokine, and surfactant protein D were increased in RA with ILD patients compared to RA without ILD (15, 16). The most important thing is to have high level of suspicion in patients who complain new or changed respiratory symptom and detect early stage ILD in RA patients, enabling to predict prognosis.

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Insight from real world : Treatment considerations of rheumatoid arthritis in an aging society

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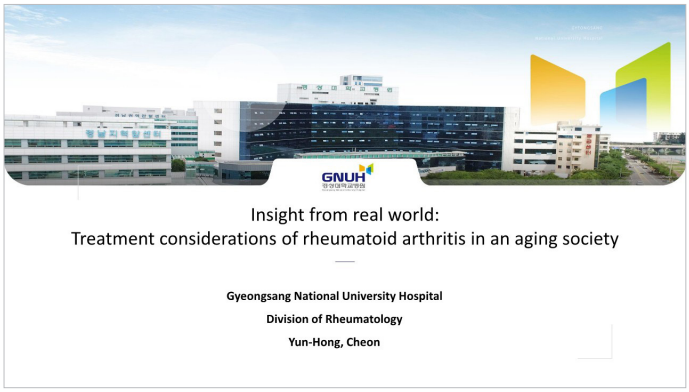
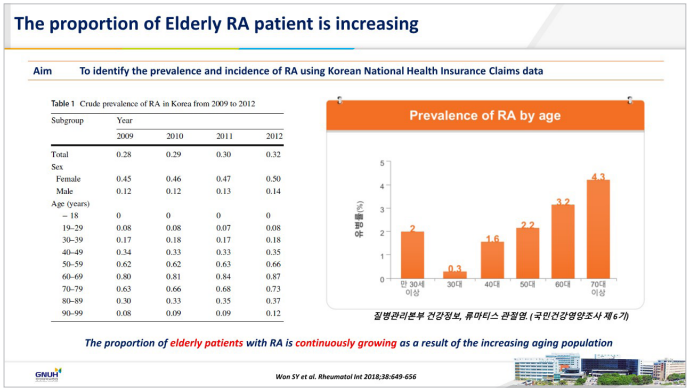
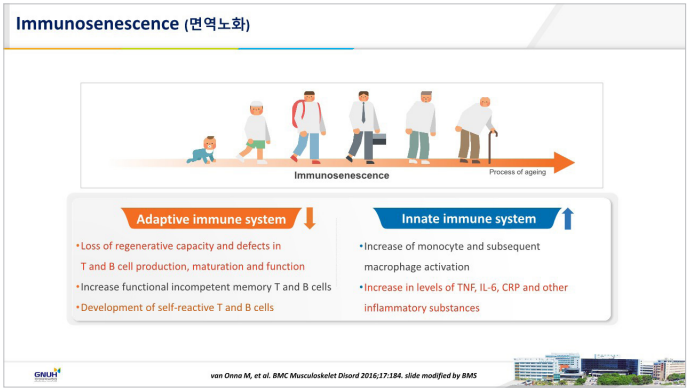
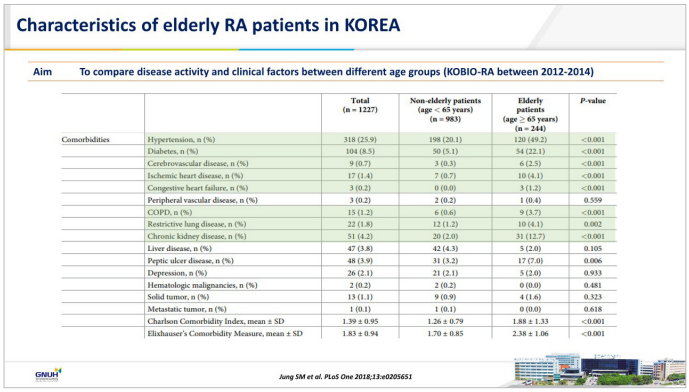
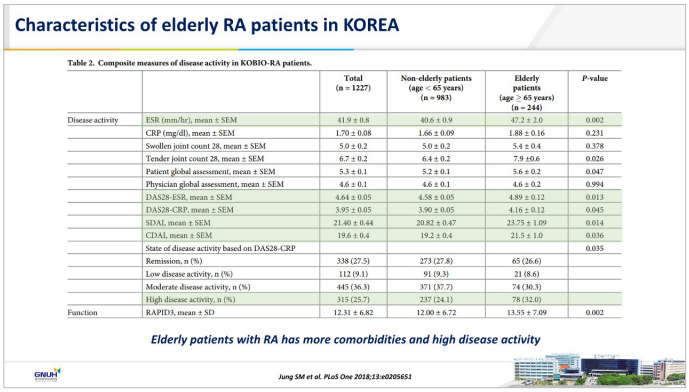










Classification of Elderly RA (YORA, EORA)

Young-onset RA

Elderly onset RA

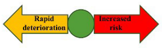
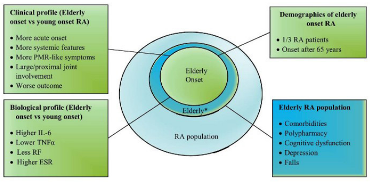


Fig. 1. Clinical approach in elderly RA patients.
Tension often occurs when balancing the likely benefit of treating elderly RA patients with active disease and increased risk of deterioration against the risk of adverse events due to comorbidities.



GNUH

Serhal L et al. Autoimmun Rev 2020;19:102528

Age-stratified treatment trend

Aim To estimate the age-stratified treatment trends in Japan using National Database of Health Insurance Claims

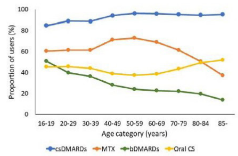


FIGURE 2 The proportion of patients with a prescription of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), methotrexate (MTX), biologic DMARDs (bDMARDs), and oral corticosteroids (CS) in each age category. The x-axis indicates the age category. The y-axis indicates the proportion (%) of patients who received at least 1 prescription of each medication between April 2017 and March 2018

TABLE 3 Medications for rheumatoid arthritis in the overall population and age-stratified groups

		Age-stratified groups								
	All	16-19	20-29	30-39	40-49	50-59	60-69	70-79	80-84	85+
Number	825 772	1626	9293	26 811	73 201	122 602	217 714	236 407	80 583	57 535
csDMARDs use, %[a]	95.0	84.9	88.9	88.7	94.1	96.1	95.8	95.1	94.6	95.2
Methotrexate	63.4	60.4	61.4	61.3	71.5	73.0	69.2	61.4	50.5	38.2
Sulfasalazine	24.9	10.9	18.7	22.5	21.4	22.2	23.0	25.6	30.1	33.9
Tacrolimus	11.9	15.4	16.3	14.3	11.4	10.3	11.1	12.8	13.5	11.8
Bucillamine	14.5	1.5	6.6	8.1	10.3	12.3	14.0	15.3	18.0	22.6
Iguratimod	9.2	3.7	7.3	8.2	9.9	9.9	9.3	9.3	8.9	7.4
bDMARDs use, %[a]	22.9	50.9	39.8	36.2	27.9	24.0	22.6	22.1	19.4	13.7
TNFIs	14.4	29.5	26.1	26.9	19.8	16.2	14.1	12.9	10.8	7.4
IL-6Is	5.7	22.7	13.2	8.8	7.0	6.2	6.1	5.3	4.2	2.7
Abatacept	3.9	1.2	2.1	2.3	2.4	2.8	3.5	5.1	5.5	4.4
Ratio of TNFIs to abatacept use[b]	3.6	24.0	12.3	11.8	8.3	5.8	4.0	2.5	1.9	1.7
Ratio of IL-6Is to abatacept use[b]	1.5	18.4	6.2	3.9	2.9	2.2	1.7	1	0.8	0.6
JAK inhibitors use, %[a]	0.90	–[c]	0.85	0.78	0.98	0.99	1.00	0.97	0.66	0.37
Intra-articular CS injection use, %[a]	11.1	4.7	7.0	8.8	9.8	11.2	10.8	11.6	12.7	12.0
Oral CS use, %[a]	42.1	45.5	45.7	44.0	38.8	37.3	38.7	43.4	49.3	52.0
NSAIDs use, %[a]	62.4	56.0	61.5	64.8	67.1	66.0	61.8	61.0	62.0	56.9
Opioid use, %[a]	7.2	2.6	3.7	4.8	5.4	5.9	5.9	8.2	10.6	10.3

GNUH

Nakajima A et al. Int J Rheum Dis 2020 doi:10.1111/1756-185X.13974

CONTENTS OF TOAST SYMPOSIUM

- Old age (≥65) : : Prevalence, characteristics
- Effectiveness and Persistence in elderly RA patients
- Safety issues

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Effectiveness of abatacept in elderly patients (1)

Aim To study the effect of age on the risk-benefit balance of abatacept in RA from French Orencia and RA registry (ORA)

Subject Patients who *failed or contraindicated to TNF inhibitors*

TABLE 1 Demographic and disease characteristics of RA patients at baseline (n = 1017)

Characteristics	Missing data, n (%)	<50 years, n = 293	50–64 years, n = 406	65–74 years, n = 215	≥75 years, n = 103	P-values (trend[a])
Age, mean (S.D.), years	0 (0)	41 (7.9)	57.3 (4)	70 (2.8)	79.3 (3)	<0.001
Female, n (%)	0 (0)	248 (84.6)	302 (74.4)	170 (79.1)	87 (84.5)	0.65
Disease duration, median (IQR), years	14 (1.4)	14 (10–22)	16 (11–23)	20 (14–29)	19 (11–26)	<0.001
DMARDs, n (%)	14 (1.4)	203 (69.5)	265 (66.3)	130 (61.9)	61 (60.4)	0.04
Corticosteroids, n (%)	18 (1.8)	217 (74.6)	304 (76)	161 (77.8)	77 (76.2)	0.51
Previous treatment with anti-TNF, n (%)	1 (0.1)	268 (91.5)	353 (87)	184 (85.6)	84 (82.4)	0.01
DAS28, mean (s.d.)	165 (16.2)	5.2 (1.3)	5.3 (1.3)	5.3 (1.4)	5.8 (1.1)	0.001
DAS CRP, mean (s.d.)	315 (31)	4.9 (1.2)	5 (1.3)	5.1 (1.3)	5.3 (1)	0.04
CRP, median (IQR), mg/l	264 (26)	10 (4–23)	13.5 (5–30)	15 (6–37)	17.8 (8–42)	<0.001
ESR, median (IQR), mm	336 (33)	24 (11–40)	27.5 (14–49)	34 (18–52)	43 (25–71.5)	<0.001
RF positivity, n (%)	181 (17.8)	164 (67.5)	236 (71.1)	130 (76.5)	66 (72.5)	0.12
RF titre, median (IQR), IU/ml	597 (58.7)	106 (41–256)	144 (64–320)	118 (46–267)	109 (40–256)	0.94
ACCP antibody positivity, n (%)	737 (27.5)	153 (69.2)	191 (67.3)	123 (78.9)	48 (63.2)	0.66
ACCP antibody titre, median (IQR)	668 (65.7)	212 (102–369)	250 (82–340)	239 (63–340)	250 (110–800)	0.93
Gammaglobulin, median (IQR)	501 (49.3)	10.9 (9.3–13.9)	10.3 (8.4–12.9)	9.6 (7.6–12.7)	10.1 (8.2–13.7)	0.006
IgG, median (IQR), g/l	672 (66.1)	12.5 (10.1–14)	10.9 (8–13.9)	10.3 (7.1–12.8)	9.5 (7.4–12.8)	<0.001
IgM, median (IQR), g/l	675 (66.4)	1.4 (0.8–1.9)	1.1 (0.7–1.6)	1.1 (0.6–1.8)	0.9 (0.6–1.4)	0.002
IgA, median (IQR), g/l	677 (66.6)	2.4 (1.8–3.4)	2.9 (2–4)	2.4 (1.8–3.6)	3.3 (2.1–4.9)	0.17

[a]Taking into account the ordered nature of age groups. IQR: interquartile range; n: number; S.D.: standard deviation.

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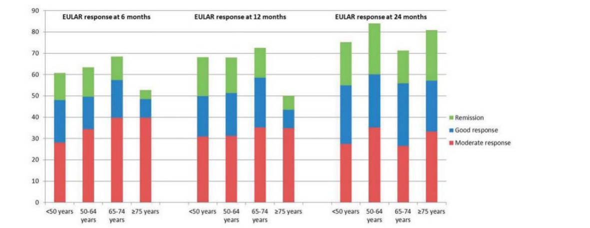
Lahaye C, et al. Rheumatology (Oxford) 2016;55:874-82.

Effectiveness of abatacept in elderly patients - ORA registry

Fig. 1 EULAR response at 6, 12 and 24 months according to age, in percent



The EULAR response** (good or moderate) **and the remission rate were not significantly different between the four age groups in the ORA registry

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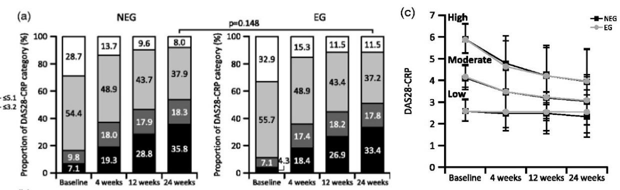
Lahaye C, et al. Rheumatology (Oxford) 2016;55:874-82

Effectiveness of abatacept in elderly patients (2)

Aim To investigate the effectiveness of abatacept in non-elderly (< 65) and elderly (≥65)

Subject Data from post-marketing surveillance in Japan (Non-elderly, n=2170, Elderly, n=1712)



Abatacept was well tolerated and similarly efficacious in the EG and NEG

GNUH

Harigai M et al. Mod Rheumatol 2019;29:747-755

CONTENTS OF TOAST SYMPOSIUM

- Old age (≥65) : : Prevalence, characteristics
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Retention rates of Abatacept in elderly RA patients - ANSWER cohort

Aim To evaluate the retention rates for 7 biological DMARDs in a real-world setting of elderly patients

Subject Multi-center, retrospective study assessed 1,098 treatment courses of 661 patients with bDMARDs from 2009 to 2018

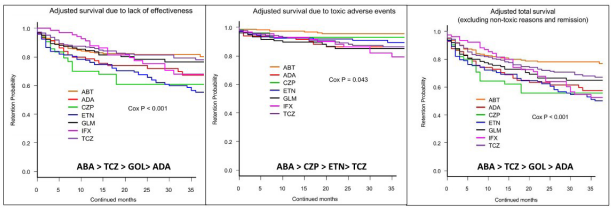
Table 1. Clinical characteristics at initiation of each biologic agent.

Variable	ABT (n = 272)	ADA (n = 97)	CZP (n = 51)	ETN (n = 184)	GLM (n = 159)	IFX (n = 101)	TCZ (n = 234)
Age (years)	73.0±6.0	69.9±4.7	73.1±6.8	71.9±5.5	72.5±5.6	69.6±3.2	71.0±5.3
Female sex (%)	79.4	79.4	90.2	81.5	86.2	79.2	76.9
BMI (kg/m^2)	21.7±3.5	21.9±3.5	22.4±3.6	22.2±3.5	22.8±3.5	22.6±3.4	22.0±3.3
Disease duration (years)	10.6±11.2	10.1±11.2	9.1±10.5	10.5±10.2	11.1±11.5	9.1±11.3	11.0±10.9
RF positivity (%)	83.4	79.0	89.4	85.2	73.7	75.3	82.8
ACPA positivity (%)	89.9	82.7	85.1	86.2	82.6	81.0	85.6
DAS28-ESR	4.5±1.2	4.5±1.2	5.1±1.5	4.7±1.3	4.4±1.3	5.0±1.5	4.8±1.3
CDAI	16.9±9.7	15.7±9.0	21.8±12.7	17.6±10.0	16.1±10.7	21.3±14.0	16.8±9.8
HAQ-DI	1.2±0.8	1.0±0.7	1.7±0.9	1.2±0.8	1.3±0.8	1.3±1.0	1.3±0.9
PSL usage (%)	46.8	41.1	37.3	47.8	41.4	48.4	47.8
PSL dose (mg/day)	3.1±7.3	2.9±4.9	1.7±2.6	2.8±3.6	2.3±3.6	3.1±5.9	2.8±3.9
MTX usage (%)	46.1	74.7	52.9	44.9	66.9	100.0	46.1
MTX dose (mg/week)	3.4±4.2	6.1±4.2	4.2±4.6	3.5±4.3	5.2±4.4	8.2±2.5	3.6±4.3
Starting date (2009–2012) (%)	16.1	54.6	0	56.5	17.0	67.3	30.8
Starting date (2013–2015) (%)	65.1	39.2	70.6	37.5	50.9	29.7	52.1
Starting date (2016–2018) (%)	18.8	6.2	29.4	6.0	32.1	3.0	17.1
1st bio (%)	66.5	59.8	58.8	71.2	45.3	86.1	43.6
2nd bio (%)	18.0	29.9	5.9	17.9	30.2	10.9	29.9
≥3rd bio (%)	15.5	10.3	35.3	10.9	24.5	3.0	26.5

GNUH

Ebina K, Hashimoto M et al. PLoS One 2019;14(5):e0216624

Aim	To evaluate the **retention rates** for 7 biological DMARDs in a real-world setting of elderly patients
Subject	Multi-center, retrospective study assessed 1,098 treatment courses of **661 patients with bDMARDs from 2009 to 2018**

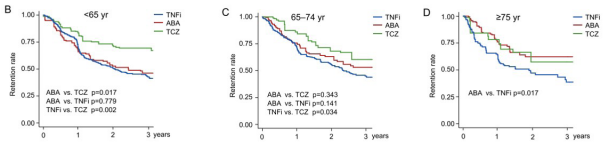


- *ABA showed lowest discontinuation rate by lack of effectiveness and by toxic adverse events.*

Ebina K, Hashimoto M et al. PLoS One 2019;14(5):e0216624

Retention rates of biologics in elderly RA patients - First cohort

Aim	To evaluate the **retention rates** for TNF inhibitors, Abatacept, Tocilizumab by age group (<65, 65-74, and ≥ 75 years)
Subject	Data from prospective observational Frist registry (2011-2017), (N= 1,362, <65 (n= 695), 65-74 (n=402), ≥ 75 (n=265)



- *Elderly RA (≥ 65) patients might be suitable candidates for ABA and TCZ therapy.*
- *Elderly RA (≥75) patietns might be suitable candidates for ABA therapy.*

Ebina K, Hashimoto M et al. PLoS One 2019;14(5):e0216624

Persistence of Abatacept : 1st line (bDMARD-naïve patients) vs 2nd line – ANSWER cohort

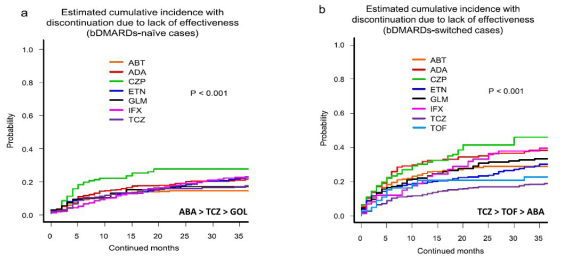
Objective	**To clarify retention rates and reasons for discontinuation of 7 biological bDMARDS and tofacitinib**
Methods	Data from ANSWER cohort study (2001 – 2019), 2377 bDMARD-naïve and 1678 bDMARDs-switcher

Table 1 Clinical characteristics at initiation of 7 bDMARDs (bDMARDs-naïve cases)

Variable	ABT (n = 390)	ADA (n = 374)	CZP (n = 135)	ETN (n = 616)	GLM (n = 208)	IFX (n = 650)	TCZ (n = 364)
Age (years)	65.5 ± 12.4	55.3 ± 12.8	58.1 ± 16.8	55.5 ± 15.9	62.0 ± 14.8	52.9 ± 13.4	56.6 ± 14.4
Female sex (%)	81.2	79.4	88.8	86.7	86.1	78.0	78.2
Disease duration (years)	9.2 ± 12.4	5.0 ± 7.5	4.7 ± 7.6	8.3 ± 8.7	7.3 ± 10.0	6.9 ± 8.4	7.4 ± 9.4
RF positivity (%)	86.6	73.8	86.2	83.1	75.6	74.2	74.0
ACPA positivity (%)	84.3	75.9	85.7	83.2	73.2	82.9	82.1
DAS28-ESR	4.4 ± 1.2	4.1 ± 1.2	4.6 ± 1.4	4.4 ± 1.4	4.3 ± 1.2	4.5 ± 1.6	4.6 ± 1.5
CDAI	17.7 ± 9.6	14.7 ± 9.1	22.2 ± 12.9	17.3 ± 8.8	17.2 ± 11.5	18.5 ± 12.4	18.1 ± 9.8
HAQ-DI	1.2 ± 0.8	0.7 ± 0.6	1.2 ± 0.8	0.9 ± 0.8	1.1 ± 0.8	1.1 ± 0.9	1.1 ± 0.8
PSL usage (%)	44.2	32.8	44.8	39.2	38.9	36.4	45.7
PSL dose (mg/day)	3.1 ± 7.3	2.9 ± 4.9	1.7 ± 2.6	2.8 ± 3.6	2.3 ± 3.6	3.1 ± 5.9	2.8 ± 3.9
MTX usage (%)	49.1	72.0	76.1	39.4	76.0	100.0	51.2
MTX dose (mg/week)	8.1 ± 2.8	9.4 ± 3.1	9.4 ± 2.9	8.0 ± 2.8	9.2 ± 2.9	8.2 ± 2.5	8.8 ± 3.0
Starting date 2001–2009 (%)	0.0	13.6	0.0	40.4	1.0	60.9	11.5
Starting date 2010–2013 (%)	35.9	53.7	12.6	42.0	40.4	30.2	47.3
Starting date 2014–2019 (%)	64.1	32.7	87.4	17.6	58.7	8.9	41.2

Ebina k et al. Arthritis Res Ther 2020;22:142

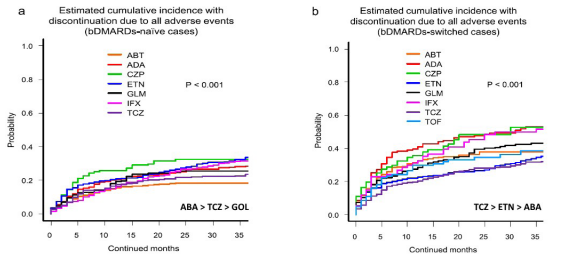
Effectiveness



- **Abatacept has better persistence when used as a 1st line biologic than 2nd line agent**

Ebina k et al. Arthritis Res Ther 2020;22:142

Adverse events

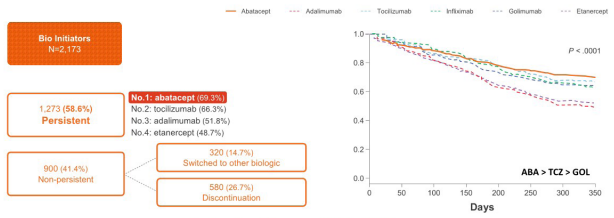


- **Abatacept has better persistence when used as a 1st line biologic than 2nd line agent**

Ebina k et al. Arthritis Res Ther 2020;22:142

Persistence of Abatacept : 1st line (bDMARD-naïve patients) – HIRA data

Objective	**To assess treatment persistence of TNF inhibitors and non-TNFR inhibitors (abatacept and tocilizumab)**
Methods	Korea National Health Insurance Claims Data (2013-2014), N=2,684 (bDMARD naive and switchers)

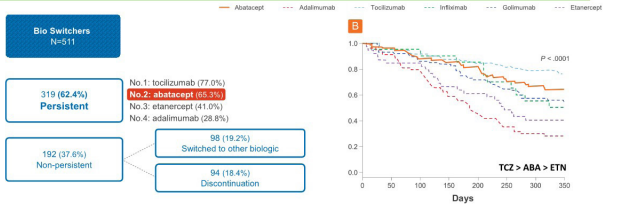


Treatment persistence was 58.6% in initiators
Abatacept showed highest persistent among biologics

Park JA et al. Curr Med Res Opin 2020;36:343-351

Drug survival of second biological DMARD therapy

Objective	**To assess treatment persistence of TNF inhibitors and non-TNFR inhibitors (abatacept and tocilizumab)**
Methods	Korea National Health Insurance Claims Data (2013-2014), N=2,684 (bDMARD naive and switchers)

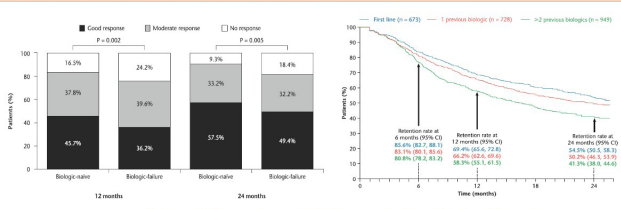


Treatment persistence was 62.4% in switchers
Non-TNF inhibitors (Tocilizumab and Abatacept) showed better persistent compared to TNF inhibitors

Park JA et al. Curr Med Res Opin 2020;36:343-351

Persistence of Abatacept : 1st line vs 2nd line – ANSWER cohort

Objective	**Evaluate abatacept retention over 2 years**
Methods	Results form the real-world ACTION study (1st line, n : 673, 2nd line, n : 728, 3rd line, n : 949



- **Abatacept in RA may achieve good EULAR response (earlier >> later line of therapy)**
- **Abatacept initiation as earlier vs later line of therapy in RA may achieve higher 2-year retention rates**
  However, earlier use of abatacept is much better for persistence

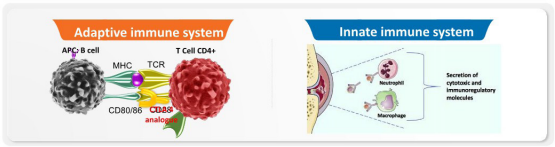
Alten R et al. Clincal Rheumatology 2019;38:1413-1424

CONTENTS OF TOAST SYMPOSIUM

- Old age (≥65) : : Prevalence, characteristics
- Effectiveness and Persistence in elderly RA patients
- Safety issues

Infection and Abatacept

- Fully human fusion protein, The Fc region of abatacept has been modified:



Suppressive adaptive immunity in a physiological manner like regulatory T cell

Innate immunity is preserved

- *ABA would be an ideal treatment option for elderly RA patients who have infection risks*

Safety - abatacept vs TNF inhibitors

Aim	To evaluate the comparative risk of hospitalized infection between ABA vs TNF inhibitor
Subject	Post-marketing surveillance in US (MarketScan from 2006-2015) (11,248 PS-matched)

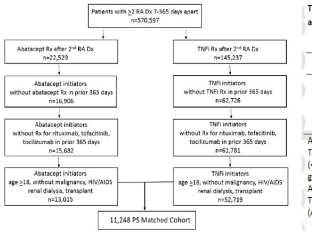


Table 3. Risk of hospitalized infection in abatacept versus TNFi initiators: 1:1 PS-matched analysis

	Abatacept (N=11,248)				TNFi (N=11,248)			
	No. Events	Person-Years	IR, per 1000 PY (95% CI)	HR (95% CI)	No. Events	Person-years	IR, per 1000 PY (95% CI)	HR (95% CI)
As-Treated (<30 days gap)	188	5,126	36.7 (31.8-42.3)	0.78 (0.64-0.95)	219	4,621	47.4 (41.5-54.1)	1.0
As-Treated (Any gap)	298	8,201	36.3 (32.4-40.7)	0.86 (0.74-1.01)	321	7,639	42.0 (37.7-46.9)	1.0

Chen SK et al. Arthritis Care Res (Hoboken) 2018 Dec 20 [Epub ahead of print]

Safety - abatacept vs Tocilizumab

Subject	Using claims data from US Medicare, IMS and MArketScan (2010-2015)

Table 3 IR and HR of composite serious infections in tocilizumab initiators vs abatacept, propensity score-matched with a 1:1 fixed ratio

	Tocilizumab				Abatacept					
	Subjects (n)	Events	Person-years	IR* (95% CI)	Subjects (n)	Events	Person-years	IR (95% CI)	HR (95% CI)	Rate difference†
As-treated analysis										
Medicare	3850	230	3231	7.12 (6.20 to 8.04)	3850	176	3659	4.81 (4.10 to 5.52)	1.25 (1.06 to 1.47)	2.31 (1.15, 3.47)
IMS	3008	90	2688	3.35 (2.66 to 4.04)	3008	54	2675	2.02 (1.48 to 2.56)	1.58 (1.19 to 2.09)	1.33 (0.45, 2.21)
MarketScan	3556	68	2680	2.54 (1.93 to 3.14)	3556	65	2760	2.36 (1.78 to 2.93)	1.14 (0.85 to 1.54)	0.18 (−0.65, 1.01)
Combined	10 414	388	8599	4.51 (4.06 to 4.96)	10 414	295	9094	3.24 (2.87 to 3.61)	1.40 (1.20 to 1.63)	1.27 (0.69, 1.85)
Intention-to-treat analysis up to 180 days										
Medicare	3850	157	1741	9.02 (7.61 to 0.43)	3850	111	1752	6.34 (5.16 to 7.51)	1.26 (1.03 to 1.55)	2.68 (0.84, 4.52)
IMS	3008	51	1376	3.71 (2.69 to 4.72)	3008	32	1389	2.30 (1.51 to 3.10)	1.34 (0.94 to 1.92)	1.41 (0.12, 2.70)
MarketScan	3556	44	1544	2.85 (2.01 to 3.69)	3556	45	1552	2.90 (2.05 to 3.75)	0.96 (0.67 to 1.37)	−0.05 (−1.24, 1.14)
Combined	10 414	252	4661	5.41 (4.74 to 6.07)	10 414	188	4693	4.01 (3.43 to 4.58)	1.34 (1.11 to 1.63)	1.40 (0.52, 2.28)

*Incidence rate (IR) is per 100 person-years.
†Rate difference per 100 patients (tocilizumab-abatacept).

Comparing TCZ with Abatacept, higher risks for composite SI, serious bacterial infection, diverticulitis, pneumonia/upper respiratory tract infection and septicaemia/bacteraemia were observed in the TCZ group

Pawar A et al. Ann Rheum Dis 2019;78:456-464

Safety - abatacept vs other biologic DMARDs

Aim	To define the risk of serious bacterial infections in patients receiving specific biological DMARDs
Subject	Analysis from RECORD study of the Italian Society for Rheumatology (N = 4,656, 2004-2013)

Table V. Events, person years (PYs), crude and adjusted HR for hospitalised infection compared to Etanercept.

Biologic exposure	Events	PYs	Incident rate *1000 PY (95%CI)	Crude HR (95% CI)	Adjusted HR (95%CI)*
Etanercept	68	8296	8.2 (6.4, 10.4)	Ref (1.0)	Ref (1.0)
Adalimumab	52	4851	10.7 (8, 14.1)	1.27 (0.88, 1.82)	1.37 (0.95, 1.96)
Infliximab	26	3199	8.1 (5.3, 11.9)	0.98 (0.62, 1.54)	0.96 (0.60, 1.56)
Certolizumab	4	406	9.9 (2.7, 25.2)	0.93 (0.34, 2.55)	1.31 (0.48, 3.58)
Golimumab	4	451	8.8 (2.4, 22.7)	0.84 (0.31, 2.32)	1.09 (0.37, 3.21)
Abatacept	4	1404	2.8 (0.8, 7.3)	0.3 (0.11, 0.83)	0.29 (0.10, 0.82)
Rituximab	13	984	13.2 (7.0, 22.6)	1.4 (0.77, 2.55)	0.95 (0.48, 1.91)
Tocilizumab	10	928	10.8 (5.2, 19.8)	1.09 (0.56, 2.12)	1.24 (0.59, 2.61)

*Adjusted for pre-specified confounders (gender, age, disease duration, NSAIDs, number of previous bDMARDs, Charlson Comorbidity Index, infections and antibiotic prescription for 14 days in the previous year); HR, hazard ratio; CI, confidence interval.

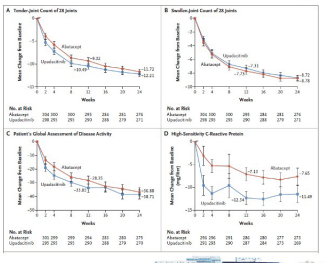
Carrara G et al. Clin Exp Rheumatol 2019;37:60-66

Safety - abatacept vs JAK inhibitor

Objective	Evaluate the efficacy and safety of upadacitinib (15mg) vs abatacept in patients with at least 1 biologic DMARDs failure
Methods	In 24-week, phase 3, double-blind, controlled trial (N=303)

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Upadacitinib (N=303)	Abatacept (N=309)
Female sex — no. (%)	249 (82.2)	253 (81.9)
Duration of rheumatoid arthritis — yr	12.4±9.5	11.8±8.3
Age — yr	55.3±11.4	55.8±11.9
No. of previous biologic DMARDs — no. (%)		
0	4 (1.3)	2 (0.6)
1	206 (68.0)	202 (65.4)
2	64 (21.1)	70 (22.7)
3	29 (9.6)	35 (11.3)
Tender-joint count of 28 joints	14.40±6.49	15.63±6.53
Swollen-joint count of 28 joints	10.45±4.72	11.26±5.09
Patient's global assessment of disease activity — mm¶	66.82±19.92	69.61±20.83
C-reactive protein — mg/liter	15.95±18.48	17.38±21.12
DAS28-CRP‖	5.70±0.90	5.88±0.94
DAS28-ESR‖	6.36±0.92	6.57±0.99
Clinical Disease Activity Index**	38.54±11.37	40.74±12.05



Rubber-Roth A et al. N Engl J Med 2020;383:1511-1521

Safety - abatacept vs JAK inhibitor

Table 3. Adverse Events through Week 24.

Event	Upadacitinib (N=303)		Abatacept (N=309)	
	no. of patients	% (95% CI)	no. of patients	% (95% CI)
Any adverse event	209	69.0 (59.9–79.0)	189	61.2 (52.8–70.5)
Serious adverse event	10	3.3 (1.6–6.1)	5	1.6 (0.5–3.8)
Adverse event leading to discontinuation of trial drug	14	4.6 (2.5–7.8)	9	2.9 (1.3–5.5)
Death‖	2	0.7 (0.1–2.4)	1	0.3 (0.0–1.8)
Treatment-emergent	1	0.3	0	
Non-treatment-emergent	1	0.3	1	0.3
Serious infection	3	1.0 (0.2–2.9)	1	0.3 (0.0–1.8)
Opportunistic infection	4	1.3 (0.4–3.4)	1	0.3 (0.0–1.8)
Herpes zoster infection	4	1.3 (0.4–3.4)	4	1.3 (0.4–3.3)
Hepatic disorder	23	7.6 (4.8–11.4)	5	1.6 (0.5–3.8)
Gastrointestinal perforation	0		0	
Cancer, including nonmelanoma skin cancer	0		0	
Major adverse cardiovascular event†	1	0.3 (0.0–1.8)	0	
Venous thromboembolic event‡	2	0.7 (0.1–2.4)	0	

Table 4. Change in Laboratory Values from Baseline to Week 24.*

Variable	Upadacitinib (N = 303)	Abatacept (N=309)
	least-squares mean change	
Hemoglobin — g/dl	−0.4±9.5	2.7±8.8
Neutrophil count — $\times 10^9$/liter	−1.08±2.31	−0.90±2.10
Lymphocyte count — $\times 10^9$/liter	0.02±0.62	0.16±0.82
Platelet count — $\times 10^9$/liter	−9.6±64.2	−17.1±64.3
LDL cholesterol — mmol/liter	0.37±0.76	0.05±0.68
LDL cholesterol — % change	15.81±28.31	4.16±24.15
HDL cholesterol — mmol/liter	0.20±0.39	0.05±0.28
HDL cholesterol — % change	16.23±27.40	5.10±20.79
ALT — U/liter	3.5±21.2	0.0±10.2
AST — U/liter	5.4±17.8	1.1±8.2
Creatinine — μmol/liter	4.6±9.7	2.2±9.4
Creatine kinase — U/liter	86.4±247.4	20.0±52.4

* Plus–values are means ±SD. To convert the values for cholesterol to milligrams per deciliter, divide by 0.02586. To convert the values for creatinine to milligrams per deciliter, divide by 88.4. ALT denotes alanine aminotransferase, AST aspartate aminotransferase, HDL high-density lipoprotein, and LDL low-density lipoprotein.

Upadacitinib was superior to ABA in the change of DAS 28-CRP, however, upadacitinib showed more serious adverse events

Rubber-Roth A et al. N Engl J Med 2020;383:1511-1521

JAK-inhibitors

Non-inferiority vs TNF inhibitor for rates of MACE was not achieved for tofacitinib in ORAL Surveillance

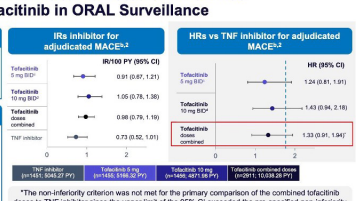
Enriched patient population[1]

- Adults ≥50 years old
- At least one CV risk factor
- Moderate-to-severe RA
- Inadequate control on methotrexate

Endpoints[1,2]

- Non-inferiority of combined tofacitinib doses compared to TNF inhibitor* regarding:
  - Adjudicated major adverse cardiovascular events (MACE) and
  - Malignancies excluding non melanoma skin cancer (NMSC)

Non-inferiority (NI) design with a margin of 1.8. Survival analysis (Cox-proportional hazards) Event driven study duration



*The non-inferiority criterion was not met for the primary comparison of the combined tofacitinib doses to TNF inhibitor since the upper limit of the 95% CI exceeded the pre-specified non-inferiority criterion of 1.8, ie, 1.94 >1.8, Dotted line, NI margin (1.8)

*TNF inhibitors: adalimumab and etanercept. †Based on Cox proportional hazard model. ‡Tofacitinib 5 mg BID is the EMA-approved label for RA and PsA. §The 10 mg BID treatment group includes patients that were switched from 10 mg BID to 5 mg BID as a result of a study modification in February 2019
EOW, every other week; EW, every week

1. NCT02092467. Available at: https://clinicaltrials.gov/ct2/show/NCT02092467 (last accessed March 2021);
2. Pfizer. Available at: https://www.pfizer.com/news/press-release/press-release-detail/pfizer-shares-co-primary-endpoint-results-post-marketing (last accessed March 2021)

Extracted from 2021 EULAR

JAK-inhibitors

FDA requires warnings about increased risk of serious heart-related events, cancer, blood clots, and death for JAK inhibitors that treat certain chronic inflammatory conditions

Approved uses also being limited to certain patients

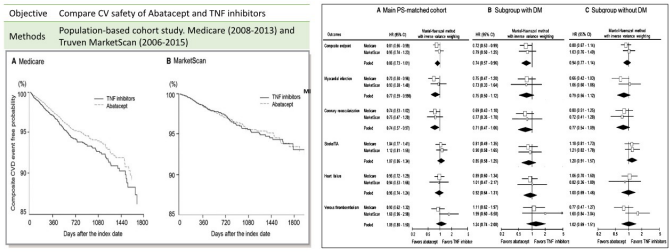
This information is an update to the FDA Drug Safety Communication issued on February 4, 2021. FDA also previously communicated about the safety clinical trial with Xeljanz, Xeljanz XR (tofacitinib) in February 2019 and July 2019.

Drug Safety Communication (PDF - 255 KB)

Effect of Abatacept on CV risk

- Improvement in lipid profile / Improve insulin sensitivity

Objective	Compare CV safety of Abatacept and TNF inhibitors
Methods	Population-based cohort study. Medicare (2008-2013) and Truven MarketScan (2006-2015)



Abatacept is associated with a modestly reduced cardiovascular risk compared with TNF inhibitors

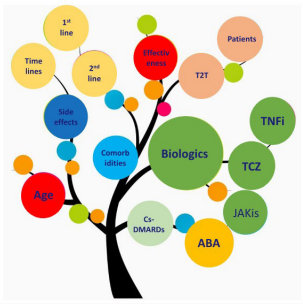
Kang EH et al. J Am Heart Assoc 2018;7:e007393

Summary for safety of biologics

	TNF inhibitors	Abatacept	Tocilizumab
Infections	Slight increase over RA patients	*Low infection risk*	Slight increase over RA patients
Tuberculosis	Increased risk of latent TB reactivation	*No increased risk*	No increased risk
NTM	No recommendation	*Recommended (ACR)*	No recommend
Opportunistic infections	Increased risk of opportunistic infections	*No increased risk*	No increased risk
Hepatitis B infection	Should be restricted	*No worsening*	No worsening
Malignancy	Similar risk as RA	*No increased risk*	No risk
CV risk	Avoid to patients with heart failure	*No worsening*	No worsening, but may increased LV ejection fraction
Dyslipidemia	Modestly increased	*No increases*	Increase Total Chol, LDL, HDL, TG
ILD	Uncertain	*Recommended (BSR, Spain)*	Uncertain

Canete JE et al. Expert Opin Biol Ther 2017;17:1089-1103, Fraenkel L et al. Arthr, Holroyd CR, et al. Rheumatology (Oxford). 2019;58:e1-e2. Itis Care and Research 2021;73:924-939, Grupo de Trabajo GUIPCAR. Sociedad Española de Reumatología 2019.

Summary : Decision of RA medications



Summary

High titer Of ACPA

Dual positive (RF/ACPA)

Elderly RA

Comorbidities such as CVD,ILD, NTM

Patient support programs are needed

Luncheon Symposium VI - Yuhan

What`s the Meaning of Adalimumab Biosimilar to Treat Rheumatoid Disease Patients

JRD Journal of Rheumatic Diseases
Vol. 28, Suppl. 1, October, 2021

The position of the 1st Adalimumab biosimilar in Europe

Ulf Müller-Lader
Justus Liebig Univ. Giessen, Germany

Since the introduction of biosimilars for the treatment of inflammatory rheumatic diseases starting with infliximab, since 2018 the numbers of prescriptions of adalimumab biosimilars increased also steadily worldwide. However, in Europe the rate of increase differs significantly from country to country with Germany being amongst the strongest prescribers. This is based on both the financial pressure on the rheumatologists, the more or less problem-free originator-to-biosimilar switching and the increasing body of data showing the positive outcome of switching in controlled clinical trials. The next developments in this evolving field were the subsequent real-world date. Of these, the most recent data originate from SB5, an adalimumab biosimilar that received EU marketing authorisation in August 2017. The actual and still ongoing non-interventional PROPER study enrolled 1000 subjects with rheumatoid arthritis, axial spondyloarthritis or psoriatic arthritis (PsA), ulcerative colitis or Crohn's disease, who initiated SB5 as part of routine clinical practice following a minimum of 16 weeks' treatment with reference adalimumab at clinics in Belgium, Germany, Ireland, Italy, Spain and the UK. Data are being captured from clinic records retrospectively for the 24 weeks prior to transition, and prospectively and/or retrospectively for 48 weeks following transition. The timely interim analysis includes 510 patients: 205 with RA, 169 with PsA and 136 with axSpA showing no alteration or decrease in efficacy after switching over an extended period of time and a safety profile comparable with the originator. Another monocentric trial from Italy, which recorded the switching from reference ADA to SB5 in real-life patients with RA, PsA, and axSpA resulted in similar profiles of control of disease activity, everyday life disability and safety, resulting in a high persistence rate. The own experience in our clinic serving around 10.000 patients per year was that prior to 2019, less than 10% of the eligible patients were on biosimilars, but at present more than 80% of the patients are on label on biosimilars, with several adalimumab biosimilars available. All of these adalimumab biosimilars are used as university rheumatology teaching center with SB5 being one of the top adalimumab biosimilars in our clinic because of the lack of unexpected problems beyond the known adalimumab-specific side effect profile, including no major injection reactions.

International Symposium

Update of Fibromyalgia

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Diagnosis of fibromyalgia

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Fibromyalgia (FM) is a complex multi-factorial syndrome characterized by chronic widespread pain accompanied by fatigue, cognitive problems and sleep disturbances causing a considerable decline in quality of life.

Over the past decades, a number of different classification and diagnostic criteria have emerged. The first 1990 American College of Rheumatology (ACR) criteria required the presence of chronic widespread musculoskeletal pain (>3 months) and tenderness on palpation in at least 11 out of 18 specified tender points. The 1990 ACR criteria were originally established as inclusion criteria for research purposes and were not intended for clinical diagnosis. In 2010, the ACR preliminary diagnostic criteria (ACR 2010 Cr) eliminated the need for eliciting tender points and introduced the Widespread Pain Index, and the Symptom Severity Scale to measure the manifold associated symptoms. In 2011, the ACR 2010 Cr was modified to eliminate the need for an interviewer and allow epidemiologic studies. A further revision (ACR 2016 criteria) added the generalized pain criterion (pain in at least four of five regions), specified somatic symptoms including headache, pain or abdominal cramps, and depression, also stating that a diagnosis of FM does not exclude the presence of other diagnoses. Recently, the Analgesic, Anesthetic, and Addiction Clinical Trial Translations Innovations Opportunities and Networks-American Pain Society Pain Taxonomy introduced new criteria focusing on: 1) six or more pain sites from a total of nine, 2) moderate-to-severe sleep prob¬lems or fatigue, and 3) multisite pain plus fatigue or sleep problems present for at least three months.

Although many criteria have been developed over the last decades, problems still are present with acceptance of criteria, delayed diagnoses, use of criteria in general practice. Discovery of a reliable biomarker for FM would be a critical step to early intervention.

References

1. Wolfe F, Smythe HA, Yunus MB et al.: The American College of Rheumatology 1990 Criteria for the Classification of Fibro¬myalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum 1990; 33:160-72.

2. Wolfe F, Clauw DJ, Fitzcharles MA et al.: The American College of Rheumatology preliminary diagnostic criteria for fibromyal¬gia and measurement of symptom severity. Arthritis Care Res 2010; 62:600-10.

3. Wolfe F, Clauw DJ, Fitzcharles MA et al.: Fibromyalgia criteria and severity scales for clinical and epidemiological studies: A modification of the ACR preliminary diag¬nostic criteria for Fibromyalgia.

J Rheumatol 2011; 38:1113-22.
4. Wolfe F, Clauw DJ, Fitzcharles MA et al.: 2016 Revisions to the 2010/2011 fibro¬myalgia diagnostic criteria. Semin Arthritis Rheum 2016; 46:319-29.
5. Alciati A, Nucera V, Masala IF et al.: One year in review 2021: fibromyalgia. Clin Exp Rheumatol 2021 May-Jun;39 Suppl 130(3):3-12.

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Fibromyalgia Update : Medical and Non-medical Therapy

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Fibromyalgia, a fairly common musculoskeletal condition, is characterized by chronic widespread pain, fatigue, sleep disturbances and complex functional symptoms. This talk presents and summarizes up-to-date literature on the clinical manifestations, pathophysiological mechanisms, and treatment options for fibromyalgia patients.

The pathophysiology of fibromyalgia involves genetic predisposition, stressful events, peripheral (inflammatory) and central (cognitive emotional) mechanisms interplay to amplify pain perception owing to neuromorphological modifications ('nociplastic pain'). The multiple components of the pathogenesis necessitate a multi-modal treatment approach. Initial management should involve patient education and nonpharmacological therapies. Based on meta-analyses, the only 'strong for' therapy-based recommendation in the 2016 EULAR guidelines was exercise. In case of non-response, further therapies should be tailored to the specific needs of the individual and may involve psychological therapies (for mood disorders and unhelpful coping strategies), pharmacotherapy (for severe pain or sleep disturbance) and/or a rehabilitation program (for severe disability). Pharmacological agents include antidepressants such as tricyclics and norepinephrine/serotonin reuptake inhibitors, anticonvulsants, muscle relaxants, analgesics (tramadol) as well as some investigational agents. Unfortunately, the size of effect for most medical therapies is relatively modest. But in real-life clinical experience, patients seldom achieve sufficient symptom relief without use of drugs. Thus, some experts suggest starting both pharmacological and non-pharmacological treatments simultaneously straightaway, rather than sequential workflow mainly because patients are usually diagnosed years after symptom onset. Considering that no consistently effective treatments are yet available, approach should be individualized, symptom-based and stepwise, establishing shared goals with the patient.

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Cognitive-behavior therapy for fibromyalgia-focusing on acceptance-commitment therapeutic approach

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Psychological and behavioral therapies are increasingly used to treat patients with Fibromyalgia (FM). For FM, integrating psychotherapy into the clinical care plan is more effective than offering medical treatments alone. A recent meta-analysis demonstrated that CBT is promising, but its effect is still moderate and additional measures to improve the patient's functioning still needs to be explored.

Empirical support for Acceptance-Commitment Therapy (ACT) is rapidly growing. ACT was listed as an empirically supported treatment for chronic or persistent pain in general by the American Psychology Association (Division12, A.P.A., 2010). ACT focuses on enhancing a patient's capability to deal with pain and suffering and to act in accordance with his/her values while accepting unwanted thoughts, feelings, and bodily sensations.

In this presentation, recent empirical findings showing the efficacy of ACT on FM and the process variables that mediate its effect are reviewed. Psychological flexibility, acceptance, and value-based action are addressed as mediators of ACT for FM. Future implications are also discussed.

Joint Symposium

KCR-JCR Joint Symposium
- Precision Medicine in Rheumatology

Big data analysis of autoimmune diseases

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Development of next generation sequencing technology provided tons of human genome and omics data of hundreds of thousands of subjects. Variations in human genome sequence define individuals' disease susceptibility. Large-scale human genome analysis successfully identified comprehensive catalogues of genetic susceptible loci, including those of autoimmune diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE; Sakaue S and Kanai M et al. Nat Genet 2021). However, little is known regarding how to develop methodology to integrate large-scale human genome data with diverse biological resources, to which statistical genetics should contribute. We have developed such methods and applied to a pioneering example of large-scale genetic association studies on a variety of human complex traits, including autoimmune diseases, clinical biomarkers, and past medical records. Tran-layer omics analysis identified the cell types and microbiomes implicated in disease biology (e.g., regulatory T cells for Graves' disease, genus Prevotella for RA, and genus Streptococcus for SLE; Kanai M et al. Nat Genet 2018, Kishikawa T et al. Ann Rheum Dis 2020, Tomofuji Y et al. Ann Rheum Dis 2021). Network analysis between the disease risk genes and the drug target genes could identify novel candidates of drug repositioning (e.g., CDK inhibitor for RA). Integration of cell type-specific gene expression profiles estimated from GWAS with compound perturbation databases can pinpoint novel therapeutic targets and compounds (Konuma T et al. Hum Mol Genet 2021). Application of the machine learning methods into population genome data can classify the samples without prior biological information (e.g., white blood cell type classification from human leukocyte antigen (HLA) gene sequences; Hirata J et al. Nat Genet 2019. Further, we demonstrated utility of deep learning in human population genomes, such as in silico estimation of HLA gene variants (Naito T et al. Nat Commun 2021). Polygenic risk score (PRS) integrating genetic risk of the genome-wide variants can stratify the samples based on disease risk, and can also identify causal factors for human longevity (e.g., blood pressure and obesity; Sakaue S and Kanai M et al. Nat Med 2020). These results should empirically show the value of statistical genetics to dissect disease biology, novel drug discovery, and personalized medicine. Finally, we would like to introduce our activity on young researcher developments ("Summer school of statistical genetics" in Osaka Univeristy).

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Pathological pathways revealed by functional genome analysis of immune-mediated diseases

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Immune-mediated diseases (IMDs) consist of a wide range of etiologies from autoimmune to autoinflammatory conditions. In spite of the development of a variety of therapeutic agents and regimens, the treatment response varies from patient to patient. The heterogeneous pathogeneses of an IMD may be associated with different outcomes. Accompanied with the maturation of genome research, functional genome analysis which evaluate relationships between genetic polymorphism and transcriptome has become a prominent approach for the understanding of autoimmune diseases. A number of attempts to stratify diseases using functional genome analysis are being carried out all over the world. In this context, we constructed a gene expression and eQTL database, ImmuNexUT, which consist of nearly 10000 RNA-seq samples derived from 28 immune cell subsets of 416 donors with 10 immune-mediated diseases (IMDs) and healthy controls. Our data integratively revealed characteristic gene expression signatures across immune cells and IMDs. When we compared the patterns of dysregulated gene modules, IMDs were divided into 2 groups, largely corresponding to clinically distinct autoimmune diseases (SLE, MCTD, SSc, SjS, IIM, and RA) and autoinflammatory diseases (BD and AOSD). Gene modules upregulated in autoimmune diseases showed significant overlap with interferon (IFN)-induced gene sets, whereas gene modules upregulated in autoinflammatory diseases showed significant overlap with interleukin (IL)-18- or IL-1β-induced gene sets. Our analysis identified eQTLs for 13,395 protein coding genes and 3,839 long non-coding RNAs at a 5% false discovery rate (FDR). A median of 7,092 genes were identified as eGenes in each cell type, which is 2.2-fold more than that identified in the previous eQTL database. Examination of context-dependent eQTL revealed transcriptionally regulated hidden modules associated with IFN signal, aging, and cell proliferation. Of the 29 suggested associated loci in recently reported Japanese SLE GWAS, 20 showed colocalization with at least one immune cell eQTL with stringent criteria. Notably, some showed subset-specific or directionally opposite eQTL effects among immune cells, and some regulated genes which have not been reported to be associated with SLE. Our results show critical role of functional genome analysis in the identification of disease-related pathways and genes in IMD.

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Optimal selection of targeted therapeutics using genetics and transcriptomics in rheumatoid arthritis

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Rheumatoid arthritis (RA) is a systemic chronic autoimmune disease that mainly involves synovial joints. RA is not homogeneous but rather heterogeneous regarding to clinical manifestation such as severity of arthritis, joint destruction, and drug responses. In addition, the underlying pathogenesis of RA is complex and may be different for each individual, which involves various cell types, cytokines, genetic predisposition, and environmental factors.

Precision medicine (PM) in RA is a highly tailored approach to patient management that need to profile all of these heterogeneous patterns of clinical manifestations, complexity of the pathogenesis, and various degree of genetics' contribution.

Biological drugs are cornerstones of RA treatment strategy. However substantial proportion of patients treated with the biologics do not reach the treatment target. Overall response rates of several biologics including TNF inhibitors (TNFi) and abatacept using the American College of Rheumatology (ACR) response criteria for 20%, 50%, and 70% improvement have been reported to be similar that is 60%, 40%, and 20%, respectively.

Therapeutics precision, the preferential treatment selection of the best biological compound for an individual patient with active disease, might increase the response rates, for example up to 70~80% ACR50 response rate instead of 40%.

We have been attempting to provide data using genetics and transcriptomics to address the unmet precision medicine; "which targeted biologics is optimal for each individual in RA?"

It has been recently reported that HLA-DRB1 could be a marker for predicting the responses of TNFi and abatacept. We analyzed the association between each HLA-DRB1 allele and treatment response of TNFi and abatacept in patients with RA, which showed the differences of response rate of the therapeutics depending on HLA-DRB1 allele. With further validation studies, the HLA-DRB1 might guide the choice of preferential targeted therapy in clinics.

Given the limitations of genetics for therapeutics precision, we performed RNA sequencing from peripheral blood cells in 62 patients, which were generated just before and 6 months after initial treatment with TNFi. Our integrative transcriptomic analysis contrasts transcriptomic differences in good responders and null responders in order to identify the biomakers and understand the underlying mechanisms in response to TNFi.

Precision medicine for targeted therapeutics choice has not yet been identified, but continuous efforts will make the molecular biomarkers in addition to the clinical markers to be useful in clinical practice in future.

Free Paper Session

Spondyloarthritis

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Well-controlled C-reactive protein level during the first 3 months is associated with slowing radiologic progression in patients with ankylosing spondylitis : 18-year real world evidence

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Background

The aim of this study was to investigate the relationship between changes in C-reactive protein (CRP) level of patients initially treated with nonsteroidal anti-inflammatory drugs (NSAIDs) and/or conventional disease modifying anti-rheumatic drugs (cDMARDs) for 3 months and spinal radiographic progression.

Methods

Of the 1,280 patients who were followed-up for 18 years in a single center, patients who were initially treated with NSAIDs and/or cDMARDs for 3 months were included. Among them, patients with CRP lower than 0.8mg/dl or half of baseline CRP at 3 months were defined as the CRP controlled group and others were defined as the CRP not controlled group. The generalized estimating equation was used to analyze the differences in the modified stoke ankylosing spondylitis spinal score (mSASSS) between the two groups.

Results

In the multivariable model (table 1), the CRP not controlled group (n=452) showed a slower increase in mSASSS compared to the CRP not controlled group (n=351) (interaction term β= -0.499, 95% confidence interval -0.699 to -0.300). Average mSASSS change was estimated to be 0.536 per year and 1.036 per year, in the CRP controlled group and the CRP not controlled group, respectively.

Conclusions

CRP levels controlled by initial treatment for 3 months were significantly associated with slowing the rate of spinal radiographic change.

Keywords

Ankylosiing spondylitis, Radiographic progression, C-reactive protein

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O-18

Computed tomography-based assessment of radiographic progression in spine and sacroiliac joints after pregnancy in women with ankylosing spondylitis

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Background

Mechanical stress are one of the pathogenesis of ankylosing spondylitis (AS). During pregnancy, the mechanical overload on the spine and pelvis increases due to gravid uterus. We aimed to investigate whether pregnancy affects radiographic progression in patients with ankylosing spondylitis (AS) based on computed tomography (CT) evaluations.

Methods

This retrospective study included women with AS aged 19-49 years who underwent at least two CT evaluations of the whole spine or sacroiliac joints (SIJs) at intervals of 2-4 years. To compare radiographic progression after delivery, we classified the patients into two groups: delivery group and controls. The delivery group was restricted to women who had the first CT ~2 years before delivery and the second CT ~2 years after delivery. The CT Syndesmophyte Score (CTSS) (0-522) and SIJ scores (0-40) were used to evaluate spinal syndesmophytes and erosion, joint space narrowing, and sclerosis of the SIJs.

Results

A total of 21 women in the delivery group and 38 women in the control group were included. The median (Q1-Q3) CTSS at baseline in the delivery group and controls was 19 (16-23) and 20 (13.25-27.75), and the median progression was 1 (0-3) and 0 (0-1) during the median 2.9-year follow-up, respectively. The median (Q1-Q3) SIJ score at baseline in the delivery group and controls was 13 (8-22) and 11 (6-22), and the median progression was 1.5 (0-3) and 1 (0-2), respectively. The CTSS and SIJ scores significantly increased in both groups; however, no difference in absolute score changes per time point was observed. The SIJ score changes were comparable according to the delivery method.

Conclusions

Pregnancy and delivery do not affect the radiographic progression of the spine and SIJs in women with AS.

Keywords

Ankylosing spondylitis, pregnancy, computed tomography

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The occurrence of acute anterior uveitis in patients initiating TNF-α inhibitor for ankylosing spondylitis: An analysis of Korean nationwide claims data

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Background

Acute anterior uveitis (AAU) is the most common extra-articular manifestation in ankylosing spondylitis (AS). This study aims to evaluate the occurrence of AAU in patients with AS during treatment with tumor necrosis factor-alpha (TNF-α) inhibitors (TNFis).

Methods

A nationwide population study was performed using the Korean National Health Insurance claims database from JAN 2009 to DEC 2019. Patients diagnosed with AS (ICD-10, M45) or with rare incurable disease registration code for AS (V140) were included. We investigated whether there was a difference in the occurrence of AAU according to the type of TNFis. In addition, we evaluated whether there was a difference in the occurrence of AAU in AS patients with a history of AAU prior to treatment with TNFi. Patients who developed AAU prior to the first TNFis prescription were classified as 'previous AAU history (+)'.

Results

A total 5,938 AS patients initiated TNFis between 2009 and 2017 and maintained them at least for two years. Among them, 1,488 (25.1%) patients had a history of AAU before starting the TNFis. The most used TNFis was adaimumab (ADA, 43.0%), followed by etanercept (ETN, 21.1%), infliximab (IFX, 20.9%), golimumab (GOL, 18.5%). Annual incidence rates of AAU in AS with TNFis were 7.3 per 100 pys (ETN 11.3, ADA 6.4, IFX 6.4 and GOL 5.6). As described in table 1, the incidence rate ratio (IRR) of AAU with ETN was significantly higher compared to ADA (IRR 1.76, $p < 0.001$). In addition, the IRR of AAU was also higher in ETN than in ADA in patients without a previous history of AAU (IRR 2.61, $p < 0.001$).

Conclusions

These population-based data suggest that anti-TNF monoclonal antibodies, including ADA decreased incidence of AAU compared with ETN independent to previous history of AAU.

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O-20

A cluster analysis in patients with axial spondyloarthritis using TNFi based on clinical characteristics

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Background

Previous studies using cluster analysis technique in axial spondyloarthritis (axSpA) patients have consistently identified distinct groups of patients in terms of their clinical characteristics: those with pure axial symptoms and those with a high frequency of peripheral manifestations [1,2]. Due to the cross-sectional nature of these studies, however, prognostic information such as drug survival of anti-TNF agents in these group were not provided.

Methods

Clinical characteristics and demographic data of axSpA patients in KOBIO registry were analyzed using hierarchical clustering analysis. After clustering, drug survivals of anti-TNF agents were compared between these groups.

Results

1,042 patients were included in the study with no missing data. The hierarchical cluster analysis classified patients in two groups; one with predominant isolated axial manifestations (axial group, n=828) and the other with more frequent extra-axial symptoms (extra-axial group, n=214). Almost all extra-axial symptoms (peripheral arthritis, enthesitis, uveitis, and psoriasis) were more frequently observed in extra-axial group than axial group. In addition, patients with shorter disease duration, late disease onset, and high disease activity were classified in extra-axial group. Interestingly, the extra-axial group had lower drug survival probability than the axial group (p=0.001, Figure 1).

Conclusions

Cluster analysis of AS patients using anti-TNF agents classified two distinct groups of patients in terms of their clinical phenotypes and revealed that the patients with prominent extra-axial manifestations had lower drug survival with anti-TNF agents.

Keywords

spondyloarthritis, cluster analysis, SpA features

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Radiographic Facet Joint Damage of the Cervical Spine in Patients with Ankylosing Spondylitis and Its Impact on Functional Status : A Longitudinal Analysis in Relation to the Damage of Vertebral Body

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Background
We aimed to identify the extent of cervical facet joint damage in patients with ankylosing spondylitis (AS) and evaluate whether it contributes to physical function impairment.

Methods
Clinical and radiographic data from 1106 AS patients followed up to 16 years at a single hospital were used. Two readers scored cervical facet joints and vertebral bodies using the method of de Vlam and the mSASSS, respectively. Facet joint damage at a given vertebral level was defined as the presence of partial and/or complete fusion. Radiographic progression over time was assessed using the radiographs measured within follow-up periods stratified into 4-year increments. Functional status at each timepoint of the radiograph was assessed according to the BASFI. The longitudinal association of facet joint fusion with the BASFI was analyzed using generalized estimating equations.

Results
In total, 4984 radiographs were obtained with a mean (SD) of 4.5 (1.2) measurements per patient. Among 220 patients with ≥1 of facet joint damage or syndesmophytes at baseline, structural damage to facet joints and vertebral bodies was seen simultaneously in 53.6%. However, the proportion with facet joint damage alone (without syndesmophyte) and those with syndesmophyte alone (without facet joint damage) accounted for 31.0% and 29.3%, respectively, in each group with corresponding structural damage. New development of ≥1 of facet joint damage and syndesmophyte were seen at all stratified follow-up periods (0–4, 4–8, 8–12, and 12–16 years); the progression rate increased gradually from 8.1% to 9.7% for facet joint and from 10.9% to 13.6% for syndesmophyte. In the multivariable analysis adjusted for bridging syndesmophytes, symptom duration, BASDAI, CRP, and hip involvement, facet joint fusion was independently associated with BASFI (β=0.215, 95% CI: 0.104, 0.327).

Conclusions
In AS, assessing the radiographic damage of the facet joints along with vertebral bodies may provide an additional value in the evaluation of functional status.

Keywords
Ankylosing spondylitis, Facet joint, Function

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O-22

Clinical features of patients with active ankylosing spondylitis who did not respond to adalimumab but responded to Ixekizumab: A post-hoc analysis

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Background

It is unknown whether there are predictors of response to TNFi or IL-17i or response after switching from TNFi to IL-17i. To evaluate whether patients who were non-responsive to adalimumab (ADA) but subsequently responded to ixekizumab (IXE) differed from those responding to both ADA and subsequent IXE.

Methods

Analysis included 341 bio-naive patients with active AS from the phase-3 COAST-V randomized trial. Patients received 80mg IXE every 2weeks (Q2W), or 4weeks (Q4W), ADA 40mg Q2W, or placebo (PBO) for the 16-week blinded-treatment period. Of these, 329 entered the double-blind Week 16-52 period. Those receiving PBO or ADA were re-randomized to IXE 80mg Q4W or Q2W. Responders or non-responders were stratified based on Weeks 16 and 52 ASAS 40 response.

Results

More patients responded to IXE than ADA at Week 16. 30.9% responded to both initial ADA and subsequent IXE, 23.5% didn't respond to initial ADA but responded to subsequent IXE, 45.9% responded to IXE at both time points, and 12.3% didn't respond to IXE at Week 16 but did at Week 52. Across groups, patients had similar age, disease duration, or disease activity but there were proportionally more females among non-responders to either ADA or IXE at Week 16. ADA non-responders at Week 16/IXE responders at Week 52 had numerically lower baseline (mean[SD]) C-reactive protein (11.2 [11.2]), lower MRI SPARCC scores of the spine (11.6 [12.1]) and sacroiliac joints (1.1 [2.2]) than ADA responders at Week16/IXE responders at Week 52 (16.0 [17.1], 24.6 [32.6], and 5.5 [9.8]), respectively.

Conclusions

Non-responders to ADA who subsequently responded to IXE exhibited overall lower levels of inflammation compared with patients who responded to ADA/subsequent IXE. Data indicate IXE is efficacious in patients with active AS irrespective of inflammation level. Lower baseline inflammation may be a predictor of delayed response.

Keywords

Ixekizumab, Ankylosing spondylitis, COAST trials

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PDGF-BB as a novel therapeutic target in pathological bone formation of AS

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Background

Abnormal bone formation in enthesis is a key pathogenic feature in ankylosing spondylitis (AS), resulting in spinal ankylosis. Platelet-derived growth factor B (PDGF-BB) is well known as an important factor promoting bone formation. The aim of this study is to investigate the pathological bone-forming role of PDGF-BB in enthesis and its association with the pathogenesis of AS.

Methods

The sera were obtained from 63 patients with AS and 25 healthy controls (HCs). The patients were divided into two groups, early or advanced AS groups according to mSASSS scores (early: <32 and advanced: >32). PDGF-BB serum levels of three groups were measured using ELISA. The enthesis cells of interspinous process were obtained from 8 AS patients and 10 disease controls. The platelet-derived growth factor receptor beta (PDGFRB) distribution in tissues was evaluated by immunohistochemistry. The impact of PDGF-BB in human primary enthesis cells was assessed using bone formation indicators. To elucidate the mechanism of bone-forming activity increased by PDGF-BB, the stimulated cells were assessed by common molecular biology and biochemistry methods.

Results

PDGF-BB sera levels were significantly higher in advanced AS group than early AS and healthy controls (HCs). Expression of PDGFRB was elevated in enthesis of AS compared to disease controls. Additional PDGF-BB treatment in enthesis dramatically promoted bone matrix mineralization as well as matrix maturation. The bone-forming activity promoted by PDGF-BB was pronounced in AS enthesis. While PDGF-BB inhibitor obviously reduced the bone-forming activity in enthesis cells of early and advanced AS group. Mechanically, the PDGF-BB treatment in enthesis regulated SOX9 protein via PDGFRB-ERK-mTOR axis and RUNX2 transcript via PDGFRB-AKT-FOXO1A axis, respectively.

Conclusions

The PDGF-BB and its signaling transduction network are critical factors for abnormal bone formation occurring in the progression of AS, thereby highlighting its pathological therapeutic target against clinically AS diseases.

Keywords

ankylosing spondylitis, PDGF-BB, abnormal bone formation

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O-24

Multicenter study for the prevalence and fracture risk of osteoporosis in patients with ankylosing spondylitis

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Background

The aims of this study are to determine the proportion of patients with high-risk of osteoporotic fractures according to World Health Organization (WHO) criteria and the fracture risk assessment tool (FRAX) in patients with ankylosing spondylitis (AS) in Korea, and to investigate clinical factors affecting fracture risk.

Methods

This is a multicenter, retrospective study including 219 AS patients from five university hospitals. The control group was selected by matching age and sex with the AS patients. The evaluation of fracture risk was based on BMD measured by dual-energy X-ray absorptiometry and calculations using the FRAX criteria.

Results

The mean age was 47.6 years, and 75 (34.2 %) of them were female, of which 43 (57.3 %) were menopause. The numbers of candidates for pharmacological treatment using the WHO criteria and the FRAX with or without BMD criteria were 45 (20.5%), 21 (13.8%), and 23 (15.1%), respectively, which is significantly higher than that of control group. Among them, the proportion of patients receiving actual treatment was 39.1 – 73.3%. On logistic regression analysis, menopause was an independent factor in increasing the risk of fractures according to WHO criteria and FRAX with/without BMD. The ESR (odds ratio [OR] 5), CRP (OR 3.8), use of glucocorticoids (OR 2.6) and use of PPI (OR 2.7) were found to associated to the high-risk of osteoporotic fractures in FRAX without BMD, and HLA-B27 positivity (OR 4.1) and CRP (OR 2.3) were related to osteoporosis based on WHO criteria.

Conclusions

Among Korean patients with AS, there was a substantial gap in the rate of actual pharmacological treatment in patient with osteoporosis in WHO criteria and patients having a high-risk of osteoporotic fractures by the FRAX criteria. AS patients with menopause, high ESR or CRP, and use of glucocorticoids or PPI may increase their risk of osteoporotic fractures.

International Symposium

Initiation or Flare of Inflammation in RA : Functions of Fibroblast

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RNA identification of prime cells predicting rheumatoid arthritis flares

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Dr. Dana Orange, MD, MSc, is an Assistant Professor at Rockefeller University and Assistant Attending of Rheumatology at the Hospital for Special Surgery. She received her medical degree from Weill Cornell Medical College, Cornell University, and her MSc from Rockefeller University. She completed her Internal Medicine Residency at New York Presbyterian Hospital and her Rheumatology Fellowship at the Hospital for Special Surgery. Dr. Orange's research aims to understand the molecular underpinnings of symptoms of rheumatoid arthritis such as pain, morning stiffness, and flares.

In this lecture, she will discuss recently developed methods to empower patients to participate in dense longitudinal genomics studies from home and describe how this approach was used to gain insights into the immune events that led to rheumatoid arthritis flares. Immune activation was detected in blood in the weeks just prior to RA flare symptom onset. Specifically, we found evidence for a previously unexplored circulating CD45-/CD31-/PDPN+, Pre-Inflammatory MEsenchymal (PRIME) cell in RA patient blood that highly overlaps with synovial sublining fibroblasts. She will review emerging data on synovial fibroblasts and their role in rheumatoid arthritis.

Inflammation or damage : Fibroblasts decide

Christopher D. Buckley
Univ. of Oxford, United Kingdom

The synovium is a thin mesenchymal membrane encapsulating the joint space and is the major site of pathology in rheumatoid arthritis. Synovial fibroblasts comprise a key cell type in the hyperplastic pannus that invades and destroys cartilage and bone via their production of matrix degrading enzymes. However, they are also major contributors to inflammation by providing an amplificatory loop that drives the production of cytokines such as IL6.

Until now, functional subclasses of fibroblasts have proven difficult to define, characterize and study in health and disease. In contrast the identification of leucocyte subsets with non-overlapping effector functions provided a molecular framework for the development of targeted therapies that have demonstrated spectacular success in immune-mediated inflammatory diseases (IMIDs). Furthermore, it remains unknown whether fibroblast mediated inflammation and tissue damage always coupled, reflecting cellular plasticity residing within a single fibroblast population or instead, are uncoupled and mediated by different subsets of fibroblasts

In this lecture I will explain the interrelationships between synovial fibroblast subsets in the lining and sub-lining layers of the synovium and observe how selective deletion of these subsets or changes in their biology alter the balance between persistent inflammation and tissue damage during the development of arthritis. Next I will describe the functional relationships between alterations in fibroblast subsets and disease outcome during the development of human rheumatoid arthritis. Finally I will speculate on how clinical trials targeting fibroblasts in patients with IMIDs might be delivered given these new findings

References:

1. Distinct fibroblast subsets drive inflammation and damage in arthritis. Croft AP, Campos J, Jansen K, Turner JD, Marshall J, Attar M, Savary L, Wehmeyer C, Naylor AJ, Kemble S, Begum J, Dürholz K, Perlman H, Barone F, McGettrick HM, Fearon DT, Wei K, Raychaudhuri S, Korsunsky I, Brenner MB, Coles M, Sansom SN, Filer A, Buckley CD. Nature. 2019 Jun;570(7760):246-251. PMID: 31142839
2. Notch signalling drives synovial fibroblast identity and arthritis pathology. Wei K, Korsunsky I, Marshall JL, Gao A, Watts GFM, Major T, Croft AP, Watts J, Blazar PE, Lange JK, Thornhill TS, Filer A, Raza K, Donlin LT; Accelerating Medicines Partnership Rheumatoid Arthritis & Systemic Lupus Erythematosus (AMP RA/SLE) Consortium, Siebel CW, Buckley CD, Raychaudhuri S, Brenner MB. Nature. 2020 Jun;582(7811):259-264. PMID: 32499639

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Mitochondrial STAT3 attenuates rheumatoid arthritis by regulation of synovial fibroblast autophagy

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Abstract

Th17 cells are activated by signal transducer and activator of transcription 3 (STAT3) factors, and these cells correlate with the pathologic changes of rheumatoid arthritis (RA). Recent studies have demonstrated the presence of STAT3 in the mitochondria, but its function is unclear. We investigated the role of mitochondrial STAT3 (mitoSTAT3) in Th17 cells and fibroblast-like synoviocytes (FLS), and analyzed the correlation of mitoSTAT3 with RA disease activity. Accumulation of autophagolysosomes, increased inflammatory cell death, and decreased mitoSTAT3 activity were observed in RA FLS treated with IL-17. The pathological changes in experimental RA, expression of Th17 and Treg cells, autophagolysosome formation, and inflammatory cell death were analyzed using mitoSTAT3 overexpression DNA vector and mitoSTAT3 inhibitor. The functions of mitoSTAT3 were analyzed in RA synovial fluid mononuclear cells and peripheral blood mononuclear cells. IL-17 induced the accumulation of autophagolysosomes and expression of inflammatory cell death factors (such as RIP1, RIP3, and p-MLKL) in RA FLS, and decreased mitoSTAT3 activation. In a collagen-induced arthritis mouse model, pathological changes (arthritis and joint inflammation) were decreased by mitoSTAT3 overexpression vector. The accumulation of autophagolysosomes and expression of inflammatory cell death factors were decreased in these mice. Zinc, a mitoSTAT3 enhancer, increased mitochondrial membrane potentials and decreased the production of reactive oxygen species and IL-17 in murine and human Th17 cells. The increased activity of STAT3 accelerated the development of arthritis and inflammatory cell death. Therefore, the activation of mitoSTAT3 induced intact autophagolysosome formation and inflammatory cell death by regulating mitochondrial function. MitoSTAT3 inhibits the development of RA through the regulation of autophagy and inflammatory cell death in human FLS. MitoSTAT3 also decreased IL-17 production in Th17 cells. Therefore, mitoSTAT3 may be a novel treatment for RA.

Keywords : Rheumatoid arthritis, Mitochondrial STAT3, Autophagolysosome, Th17, Cell death

Free Paper Session

Vasculitis and Metabolic Bone Disease

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O-25

Vascular uptake on 18F-FDG PET/CT during the clinically inactive state of Takayasu arteritis is associated with a higher risk of relapse

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Background

To evaluate whether vascular uptake on 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) during the clinically inactive state of Takayasu arteritis (TAK) is associated with disease relapse.

Methods

Patients with TAK who underwent 18F-FDG PET/CT during the clinically inactive state of the disease between 2006 and 2019 were included. Clinically inactive disease was defined as a status not fulfilling the National Institutes of Health (NIH) criteria for active disease in TAK. Relapse was defined as recurrence of clinically active disease after a clinically inactive period, requiring change in the treatment regimen. Vascular uptake on 18F-FDG PET/CT was assessed using target/background ratio (TBR), calculated as arterial maximum standardized uptake value (SUV)/mean SUV in venous blood pool. Multivariable Cox regression analysis was performed to identify factors associated with relapse.

Results

A total of 33 patients with clinically inactive TAK were included. During a median observation period of 4.5 (0.9–8.1) years, relapse occurred in nine (27.3%) patients at median 1.3 (0.7–6.9) years. Notably, TBR (1.5 [1.3–1.8] vs. 1.3 [1.1–1.4], p=0.044) was significantly higher in patients who relapsed than those who did not. On multivariable Cox regression analysis, the presence of NIH criterion 2 (adjusted HR: 7.044 [1.424–34.855], p=0.017) and TBR (adjusted HR: 11.533 [1.053–126.282], p=0.045) were significantly associated with an increased risk of relapse.

Conclusions

Vascular uptake on 18F-FDG PET/CT and the presence of NIH criterion 2 are associated with future relapse in patients with clinically inactive TAK.

Keywords

PET/CT, inactive, Takayasu arteritis

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Surgical outcomes after operative procedures in patients with Behcet's disease

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Background

Behcet's disease (BD) is characterized by hyper-inflammatory response to trauma, which is called the pathergy phenomenon. Therefore, there are concerns about postoperative complications when the affected patients undergo surgical procedures. Here, we comprehensively investigated the incidences of postoperative complications after surgical procedures.

Methods

We retrospectively reviewed all the patients with BD who underwent surgeries at Seoul National University Hospital between January 2003 to December 2019. Diagnosis of BD was based on the International Study Group criteria or revised diagnostic criteria for the Behcet's Disease Research Committee of Japan. The incidence of surgical complications and the associated factors of surgical wound complications were analyzed.

Results

The patients were composed of 270 patients (49.1 ± 13.6 years at operation, 107 men) and they underwent 356 surgeries. A total of 38 cases (10.7 %) of postoperative complications were found, of which 32 (9 %) were surgical wound complications including 16 wound dehiscences (50 %), 11 bleedings (34.4 %), 6 anastomotic dehiscences (18.8 %), 3 wound infections (9.4 %), 2 graft occlusions (6.3 %), and 1 fistula formation (3.1 %) with median time interval 10 days from the operation date (interquartile range (IQR) 5 to 19 days). Sixteen cases (4.5 %) required reoperations due to wound problems, and there were four operation-related deaths (1.1 %). Seventeen cases of long-term surgical recurrences were identified within the median follow-up of 21.5 months (IQR 16.8 to 52.5 months). Most postoperative wound complications occurred after cardiac (33.3 %), vascular (26 %), and gastrointestinal (12.5 %) surgeries, while those rarely occurred after orthopedic, thoracic, endocrinologic, and breast surgeries.

Conclusions

Incidences of postoperative complications vary among different surgeries in BD. The incidences of surgical wound complications are higher in cardiac, vascular, and gastrointestinal surgeries in patients with BD. Special perioperative care is recommended for these surgeries in BD patients.

Keywords

Behcet's disease, surgery, complication

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O-27

Clinical characteristics and radiographic outcome of vascular Behcet's disease involving aorta and its major branches

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Background

Behcet's disease (BD) is an immune-mediated systemic vasculitis affecting any size of blood vessels. Previous studies showed that BD may involve large arterial vessels but the radiographic outcome has not been well known due to its low prevalence. We aim to describe the clinical characteristics and radiographic outcomes of vascular BD involving the aorta and its major branches.

Methods

This retrospective cohort study was performed in patients with vascular BD involving the aorta and its major branches. All included patients underwent computed tomography angiography (CTA) at least two times with a 2–5-year interval. Radiographic progression was defined as newly developed and/or aggravated (> 20%) characteristic features on CTA.

Results

The cohort included 22 patients with BD with a mean interval of 3.54 years between the initial and follow-up CTA. Five patients (22.7%) showed radiographic progression. Patients with radiographic progression had a longer disease duration at baseline than those without (6.61 vs. 1.63 years, p = 0.010, Table 1). Of all patients, 21 (95.5%) had vascular aneurysms/pseudoaneurysms and 11 (50.0%) had thrombosis. The most frequently involved arteries were the abdominal aorta and iliac arteries (observed in nine patients [40.9%] each), followed by the ascending aorta and femoral arteries (observed in six patients [27.3%] each). The characteristics and locations of vascular involvement did not significantly differ according to the radiographic outcome (Table 1).

Conclusions

A considerable proportion of patients with BD with arterial involvement showed radiographic progression within 2–5 years. Patients with radiographic progression had a longer disease duration at baseline. The most common form of arterial involvement of BD was aneurysmal change, followed by thrombus formation.

Keywords

Behcet's disease, CT angiography, large vessel vasculitis

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Soluble immune checkpoint molecules in patients with antineutrophil cytoplasmic antibody-associated vasculitis

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Background

Immune checkpoint molecules balances the immune effector responses and the regulatory reactions. We speculated that soluble checkpoint molecules involve in the dysregulation of immune response and autoimmunity. Herein, we evaluated the association between soluble checkpoint molecules and antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV).

Methods

Total 56 patients with AAV from a prospective observational cohort and 40 healthy controls were analysed. Soluble types of PD-1, PD-L1, PD-L2, CTLA-4, CD28, CD80, CD86, ICOS, TIM-3, BTLA, CD40, LAG-3, TLR-2, and CD27 were measured in stored sera using Milliplex MAP assay. Paired analyses were performed before and after treatment. AAV-specific indices including BVAS, FFS, vasculitis damage index and blood samplings were collected.

Results

The levels of sPD-L1, sCD28, sCD80, sCD86, sICOS, sTIM-3, sLAG-3, sTLR-2, and sCD27 were higher and sCTLA-4 was lower in patients with AAV than in healthy control ($p < 0.05$) (Table 1). Levels of sPD-L2 and sCTLA-4 was lower in patients with AAV than in healthy control at baseline, which recovered after treatment (Table 2). Levels of sCD28, sTIM-3, and sCD27 were higher in patients with AAV than in healthy control at baseline, which decreased after treatment. Furthermore, levels of sCD28 significantly correlated with BVAS ($r = 0.281$) and sTIM-3 significantly correlated with BVAS ($r = 0.485$) and five factor score ($r = 0.738$).

Conclusions

The levels of various soluble checkpoint molecules are altered in patients with AAV and these soluble checkpoint molecules could potentially act as a surrogate marker of AAV disease activity.

Keywords

soluble checkpoint molecules, antineutrophil cytoplasmic antibody-associated vasculitis

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O-29

Ncoa6 is a novel regulator of NLRP3 inflammasome and gouty arthritis

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Background
Nuclear receptor coactivator 6 (Ncoa6), a transcriptional coactivator of nuclear receptors, plays roles in apoptosis, embryonic growth, and insulin secretion, however, its role in immune system remains unclear. Here, we investigated whether Ncoa6 controls innate immunity and immunologic diseases.

Methods
Intracellular localization of Ncoa6 was determined by immunocytochemistry and confocal microscopy. IL-1β and p20 concentrations were measured in the culture supernatants of human monocytes or mouse macrophages. Immunoprecipitation assay was conducted to assess molecular interactions between Ncoa6 and NLRP3. Animal models of acute tubular necrosis (ATN) of the kidney and MSU crystal-induced arthritis were induced in Ncoa6-deficienct and control mice.

Results
: In activated monocytes/macrophages, Ncoa6, a nuclear protein, was trans-localized from the nucleus into the cytoplasm and its expression was increased by LPS and pro-inflammatory cytokines. Interestingly, Ncoa6 actively formed aggregates ('specks') in the cytoplasm of activated monocytes, which were co-localzied with inflammasome components, including ASC and NLRP3. Specifically, Ncoa6 protein was directly bound to NACHT domain of the NLRP3, but not to ASC. Transcriptomic profiling of Ncoa6-deficient macrophages suggests that Ncoa6 is involved in innate immunity, macrophage activation, and inflammasome. In parallel with this, production of IL-1β and p20 was markedly reduced in Ncoa6-deficient human monocytes. The macrophages of Ncoa6fl/flLysMCRE mice also showed a decreased secretion of IL-1β and p20. Mechanistically, Ncoa6 deficiency inhibited the assembly of NLRP3 inflammasome by suppressing ASC speck formation and oligomerization. Moreover, MSU crystal-induced arthritis was dramatically reduced in Ncoa6fl/flLysMCRE mice; ATN of the kidney, anther model of NLRP3 inflammasome, showed similar results. By contrast, Ncoa6 expression, in addition to speck formation, was substantially increased in the synovial macrophage of patients with gouty arthritis, correlating with IL-1β expression, and it was completed blocked by colchicine.

Conclusions
Our data demonstrate first that Ncoa6 is a novel, critical regulator of NLRP3 inflammasome and gouty arthritis

Keywords
Ncoa6, inflammasome, gout arthritis

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Increased risk of cardiovascular events and death in the initial phase after discontinuation of febuxostat or allopurinol: another story of the CARES trial

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Background

The Cardiovascular Safety of Febuxostat or Allopurinol in Patients with Gout (CARES) trial suggested a higher risk of cardiovascular (CV) death from febuxostat than from allopurinol. (1) Consequently, the FDA added a boxed warning to febuxostat regarding the increased mortality risk. However, the mortality rate was increased by up to 40-fold after the discontinuation of allopurinol or febuxostat in simple re-calculation of the CARES trial data. The sharp increases in mortality were assumed to be associated with rapid changes in the serum uric acid levels arising from drug discontinuation (rebound hyperuricemia). (2) We investigate whether major adverse cardiovascular events (MACE) and CV death were in the initial stage after discontinuation of febuxostat or allopurinol.

Methods

The CARES trial was a multicenter, randomized, double-blind non-inferiority trial. As in the CARES trial, we used the data of patients with gout and a history of major CV disease to perform a modified intention-to-treat analysis. We compared the MACE that occurred during administration and the initial phase after discontinuation to determine the impact of discontinuation of febuxostat or allopurinol.

Results

Among 6190 patients, the incidence rate per 100 person-years for MACE was 3.11 during administration and 6.71 after discontinuation of the study drugs. A higher risk of MACE was observed after discontinuation of the study drugs than that observed during administration (hazard ratio [HR], 2.32; 95% confidence interval [CI], 1.94–2.77; $P < 0.001$). MACE was significantly increased after discontinuation compared with during administration within 1 month (HR, 7.40; 95% CI, 5.38–10.17), 3 months (HR, 6.05; 95% CI, 4.78–7.67), and 6 months (HR, 5.22; 95% CI, 4.26–6.39).

Conclusions

In patients with gout and major coexisting CV conditions, MACE was increased in the initial stage after discontinuation of febuxostat or allopurinol.

Keywords

Gout, Cardiovascular Diseases

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O-31

The appropriate starting dose of urate lowering treatment

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Background

The goal of gout treatment is to reduce the frequency of gout attacks and prevent complications. In general, gout attacks are more likely to occur when there is an abrupt fluctuation in serum urate level. Guidelines and expert opinions recommend starting treatment with low-dose urate lowering agents. The occurrence of gout attacks at the start of treatment is a factor that worsens treatment compliance. This study was conducted to determine the appropriate dose of a febuxostat that can reduce the occurrence of gout attacks during initial treatment.

Methods

We retrospectively analyzed patients who were diagnosed with gout and started treatment at Jeju National University Hospital from May 2018 to May 2020.

Results

Two hundred twenty-seven patients were included in this study, their mean age was 53.15±16.4 years, and 219 (96.5%) were male. When divided into two groups according to the starting dose of febuxostat (20mg vs. 40mg), there were no significant differences in mean age {56.5±16.8 vs 50.8±15.8 (years), p=0.210}, disease duration{3.8±5.6 vs 3.6±5.2 (years), p=0.459}, colchine {69 (73.4%) vs 111 (83.5%), p=0.066}, creatinine clearance {74.7±28.9 vs 89.3±28.3 (mL/min), p=0.141}, initial urate level{9.5±1.5 vs 8.8±1.3 (mg/dL), p=0.250}, subcutaneous tophi {13(13.8%) vs 16(12.0%), p=0.689} between the two groups. There were significantly more patients with gout attacks in the 20mg group than in the 40mg group during 1 year {43(45.7%) vs 34(25.6%), p=0.002}, especially in the period of 0~1month {19(20.2%) vs 9(6.8%), p=0.002}, 1~3months {19(20.2%) vs 14(10.5%), p=0.041}. Multivariate logistic regression analysis showed that the starting dose of febuxostat (40mg) (Odds ratio 0.482; 95% CI, 0.249-0.933; p=0.030) and the use of colchicine (Odds ratio 0.348; 95% CI, 0.154-0.782; p=0.011) were predictors of fewer gout attacks.

Conclusions

When starting urate lowering treatment, starting with febuxostat 40mg may reduce the incidence of early gout attacks compared to starting with 20mg.

Keywords

Urate lowering treatment, gout attack, starting dose

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Catch-up growth of infants born to mothers with autoimmune rheumatic disorders

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Background

To assess demographic neonatal characteristics and height and weight growth pattern of babies born to autoimmune rheumatic disorders (ARD) mothers.

Methods

Retrospective analysis of medical records of babies born to ARD mothers and gestational age matched babies at the two hospitals of The catholic university of Korea between 2010 and 2017. Demographic data for mothers and newborns, as well as autoimmune laboratory of ARD mothers' baby were assessed. The growth measurements included height and weight of each neonate at birth and follow ups.

Results

A total of 142 infants from ARD mothers and 149 infants from healthy mothers were enrolled in the study. Among maternal parameters, there was no significant difference for delivery age, parity, abortion and premature delivery history between ARD and healthy mothers. The diseases diagnosed of enrolled ARD mothers in this study were SLE (81%), Sjogren syndrome (6%), and other autoimmune phenomenon. The overall neonatal characteristics between the two groups were significantly different in prematurity, gestational age, birth weight and height, but not different in Apgar score and delivery type. For most neonates, autoimmune laboratory results were normalized within 1 year follow up except anti-SSB antibody. The height and weight for age z-score was lower than the normal age groups at birth but was showed catch up growth around 2 year of age.

Conclusions

The weight and height differences at birth could be caught up by 2 years of age in neonates born to ARD mothers and maternal ARD does not affect the growth of their offspring.

Keywords

Autoimmune diseases, Growth

Symposium

Medical humanities Symposium - COVID-19 and Inequality

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Justice and fairness in the era of COVID-19

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What is justice? What is fairness? These concepts has been defined in many different ways. Even recently, John Rawls defined justice from his liberal stance, but was criticized by Michael Sandel for his lack of proper understanding of humans. In the era of covid-19, a new issue has been raised in this field: meritocracy and its relation to justice and fairness.

The issue of meritocracy was first raised by Michael Young. In his book The Rise of the Meritocracy (1958) Young depicted a future England where meritocracy would be taken as the main principle of society. Merit is defined as the sum of I.Q.(talents) and efforts. The English people took it because meritocracy was proven as an effective social principle that ended the aristocratic and plutocratic inefficiency from the traditional England. The future society of England, however, was described as a dystopia,

Michael Sandel, in his book The Tyranny of Merit, developed Young's idea in the context of contemporary society, especially in the era of the covid 19. He values merit for the good of society, but criticizes meritocracy because it will lead to the collapse of solidarity among citizens and eventually lead us to an unhappy society. For it will deepen the discrepancy of the have's and the have-not's, and meritocracy will justify the hubris of the winners and the humility of the losers.

Sandel's remedy for meritocratic harms is to promote virtues for democratic citizens by letting them realizing that their merits are not entirely from their endeavors and that they have good reasons to be thankful to other members of the society. In a nutshell, he tries to form a culture in which people may collaboratively pursue a society that values merits and equality as well.

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Ethics of vaccine refusal

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Univ. of Seoul, Korea

It has been nearly two years since COVID-19, which was first reported in Wuhan, China in December 2019, became a pandemic. Vaccination is currently considered a decisive factor that could turn the tide, that is, a game changer. However, vaccination is associated with many ethical and legal issues. In this presentation, I will first explore ethical issues related to "vaccine refusals." For example, is it someone who refuses to vaccinate against COVID-19 a free-rider? Isn't it unfair not to do one's share while receiving the benefits of herd immunity? On the other hand, is vaccination self-regarding "risk avoidance,"or other-regarding "risk transfer", or using others as a merely means of self-protection, that is "use others as a shield"? Focusing on these questions, I will discuss the issues of fairness and ethical evaluation of vaccination and vaccine refusals.

Next, I will review legal issues relating to vaccine refusals. In order to cope with future pandemics, I will examine whether the duty of safety can be accepted as the fundamental duty of the people. The current Infectious Disease Prevention Act requires up to one year in prison or up to 10 million won in fines if a COVID-19 patient, so-called confirmed patient, refuses to medical treatment without reasonable reasons. For example, suppose that it is the time when herd immunity is expected to fail in light of the current inoculation situation. In such a situation, should vaccination be legally mandatory? I will examine the question of what legal or administrative response can be made to the refusal of vaccination. (Of course, it is possible to say that the state cannot intervene because vaccine refusal belongs to an individual's basic rights.)

COVID-19 Pandemic calls for fundamental reflection on the concepts and thinking systems that we have undoubtedly accepted. As you know, a liberal democratic society has regarded the protection and enhancement of individual human rights as the highest virtues of society based on the dichotomy of individual and society. The dichotomous frame of individuals and society did not have the opportunity to face fundamental academic challenges, but now the situation has changed due to COVID-19. The current long-term (and expected repetitive) outbreak of infectious diseases such as COVID-19 makes us fundamentally skeptical of the validity of individual/social dichotomy. In order to philosophically examine the legitimacy of vaccination refusal, this presentation aims to find a 'new' frame that can overcome the limitations of the conventional individual/social dichotomy.

KCR 2021

41st Korean College of
Rheumatology Annual Scientific Meeting
and the 15th International Symposium

October 21(Thu) - 23(Sat), 2021
Seoul Dragon City, Seoul, Korea

DAY 03

PROGRAM

October 23(Sat)

Breakfast Symposium IV - Yuhan

The Treatment Companion of Rheumatoid Disease Patients

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RA/AS treatment journey with biosimilars

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Hanyang Univ., Korea

In recent years, number of biosimilars for treatment of rheumatic diseases has been approved and are available for use. They have demonstrated sufficient comparability to their reference products through vigorous examinations as well as extensive clinical assessments. There are growing evidence of long-term efficacy and safety of biosimilars from real-world data. Comparable long-term retention rates of etanercept biosimilar SB4 (Etoloche) was observed in the non-medical mandatory switching in the DANBIO registry as well as non-mandatory switching in the BIO-SPAN study. Sustained and stable clinical disease activity in both rheumatoid arthritis and ankylosing spondylitis was observed in European patients in the BENEFIT study. Infliximab biosimilar SB2 (Remaloce) also demonstrated long-term real-world evidence of long-term efficacy and safety comparable to the originator.

Breakfast Symposium V - Astellas

Lupus Nephritis

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Calcineurin inhibitors in systemic lupus erythematosus : A revisit

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The calcineurin inhibitors (CNIs) belong to a class of immunosuppressive agents that inhibit T-cell activation through the suppression of the calcium/calcimodulin-dependent phosphatase calcineurin. Tacrolimus (TAC) is preferred to cyclosporine A (CSA) for treating SLE because of fewer cosmetic, hypertensive and dyslipidemic side effects. Recent randomized controlled trials (RCTs) have demonstrated non-inferiority of TAC to mycophenolate mofetil (MMF) or cyclophosphamide (CYC) as induction therapy of lupus nephritis. Combination of TAC and MMF is superior to intravenous CYC pulses in inducing remission of lupus nephritis. Newer generation CNIs have recently emerged. Voclosporin is a chemical analogue of CSA with an improved pharmacokinetic profile. A recent phase 3 RCT has demonstrated superiority of voclosporin to placebo when combined with MMF and moderate dose of glucocorticoids in lupus nephritis at week 52, particularly in the Asian subgroup. Although no increase in infection was demonstrated, results were inconsistent with the earlier phase 2 trial of the same treatment protocol. Close surveillance for infective complications is warranted when CNIs are combined with other immunosuppressive drugs. Low-dose TAC was shown to be as effective as azathioprine as maintenance therapy of lupus nephritis. Open-label single arm studies from Asian countries have reported tolerability of long-term therapy with TAC in various SLE manifestations. In the APLAR consensus statements, TAC is an option for maintenance therapy of SLE when other immunosuppressive drugs are intolerant or contraindicated. TAC does not affect fertility and is relatively safe in pregnancy. However, drug level monitoring is required to ensure drug exposure and minimize toxicities. There are still no safety data of voclosporin in pregnancy yet.

In summary, TAC is an option for induction therapy of lupus nephritis. Combining TAC with MMF may be considered for refractory disease. TAC may also be considered in situation when persistent leukopenia precludes the use of adequate doses of other immunosuppressive drugs. The cost-effectiveness of combining the CNIs with MMF as induction therapy of lupus nephritis requires further evaluation.

KCR 2021 | October 21(Thu) - 23(Sat), 2021
Seoul Dragon City, Seoul, Korea

Breakfast Symposium VI - Lilly

Up-to-date Treatment of SpA

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Ixekizumab : New treatment option for patients with axial SpA

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Ankylosing spondylitis usually starts with sacroiliac joint inflammation and progresses to irreversible spinal ankylosis, and it is also a disease that seriously degrades the patient's quality of life. Following the TNF inhibitors that have been prescribed primarily as a treatment for ankylosing spondylitis, a new IL-17A inhibitor, ixekizumab, has been approved for the reimbursement from October 1st, 2020 in Korea. This lecture addresses the efficacy and safety of ixekizumab for up to 52 weeks in two phase III studies of patients with active radiographic axial spondyloarthritis (r-axSpA) who were biological disease-modifying antirheumatic drug (bDMARD)-naive (COAST-V) or tumour necrosis factor inhibitor (TNFi)-experienced (COAST-W). And this lectures also addresses the long-term efficacy and safety of ixekizumab for up to 104 weeks in COAST-Y, 2 years extension of the COAST-V, -W trials, recently updated in EULAR 2021.

Adult patients with active r-axSpA were randomised 1:1:1:1 (n=341) to 80 mg ixekizumab every 2 (IXE Q2W) or 4 weeks (IXE Q4W), placebo (PBO) or 40 mg adalimumab Q2W (ADA) in COAST-V and 1:1:1 (n=316) to IXE Q2W, IXE Q4W or PBO in COAST-W. At week 16, patients receiving ixekizumab continued their assigned treatment; patients receiving PBO or ADA were rerandomised 1:1 to IXE Q2W or IXE Q4W (PBO/IXE, ADA/IXE) through week 52. All patients entered into COAST-Y and received IXE and used for baseline characteristics data. n=773 (IXE Q4W, N=350; IXE Q2W, N=423) Patients who, at Week 24, were eligible for randomization to IXE withdrawal (PBO) or to continued IXE treatment. n=155 (IXE Withdrawal [PBO], N=53; IXE Q4W, N=48; IXE Q2W, N=54)

In COAST-V, assessment of SpondyloArthritis international Society 40 (ASAS40) responses rates (intent-to-treat population, non-responder imputation) at weeks 16 and 52 were 48% and 53% (IXE Q4W); 52% and 51% (IXE Q2W); 36% and 51% (ADA/IXE); 19% and 47% (PBO/IXE). Corresponding ASAS40 response rates in COAST-W were 25% and 34% (IXE Q4W); 31% and 31% (IXE Q2W); 14% and 39% (PBO/IXE). These ASAS40 responses were sustained through Week 116 in COAST-Y. Both ixekizumab regimens sustained improvements in disease activity, physical function, objective markers of inflammation, QoL, health status and overall function up to 52 weeks. Most patients treated with ixekizumab for 2 years did not show radiographic progression. Safety through 52 weeks of ixekizumab was consistent with safety through 16 weeks. Ixekizumab treatment led to consistent and sustained long-term improvements in disease activity and quality of life in patients with r-axSpA, with no new safety signals after up to 2 years of treatment.

Ixekizumab is a novel alternative for treatment of axSpA in Korea. Significant improvements in ASAS40 response rate vs. placebo were seen as early as Week 1 for TNFi-experienced and Week 2 for bDMARD-naïve patients. Responses were sustained through Week 116. Ixekizumab reduced objective inflammatory markers and improved symptoms, functioning, quality of life, and patient-reported outcome measures. There were no unexpected safety signals reported in COAST-V, -W and COAST-Y trials.

Keynote Lecture

EULAR Participates in KCR's 40th-anniversary Celebrations

JRD Journal of Rheumatic Diseases
Vol. 28, Suppl. 1, October, 2021

EULAR strategy, collaborations and activities in the COVID-19 era

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Univ. of Turin, Italy

The EULAR COVID-19 Recommendations

In the early stages of the pandemic a EULAR Task Force was convened to address several aspects of the severe acute respiratory syndrome, the virus, and the disease caused by SARS-CoV-2, COVID-19 in the context of rheumatic and musculoskeletal diseases (RMDs), developing the following work:

- EULAR provisional recommendations for the management of RMDs in the context of SARS-CoV-2 (first published June 5, 2020), meant for patients with RMDs and their caregivers, agreeing on five overarching principles and 13 recommendations.
- EULAR View-points on SARS-CoV-2 vaccination in patients with RMDs (first published February 9, 2021) addressing key questions, especially for patients with inflammatory RMDs and patients that are treated with drugs that may influence their immune system.
- First update of the EULAR Recommendations for the management of RMDs in the context of SARS-CoV-2 (work finalised by July 16, 2021), a bullet-list with overarching principles and recommendations. A detailed explication will be published, together with the results of the systematic literature research underpinning these recommendations, later in 2021.

EULAR Advocacy

Marking World Arthritis Day on 12 October, EULAR held the EULAR Brussels Forum 2020, with a digital debate, on the topic 'Employment risks and impacts for Europeans with RMDs during the COVID-19 recession' providing a fully online space for ideas and views to be exchanged and shared with society at large and thereby contribute to bringing change forward for those with an RMD in the workplace.

The EULAR COVID-19 repositories for clinicians and patients

EULAR created the COVID-19 Repository for clinicians and COVID-19 Repository for patients providing guidance and an array of useful resources about the COVID-19 outbreak, such as reading materials, webinars and infographics, to give clinicians and people with RMDs the best possible care.

The EULAR COVID-19 and COVAX registries

With the identified need for data to address the lack of information on the relationship between COVID-19 outcomes, RMDs and their associated treatments, the EULAR COVID-19 Registry was created in early 2020. In 2021 the EULAR COVAX Registry was established to gather vaccination outcomes data.

These physician-reported registries gather European paediatric and adult data and were established in collaboration with the Paediatric Rheumatology European Association (PReS) and the COVID-19 Global Rheumatology Alliance. The registries demonstrated the strength in collaboration across Europe and beyond, acting as catalysts to build on these networks for both COVID-19 and other RMD research.

The EULAR virtual congresses 2020 and 2021

The COVID-19 pandemic has imposed unprecedented changes in our personal and professional lives. After careful consideration and evaluation of the risks and alternatives, EULAR decided to offer virtual congress experiences in 2020 and 2021, remaining committed to meeting our scientific, educational, and training obligations with a scientific programme of the highest level.

The whole rheumatology community ensured these congresses were real successes. Thanks to the amazing collaboration and commitment by the speakers and abstract presenters to ensure all material was up on our congress platform in time, we were ready to welcome over 18,000 (2020) / 17,000 (2021) from more than 140 countries. Thus, these meetings saw more delegates than ever before.

But while scientific sessions can be watched on a screen, real live face to face interaction is dearly missed and we are enthusiastically planning for the 75th anniversary of EULAR. We welcome you to celebrate with us in Copenhagen from 1-4 June 2022.

See EULAR 2022 – Previous congresses.

KCR 2021 | October 21(Thu) - 23(Sat), 2021
Seoul Dragon City, Seoul, Korea

International Symposium

Osteoporosis Update

Osteoporosis update. Clinical update

Peter Ebeling
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Osteoporosis is a global public health problem, with fractures contributing to significant morbidity and mortality. It is particularly important in Asia, as ageing of the population and increasing urbanization mean that >50% of hip fractures will occur in Asia by 2050. Although post-menopausal osteoporosis is most common, up to 30% of post-menopausal women, >50% of premenopausal women, and between 50-80% of men have secondary osteoporosis. Exclusion of secondary causes is important as treatment of such patients often commences by treating the underlying condition. These are varied but often neglected, ranging from endocrine to chronic inflammatory and genetic conditions. In addition, recent head-to-head trials of antiresorptive and anabolic drugs in women with post-menopausal osteoporosis show that anabolic drugs are more effective in reducing vertebral fractures, and in some cases, also non-vertebral and hip fractures, than oral bisphosphonates. Unfortunately, despite having such effective treatments, osteoporosis remains under-diagnosed and undertreated. The challenge is to identify the patients most at risk of a fragility fracture, i.e. those with a pre-existing fragility fracture, so that they can be investigated for osteoporosis and treatment initiated. The most effective way of doing this is with a fracture liaison or refracture prevention service to identify patients coming into a health service with a fragility fracture and directing them to osteoporosis investigations and treatment initiation. Another challenge is to identify which groups of patients may benefit the most from anabolic therapy. Recent osteoporosis management guidelines have identified patients with very high fracture risk as the most likely to benefit. However, the guidelines differ in their definition of very high fracture risk. The American Association of Clinical Endocrinologist (AACE) guidelines recommend anabolic therapy, including romosozumab, for very high fracture risk defined as one of the following: recent fracture (<12 months); multiple (≥2) fractures while on therapy; use of drugs that cause skeletal harm; BMD T-scores <−3.0; FRAX® score >4.5% (hip) or >30% (major osteoporotic fracture); high fall risk. By contrast, the US Endocrine Society guidelines definition of very high fracture risk includes one of the following: severe or multiple vertebral fractures; T-score <-2.5 and any fracture(s); bisphosphonate failure (fractures or loss of BMD while on treatment); medication-related osteonecrosis of the jaw or atypical femur fracture while on antiresorptive drugs. However, it is important to remember that anabolic therapy should always be followed by antiresorptive therapy to either maintain or increase the foundational increases in both bone density and bone strength afforded by anabolic therapy. In Asia, the Asian Pacific Consortium on Osteoporosis (APCO) has developed a Framework to standardize osteoporosis management guidelines in the region to improve health outcomes and to reduce the predicted tsunami in hip fractures.

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New insights into the Osteocyte

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Even though considerable progress has been made in the last two decades regarding the biology and function of osteocytes, these cells are still difficult to study and resistant to standard experimental approaches. Whereas several useful cell line models have been generated, to date few Cre mouse models have been generated, mainly using the Dentin Matrix Protein, Dmp1 Cre and the isolation of primary osteocytes from bone, especially mature, hypermineralized bone, has proved difficult. In spite of these obstacles, new discoveries are still being made about this elusive bone cell.

Osteocytes make up over 90-95% of bone cells in the adult skeleton and their total mass of cell body and dendritic processes is greater than the mass of the brain. These cells can exist for decades in the bone matrix, making them long-lived cells, much longer than osteoblasts or osteoclasts. As these cells age, they convert from highly mechanosensitive cells to less mechanically sensitive cells while losing their connectivity through their dendritic processes. In the aged skeleton, not only are senescent cells present, but also, empty lacunae where previous cells existed. This may be the explanation for the skeletal resistance to exercise with aging.

Osteocytes are also secretory cells. One of the most famous osteocyte factors is sclerostin that inhibits osteoblastic bone formation. Another is Rankl, the major activator of osteoclasts. Luckily, mechanical loading reduces both sclerostin and Rankl expression, while increasing release of positive regulators of bone formation such as prostaglandin E2, ATP, and nitric oxide. Another product of osteocytes is fibroblast growth factor 23, which targets the kidney to regulate phosphate metabolism. So not only do osteocytes produce factors that regulate bone, but also factors that can target distant organs such as the kidney. Neutralizing antibodies to sclerostin, Rankl, and FGF23 have been approved as therapeutics, all three are osteocyte factors.

Osteocytes are also regulators of calcium. Parathyroid hormone, PTH, or PTH related protein working through high expression levels of the PTH type 1 receptor in osteocytes compared to osteoblasts, can induce a sequence of events resulting in the osteocyte becoming like and functioning similar to the osteoclast. The osteocyte can reduce the pH in its lacunae and generate enzymes that will degrade the matrix such as Cathepsin K, Trap, and MMPs in order to release calcium into the circulation especially under calcium demanding conditions such as lactation. In fact, a recent publication has shown that the major difference between male and female osteocytes is the elevated expression of these genes in females. Osteocytes may account for some of the sex differences in male bone as compared to female bone.

New avenues of osteocyte biology are being investigated such as the role of osteocytes in various forms of cancer, the role of osteocytes in regulating adipogenesis, myogenesis and muscle function, potential crosstalk with the brain, the role of osteocytes in diseases such as osteoarthritis where they may function as inflammatory cells, the kind of energy metabolism in loaded versus unloaded osteocytes and how osteocyte metabolism affects whole body metabolism, and others. These studies should lead to future additional therapeutics, again targeting osteocytes.

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Novel approach for evaluating bone mineral density of hips based on Sobel gradient-based map of radiographs utilizing convolutional neural network

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Osteoporosis, which is a common disorder associated with low bone mineral density (BMD), is one of the primary reasons for hip fracture. It not only limits mobility, but also makes the patient suffer from pain. Unlike traditional methods, which require both expensive equipment and long scanning times, this study aims to develop a novel technique employing a convolutional neural network (CNN) directly on radiographs of the hips to evaluate BMD. To construct the dataset, X-ray photographs of lower limbs and dual-energy X-ray absorptiometry (DXA) results of the hips of patients were collected. The core of this research is a deep learning-based model that was trained using the pre-processed X-rays images of 510 hips as the input data and the BMD values obtained from DXA as the standard reference. To improve performance quality, the radiographs of the hips were processed with a Sobel algorithm to extract the gradient magnitude maps, and an ensemble artificial neural network which analyses the outputs of CNN models corresponding to three Singh sites and biological parameters was utilized. The superior performance of the proposed method was confirmed by the high correlation coefficient of 0.8075 ($p<0.0001$) of the BMD measured by DXA in a total of 150 testing cases, with only 0.12 s required for applying the computing configuration to a single X-ray image.

Keywords: Convolution neural network, radiographs, osteoporosis, bone mineral density, hip fractures.

Free Paper Session

Rheumatoid Arthritis Clinical Research

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Incident and recurrent herpes zoster for first-line bDMARDs and tsDMARD users in seropositive rheumatoid arthritis patients: a nationwide cohort study

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Background

There is limited information regarding disease-modifying antirheumatic drugs (DMARD)-dependent risks of the overall, incident, and recurrent herpes zoster (HZ) during first-line biologic DMARD (bDMARD) or targeted synthetic DMARD (tsDMARD) treatment among seropositive rheumatoid arthritis (RA) patients in terms of HZ risk.

Methods

A total of 11,720 patients with seropositive RA who were prescribed bDMARD or tofacitinib between January 2011 and January 2019 from the Korean Health Insurance Review and Assessment Service database were studied. Multivariate Cox proportional hazards regression model was adopted to evaluate the adjusted hazard ratio (aHR) with 95% confidence interval (CI) for risk of HZ dependent on the choice of first-line bDMARDs or tsDMARD, including etanercept, infliximab, adalimumab, golimumab, tocilizumab, rituximab, tofacitinib, and abatacept.

Results

During 34,702 person-years of follow-up, 1,686 cases (14.4%) of HZ were identified, including 1,372 (11.7%) incident and 314 (2.7%) recurrent HZs. Compared to the abatacept group, tofacitinib increased risks of overall (aHR, 2.46; 95% CI, 1.61-3.76; P<0.001), incident (aHR, 1.99; 95% CI, 1.18-3.37; P=0.011), and recurrent (aHR, 3.69; 95% CI, 1.77-7.69; P<0.001) HZ. Infliximab (aHR, 1.36; 95% CI, 1.06-1.74; P=0.017) and adalimumab (aHR, 1.29; 95% CI, 1.02-1.64; P=0.032) also increased overall HZ risk. In addition, history of HZ was found to be an independent risk factor for HZ (aHR, 1.54; 95% CI, 1.33-1.78; P<0.001).

Conclusions

HZ risk is higher after tofacitinib treatment during first-line bDMARD or tsDMARD treatment among RA patients. Individualized characteristics and history of HZ need to be considered when selecting bDMARDs or tsDMARDs for RA patients in terms of HZ risks.

Keywords

herpes zoster, arthritis, rheumatoid, biological products

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O-34

Safety of JAK inhibitor in patients with rheumatoid arthritis who developed reactivation of herpes zoster after receiving JAK inhibitor

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Background

Janus kinase inhibitor (JAKi) increases the risk of the reactivation of herpes zoster (HZ) virus and may thus be temporarily discontinued in cases of HZ infection. In this study, we sought to determine the safety of JAKi during or following an HZ reactivation.

Methods

Medical records of all patients (n = 417) who received JAKi at a tertiary referral center between August 2015 and May 2021 were retrospectively reviewed. Among them, data from patients who developed HZ reactivation were collected and the clinical outcomes were evaluated for those who continued or resumed JAKi after HZ reactivation.

Results

Of 417 patients who received JAKi, 33 (7.9%) developed HZ reactivation during JAKi treatment (tofacitinib, n = 22; baricitinib, n = 11). The median age of the patients was 61 years (IQR, 53–69); 14 patients received glucocorticoids, and the mean dose of prednisone was 4.0 ± 2.3 mg. The median duration of JAKi administration before HZ reactivation was 11 months (IQR, 4–29). JAKi was continued in 24 (72.7%) patients during the HZ reactivation, and 5 (15.2%) patients temporarily discontinued the JAKi and then resumed it after episode of HZ. Three patients with HZ reactivation had acute complications such as encephalitis with HZ ophthalmicus. Four patients, including the three patients with complications, permanently discontinued JAKi. Of the 27 patients who were followed up for a median of 12 months (IQR, 5.5–22.5) after the HZ reactivation, HZ reactivation recurred in one patient; this patient maintained JAKi treatment for further 18 months, during which additional HZ recurrence was not observed.

Conclusions

JAKi was commonly continued or re-administered in patients with HZ reactivation, and the majority of patients did not experience significant complications or a recurrence of HZ reactivation. Thus, the use of JAKi after HZ reactivation may be generally safe and well-tolerated.

Keywords

Rheumatoid arthritis, JAK inhibitor, Herpes zoster

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Comparison between non-TNF-targeted treatment and use of a second Anti-TNF inhibitor for rheumatoid arthritis patients showing an insufficient response to the first Anti-TNF inhibitor

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Background

Despite improved quality of care for rheumatoid arthritis (RA) patients, many still experience treatment failure with biologic disease-modifying antirheumatic drugs (bDMARDs) or targeted synthetic DMARDs (tsDMARDs; typically JAK inhibitors [JAKi]), and eventually switch to another agent. We compared the efficacy between a second TNF inhibitor (TNFi) and non-TNF-targeted treatment as the second-line treatment for patients showing an insufficient response to the first TNFi.

Methods

The analysis was based on the prospective observational Korean Biologics (KOBIO) registry. Patients were included if they had received at least one prescription for a TNFi, and at least one follow-up prescription for a second TNFi or non-TNF-targeted treatment after discontinuation of the first. In total, 209 patients were analyzed, including 69 with a second TNFi and 140 with a non-TNF-targeted treatment (106 non-TNFi biologics and 34 JAKi). Cox regression was used to estimate the hazard ratio (HR) for discontinuation.

Results

The mean follow-up after switching drugs was 28.0 months (range: 0–80 months) and 53 (24.4%) of the 209 patients switched or discontinued the second drug. In multivariate Cox proportional hazard analysis, the non-TNF-targeted treatment group (including non-TNFi biologic and JAKi groups) had a lower likelihood of discontinuing their treatment than the second TNFi group (HR = 0.326, 95% CI: 0.170–0.626, p=0.001). When analyzed separately, the risk of discontinuation was significantly lower in both the non-TNFi biologic (HR = 0.318, 95% CI: 0.160–0.633, p=0.001) and JAKi (HR = 0.356, 95% CI: 0.129-0.980, p=0.046) groups than in the second TNFi group.

Conclusions

Our study supports switching to a non-TNF-targeted treatment instead of TNFi cycling in patients showing an inadequate response to the initial TNFi.

Keywords

comparison, Non-TNF-targeted, anti-TNF inhibitor

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Comparison of efficacy and drug retention between JAK inhibitors in rheumatoid arthritis: from the nationwide Korean College of Rheumatology BIOlogics (KOBIO) registry

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Background

JAK inhibitors (JAKi) have been expected to change the management patterns and prognosis in chronic rheumatic diseases. This study tried to compare the efficacy and drug survival of the approved JAKi, tofacitinib and baricitinib, for rheumatoid arthritis (RA) from the Korean nationwide database.

Methods

Data was extracted from the Korean College of Rheumatology Biologics registry, including clinical characteristics and disease activity markers for RA.

Results

Three hundred sixty three patients were treated with a JAKi (tofacitinib: n = 300; baricitinib: n = 63); 16.3% male; mean age 55.4 ± 11.9 years. Among them, 105 patients were biological disease-modifying antirheumatic drug (bDMARD)-naïve patients (tofacitinib: n = 91; baricitinib: n = 14). Baseline disease activity markers and proportion with conventional DMARDs (cDMARDs) were not different between patients treated with JAKi as bDMARD-naïve or previous bDMARD-failure conditions. Baseline disease activity markers and the proportion with cDMARDs were not different between tofacitinib and baricitinib groups, while more proportion were taking glucocorticoids in patients with tofacitinib (251/300, 83.7%) compared in those with baricitinib (38/63, 60.3%, $p < 0.01$). While any patients with baricitinib did not discontinue or switch, 7 patients with tofacitinib discontinued or switched due to lack of efficacy, and adverse event was reported in follow-up patients. In drug survival, Kaplan-Meier curve was not different between tofacitinib biological-naïve and previous biological-failure groups (Log- rank test $p = 0.202$). The efficacy was similar between tofacitinib and baricitinib groups.

Conclusions

Tofacitinib and baricitinib had no significant difference in efficacy for RA. In addition, drug survival was not different between bDMARD-naïve or previous bDMARD-failure patients among tofacitinib users in a real world practice.

Keywords

rheumatoid arthritis, JAK inhibitor, drug retention

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Association of first, second, and third-line bDMARDs and tsDMARD with drug survival among seropositive rheumatoid arthritis patients: Cohort study in a real world setting

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Background

To determine the association of first, second, and third-line biologic disease-modifying antirheumatic drugs (bDMARDs) and tofacitinib with drug survival among seropositive rheumatoid arthritis (RA) patients.

Methods

The study population was composed of 8,018 seropositive RA patients who were prescribed bDMARDs or tofacitinib between January 2014 and January 2019 from the Korean Health Insurance Review and Assessment Service database. First, second, and third-line choice of tumor necrosis factor inhibitors (TNFi) including etanercept, infliximab, adalimumab, and golimumab, as well as non-TNFi including tocilizumab, rituximab, tofacitinib, and abatacept were assessed. Multivariate Cox proportional hazards regression was used to determine the adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) for drug failure according to bDMARD or tofacitinib choice starting from the initial prescription date.

Results

Compared to first etanercept users, patients with first tocilizumab (aHR 0.56, 95% CI 0.46-0.68), tofacitinib (aHR 0.27, 95% CI 0.18-0.42), or abatacept (aHR 0.83, 95% CI 0.69-0.99) had lower risk of drug failure. Second choice of tocilizumab (aHR 0.38, 95% CI 0.25-0.55), tofacitinib (aHR 0.23, 95% CI 0.15-0.37), or abatacept (aHR 0.54, 95% CI 0.35-0.84) was associated with lower drug failure risk compared to second etanercept users. Finally, third choice of tocilizumab (aHR 0.32, 95% CI 0.16-0.62) or tofacitinib (aHR 0.35, 95% CI 0.19-0.63) was associated with lower drug failure risk compared to third TNFi users.

Conclusions

First and second-line tocilizumab, tofacitinib, or abatacept may lead to improved drug survival. Third-line use of tocilizumab or tofacitinib may be beneficiary in reducing drug failure risk among seropositive RA patients.

Keywords

drug failure, bDMARD, tsDMARD

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The effects of biologic DMARDs on hemoglobin and disease activity index in rheumatoid arthritis patients

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Background

Disease activity and anemia were improved when biologic DMARDs were used in RA patients. In particular, tocilizumab has been reported to be the most effective in increasing hemoglobin in RA patients with anemia. The purpose of this study is to investigate the effect of the biologic DMARDs on changes in hemoglobin and disease activity in rheumatoid arthritis patients. We also aimed to determine whether tocilizumab is more effective in controlling disease activity in RA patients with anemia.

Methods

A total of 948 RA patients using the biologic DMARDs were enrolled in this study from the KOBIO registry. Patients who started the first biologic DMARD and have been using one biologic DMARD for more than 1 year were included in this study. Patients were divided into three groups according to the biologics they used ; tocilizumab , TNF inhibitor and other biologics group.

Results

They were divided into 247 patients in the tocilizumab group and 504 patients in the TNF-i group and 197 patients in other biologics group. Hb, Hct, disease activity index scores were compared at baseline and follow-up. Hb and Hct was significantly elevated in tocilizumab-treated group compared to other groups among patients with anemia on the index date. ESR and DAS 28 ESR also decreased the most in the tocilizumab group. TJC decreased the most in the TNFi group. Among the disease activity index scores, SJC, PGA, PhGA, CRP, SDAI, CDAI, and RAPID3 were not significantly different between the three groups among patients with anemia.

Conclusions

Tocilizumab was most effective in increasing Hb and Hct and decreasing ESR and DAS 28 ESR in patients with RA anemia. But other disease activity index scores including SJC, PGA, PhGA, CRP, SDAI, CDAI, and RAPID3 were not significantly different between the three groups.

Keywords

biologic DMARDs, Hemoglobin, Disease activity index

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Time-integrated cumulative parameters predictive of radiographic progression of rheumatoid arthritis: Real-world data from a prospective single-center cohort

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Background

For many chronic inflammatory diseases, outcomes are determined by assessing both disease activity at presentation and cumulative activity over time. Here, we investigated whether cumulative activity better reflects radiographic progression (RP) of rheumatoid arthritis (RA) than measurement of activity at a single timepoint.

Methods

From a prospective cohort of RA patients, most of whom were treated with anti-rheumatic drugs, we retrospectively selected 117 subjects for whom laboratory, clinical, and radiographic parameters potentially influencing RP were monitored serially for more than 1 year. X-ray images of both hands and both feet were scored using the modified Sharp score (mSS). In addition to cross-sectional values at baseline, longitudinal and cumulative values for each parameter were calculated in a time-integrated and averaged manner.

Results

Among the values measured at baseline, mSS, but not the baseline erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) level, was associated with RP. By contrast, multivariate analyses identified cumulative values such as the cumulative tender joint count (TJC), cumulative swollen joint count (SJC), and cumulative Disease Activity Score 28 (DAS28)-ESR as major determinants of RP. In particular, the cumulative SJC showed the best predictive performance for RP. Moreover, the cumulative ESR, CRP, DAS28-ESR, and TJC correlated positively with the extent of RP.

Conclusions

This study highlights the importance of cumulative indices for predicting progression of RA. Specifically, dynamic and cumulative values of RA activity-related factors, particularly the cumulative SJC, may be the major determinants of RP in real practice.

Keywords

Rheumatoid arthritis, radiographic progression, cumulative values

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O-40

Drug survival of biologics depending on shared epitope in Korean patients with rheumatoid arthritis

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Background

Shared epitope (SE) is associated with the generation of anti-citrullinated peptide antibody (ACPA) and has many implications for the pathogenesis and clinical manifestation of rheumatoid arthritis (RA). But less attention has been paid to association between SE and treatment response, so we compared the drug retention rate of biologic disease modifying anti-rheumatoid drugs (bDMARDs) depending on SE positivity.

Methods

The medical chart of 762 RA patients with HLA-DRB1*04 allele results were reviewed retrospectively. We investigated the association of SE with bDMARDs initiation and drug survival rate between bDMARDs. SE was defined as *0401, *0404, *0405, *0408, *0410 allele.

Results

Of 762 patients, 338 (44.4%) patients were SE positive and 635 (83.3%), 578 (75.9%) patients were ACPA positive, high-ACPA positive, respectively. When comparing patients who started bDMARDs with patients who received only conventional DMARDs (cDMARDs), patients with female, younger onset age, rheumatoid factor (RF) and high RF positivity, high ACPA positivity and SE positivity had a higher rate of initiation of bDMARDs. We analyzed each of the HLA-DRB1*04 SE alleles, only patients with *0405 allele started more bDMARDs. We analyzed whether there was a difference in the treatment response of tumor necrosis factor (TNF) inhibitor and abatacept according to the presence or absence of SE positivity and *0405 allele positivity. In the *0405 positive and *0405/ACPA positive patient groups, the 1-year retention rate for abatacept tended to be higher than for TNF inhibitors (p=0.056 and p=0.052, respectively).

Conclusions

SE, especially *0405 allele, positive patients were more likely to initiate bDMARDs and *0405 allele and ACPA positivity may be associated in better drug survival rate of abatacept.

Keywords

Rheumatoid arthritis, Shared epitope, Treatment response

Free Paper Session

Osteoarthritis, Orthopedics, and Osteoporosis

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O-41

The functional role of DKK1 In mineralization of osteoblast differentiation

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Background

Dickkopf-1 (DKK1) is a secreted protein and known as antagonist of canonical WNT/β-catenin pathway. We previously reported that Transforming growth factor β1 (TGFβ1) suppresses mineralization of osteoblast differentiation by regulating DKK1 expression. Although we have identified the DKK1 gene as important for matrix mineralization, further studies are needed on the DKK1 function. We here explore the functional role of DKK1 on the mineralization of osteoblasts differentiation.

Methods

Primary osteoprogenitor cells were isolated from human spinal bone tissues. To investigate the functional role of DKK1 in mineralization of osteoblasts differentiation, we established the stable DKK1 knockdown in SaOS2 cells line and transiently transfected with human DKK1 in osteoprogenitor. The DKK1 gene manipulated cells were differentiated into mature osteoblasts with conditional medium. For matrix maturation of osteoblast differentiation, the cells were stained with Alkaline phosphatase (ALP) and Collagen (COL) staining. For matrix mineralization of osteoblast differentiation, the cells were stained with Alizarin Red S (ARS), Von Kossa (VON) and Hydroxyapatite (HA) staining.

Results

During osteoblasts differentiation, the protein and mRNA expressions of DKK1 were dramatically increased at matrix mineralization stage accompanied by expression of osteocalcin, a marker of bone mineralization. Furthermore, DKK1 overexpression in osteoprogenitor exhibited the promoting matrix mineralization of osteoblast differentiation but not in matrix maturation. In contrast, stable DKK1 knockdown in SaOS2 cells showed the reduction of matrix mineralization during osteoblast differentiation.

Conclusions

Manipulating DKK1 expression regulates the matrix mineralization of osteoblasts differentiation, suggesting that DKK1 is a critical gene for bone mineralization of osteoblasts.

Keywords

Matrix mineralization, Osteoblast differentiation, DKK1

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Status of glucocorticoid-induced osteoporosis preventive care in Korea : A nationwide population-based retrospective cohort study using the Korean national health insurance service database

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Background

It is crucial to prevent osteoporosis in patients receiving long-term glucocorticoid treatment. The objectives of this study were to investigate the frequency and associated factors of preventive care in Korean patients with glucocorticoid-induced osteoporosis (GIOP).

Methods

Using National Health Insurance Service database, we identified 37,133 individuals aged 20 years and over who started new long-term (≥ 90 days) systemic glucocorticoids (GCs) from 2011 to 2012. High quality GIOP preventive care was defined as by the composite of 1) bone mineral density (BMD) test, 2) prescription osteoporosis medications such as bisphosphonates and selective estrogen receptor modulators or 3) calcium and/or vitamin D within 6 months of GCs initiation.

Results

Mean age was 49.8 years and 18,476 (49.8%) subjects were female. Mean cumulative GCs dose was 0.203 g. The frequency of high quality GIOP preventive care was only 3.68% (BMD test: 1.46%, osteoporosis medications: 1.65% and calcium/vitamin D: 1.63%). Multivariable logistic regression models showed that increasing age (OR=2.53, 95% CI=2.02-3.17, p<0.001; 40~49 years, OR=4, 95% CI=3.23-4.92, p<0.001; 50~59 years, OR=5.17, 95% CI=4.16-6.43, p<0.001; 60~69 years and OR=8.01, 95% CI= 6.5-10.03, p<0.001; ≥70 years, respectively), systemic autoimmune disease (OR=3.01, 95% CI=2.49-3.8, p<0.001), concomitant hyperthyroidism (OR=1.58, 95% CI=1.13-2.21, p=0.007), rural residence (OR=1.19, 95% CI=1-1.42, p=0.046) were significantly associated with higher likelihood of receiving high quality GIOP preventive care. Otherwise, male (OR=0.26, 95% CI=1.23-0.3, p<0.001) and GC prescription in primary care clinic/nursing hospital (OR=0.66, 95% CI=0.57-0.75, p<0.001) was related with lower likelihood of high quality GIOP preventive care. Cumulative GCs dose tended to be associated with a higher frequency of receiving high quality GIOP preventive care (OR=1.25, 95% CI=0.91-1.71, p=0.075).

Conclusions

The majority of Korean patients treated with GCs did not receive appropriate preventive care for GIOP in real practice. Thus, special attention should be paid to the screening and management of GIOP.

Keywords

Glucocorticoids, Osteoporosis, Prevention

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O-43

Muscle exercise mitigate the negative influence of low socioeconomic status on muscle strength

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Background

Socioeconomic status (SES), including household income and education level, is an important factor for skeletal muscle strength as a discriminator of sarcopenia. Even though the beneficial effects of exercise on muscle strength are well recognized, the influence of exercise for people of different SES has not been fully elucidated. Thus, This study was conducted to assess the degree of impact of exercise on muscle strength according to the different SES.

Methods

Total 6,081 subjects with complete data on measures of hand grip strength (HGS) and other relevant variables were included from the Korea National Health and Nutrition Examination Surveys (KNHANES) VII-3. Multivariable logistic regression analysis was performed to assess the effect of SES on HGS and the interaction of muscle exercise with HGS according to the degree of SES. Three-step logistic regression analysis using Baron and Kenny mediation method was performed to check the mediating effect of exercise with HGS, and the significance was confirmed by the Sobel test.

Results

In multivariable analysis, Low household income (OR 1.637, $p=0.005$) and low education state (OR 2.351, $p<0.001$) had poor HGS compared to high SES. Comparing with high SES, the difference in HGS by muscle exercise interaction was greater for low household income (OR 7.082 vs. 3.619, $p<0.001$) and low education state (OR 14.711 vs. 6.383, $p<0.001$). In three-step logistic regression analysis, Muscle exercise mediated the relationship of muscle strength with low household income (OR from 1.772 to 1.736, $z=2.373$, $p=0.017$) or low education state (OR from 2.368 to 2.309, $z=2.489$, $p=0.012$).

Conclusions

This study confirmed that exercise improves negative effect of low income and education levels on muscle strength, thus suggest greater importance of muscle exercise in the people with low SES.

Keywords

Sarcopenia, Socioeconomic status, Muscle exercise

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Skeletal muscle atrophy and its relationship with osteoarthritis

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Background

A growing evidence shows that knee Osteoarthritis (OA) is associated with changes in peri-articular muscle including loss of muscle mass and pain. However, it remains unclear whether the muscle atrophy is responsible for the disease progression or is a consequence of the degenerative joint. In this study, we investigated the correlation between muscle atrophy and knee OA progression in the destabilization of the medial meniscus (DMM) knee OA model mice with peri-articular muscle atrophy.

Methods

C57BL/6, male mice (10 weeks old) were used for the induction of Knee OA (KOA) by DMM. At both acute and chronic phase of OA, muscle atrophy in TA and quadricep muscle was measured and knee histology was performed. The quadricep muscle atrophy was induced by repeated injection of Bacl2 (1.2%, 4 times injection with 10 days intervals) and the atrophy of peri-articular TA muscle in the mice with knee OA was measured.

Results

The muscle mass and size of the quadricep and TA muscle were decreased in KOA group at both early and late stage with a morphological alteration including muscle fibrosis. The gene expression of skeletal muscle proteolysis, atrogin-1 and inflammatory cytokines including IL-1β and IL-6 were increased with appearance of inflammatory infiltration in both quadricep and TA muscle at early stage of OA. This inflammatory sign has been resolved a bit at late stage of OA, nevertheless OA was accelerated. The expression of skeletal muscle regeneration marker, pax7, was decreased in both quadricep and TA muscle at late stage of OA, which suggest that muscle repair capacity was impaired in KOA. Interestingly, cartilage degeneration seems to be more exacerbated following the quadricep and TA muscle atrophy.

Conclusions

DMM induced KOA promotes peri-articular muscle atrophy at both acute and chronic phase of knee and Knee OA is more aggravated by weakness of the muscle. Therefore,

Keywords

Osteoarthritis, Muscle atrophy, DMM

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O-46

Female reproductive factors and risk of joint replacement arthroplasty of the knee and hip due to osteoarthritis in postmenopausal women : A nationwide cohort study of 1.36 million women

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Background

Previous studies of the relationships between female reproductive factors and osteoarthritis (OA) have shown conflicting results. In this study, we aimed to explore the relationships between reproductive factors and joint replacement arthroplasty of the knee (TKRA) and hip (THRA) in a large nationwide population-based cohort of postmenopausal Korean women.

Methods

We included 1,218,257 subjects who participated in national health examinations in 2009 in the study. The study outcomes were incident THRA or TKRA due to severe hip or knee OA. The relationships between reproductive factors and THRA or TKRA were evaluated using a multivariate-adjusted proportional hazards model.

Results

During a mean follow-up duration of 8.2 years, 1,733 incident THRA cases and 65,108 incident TKRA cases were observed. Later age at menarche, longer breastfeeding, HRT and OC use were associated with increased risk of TKRA for severe knee OA, while later age at menopause and longer reproductive span were associated with decreased risk. With regard to THRA for severe hip OA, later menarche, longer breastfeeding, and HRT more than 5 years were associated with higher risk. The associations between reproductive factors and severe OA were more pronounced in underweight and younger subjects.

Conclusions

We found that shorter estrogen exposure was associated with higher risk of joint replacement therapy due to severe OA, and such associations were more pronounced in underweight and younger subjects.

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The association of index-to-ring finger ratio with trapeziometacarpal joint osteoarthritis in a Korean elderly population

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Background

Index-to-ring finger ratio (IRFR), a possible indicator of prenatal testosterone levels, has been reported to be associated with risk of osteoarthritis (OA) involving hip, knee, and hand interphalangeal joints. Trapeziometacarpal joint (TMCJ) OA is common in elderly and can cause significant pain, weakness and functional limitations. We aimed to evaluate the association between IRFR and TMCJ OA in a Korean elderly population.

Methods

A population-based sample included 318 males (mean age 75.1 ± 8.6) and 286 females (mean age 74.4 ± 8.3) who had participated in a Korean Longitudinal Study on Health and Aging. After collecting their hand X-rays, IRFR was visually classified as either type 1 (index finger longer than or equal to the ring finger) or type 2 (index finger shorter than the ring finger), and was radiographically measured by the ratio of length of the right second to fourth phalangeal bones ("phalangeal IRFR") and metacarpal bones ("metacarpal IRFR"). TMCJ OA was defined according to Kellgren-Lawrence (KL) grade. We assessed the odds ratios (ORs) and 95% confidence intervals (95% CIs) for presence of OA (KL grade > 1) and for severe OA (KL grade > 2) using logistic regression with age, gender, visual, phalangeal, and metacarpal IRFR as independent variables.

Results

Logistic regression analysis showed that TMCJ OA was significantly associated with age (OR = 1.036, 95% CI 1.011 to 1.061) and metacarpal IRFR (OR = 0.001, 95% CI 0.000 to 0.401), and that severe TMCJ OA with age (OR = 1.077, 95% CI 1.034 to 1.122) and type 2 IRFR (OR = 2.834, 95% CI 1.098 to 7.313). Other variables did not show any statistically significant associations.

Conclusions

IRFRs evaluated visually and radiographically were both independent risk factors of TMCJ OA. They might serve as an easy measurable biomarker to identify patients vulnerable to TMCJ OA.

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O-48

Folate deficiency is associated with increased radiographic severity of osteoarthritis in the knee joints, but not in the hand joints

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Background

Folate deficiency promotes the expression of pro-inflammatory cytokines and increases the serum homocysteine concentration, triggering oxidative stress and increasing metalloproteinase synthesis. However, no clinical studies have explored the effect of folate deficiency on the severity of osteoarthritis (OA). Therefore, this study investigated the relationship between folate levels and radiographic features of the knee and hand in a large, population-based OA cohort.

Methods

We recruited 2,334 participants from the Dong-gu Study. Baseline characteristics were collected via a questionnaire, and hand and knee X-rays were scored using a semi-quantitative grading system. Linear regression analysis was performed to assess the relationships between the serum folate level and knee and hand radiographic scores after adjusting for age, gender, body mass index, smoking, alcohol consumption, education, and physical activity.

Results

Regarding the knee joints, subjects with folate deficiency had higher total ($p<0.001$), osteophyte ($p=0.001$), joint space narrowing ($p=0.007$), tibial attrition ($p<0.001$), and sclerosis ($p=0.008$) scores than those with normal folate levels after adjusting for confounders. However, the radiographic scores for the hand joints, except the subchondral cyst score, did not differ between the groups after adjustment.

Conclusions

Folate deficiency was associated with the radiographic severity of OA in the knee joints, but not in the hand joints. Future studies should explore the differential effects of folate on the development of knee and hand OA.

Keywords

folate deficiency, radiographic, osteoarthritis

Luncheon Symposium VII - Novartis

Reimagining AS Management

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IL-17 pathway : A voyage towards understanding its role in AS

Xenofon Baraliakos
Rheumazentrum Ruhrgebiet, Germany

Axial spondyloarthritis (axSpA) describes a group of chronic inflammatory rheumatic diseases primarily involving the axial skeleton. IL-17 is involved in the pathogenesis of numerous inflammatory diseases, including inflammatory arthritis. Until a few years ago, the only biological agents licensed for the treatment of axSpA and nr-axSpA were TNF inhibitors. The introduction of IL-17 inhibitors has extended the treatment options. The last ten years have seen the development of a number of therapeutic recommendations that aimed at improving the management of axSpA patients. The aim of this presentation is to provide a comprehensive picture of the clinical efficacy and safety of the concept of IL-17 inhibition and its position as a disease modifying treatment strategy in the international treatment guidelines.

Luncheon Symposium VIII - GSK

Benlysta

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Benlysta : Shaping new SLE treatment paradigm in Korea

Seung-Ki Kwok
The Catholic Univ. of Korea, Korea

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the production of diverse autoantibodies and immune complex deposit in target tissues. It affects multiple organs and has significant morbidity and mortality. Identification and development of new treatment strategy for SLE is currently an area of intense investigation. Belimumab (Benlysta) is a human monoclonal antibody that inhibits B cell activating factor (BAFF) also known as B-lymphocyte stimulator (BLys). It is the first biologic drug for the treatment of SLE. In this talk, I am going to briefly introduce the pathogenesis of SLE and review the mode of action of Belimumab. In addition, I am also going to summarize not only the pivotal clinical trials which play major roles in the approval by regulatory agency but also real word data of Belimumab. Finally, I am going to present the possible best strategy for Belimumab in the treatment of SLE.

Luncheon Symposium IX - Amgen

Prolia, Osteoporosis

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Breaking myths, not bones

Peter Ebeling
Monash Univ., Australia

Denosumab has been available in the Asia-Pacific as a treatment for osteoporosis for >11 years. In some countries such as Australia, the combination of medication reimbursement as a first-line treatment and family physician management of osteoporosis has meant most patients with osteoporosis (>82%) are now treated with denosumab. Clinical trial data for denosumab are limited to 10 years but these show important differences to oral or intravenous bisphosphonates. The open-label FREEDOM Extension Study showed that both vertebral and non-vertebral fractures remained at similar levels in the denosumab treatment group to that seen in the double-blind FREEDOM study. In addition, there were further decreases in non-vertebral fractures after 3 years of denosumab treatment in both the seven- or ten-year treatment groups. Increases in bone mineral density (BMD) continued throughout the seven or ten years of treatment to 21.7% and 9.2% at the spine and femoral neck, respectively, after 10 years. This progressive increase in BMD is different to that seen with oral and intravenous bisphosphonates where a plateau in increases in spine and hip BMD occurs at 5-6 years of treatment. Another important difference between denosumab and bisphosphonates is the rapid offset of action of the former following treatment discontinuation. In phase 2 studies all BMD befits gained following 2 years of denosumab treatment were lost after 12 months of discontinuation. In addition, levels of the bone resorption marker, CTX, increased above baseline. This effect was also seen after 8 years of denosumab treatment with about 40% of the increase in spinal BMD lost in 12 months after treatment discontinuation. Case series and data from the FREEDOM and FREEDOM extension studies also show an increase in vertebral fractures and multiple vertebral fractures following denosumab treatment discontinuation. This increase in vertebral fractures begins about 5-6 weeks after the missed denosumab dose and is most marked >16 weeks after the missed dose. Observational and randomized trials suggest that transitioning to either an oral or intravenous bisphosphonate can ameliorate bone loss and may reduce the risk of vertebral fractures following denosumab cessation. After switching to oral alendronate following only one year of denosumab, spine and hip BMD were generally maintained and did not fall below pretreatment baseline in most trial participants. In another trial switching to intravenous zoledronic acid either at the time of the missed dose or 3 months later ameliorated, but did not completely prevent, bone loss at the spine or hip. A recent observational study showed therapy with either oral alendronate or a single intravenous zoledronic acid infusion is partially effective in reducing the increased vertebral fracture risk after denosumab withdrawal. In conclusion, to maintain its anti-fracture efficacy, denosumab treatment needs to be continued in the long-term; this has been demonstrated for up to 10 years in trials. If a target BMD has been attained and a decision to stop denosumab has been made, transition to an oral bisphosphonate for 12-24 months or intravenous zoledronic acid is required and BMD should then be monitored. Adverse events associated with long-term denosumab therapy such as atypical femur fractures or medication-related osteonecrosis of the jaw are very rare and treatment benefits far outweigh the risk of these events.

International Symposium

Gout : Comorbidity Matters and Optimal Management Strategies

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Epidemiologic study for gout and comorbidities in Korea

Ki Won Moon
Kangwon Nat'l Univ., Korea

Gout is the most common inflammatory arthritis in adults worldwide. The prevalence and incidence of gout vary widely according to the population. The prevalence and incidence of gout increased in Korea in recent years. Especially, the incidence of gout in the younger generation has increased rapidly in Korea. Gout is associated with metabolic syndrome including obesity, hypertension, hyperlipidemia and impaired glucose tolerance. The prevalence of metabolic syndrome in gout patients was 50.8%, which is higher than the prevalence of general Korean population. In addition to metabolic syndrome gout patients have various comorbidities, such as urolithiasis, chronic kidney disease, cardiovascular disease and peripheral vascular diseases. These comorbidities contribute to increased mortality in gout patients. Previous epidemiologic studies have reported that cardiovascular mortality is increased in gout patients. However, epidemiologic data on clinical features and mortality of Korean patients are insufficient. A large scaled study on clinical features and outcomes of Korean gout patients is needed for effective management of gout

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Cardiovascular risk of urate-lowering therapy in gout

Tuhina Neogi
Boston Univ., USA

In this talk, we will review the high prevalence of cardiovascular morbidity in patients with gout and high rates of mortality due to cardiovascular disease in gout. We will discuss potential biologic mechanisms by which serum urate may increase risk of cardiovascular disease. We will review trial and observational data regarding the risks of adverse cardiovascular outcomes related to different urate-lowering therapies and some of the methodologic challenges interpreting these data. Finally, we will discuss potential cardiovascular benefits of using anti-inflammatory therapy such as colchicine.

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What's new in gout management

Nicola Dalbeth
Univ. of Auckland, New Zealand

This lecture will provide a state-of-the-art summary of advances in approaches to gout management. The general concepts of gout management will be described. The update will cover gout flare management, indications for urate-lowering therapy, choice of first line urate-lowering therapy, and use of anti-inflammatory prophylaxis. The lecture will also discuss the impact of the COVID-19 pandemic on gout management, and provide strategies for improved gout management.

Joint Symposium

KCR-ARA-NZRA Joint Symposium
- Digital Healthcare in Rheumatology

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Digital health and rheumatoid arthritis – Current state, future horizons

Rebecca Grainger
Univ. of Otago, New Zealand

Digital health technology (DHT) is beginning to be explored in rheumatology. Mobile health, wearables, telemedicine visits, online and digital interventions, and machine learning and artificial intelligence – individually or collectively –could reshape rheumatology care. This talk will give an overview of the emergent literature providing insights into applications of DHT to assessment or care of people with rheumatoid arthritis (RA), organised at a micro (person), meso (patient care) and macro (patient population) level. While DHT seems to hold promise for supporting patient self-care and empowerment, providing care at the right time for the right people, and enhancing quality of care, much still needs to be known to realise the potential.

Apps and wearables can provide people with RA means to self-manage their disease and support healthful behaviours. People with rheumatic disease are clear what they might want in an app for their disease, often with complex functionality. However, many apps for designed for people with RA lack basic functions based on best practice approaches, or fail to include a variety of persuasive design features or behaviour change strategies. There are emerging data in rheumatic disease to suggest that activity tracking wearables might be a useful strategy for increasing physical activity in people with RA. Sensing smart gloves that can evaluate hand synovitis have also been explored but are currently too expensive and impractical for use outside research settings.

There are many ways DHT can support patient care. Preliminary telehealth studies, predating the urgent change to telehealth during the COVID-19 pandemic, have shown the telehealth via phone, video, or supported via app-report electronic Patient Reported Outcomes (ePROs) have similarly good RA disease outcomes over the short term. Wearable data may also be useful in identifying patients experiencing RA flare remotely-monitored between visits. Health interventions delivered via web-portals or apps may also be a feasible way to provide care to more people at great convenience.

At a service or national level, Clinical Quality Registries have enormous potential for improving care quality for people with RA. The American College of Rheumatology RISE Registry is already impacting on clinical care quality and providing the "Big Data" with enormous research opportunities.

While much has been achieved, the true transformation of care for people with RA will require both more work, and different work. More focus will be required on developing digital health ecosystems, new models of care with sound business models, and more emphasis on user perspectives.

Background and application of MyRA in the digital healthcare in rheumatology

Catherine Hill
The Queen Elizabeth and Royal Adelaide Hosp

This talk will cover the aims and development of myRA: a communication platform for patients with rheumatoid arthritis in Australia.
It is a free online support program for people with rheumatoid arthritis (RA) with aims to empower people with RA to understand RA, how to manage it and where to access support. There is an option to register for tailored information and support. It was developed by Arthritis Australia, with people with RA and the Australian Rheumatology Association (ARA).

The Development Process encompassed:

1. Workshop with experts and consumers (Journey mapping and needs analysis)
2. MyRA Consumer Survey (Online consumer survey using validated Arthritis Educational Needs Assessment Tool (ENAT) to evaluate and prioritise information needs; use of other metrics (e.g. age at diagnosis, effect of arthritis, confidence) to develop a profiling algorithm
3. Content preparation
4. Consumer profiling. Sixteen different patient profile algorithms developed with information needs and content mapping for each profile
5. MyRA Site development: Registration process to capture information for profiling algorithms; content served according to profile and adjusted when a user updates their profile, tools to assess and track patient reported outcome measures (PROMs), back-end database for collecting and reviewing user data for quality improvement
6. User testing.

The site includes content structure developed using data from survey of ENAT.
Consumers who register for the site allows personalised reports, personalised content sorted by personal profile and situation. This allows invaluable support for consumers with RA using the online support program.

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Application of ICT in the clinical practice of Korea

Ji Hyeon Ju
The Catholic Univ. of Korea

Free Paper Session

Systemic Lupus Erythematosus

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A high genetic risk burden is associated with diverse clinical manifestation in Systemic lupus erythematosus

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Background

Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease caused by gene-environment interactions. More than 100 SLE loci have recently been identified in the genome-wide association research (GWAS) of SLE. However, the genetic load on the American College of Rheumatology (ACR) classification criteria for SLE is not fully assessed. Our objective in this study was to examine the associations between weighted genetic risk scores (GRS) and ACR criteria in patients with SLE.

Methods

A total of 1243 patients with SLE from the Hanyang BAE Lupus cohort were newly genotyped with a custom designed genotyping array, Korea Biobank Array. Weighted GRS was calculated from 112 non-HLA loci on most updated East Asian study and HLA-DRβ1 haplotypes in amino-acid positions 11, 13, and 26. Multivariable logistic or linear regression was performed using covariates including sex, at diagnosis of SLE, disease duration, and genotype PC1~PC4.

Results

We observed the association between a weighted GRS and 11 SLE subphenotypes defined by the ACR classification criteria. We showed that a significant association between the weighted GRS and the cumulative number of ACR classification criteria in a multivariable linear regression model (β coefficient = 0.139, $p = 2.1 \times 10-5$). Patients in higher weighted GRS had malar rash (OR =1.21, $p = 4.0 \times 10-4$), renal disorder (OR =1.17, $p = 2.0 \times 10-3$), and production of and anti-Sm (OR =1.24, $p = 4.8 \times 10-4$) and anti-DNA antibody (OR =1.24, $p = 2.9 \times 10-3$).

Conclusions

The high genetic burden of SLE is more prevalent in individuals with diverse clinical and serological manifestations. These results suggested that genetic profiling could be utilized to predict the clinical outcome of SLE.

Keywords

ACR criteria, Genetic risk score, systemic lupus erythematosus

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Clinical and genetic risk factors associated with the presence of lupus nephritis

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Background

To elucidate whether clinical features and the weighted genetic risk score (wGRS) were associated with the presence of lupus nephritis (LN).

Methods

We retrospectively divided patients with systemic lupus erythematosus (SLE, n=1,078) into biopsy-proven LN (n=507) and non-LN groups (non-LN, n=571). Baseline clinical features, serologic markers, and the wGRS were collected. The wGRS was calculated from 112 non-human leukocyte antigen (non-HLA) loci and HLA-DRβ1 amino acid haplotypes for SLE. Associations among clinical features, wGRS, and the presence of LN were identified.

Results

In the multivariate analysis, patients with LN were younger at diagnosis (odds ratio [OR]=0.97, $p<0.001$), had more pleuritis (OR=2.44, $p<0.001$) and pericarditis (OR=1.62, p=0.029), had a higher detection rate of anti-double stranded deoxyribonucleic acid (anti-dsDNA antibodies, OR=2.22, $p<0.001$), anti-Smith antibodies (anti-Sm antibodies, OR=1.70, p=0.002), low level of complement (OR=1.37, p=0.043) and absence of antiphospholipid antibodies (aPL antibodies, OR=1.60, p=0.002), and had higher wGRS (OR=1.16, p=0.012). Mediation analysis suggested that anti-Sm antibodies and low complement could be mediators in the relationship between high wGRS and the presence of LN.

Conclusions

Onset age, pleuritis, pericarditis, several serologic markers, and wGRS were associated with the presence of LN. Anti-Sm antibodies and low complement appeared to mediate the indirect relationship between wGRS and the presence of LN.

Keywords

Systemic lupus erythematosus, Lupus nephritis, Associated factors

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Risk of bloodstream Infection in patients with systemic lupus erythematosus exposed to prolonged moderate to high dose glucocorticoids

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Background

To investigate the incidence and risk factors of bloodstream infection in patients with systemic lupus erythematosus (SLE) receiving moderate-to-high dose of glucocorticoids.

Methods

This study included 1109 treatment episodes with prolonged (≥4 weeks), moderate-to-high dose glucocorticoids (≥ 15mg/day prednisolone) in 612 patients with SLE over 14-year period. Clinical features regarding disease activity (SLEDAI-2K), immunosuppressant use and laboratory results were collected from the electronic medical database. Baseline date was defined as the date of initiating moderate-to-high dose steroid. Incidence rate and risk factors for bloodstream infection were investigated using generalized estimating equation.

Results

At baseline, the mean (SD) age was 37.0 (12.7) years and 83.4% were female. The mean (SD) SLEDAI-2K score was 10.4 (6.3). During a total of 1078.64 person-years, 33 cases of bloodstream infection occurred in 29 treatment episodes, with an incidence rate of 3.06 (2.11-4.30) per 100 person-year. When the incidence rate was stratified by SLE manifestation, treatment episode with neuropsychiatric manifestations and serositis showed a higher incidence of bloodstream infection compared to those with other manifestations (Figure). Multivariable analysis showed that older age (incidence rate ratio [IRR]: 1.06; 95% CI 1.03-1.08), and baseline azotemia (5.66; 95% CI 2.72-11.75) were associated with increased risk of the bloodstream infection. As for effect of immunosuppressive treatment, bloodstream infection occurred more frequently in the treatment episodes with higher cumulative dose of steroids during previous 6 months from the baseline (≥ 15mg/day prednisolone) (3.09; 95% CI 1.47-6.52). Higher SLEDAI, concomitant cyclophosphamide pulse treatment and baseline dose of steroid tended to increase the outcome, but not statistically significant.

Conclusions

In SLE patients exposed to prolonged moderate-to-high dose glucocorticoids, older age, impaired renal function, and higher previously used steroids are important factors that increase the risk of bloodstream infection.

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Depression is associated with frailty in systemic lupus erythematosus patients: Multicenter retrospective analysis using systemic lupus erythematosus international collaborating clinics-frailty index

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Background

Systemic Lupus Erythematosus International Collaborating Clinics-Frailty Index (SLICC-FI) is a novel health measure in systemic lupus erythematosus (SLE) and was reported to have impact on outcomes including mortality. The objective of the study was to identify modifiable factors including depression and evaluate the association with frailty in SLE.

Methods

SLE patients who fulfilled 1997 American College of Rheumatology (ACR) classification criteria were enrolled from five tertiary hospitals in Korea and the participants filled out questionnaires at outpatient clinic. Electronic medical records were reviewed for laboratory results, disease activity at enrollment and medications. The SLICC/ACR damage index score and SLICC-FI was calculated based on questionnaires and medical records. To assess the severity of depression, patient health questionnaire-9 (PHQ-9) was used. Logistic regression analysis was used to evaluate the factors associated with frailty in SLE patients.

Results

In total, 247 patients were recruited. Mean (standard deviation, SD) age of the cohort was 50.5 (1.6) and 91.9% of the cohort was female. The mean (SD) of SLE disease activity index-2000 (SLEDAI-2K) was 3.5 (4.0). According to SLICC-FI, 36 (14.6%) patients were classified as frail (SLICC-FI > 0.21) and others were classified as non-frail (SLICC-FI $\leq$ 0.21), which include least fit (0.10 < SLICC-FI $\leq$ 0.21), relatively less fit (0.03 <SLICC-FI $\leq$ 0.10) and robust (SLICC-FI $\leq$ 0.03) patients. In multivariable logistic regression analysis, age (1.09), ESR (1.03), SLEDAI-2K (1.18), PHQ-9 score (1.27) and SLICC/ACR damage index (3.22) were associated with frailty

(odds ratio in parenthesis). Mild depression (PHQ-9 score ≥ 5) was observed in 97.2% of frail patients and 54.5% of non-frail patients. Severe depression (PHQ-9 ≥ 20) was observed in 22.2% of frail patients and 1.4% of non-frail patients.

Conclusions

Depression in SLE patients was associated with frailty. Rheumatologists should pay attention to early detection and intervention of depression in SLE patients to improve outcomes.

Keywords

Systemic lupus erythematosus, frailty, depression

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Discovery of urine biomarkers of lupus nephritis via quantitative and comparative proteome analysis

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Background
The need for a biomarker with robust sensitivity and specificity in diagnosing lupus nephritis (LN) remains unmet. Compared with blood samples, urine samples are more easily collected; thus, we aimed to identify urine biomarkers of LN based on proteome analysis.

Methods
Potential urinary biomarkers of LN were screened via sequential window acquisition of all theoretical mass spectra combined with liquid chromatography (SWATH LC-MS)-based proteome analysis, an updated platform of quantitative proteome analysis. Among the urine proteins that were differentially expressed in common between healthy controls (HCs, n=20) vs. systemic lupus erythematosus (SLE, n=22) patients without nephritis, and SLE patients without nephritis vs. patients with newly diagnosed LN (n=17), five proteins were selected for further validation using enzyme-linked immunosorbent assay (ELISA) in a validation cohort. Receiver operating characteristic analyses were performed to evaluate discriminatory ability and Spearman's rank correlation analyses were conducted to assess correlation between biomarkers and histologic activity/chronicity indices.

Results
A total of 23 differentially expressed proteins were observed in common between HCs vs. SLE patients without nephritis, and SLE patients without nephritis vs. patients with LN. Among these, urine alpha-1-acid glycoprotein 1 (ORM1), antithrombin-III (SERPINC1), ceruloplasmin (CP), hemoglobin subunit beta (HBB), and hemoglobin subunit delta (HBD) were selected for validation study. ELISA revealed upregulated urine ORM1, SERPINC1, CP, and HBD in LN compared with SLE without nephritis. Urine ORM1 had the highest area under the curve (AUC) in distinguishing LN from SLE without nephritis (AUC=0.914), followed by CP (AUC=0.896), SERPINC1 (AUC=0.874), and HBD (AUC=0.757). In terms of histology, urine HBD was the only protein that accurately discriminated proliferative LN from non-proliferative LN (AUC=0.964), and the only protein that showed significant correlation with activity index (r=0.549, p=0.024).

Conclusions
Urine ORM1 could be useful in early detection of LN, while urine HBD could provide histologic information when renal biopsies are unavailable.

Keywords
lupus nephritis, biomarker, proteomics

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Increased expression of NRP-1 in systemic lupus erythematosus and its correlation with disease activity

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Background

Neuropilin-1 (NRP-1) is a transmembrane glycoprotein that acts as a receptor of class III/IV semaphorins which role in the pathogenesis of autoimmune diseases. There have been limited studies on the role of NRP-1 in autoimmune inflammatory rheumatic disease, including systemic lupus erythematosus (SLE). This study was aimed to investigate the expression and the clinical implication of NRP-1 in lupus mouse models and patients with SLE.

Methods

The expression of NRP-1 was measured in T cells in spleen and renal tissue from the control mouse and TLR-7 agonist-induced lupus mouse by flow cytometry, PCR, and immunofluorescence. CD4+ T cells from human peripheral blood were isolated to investigate the expression of NRP-1 in healthy control and the patients with SLE (n=40).

Results

The frequency of NRP-1 positivity in CD4+ T cells in spleen was significantly higher in lupus mouse group compared to vehicle mouse group. The quantitative analysis of NRP-1 fluorescence intensity in the kidney revealed an increased level in the lupus group compared to the control group.

The CD4+ T cells from peripheral blood mononuclear cells in the patients with lupus also showed a significantly higher frequency of NRP-1 positive CD4+ T cells than those from healthy controls. Comparing the correlation of the expression of NRP-1 and disease activity with SLEDAI, C3, C4, and anti-DNA antibodies, the significant correlation between NRP-1 and disease activity markers was confirmed.

Conclusions

Our results show that NRP-1 is highly expressed in the CD +T cells in the patients with SLE and the expression significantly correlates with the disease activity. These results indicate the significant contribution of NRP-1 in the pathogenesis of SLE and the potential of targeting NRP-1 for the treatment of SLE.

Keywords

Neuropilin-1, Mouse model of lupus, TLR-7 agonist

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A novel spleen tyrosine kinase inhibitor SKI-O-703 attenuates lupus and rheumatoid arthritis in murine models

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Background

Spleen tyrosine kinase (Syk) plays a pivotal role in the activation of B cells and myeloid-lineage cells by transducing BCR- and FcγR-triggered signals to diverse downstream pathways. Dysregulated activity of Syk can cause the development of antibody-mediated autoimmune diseases, such as rheumatoid arthritis and systemic lupus erythematosus. Therefore, Syk is regarded as a druggable target for therapeutic intervention in such diseases, but it remains to be fully evaluated.

Methods

This study was undertaken to examine the efficacy of a novel Syk inhibitor SKI-O-703 in two models of such diseases.

Results

First, BALB/c mice were injected with K/BxN serum to induce arthritis and orally administered with SKI-O-703. Upon treatment with SKI-O-703, clinical and histopathological scores were significantly decreased, with less numerous neutrophils and macrophages infiltrated into synovial tissue. SKI-O-703 at a lower dose had a synergistic effect with anti-TNF antibody. Second, to examine the effect of SKI-O-703 on the progression of lupus nephritis, NZB/W F1 female mice at the autoimmunity-established phase were orally administrated with SKI-O-703. The levels of serum anti-dsDNA antibody, serum BAFF, and proteinuria and histopathologic manifestations of glomerulonephritis were significantly decreased in SKI-O-703-treated mice, and these effects were associated with hypoactivation of B cells, especially germinal center B cells, in the spleen.

Conclusions

Thus, these results provide evidence that a novel Syk inhibitor SKI-O-703 can attenuate the progression of autoantibody-mediated autoimmune diseases by inhibiting activation of B and innate inflammatory cells.

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Efficacy and safety of belimumab in Korean patients with systemic lupus erythematosus : Subgroup analysis of a phase 3, randomized, placebo-controlled trial

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Background

To assess efficacy and safety of belimumab versus placebo in patients from Korea with systemic lupus erythematosus (SLE).

Methods

This was a post hoc subgroup analysis of Korean patients from a Phase 3, multicenter, double-blind, placebo-controlled, 52-week study conducted in North East Asia (GSK Study BEL113750; NCT01345253). Adults with active SLE despite standard therapy were randomized 2:1 to intravenous belimumab 10 mg/kg/month or placebo, both with standard therapy, to Week 48. The primary endpoint was SLE Responder Index (SRI)-4 response rate at Week 52. Secondary endpoints included: percentage of patients with ≥4-point reduction in Safety of Estrogens in Lupus Erythematosus National Assessment-SLE Disease Activity Index (SELENA-SLEDAI), SRI-7 response rate, time to first severe flare, and cumulative prednisone dose. Also, safety was assessed.

Results

Korean patients composed 14.1% (n=100/707) of those randomized (belimumab, n=66; placebo, n=34). In this subgroup, more patients achieved an SRI-4 response at Week 52 with belimumab than placebo (53.0% vs 23.5%; odds ratio [OR] 3.67 [95% confidence interval, CI]: 1.45, 9.28]; p=0.0061; Figure). The percentage of patients with a ≥4-point reduction in SELENA-SLEDAI was greater with belimumab than placebo (56.1% vs 26.5%; OR 3.54 [95% CI: 1.44, 8.75]; p=0.0061). Although the sample size was not powered for this subgroup, other secondary endpoint outcomes trended toward improvement with belimumab (belimumab vs placebo, respectively): achieving SRI-7 at Week 52 (29.4% vs 16.1%; p=0.1802),

experiencing a severe flare through Week 52 (16.7% vs 26.5%, hazard ratio 0.61 [95% CI: 0.25, 1.48]; p=0.2784), and cumulative prednisone dose over 52 weeks (median 2777.5 mg vs 3258.1 mg; p=0.1088). No new safety issues were identified.

Conclusions

Belimumab reduced SLE disease activity compared with placebo in this subgroup of Korean patients. Efficacy and safety outcomes were consistent with pivotal Phase 3 trials, suggesting that belimumab is a useful treatment option for this population.
Funding: GSK

Keywords

Systemic lupus erythematosus, treatment, randomized controlled trial

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International Symposium

Targeted Therapy of Spondyloarthritis

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Polygenic risk scores and the practice of rheumatology

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Polygenic risk scores (PRS) are quantitative scores that measure an individual's genetic risk for the condition or trait involved. Whilst PRS have typically been developed with their use to diagnose disease cases, they have multiple other potential clinical and research uses. These include in improving disease classification, predicting likelihood of future development of disease, stratifying people according to need and optimal frequency of screening tests, prediction of natural history of disease, pharmacogenomics and more. PRS are stable from the point of conception, and therefore have predictive ability for disease, and do not depend on development of the disease to have utility. This means they can be applied to determine the optimal frequency of screening tests for the disease, and there are currently studies underway for example to stratify people for breast or prostate cancer screening frequency according to their PRS. Additionally they can be used to predict the likelihood of future development of disease, enabling preventative therapy where such exists.

As PRS are typically developed in carefully assessed, clinically homogenous GWAS datasets, they can be used in disease classification, as people with clinical similar conditions with low PRS have a different though potentially overlapping aetiopathogenesis for their disease. This suggests they either have a different disease, or a disease subset.

PRS for many rheumatological diseases have demonstrated high discriminatory capacity (Table 1). Very few though have been developed or validated for other than European ethnicities, and there are still many major rheumatic diseases for which no PRS has been published to date.

Table 1: PRS for common rheumatic diseases in European and East Asian ancestry groups

Disease	Ethnicity	AUC
Ankylosing spondylitis	European	0.924[1]
Ankylosing spondylitis	East Asian	0.948[1]
Acute anterior uveitis	European	0.96[2]
Systemic sclerosis	European	0.673[3]
Systemic lupus erythematosus	European	0.67-0.72[4]
Systemic lupus erythematosus	East Asian	0.76[5]
Rheumatoid arthritis	European	0.78[6]
Gout	European	0.664[7]
Osteoporotic hip fracture	European	0.798[8]
Psoriatic arthritis	European	0.91-0.92[9]

These scores are already potentially of clinical utility. The current ankylosing spondylitis PRS is more informative than HLA-B27 testing alone, which has AUC of 0.869-0.901 in Europeans and East Asians respectively 1. As the PRS is easily calculated from anyone who has had a SNP microarray performed, it's cost to these people is far lower than that of HLA-B27 genotyping. Even in those who have not had SNP microarray genotyping performed, its cost is already lower than current HLA-B27 testing costs and so clearly should replace it.

The main priority now is to work out best how to use them as diagnostic and predictive tools, and integrate the tests into our clinical pathways. This will significantly benefit prediction, diagnosis and treatment of disease, and potentially enable accurately targeted preventative or early intervention approaches to disease management.

1. Li Z, Wu X, Leo PJ, et al. Polygenic Risk Scores have high diagnostic capacity in ankylosing spondylitis. Ann Rheum Dis. 2021.
2. Huang XF, Li Z, De Guzman E, et al. Genomewide Association Study of Acute Anterior Uveitis Identifies New Susceptibility Loci. Investigative ophthalmology & visual science. 2020; 61(6):3.
3. Bossini-Castillo L, Villanueva-Martin G, Kerick M, et al. Genomic Risk Score impact on susceptibility to systemic sclerosis. Ann Rheum Dis. 2021; 80(1):118-127.
4. Chen L, Wang YF, Liu L, et al. Genome-wide assessment of genetic risk for systemic lupus erythematosus and disease severity. Hum Mol Genet. 2020; 29(10):1745-1756.
5. Wang YF, Zhang Y, Lin Z, et al. Identification of 38 novel loci for systemic lupus erythematosus and genetic heterogeneity between ancestral groups. Nat Commun. 2021; 12(1):772.
6. Yarwood A, Han B, Raychaudhuri S, et al. A weighted genetic risk score using all known susceptibility variants to estimate rheumatoid arthritis risk. Ann Rheum Dis. 2015; 74(1):170-176.
7. Sinnott-Armstrong N, Tanigawa Y, Amar D, et al. Genetics of 35 blood and urine biomarkers in the UK Biobank. Nat Genet. 2021; 53(2):185-194.
8. Lu T, Forgetta V, Keller-Baruch J, et al. Improved prediction of fracture risk leveraging a genome-wide polygenic risk score. Genome Med. 2021; 13(1):16.
9. Patrick MT, Stuart PE, Raja K, et al. Genetic signature to provide robust risk assessment of psoriatic arthritis development in psoriasis patients. Nat Commun. 2018; 9(1):4178.

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Appropriate assessment for treatment

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The impact of spondyloarthritis (SpA) is considerable in many aspects of the life. Over the last decades, assessment of disease status and response to therapy in SpA is a rapidly expanding area of research. Instruments currently available for the assessment of patients with SpA focus predominantly on specific aspects of health such as pain, disease activity, and physical function and measure specific concepts like physical function and health-related quality of life. Thankfully, the Ankylosing Spondylitis Assessment Study group has contributed to this development, defining core sets of health domains for use in daily practice and in clinical trials, developing and validating measurement instruments corresponding to these health domains, and developing response and remission criteria for use in clinical trials.
This lecture reviews available measures of major areas of disease impact in SpA (disease activity, structural damage and functioning), and discusses which measures are relevant for use in clinical practice.

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Translational researches for new target treatment

Dennis Mcgonagle
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Free Paper Session

Rheumatoid Arthritis Basic Research

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Soluble immune checkpoint molecules in patients with rheumatoid arthritis and their association with autoantibodies

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Background

Immune checkpoints regulate the induction and maintenance of immune tolerance. We hypothesized that soluble checkpoint molecules participate in the dysregulation of immune homeostasis. Herein, we investigated the role of soluble checkpoints in rheumatoid arthritis (RA).

Methods

Total 118 patients with RA and 38 healthy controls were analysed. Soluble types of programmed cell death protein 1 (PD1), programmed death-ligand 1 and 2 (PD-L1 and PD-L2), cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), cluster of differentiation (CD) 28, CD80, CD86, inducible T-cell costimulator, T cell immunoglobulin and mucin domain-containing protein 3, herpesvirus entry mediator, B- and T-lymphocyte attenuator, CD40, lymphocyte-activation gene 3 (LAG-3), toll-like receptor 2 (TLR-2), and CD27 were quantified in stored sera using Milliplex MAP assay. Additionally, RA-related autoantibodies, (RA, anti-CCP, anti-citrullinated vimentin, anti-citrullinated α-enolase peptide 1 [anti-CEP], and anti-carbamylated protein [anti-CarP]) were analysed.

Results

The levels of all the tested soluble checkpoint molecules, except sPD-L2 and sCTLA-4, were higher in patients with RA than in healthy controls ($p < 0.05$). Furthermore, positivity of sPD1, sCD28, sTLR2 associated with higher reactivity to RA-related autoantibodies, whereas sLAG3 positivity associated with lower reactivity to RA-related autoantibodies. sPD-1 positive RA patients reacted more frequently to anti-CEP (69.7% vs. 28.6%, $p = 0.003$) and had higher number of ACPAs than sPD-1 negative RA patients ($p = 0.09$). sCD28 positive patients reacted more frequently to anti-CEP and anti-CarP (75.4% vs. 42.9%, $p = 0.001$; 64.6% vs. 40.0%, $p = 0.018$, respectively) than sCD28 negative RA patients. In contrast, sLAG-3 positive patients reacted less frequently to anti-CarP (40% vs. 73.5%, $p = 0.001$), and the number of autoantibodies was lower than in sLAG-3 negative patients ($p = 0.002$).

Conclusions

The levels of various soluble checkpoint molecules are elevated in RA patients and these molecules are associated with RA-related autoantibodies. These soluble checkpoint molecules may be implicated in RA autoimmune process.

Keywords

soluble checkpoint molecules, rheumatoid arthritis, autoantibodies

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Several certain substances within MSCs secretome can restrain IL-2-mediated NK cells activity

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Background

Mesenchymal stem cells (MSCs) are well-known for their immunomodulatory functions in innate and adaptive immunity. Although early MSC research focused on multipotency of stem cells, it was found that paracrine factors of MSCs have functional advantage of disease remission and recovery. MSCs-derived secretome consists of a variety of materials such as cytokine, chemokine, exsosome, and immune modulatory factors. In order to clarify the immunoregulatory effect of this secretome and its specific mechanism, most in vitro experiments using several immune cells are on T cells, B cells and macrophages, but only a few are on natural killer (NK) cells. To date, the effect of MSCs on NK cells is still controversial, so we are going to identify active components in MSCs secretome showing the ability to affect NK cells activity and to investigate their concrete action mechanisms in this study.

Methods

Human MSCs were derived from adipose tissue of healthy donors and cultured medium was concentrated using TFF filtering device to obtain MSCs secretome.

Results

MSCs secretome had no effect on survival and proliferation of NK-92 cells but merely diminished cell activity, as evidenced by lower secretion of cytotoxic granules and effector cytokines and also reducing killing ability. Moreover, as a result of qualitative analysis of MSCs secretome, seven candidates for modulating inflammation were identified, and interestingly, they are totally different factors from those known as MSC's immunomodulatory factor. In order to lose the function of these candidates, we utilized neutralizing antibodies to each candidate. Here, we observed that only three of the groups with neutralizing antibodies recovered cytokine secretion and cytotoxic ability of NK cells.

Conclusions

MSCs secretome can specifically inhibit the effector functions of NK cells due to some particular molecules previously unknown, which are increasing expression of inhibitory receptor CD96 on NK cells, consequently activating inhibitory signal.

Keywords

MSCs secretome, Immunomodulation, Natural killer cell

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O-59

Reduced levels of reactive oxygen species in peripheral blood mononuclear cells supresses inflammatory response of fibroblast-like synoviocytes in rheumatoid arthritis patients

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Background

The production and the oxidation mechanisms of reactive oxygen species (ROS) were out of balance in rheumatoid arthritis (RA). The aim of the study was to compare ROS productions in T cell subsets in peripheral blood mononuclear cells (PBMC) between RA patients and healthy controls.

Methods

PBMC and synovial fluid-derived mononuclear cells (SFMC) were obtained from RA patients (n=40) and healthy controls (n=10). Isolated cells were examined for the repartition of T cell subsets and expression of ROS according to RA activity. IL-10 and IL-17 levels in serum and synovial fluid were analyzed by ELISA. Following incubation with PBMC, RA fibroblast-like synoviocytes (FLS) were examined for the mRNA levels of inflammation-related genes by RT-qPCR.

Results

Among RA subgroups by disease activity, Moderate (5.1>DAS28≥3.2) group showed the highest expression of mitochondrial ROS in Treg cells. Although ROS level was steadily increased with RA activity, there was a slight decline in Severe (DAS28≥5.1) group compared to Moderate group. When PBMC and SFMC from paired-samples of Severe group were compared, these cell populations and ROS expression were higher in SFMC than PBMC (n=2). Therefore, slightly decreased Treg population in Severe group may be due to their transmigration from blood into inflamed synovial tussue. To suppress ROS production, RA PBMC was treated with mitochondrial specific ROS inhibitor (MioTEMPO) or cellular ROS scavenger (N-acetylcysteine: NAC) and then incubated with RA FLS using transwell for 24 hr. Co-cultured FLS showed significantly reduced expression of inflammation-related cytokines, including IL-1β, IL-6, IL-8, TNF-α, GM-CSF, and MMP-1 (n=3 and $p<0.05$).

Conclusions

Mitochondrial ROS production was increased according to disease activity in Treg cells among T cell sbusets of RA patients. When ROS production was suppressed in PBMC, inflammatory response was significantly reduced in RA FLS. These findings provide a novel approach to alleviate RA inflammation through ROS regulation in PBMC.

Keywords

rheumatoid arthritis, reactive oxygen species, T cell subsets

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Interleukin (IL)-18 binding protein regulates IL-17 induced osteoclastogenesis and type 17 helper T cell / regulatory T cell imbalance in rheumatoid arthritis

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Background

To evaluate the regulatory role of interleukin-(IL)-18 binding protein (BP) in osteoclastogenesis and helper T cell regulation of rheumatoid arthritis (RA).

Methods

Serum and synovial fluid (SF) of RA, osteoarthritis (OA) patients were collected to compare IL-18 and IL-18BP levels by enzyme-linked immunosorbent assay (ELISA). Peripheral blood mononuclear cells (PBMCs) of healthy control and SF mononuclear cells (SFMCs) of RA patients were cultured under type 17 helper T cell (Th17) polarization condition with or without IL-18BP. Also, PBMC was cultured under RANKL + M-CSF or IL-17A + M-CSF with or without IL-18BP, then tartrate-resistant acid phosphatase (TRAP) stain and real-time quantitative polymerase chain reaction for osteoclast related gene were evaluated.

Results

The level of IL-18 was higher in serum and SF of RA patients, whereas IL-18BP was lowered in SF of RA patients than control groups. The administration of IL-18BP decreased CD4+ IL-17A+ and CD4+ RANKL+ T cells, whereas CD4+CD25highFoxp3+ T cells population increased dose-dependently. These change in CD4+ T cell differentiation were also presented in vitro experiments of SFMC of RA patients. The IL-17A and soluble RANKL levels of culture soup (both PBMC and SFMC) significantly decreased by IL-18BP administration. TRAP+ cells were decreased in IL-18BP administration group dose dependently both in RANKL and IL-17A stimulated condition. Also, the gene levels of TRAP, NFATc1, Cathepsin K, and RANK were lowered in IL-18BP treated group.

Conclusions

We demonstrated that IL-18BP regulates Th17/Treg imbalance and IL-17 induced osteoclastogenesis. Therefore, IL-18BP may has therapeutic potential on RA treatment.

Keywords

Interleukin-18 binding protein, Rheumatoid arthritis, Th17/Treg

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O-61

Therapeutic potential of a novel Bifidobacterium strain identified through microbiome profiling of rheumatoid arthritis patients with different rheumatoid factor levels

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Background

The potential therapeutic effects of probiotic bacteria in rheumatoid arthritis (RA) remain controversial. Thus, this study aimed to discover potential therapeutic bacteria based on the relationship between the gut microbiome and rheumatoid factor (RF) in RA.

Methods

Bacterial genomic DNA was extracted from the fecal samples of 93 RA patients and 16 healthy subjects. Microbiota profiling was conducted through 16S rRNA sequencing and bioinformatics analyses. The effects of heat-inactivated Bifidobacterium strains on human peripheral blood mononuclear cells and collagen-induced arthritis (CIA) mice were assessed.

Results

Significant differences in gut microbiota composition were observed in patients with different RF levels. The relative abundance of Bifidobacterium was lower in RF-high than in RF-low and RF-negative RA patients. Among 10 differentially abundant Bifidobacterium, B. longum RAPO exhibited the strongest ability to inhibit IL-17 secretion. Oral administration of B. longum RAPO in CIA mice, obese CIA and humanized avatar model significantly reduced RA incidence, the arthritis score, inflammation, bone damage, cartilage damage, Th17 cells, and inflammatory cytokine secretion. Additionally, B. longum RAPO significantly inhibited the Th17 cells and th17 related genes-IL-17A, IRF4, RORC, IL-21 and IL-23R in rheumatoid arthritis patients PBMC.

Conclusions

Our findings suggest that B. longum RAPO may alleviate RA by inhibiting the production of IL-17 and other proinflammatory mediators. The safety and efficacy of B. longum RAPO in patients with RA and other autoimmune disorders merit further investigation.

Keywords

B. longum, Th17, Rheumatoid Arthritis

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Identification of osteoclast suppression by Kynurenine through the AHR pathway

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Background

Aryl-hydrocarbon receptor (AhR) is a ligand-activated transcription factor and regulates differentiation and function of various immune cells such as regulatory T cells, Th17 and dendritic cells. In recent study, AhR is involved in bone remodeling through regulating both osteoblasts and osteoclasts. However, the effects and mechanisms of AhR activation in human osteoclastogenesis remain unknown. Thus, we aimed to investigate the effects of AhR in human osteoclasts.

Methods

Monocytes were purified form peripheral blood mononuclear cells (PBMCs) of healthy donor. The isolated monocytes were used for the induction of osteoclast with M-CSF and RANKL. To examine the effect of AhR in osteoclastogenesis, monocytes were treated AhR ligands under osteoclast differentiation conditions. Multinucleated (more than three nuclei) TRAP-positive osteoclasts were counted as mature osteoclasts. Marker of osteoclasts was analyzed by using immunoblotting and quantitative reverse transcription PCR (RT-qPCR).

Results

AhR is activated by various exogenous and endogenous ligands such as kynurenine (Kyn), formylindolo[3,4-b] carbazole (FICZ), and benzopyrene (BaP). We found that Kyn, FICZ and BaP inhibit osteoclast formation and Kyn suppresses osteoclast differentiation during early stage. Also, the expression of AhR protein was increased in the early stage of osteoclastogenesis and decreased in mature osteoclasts. Blockade of AhR signaling through CH223191, AhR antagonist, and knockdown of AhR expression reversed Kyn-induced inhibition of osteoclast differentiation.

Conclusions

Our study is the first report that AhR agonists inhibit human osteoclast differentiation. Thus, AhR agonists could be a good therapeutic drugs to prevent bone destruction diseases such as rheumatoid arthritis (RA).

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Secretome of adipose-derived mesenchymal stem cells shift macrophage polarization toward M2b/c subtype

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Background

Mesenchymal stem cells (MSCs) express immunomodulatory and anti-inflammatory effect by secreting several bioactive molecules containing secreted proteins (secretome). Distinct mechanisms of their immune actions, however, are not fully understood. Macrophages play a vital role in innate immunity with two functional phenotypes, classically activated M1 and alternatively activated M2 macrophages. Recent studies show that MSCs polarize macrophage toward M2 phenotype. In this study, immunomodulatory ability of adipose-derived MSCs secretome toward peritoneal macrophage was studied.

Methods

Secretome was obtained from human AD-MSCs using 3K TFF membrane. Murine peritoneal macrophages were isolated from DBA1 or C57BL/6 mouse and cultured for 24 hours with secretome of AD-MSCs. Viability test of secretome toward macrophage was performed by CCK-8 assay. Macrophage polarization was analyzed by flow cytometry, enzyme-linked immunosorbent assay, and real-time PCR. LC-MS/MS proteomics analysis of secretome was performed and acquired protein sets were analyzed by DAVID Bioinformatics.

Results

Secretome of AD-MSCs increased cell viability of peritoneal macrophages. Secretome treated peritoneal macrophages resulted in reduced M1 markers such as CD86, iNOS, and TNFα and increased M2 markers such as CD206, arginase-1, and IL-10. Also, peritoneal macrophage expressed upregulation of mRNA level of LIGHT and MertK, M2b and M2c markers, respectively. According to proteomic analysis, 83 proteins were identified in secretome and seven candidates were selected for further studies.

Conclusions

Secretome of AD-MSCs induced polarization of peritoneal macrophages from M1 macrophages to M2 macrophages and made them create anti-inflammatory milieu by several key secreted proteins

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Etanercept improve cognitive dysfunction through the suppression of peripheral inflammation and neuroinflammation in a mouse model of rheumatoid arthritis

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Background

Previous studies demonstrated that patients with rheumatoid arthritis showed an increased risk of cognitive dysfunction and TNF inhibitors may decreased the risk of cognitive dysfunction. Here we examine the effect of etanercept on cognitive dysfunction and possible mechanism in a collagen-induced arthritis (CIA) mice model.

Methods

We induced CIA mice and randomly divided into three groups: Normal (n=25), CIA (n=25), CIA/Etanercept (n=25). We evaluated severity of arthritis using clinical scoring system. Joint inflammation and cartilage damage has checked by staining with H&E, Safranin-O. Level of pro-inflammatory cytokines (TNF-α, and IL-6) checked in mice sera using enzyme-linked immunosorbent assay. The expression of pro-inflammatory cytokines in ankle and hippocampus analyzed using real-time PCR. Cognitive impairment determined by morris water maze (MWM) test. Measuring blood-brain-barrier (BBB) permeability using evans blue (EB), the expression of tight junction (Zo-1, occludin) disruption in brain analyzed using immunofluorescence. The activation of microglia (Iba-1) and astrocyte (GFAP) in hippocampus analyzed using immunohistochemistry. NF-kB signaling pathway was investigated in hippocampus using western blot.

Results

Etanercept decreased severity of arthritis and joint inflammation of CIA mice (Figure 1A). In MWM test, etanercept improved memory and cognitive deficits of CIA mice (Figure 1B). Etanercept ameliorated BBB leakage and tight junction (ZO-1, occludin) disruption in brain of CIA mice (Figure 1C). The level of pro-inflammatory cytokines significantly decreased in both peripheral tissues and hippocampal tissues. Activation of Iba-1, GFAP were decreased after treatment of etanercept. Etanercept treatment suppressed neuro-inflammation via NF-kB signaling pathway (TNFR-1/NF-kB p65/COX-2) in the hippocampus of CIA mice (Figure 1D).

Conclusions

Increased peripheral inflammation influenced the development of neuroinflammation causing cognitive dysfuction. Treatment of etanercept attenuated the risk of cognitive dysfunction via regulation of NF-kB signaling pathway

Keywords

Cognitive dysfuction, Rheumatoid arthritis, Tumor necrosis alpha inhibitor

Symposium

Visiting Scholarship Symposium

IL-12 driven cytolytic CD4+ T cell program in SLE

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IL-12 is a proinflammatory cytokine critical for Th1 and Tfh cell differentiation. Dysregulation of Th1 and Tfh cells is associated with development of autoimmune diseases, such as lupus, suggesting IL-12 and its associated signaling pathways may be a therapeutic target in SLE. Here we demonstrate the existence of IL-12-driven human CD4+ T cells that display a cytolytic phenotype. In vitro stimulation of naive CD4+ T cells in the presence of IL-12 upregulated Bcl-6 and T-bet, the canonical transcription factors for Tfh and Th1 cells, respectively, and promoted production of signature cytokines, IL-21 and IFN-γ, resulting in three cell populations; IL-21+, IFN-γ+, or IL-21+ IFN-γ+. IFN-γ+ and IL-21+ IFN-γ+ also produced granzyme B (GZMB; > 70%), with robust upregulation of RUNX3, a transcription factor critical for driving cytolytic CD4+ T cell phenotypes. Reduced RUNX3 expression via CRISPR-Cas9-mediated gene knockout suppressed GZMB as well as IFN-γ in a manner dependent on RUNX3 expression. Likewise, reduction of Bcl-6 suppressed IL-21, but also GZMB production in a BCL6-dependent manner. Expression of Bcl-6 and RUNX3 was positively correlated with their expression was critical for optimal cytokine production. RUNX3 loci contained accessible chromatin for Bcl-6 binding, as determined by ATAC-seq, suggestive a cross-regulation of RUNX3 and BCL6. Moreover, epigenetic regulation by IL-12 was evident at the IFNG, IL21, and GZMB loci, compared to the cells stimulated with anti-CD3/CD28 alone. Inflamed renal tissues of patients with lupus contained cytolytic CD4+ T cells, with characteristic expression of RUNX3 and GZMB as well as other cytolytic genes. SLE patients responded to IL-12 blockade treatment with loss of similar cytolytic gene profile in peripheral blood mononuclear cells.

In summary, IL-12 induces genesis of IL-21+ IFN-γ+ and IFN-γ+ CD4+ T cells, with granzyme B positivity via coordination of TFs, including BCL6, RUNX3, and T-bet. These cells are presumably pathogenic, as their gene signature is in lupus nephritis. These data provide insight into context-dependent T-cell polyfunctionality, important for pathogen clearance but tissue damage in autoimmunity. These data also demonstrate development of a platform to interrogate a therapeutically relevant IL-12 signaling pathway, then determine the relevant transcriptional control including its CRISPered confirmation, with confirming ATAC data, and presence of the pathway in renal tissue from lupus patients. This platform can be applied to other signaling pathways and cells.

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Using claims databases for rheumatology research questions

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Large claims databases have been used increasingly to generate real-world evidence on the various clinical research; epidemiology and disease burden; treatment patterns and health outcomes in special population; comparative effectiveness and safety of drug. The purpose of this presentation was to present the result of the clinical research on the interstitial lung disease (ILD) in patients with rheumatoid arthritis (RA) using US claims database.

While dyspnea and cough are the most common symptoms in patients with ILD, up to 30-40% of RA patients with and without respiratory symptoms have subclinical ILD noted on highresolution computerized tomography scans. Due to this large variation in the clinical course of RA-ILD, evidence on the early detection and treatment of ILD is lacking, and there are no standard guidelines on how to screen RA patients for asymptomatic or subclinical ILD.

First, we developed and validated claims-based algorithms to identify ILD among patients with RA. A validated, well-performing claims-based algorithm will enable future studies to generate clinically important and relevant real-world data for the management of RA patients with ILD. Second, we performed epidemiologic study in RA-ILD patients using this validated algorithm. Clinical research using claims database will provide real-world evidence on RA-ILD, and can complement the results of a well-designed randomized clinical trial, and patients' registry

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Periodontal inflammation and microbiome in individuals at serologically increased risk of rheumatoid arthritis

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Objective. To evaluate an association between periodontal inflammation and anti-cyclic citrullinated protein antibody (ACPA)-positivity in the absence of inflammatory arthritis and to examine the generation of rheumatoid arthritis (RA)-related autoantibodies in association with specific bacterial organisms of periodontium.

Methods. Periodontal evaluations including bleeding points, clinical attachment loss (CAL) and pocket probing depths (PPD) were performed in 56 healthy controls (HC), 32 ACPA positive non-RA subjects, and 15 subjects with early RA. Simultaneous collection of serum and gingival crevicular fluid (GCF) was performed, and samples were tested for ACPA3.1. Microbiologic evaluation was done in GCF.

Results. There were no significant differences in the severity of periodontal diseases (PD) across the three groups. The level for gingival ACPA3 and ACPA3.1 was significantly higher in ACPA positive non-RA subjects compared to HC. There were no significant differences in bacterial diversity among the HC, ACPA positive non-RA, and early RA subjects. Additionally, the gingival ACPA3 and ACPA3.1 levels were significantly different according to the PD status.

Conclusion. This study suggests that the oral mucosa may serve as another extra-articular site according to PD for ACPA production in HC, despite no statistical difference of PD and microbiome in HC, ACPA positive non-RA, and early RA subjects.

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Conventional radiography in clinical study of RA

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Rheumatoid arthritis (RA) is a chronic inflammatory disorder characterized by synovitis and destruction of synovial joints, leading to severe disability and premature mortality. The introduction of disease modifying antirheumatic drugs (DMARDs) in the treatment of patients with RA has led to improved management of RA, making not only (complete) symptom relief, but in addition the prevention of long-term structural damage the current goal of therapy. To date, radiographs are still considered the most appropriate method to assess structural damage in RA. Validated radiographic scoring methods exist and are widely used for assessment and follow-up of joint damage in RA. Several scoring methods have been developed; however, the most widely used is a composite score of aggregated ordinal scales originally described in 1971 by John Sharp, which separately grades bone erosion and JSN in a number of locations in the hands and wrists. Modifications of this scoring method, including extension to the feet, have been described by Genant et al. and van der Heijde et al. I studied the subject of radiographic outcome assessment in RA at Leiden University in the Netherlands. I would like to overview several scoring methods are currently used and summarise radiographic data in randomized controlled trials (RCT)s performed by pharmaceutical companies, usually to obtain the claim of radiographic inhibition, of all DMARDs approved for patients with RA.

KCR 2021

41st Korean College of
Rheumatology Annual Scientific Meeting
and the 15th International Symposium

October 21(Thu) - 23(Sat), 2021
Seoul Dragon City, Seoul, Korea

E-poster Presentation

October 21(Thu)

E-poster Presentation

RA-pathogenesis and animal model & Cytokines and mediators

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P-001

Dasatinib prevents joint destruction through regulation of T cell differentiation and attenuation of osteoclastogenesis in collagen-induced arthritis model

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Background
To evaluate the preventive role of tyrosine kinase inhibitor, dasatinib, in rheumatoid arthritis mice model (collagen-induced arthritis [CIA] model).

Methods
CIA was provoked in DBA/1J mice by injecting bovine type II collagen. Mice were grouped as normal non-CIA, vehicle treated CIA, dasatinib pretreatment, and dasatinib posttreatment groups. Clinical arthritis score was assessed twice a week for 5 weeks after collagen immunization. H&E, safranin O, toluidine blue stain were done to assess histology score. In vitro CD4+ T cell culture was performed. Flow cytometry of mice splenocytes and human T cells were performed. Osteoclast formation was evaluated by TRAP stain, and pit area after in vitro culture of bone marrow derived mononuclear cell of each groups.

Results
The clinical arthritis score was suppressed in dasatinib pretreatment group than vehicle group. Also, inflammation and cartilage erosion scores were lower in dasatinib pretreatment group. In flow cytometry, FcεR1+ cells were downregulated, whereas regulatory T cell (Treg) population were upregulated in splenocyte of dasatinib pretreatment group. In addition, type 17 helper T cell decrease with Treg increase by dasatinib administration was confirmed in vitro CD4+ human T cell culture. When bone marrow cells were differentiated into osteoclasts, TRAP+ mature osteoclasts and bone resorbing reaction were decreased in dasatinib pretreatment group.

Conclusions
Dasatinib demonstrated preventive effect in RA mice model via regulating Treg population and osteoclastogenesis. The present study suggests therapeutic potential of tyrosine kinase inhibitor, dasatinib, in early treatment of RA.

Keywords
Rheumatoid arthritis, tyrosine kinase inhibitor, dasatinib

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PLAG as a regimen to prevent the development of interstitial lung disease in autoimmune arthritis model

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Background

Interstitial lung disease (ILD) is the main cause of morbidity and mortality among rheumatoid arthritis (RA) patients. However, limited data are available about the treatment of RA-associated ILD. PLAG (acetylated diacylglycerol 1-palmitoyl-2-linoleoyl-3-acetyl-rac-glycerol) is a lipid molecule from the antlers of sika deer that might reduce inflammation by effectively controlling neutrophil infiltration, endothelial permeability, and inflammatory chemokine production. Therefore, we evaluated the modulatory effect of PLAG on arthritis and ILD in autoimmune arthritis model.

Methods

We injected curdlan (3 mg/mouse) into 8-week-old male SKG mice and identified ILD by histological analysis at 20 weeks post-injection. PLAG (250 mg/kg/day) was orally administered every day from 3 weeks to 20 weeks after curdlan injection and the arthritis score was measured every week after curdlan injection. At 20 weeks post-injection, lung specimens were evaluated with hematoxylin and eosin, Masson's trichrome, and multiplexed immunofluorescent staining. Serum cytokines were analyzed using a Luminex multiple cytokine assay 20 weeks after curdlan injection.

Results

Oral PLAG administration decreased the arthritis score until 8 weeks after curdlan injection. However, the effect was not sustained thereafter. Lung histology revealed severe inflammation and fibrosis in curdlan-induced SKG mice, which was attenuated in PLAG treated mice. Furthermore, immunofluorescent staining of lung tissue showed GM-CSF+ neutrophil accumulation and decreased citrullinated histone 3 expression (NETosis) after PLAG treatment. PLAG treatment also downregulated levels of IL- 6 and TNF-α and upregulated the level of soluble IL-7Rα (an anti-fibrotic molecule).

Conclusions

Our results indicate that PLAG might have a preventative effect on ILD development through the resolution of NETosis in the lung.

Keywords

interstitial lung disease, PLAG, rheumatoid arthritis

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P-003

Soluble CD27 as a biomarker of rheumatoid arthritis

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Background

CD70 is a member of the tumor necrosis factor superfamily and ligand for CD27. CD27 is constitutively expressed by conventional T lymphocytes, while CD70 is only transiently expressed after T cell activation. Co-stimulation through CD70-CD27 interaction can directly regulate T cell–T cell interaction and influence the development of effector T cell.

CD27 and CD70 interaction produces soluble CD27 (sCD27). High concentration of sCD27 in the serum was known as a predictive marker of a poor prognosis in malignancy such as renal cell carcinoma, brain tumor and lymphoma.

The level of sCD27 was higher in the serum of patients with poly-articular juvenile idiopathic arthritis (JIA) than in the serum of healthy controls. In patients with JIA, the level of sCD27 was higher in the synovial fluid (SF) than in the peripheral blood (PB).

In this study, we try to examine the effectiveness of sCD27 as a biomarker for the diagnosis of rheumatoid arthritis (RA).

Methods

The concentration of sCD27 in the serum of PB or supernatant of SF of healthy control, RA, osteoarthritis (OA) and ankylosing spondylitis (AS) was measured using an sCD27 enzyme-linked immunosorbent assay (ELISA) kit.

Results

The level of sCD27 in the supernatant of RA-SF was higher than that of OA-SF, AS-SF and in the serum of RA-PB and healthy control. The level of sCD27 in the serum of RA-PB was higher than that of healthy control or the supernatant of OA-SF. There was no difference between OA-SF and AS-SF.

Conclusions

From these results, we suggest that sCD27 may be a good marker for the diagnosis of RA, especially in SF and can be a new therapeutic target of RA.

Keywords

soluble CD27, rheumatoid arthritis, synovial fluid

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Identification of differentially expressed genes contributing to immune reaction in 232 patients with rheumatoid arthritis

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Background

Characterizing differentially expressed genes of rheumatoid arthritis (RA) is necessary to understand immunogenic interactions, and how several key immune genes were closely associated with the susceptibility of RA. This study seeks to identify RNA expression based computational methodologies for analyzing RA-immune interactions, which affected the development and progression of RA.

Methods

In the present study, 232 RA patients and 43 healthy controls microarray data (GSE93272, 93772, 93776) from the Gene Expression Omnibus (GEO) database were used to detect novel candidate risk genes for RA susceptibility. All raw files (CEL files) were directly downloaded from NCBI-GEO web site. The up- or down-regulated differentially expressed genes (DEGs) were identified and visualized by R packages 'affy' and 'ggplot2', windows based tools "cluster 3.0" and "JAVA treeview" in RA patients compared to healthy control samples. The significantly enriched Gene Ontology gene sets were computed and visualized by using the DEGs from the Gene Set Enrichment Analysis.

Results

Overall, the 92 DEGs, which were 86 up-regulated and 6 down-regulated, were identified in RA patients compared to the expression of healthy control samples. The Gene Ontology enrichment analysis demonstrated that 86 up-regulated genes significantly implicated in the immune reactions included immune effector process, toll like receptor binding, leukocyte mediated immunity, myeloid leukocyte mediated immunity, myeloid leukocyte activation, and defense response to other organism. In addition, they also implicated in the oxidative phosphorylation, apoptosis, and respiratory chain complex.

Conclusions

Identifying novel candidate immune genes and its immune interactions in RA patients will shed light on the underlying pathogenic mechanism of RA and provide clinical tools for assessing RA in patients.

Keywords

Rheumatoid arthritis, Differentially expressed gene, Immune reaction

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P-006

Lactobacillus sakei suppresses collagen-induced arthritis and modulates the differentiation of T helper 17 cells and regulatory B cells

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Background

To evaluate the immunomodulatory effect of Lactobacillus sakei in a mouse model of rheumatoid arthritis (RA) and in human immune cells.

Methods

We evaluated whether L. sakei reduced the severity of collagen-induced arthritis (CIA) and modulated interleukin (IL)-17 and IL-10 levels, as well as whether it affected the differentiation of CD4+ T cells and regulatory B cells. We evaluated osteoclastogenesis after culturing bone marrow-derived mononuclear cells with L. sakei.

Results

The differentiation of T helper 17 cells and the serum level of IL-17 were suppressed by L. sakei in both human peripheral blood mononuclear cells and mouse splenocytes. The serum level of IL-10 was significantly increased in the L. sakei-treated group, whereas the regulatory T cell population was unchanged. The population of regulatory B cells significantly increased the in L. sakei-treated group. Oral administration of L. sakei reduced the arthritis incidence and score in mice with CIA. Finally, osteoclastogenesis and the mRNA levels of osteoclast-related genes were suppressed in the L. sakei-treated group.

Conclusions

L. sakei exerted an anti-inflammatory effect in an animal model of RA, regulated Th17 and regulatory B cell differentiation, and suppressed osteoclastogenesis. Our findings suggest that L. sakei has therapeutic potential for RA.

Keywords

Lactobacillus sakei, Microbiome, Regulatory B cell

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P-007

EC-18 ameliorates autoimmune arthritis by suppressing inflammatory cytokines and osteoclastogenesis

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Background

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Methods

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Results

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Conclusions

L. sakei exerted an anti-inflammatory effect in an animal model of RA, regulated Th17 and regulatory B cell differentiation, and suppressed osteoclastogenesis. Our findings suggest that L. sakei has therapeutic potential for RA.

Keywords

Lactobacillus sakei, Microbiome, Regulatory B cell

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P-008

Resveratrol loaded chitosan nanoparticles attenuates severity of collagen induced arthritis in animal model : Role of NF-jB and STAT3 signaling pathway

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Background

Rheumatoid arthritis is the common occurring autoimmune diseases which affects the 1 % of world population. Resveratrol is naturally found flavonoid and reported to reduce the RA in patients. Although, the bioavailability of RV is too low in humans. The present study was carried out to explored the fabricate and characterize the resveratrol loaded chitosan nanoparticles (RV-Chi NPs) and comparison between RV-Chi NPs and RV to evaluate the therapeutic index in collagen induced RA in animal model.

Methods

Ionic gelation method was used for the preparation of RV-chi NPs and characterization was done by TEM, SEM, DLS and zeta potential. Rats were categorized into various groups and Collagen was used to induced the arthritis. Measurement of anti-inflammatory, biochemical parameter and proinflammatory cytokines was measured. Estimation of Heme Oxygenase-1(HO-1), nuclear factor erythroid 2–related factor 2 (Nrf2), expression of Nuclear factor-jB (NF-jB) expression and Receptor activator of nuclear factor kappa-B ligand (RANKL) were also performed.

Results

There was ($p < .001$) significant reduction was observed in the arthritic index, paw edema and gain body weight in RV-Chi NPs treated rat. RV-Chi NPs also upregualted the redox status and enhance the MDA content, and other antioxidant parameter (SOD, GSH, CAT) whereas downregulation in the content of cytokines i.e. interleukin-1b (IL-1b), interleukin-2, interleukin-17, interleukin-16, and tumor necrosis factor-a (TNF-a) and higher level of Transforming growth factor beta (TGF-b), and IL 10. NPs also enhances the HO-1,Nrf2 expression and reduced the STAT3, RANKL and NF-jB expression.

Conclusions

Overall, the finding indicates that RV-Chi NPs significantly reduced the arthritis severity which was induced by collagen via ameliorated oxidative stress and inflammation and RV-Chi NP improved the efficacy in comparison to RV

Keywords

Resveratrol, chitosan nanoparticles, Rheumatoid arthritis

E-poster Presentation

RA-clinical aspects

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P-009

Which cardiovascular disease risk calculator best reflects the subclinical atherosclerosis of coronary artery in rheumatoid arthritis patients? : Pilot study

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Background

Cardiovascular disease (CVD) are the leading cause of death in rheumatoid arthritis (RA) patients. Therefore, proper estimation of CVD risk is important in RA patients, however the traditional CVD risk calculators have limitation. Coronary artery calcium (CAC) score quantifies severity of atherosclerosis, and provide additional information for planning primary prevention for CVD. We estimated CVD risk via several methods and compared these with CAC score to identify most suitable CVD risk calculator in RA patients.

Methods

We recruited RA patients and collected demographic, laboratory, and RA-specific parameters, and patients were divided into two groups (CAC score ≥ 100 vs < 100). The 10-year CVD risk was measured by Framingham, SCORE, ASCVD-plus, QRISK3, ERS-RA, Reynold methods. Computed tomography was used to quantify CAC score of each enrolled patients. Correlation between CAC score and each CVD risk estimations were performed by Spearman correlation method. Linear regression analysis was used to elucidate the association between traditional CVD risk factors and CAC score.

Results

A total 54 RA patients were enrolled, and 7 patients showed CAC score higher than 100. RA patients with CAC score ≥ 100 group showed older age, higher ESR and hsCRP, higher DAS28-ESR, and lower total cholesterol / low density lipoprotein cholesterol. Among CVD risk estimations, ERS-RA showed the highest correlation coefficient (Rho = 0.430, P = 0.001). In multivariate linear regression analysis, ERS-RA (β = 10.30, 95% confidence interval [CI] 5.51-15.10) showed positive association with CAC score in RA patients.

Conclusions

In present study, ERS-RA method could reflect CAC score most properly in RA patients. Therefore, applying ERS-RA method may be suitable to predict subclinical atherosclerosis and CVD risk in RA patients.

Keywords

Rheumatoid arthritis, Cardiovascular diseases, Coronary artery calcium score

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P-010

Diffusion tensor imaging analysis in rheumatoid arthritis to determine the alteration of microstructural white matter integrity

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Background

CNS involvement in rheumatoid arthritis is rare & imaging is reported sparingly, limited to case reports only (1). The MRI findings are also nonspecific and the majority of the MR imaging does not demonstrate any abnormality (1,2). At autopsy, the medium & small vessels involve in almost all rheumatoid patients with neuropsychiatric symptoms (3). Thereby, there is an insight of research on quantitative assessment to detect the microstructural abnormalities, which may be missed by conventional MRI. The study aimed to assess the white matter microstructural integrity changes in

Methods

This was a prospective cross-sectional study for a duration of 3 years from March 2018 to March 2021. Group, I consisted of 8 patients who fulfil the ACR criteria for RA (2010) with neuropsychiatric symptoms, Group II consisted of 7 patients with RA according to ACR criteria (2010) without neuro-psychiatric symptoms and Group III was the healthy control consisted of 15 patients. The different DTI parameters like ADC, FA, RA, Trace, RD, AD, VR and GA were obtained from six different regions of white matter at the level of centrum semiovale. Intergroup significant difference was determined by one-way ANOVA followed Tukey post hoc test. Receiver operator characteristic curves were constructed to determine the accuracy of the DTI matrices.

Results

There was a significant decrease in FA, RA, AD and GA as well as an increase of RD, ADC and VR in the white matter in RA patients with neuropsychiatric symptoms compare to the control. (p-value <0.001). The maximum sensitivity of the DTI parameters is 81% and specificity 81%.

Conclusions

There was an alteration of white matter integrity in RA patients with Neuropsychritic symptoms that represents axonal degeneration, myelin breakdown and neuronal degeneration. The DTI may be a useful tool to detect white matter abnormality in clinical practice particularly in patients with negative conventional MRI

Keywords

Diffusion Tensor Imaging, rheumatoid Arthritis, Anisotropy

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P-011

Modification of auto-antibody profiles in rheumatoid arthritis : Data from a Malaysian 10-year follow-up study

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Background
Anti-cyclic citrullinated peptide2 (anti-CCP2) and rheumatoid factor (RF) are established serological markers for rheumatoid arthritis (RA). With treatment, evidence is needed to support disease modification claims, requiring knowledge of autoantibody profile stability and/or change over time. We aimed to investigate the alterations of anti-CCP2 and RF isotypes (IgG, IgA and IgM) in a multi-ethnic Malaysian RA patient cohort with 10-year follow-up.

Methods
A total of 320 RA patients from the Malaysian Epidemiological Investigation of Rheumatoid Arthritis (MyEIRA) case-control study was included in this study. The presence of anti-CCP2, IgM RF, IgG RF, and IgA RF autoantibodies at baseline and at later time point (duration between 2005 and 2019) were determined using the similar enzyme-linked immunosorbent assays at both occasions.

Results
Anti-CCP2 occurrence was comparable at baseline and follow-up study (72% vs 71%). Among all RA patients, there was a significant increased proportion for IgM RF positive (57% at baseline and 73% during follow-up, difference=16%, $p<0.0001$), and for IgA RF positive (44% at baseline and 60% during follow-up, difference=16%, $p=0.0001$). These significant changes in IgM and IgA RF isotypes proportions were observed in all RA ethnic groups (IgM RF: Malays, $p<0.05$, Chinese, $p<0.05$ and Indians, $p<0.05$; IgA RF: Malays, $p<0.05$, Chinese, $p>0.05$ (ns) and Indians, $p<0.001$). Overall, we observed constant autoantibody status over time mainly for anti-CCP2 (92.2%) followed by IgM RF (76.6%), IgG RF (74.1%) and IgA RF (68.8%).

Conclusions
Autoantibody status generally remained stable over time, with the exception for a decrease in anti-CCP2 among Chinese RA patients. The reason for this has to be explored in the future.

Keywords
Rheumatoid arthritis, Anti-CCP2, Rheumatoid factor

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P-012

Incidence rate and characteristics of herpes zoster in patients including Japanese with moderate-to-severe rheumatoid arthritis: Update from baricitinib clinical studies

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Background

To evaluate herpes zoster (HZ) in moderately to severely active RA pts including Japanese (JP) treated with baricitinib (Bari).

Methods

Incidence rate per 100 pt-years (IR) of HZ was calculated for Bari-treated RA pts pooled from Ph1-3 trials and long-term extension study. Risk factors for HZ were assessed by Cox proportional hazard models.

Results

HZ was reported in 323 of 3770 pts exposed to Bari as of Feb 2018 (IR=3.3). Of 323, 4% had a history of HZ, 3% had prior live HZ vaccination, 79% and 52% were on concomitant MTX and corticosteroids (CS), respectively. The median time to first HZ was 538 days. While the percentage of pts with HZ increased over time, the IR of HZ did not increase over time. Of 323, 8% were multidermatomal, 2% had involvement of the ophthalmic area, none had visceral involvement, and 3% had recurrent HZ during the study. A higher risk of HZ was associated with older age and Asia region but not with use of CS, history of HZ, or baseline lymphocytes. HZ rate for Bari in JP (81/514 pts, IR=6.8) appeared higher than overall pts.

Conclusions

IR of HZ in Bari-treated RA pts did not increase over time and the majority of HZ were monodermatomal and uncomplicated. HZ rate for Bari appeared higher in JP

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P-013

Machine learning based prediction model for responses of bDMARDs in patients with rheumatoid arthritis and ankylosing spondylitis

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Background

Few studies on rheumatoid arthritis (RA) have generated machine learning models to predict biologic disease-modifying antirheumatic drugs (bDMARDs) responses; however, these studies included insufficient analysis on important features. Moreover, machine learning is yet to be used to predict bDMARD responses in ankylosing spondylitis (AS). Thus, in this study, machine learning was used to predict such responses in RA and AS patients.

Methods

Data were retrieved from the Korean College of Rheumatology Biologics therapy (KOBIO) registry. The number of RA and AS patients in the training dataset were 625 and 611, respectively. We prepared independent test datasets that did not participate in any process of generating machine learning models. Baseline clinical characteristics were used as input features. Responders were defined as those who met the ACR20% improvement response criteria (ACR20) and ASAS20% improvement response criteria (ASAS20) in RA and AS, respectively, at the first follow-up. Multiple machine learning methods, including random forest (RF), were used to generate models to predict bDMARD responses, and we compared them with the logistic regression model.

Results

The RF model had superior prediction performance to logistic regression model (accuracy: 0.726 [0.725–0.730] vs. 0.689 [0.606–0.717], area under curve (AUC) of the receiver operating characteristic curve (ROC) 0.638 [0.576–0.658] vs. 0.565 [0.493–0.605], F1 score 0.841 [0.837–0.843] vs. 0.803 [0.732–0.828], AUC of the precision-recall curve 0.808 [0.763–0.829] vs. 0.754 [0.714–0.789]) with independent test datasets in patients with RA (Figure 1). However, machine learning and logistic regression exhibited similar prediction performance in AS patients. Furthermore, the patient self-reporting scales, which are patient global assessment of disease activity (PtGA) in RA and Bath Ankylosing Spondylitis Functional Index (BASFI) in AS, were revealed as the most important features in both diseases.

Conclusions

Our findings indicate that machine learning shows promise in guiding treatment decisions in clinical practice, based on clinical profiles.

Keywords

Rheumatoid arthritis, ankylosing spondylitis, machine learning

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Lactobacillus sakei suppresses collagen-induced arthritis and modulates the differentiation of T helper 17 cells and regulatory B cells

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Background

To assess no-show rate and to identify factors associated with no-show in patients with rheumatoid arthritis (RA) during one year in a routine clinical setting.

Methods

This prospective observational study has been conducted in the rheumatology center of a local tertiary hospital during one year from January 2019. No-show was defined as a missed appointment that was not previously cancelled by the patient. Several variables that might affect no-show were examined.

Results

A total of 387 patients and 2228 appointments for one year were evaluated. Among 387 patients, 179 patients (46.0%) missed appointment more than one time and there were 271 no-shows (12.2%). No-show patients were younger (53.8 vs 56.4 years, $p = 0.007$) than show-up patients and the medical history of malignancy was fewer in the no-show patients (3.4 vs 9.6%, $p = 0.015$). The number of comorbidities of no-show patients was significantly lower (0.5 vs 0.7, $p = 0.007$) than that of show-up patients. Patients who had missed appointment were more likely to miss their appointment again comparing to patient who keep their appointment (46.6 vs 21.1%, $p < 0.001$). The logistic regression analysis identified previous history of no-show, absence of medical history of malignancy and younger age as the independent factors associated with no-show.

Conclusions

Accurate assessment of no-show rate and its associated factors in a routine clinical setting is a necessary first step towards improving effectiveness to RA treatment. Physicians should emphasize the need for continuous medication use to their patients and modify no-show behaviors during follow-up appointments.

Keywords

No-show, Rheumatoid arthritis

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P-015

The value of the simplified RAMRIS-5 in RA patients using 3T MRI

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Background

The aim of the study was to evaluate a simplified version of the Rheumatoid Arthritis Magnetic Resonance Imaging Score (RAMRIS) for five joints of the hand (RAMRIS-5) in patients with rheumatoid arthritis (RA) 3-T magnetic resonance imaging (MRI).

Methods

Eighteen patients with a seropositive RA according to 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria (mean age 54.4 years, range 40–76) were retrospectively assessed with 3-T MRI of the clinically dominant hand. MRI scans were analyzed in accordance with RAMRIS and the simplified RAMRIS-5.

Results

There was a strong correlation between the total RAMRIS-5 and RAMRIS ($r = 0.897$; $P < 0.001$). RAMRIS and RAMRIS-5 demonstrated a similar ability to detect changes for all subgroups (bone edema, erosion, and synovitis). RAMRIS-5 and RAMRIS time-comparative analysis demonstrated significantly lower time consumption for RAMRIS-5 compared with RAMRIS (48.4 ± 8.00 s versus 280.2 ± 22.4 s; $P < 0.05$)

Conclusions

Three-Tesla MRI-based RAMRIS-5 is a simplified and resource-saving RAMRIS score that compares favorably with the total RAMRIS.

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P-016

Muscle mass and function in patients with rheumatoid arthritis

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Background

Muscular dysfunction affects the quality of life and comorbidities of patients with rheumatoid arthritis (RA). We aimed to determine the associations between low muscle mass and several clinical features in patients with RA.

Methods

We evaluated muscle mass which was measured by bioelectrical impedance analysis, grip strength, and physical performance in patients with RA.

Results

Among 320 patients with RA, 7 (2.2%) and 21 patients (6.6%) were determined to have sarcopenia, as defined by the AWGS and EWGS, respectively; 54 patients (16.9%) were determined to have low muscle mass with normal muscle function, as determined by the EWGS; and 38 patients (11.9%) reported sarcopenia using the SARC-F. With adjustments, male sex (OR 140.65, $p < 0.001$), low BMI (0.41, < 0.001), and use of tumor necrosis factor (TNF) inhibitors (4.84, 0.037) were associated with a low muscle mass as determined by the EWGS, while male sex, old age, and low BMI were associated with sarcopenia as determined by the AWGS. With adjustments, old age (1.11, < 0.001), high BMI (1.13, 0.015), and a high Disease Activity Score (DAS) 28 (1.95, < 0.001) were associated with sarcopenia as reported on the SARC-F. Mean grip strength was weaker in patients with a DAS28 of ≥ 3.2 (17.77 ± 5.9 vs 20.53 ± 5.36 kg, $p < 0.001$) and in patients with bony erosion (17.27 ± 5.46 vs 19.95 ± 5.72 kg, p =

Conclusions

Sarcopenia and low muscle mass occurred less frequently in RA in current clinical setting using upgraded treatment guidelines. Male sex, low BMI, and use of TNF inhibitors were associated with a low muscle mass in patients with long-standing RA. Disease activity and joint damage may contribute to a decrease in muscle strength, but not a loss of muscle mass in patients with RA.

Keywords

rheumatoid arthritis, sarcopenia, myopenia

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P-017

Disassociation between intensity of morning stiffness and various disease activity indices in Korean patients with rheumatoid arthritis

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Background

Morning stiffness (MS) is an important, nevertheless understated complaint witnessed in patients visiting the Rheumatology clinic. We aimed to fully explore the clinical characteristics of MS in patients with rheumatoid arthritis(RA).

Methods

Patients whose MS duration was equal or above 30 min completed a questionnaire of MS guided by a Rheumatologist and a skilled nurse practitioner (from July to Dec 2020). Patient-reported outcomes (PRO) including pain, functional disability, global assessment and mental health, and joint count, physician's global assessment, laboratory results, and prescription information were collected. Logistic regression analyses were implemented to investigate the association between the clinical parameters and MS intensity and duration. DAS-based disease activities, SDAI, CDAI, and RAPID3 were separately applied to multivariable models. We also performed a subgroup analysis of MS based on CDAI of the subjects.

Results

A total of 60 patients with RA completed the questionnaire. Mean age of the subjects was 59.2 years, 83.3% of which were female and mean CDAI was 12.50. Mean NRS (0-10) for MS intensity was 4.4 and mean duration of MS was 85.2 min. Intriguingly, the duration of MS was not fully in concordance with CDAI of patients (p=0.065). In the multivariable logistic regression analyses, glucocorticoid use was a key factor associated with lower MS intensity in all models. Among disease activity measures, RAPID3 was the only significant index that predicted (NRS≥4) intensity of MS in the multivariable model (OR 4.71, CI 1.97-11.27, p<0.01)(Table). RAPID3 was also an independent, significant parameter associated with (≥60 min) duration of MS (OR 1.82, CI 1.24-2.69, p=0.003)

Conclusions

MS is an important, yet often overlooked clinical feature affected by multifaceted aspects. A strictly PRO-based composite index better reflects the intensity and duration of MS in patients with RA in clinical practice.

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Sustained remission in patients with rheumatoid arthritis treated with targeted therapy : Results from the KOBIO registry

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Background

We now have a long list of targeted therapies in our disposal for patients with rheumatoid arthritis (RA), yet there are few studies showing real-world data of sustained remission achieved after their use.

Methods

Remission rates of five different criteria were compared in patients with RA using data from the KOBIO registry. Yearly change of remission rates after initiating targeted therapy was measured for 5 years in 1) total patients and in 2) subgroups divided into four distinctive class of agents (TNF-α inhibitors, tocilizumab, abatacept and tofacitinib). Sustained remission was defined as remission maintained for two consecutive yearly visits.

Results

Patients (N = 1805) who completed at least a single follow-up visit were analyzed (median age, 56 years; female, 83.2%). At month 12, 56.0% of patients achieved remission by the disease activity score in 28 joints (DAS28)-C-reactive protein (CRP), 36.2% by the DAS28-erythrocyte sedimentation rate (ESR), 10.4% by the clinical disease activity index (CDAI), 12.7% by the simplified disease activity index (SDAI), and 12.9% by the Boolean criteria (Figure). Whereas roughly 62% of the patients achieved sustained remission by the DAS28-CRP, the percentage was lower when using the DAS28-ESR, CDAI, SDAI, and the Boolean criteria: 40%, 8%, 11%, and 13%, respectively. In addition, DAS28 remission rates were highly variable in the aforementioned subgroups during the 5-year follow-up.

Conclusions

Assessing sustained remission using the CDAI, SDAI, or the Boolean criteria is more stringent, yet congruous than the DAS28-based criteria in RA patients treated with targeted therapy.

E-poster Presentation

RA-Treatment

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P-019

Significant factors predicting the trend of disease activity in rheumatoid arthritis patients treated with biologics: Trajectory-based clustering approaches for KOBIO registry

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Background

Background/Objective: The purpose of this study is to divide the trend of disease acitivity into groups by trajectory-based clustering and to find a predictor related to treatment response for biologics in patients with rheumatoid arthritis (RA).

Methods

Methods: The cohort data of 1204 patients treated with biologic disease modifying anti-rheumatic drugs (bDMARDs) and targeted synthetic disease modifying anti-rheumatic drugs (tsDMARDs) from the Korean College of Rheumatology Biologics and Targeted Therapy (KOBIO) registry. Trajectory modeling for clustering were used for grouping of the trends of disease activity in each individual. Among groups, logistic regression was used to find predictors in baseline clinical characteristics for trajectories.

Results

Results: A total of 688 patients who started treatment with bDMARDs or tsDMARDs were included in this study. Using tajectory modeling, the disease activity trend was clustered into 4 groups (Figure 1); Disease activity decreased rapidly (group 1), decreased and then increased again (group 2), decreased slowly (group 3), and remained high (group 4). In multivariable analysis with group 1 as reference, increased ESR were associated with group 2, increased BMI, cholesterol and initial DAS28 and decreased hemoglobin, and blood urea nitrogen were associated with group 3 and current smoking and increase initial DAS28 were associated with group 4 (Table 1).

Conclusions

Conclusions: Four trajectories of disease activity trends and predictors for treatment response were identified using a trajectory-based approach. Trajectory-based clustering was a useful method for predicting treatment response in patients with RA.

Keywords

Rheumatoid arthritis, KOBIO, Treatment response

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P-020

Revealing a portrait of a patient with refractory arthritis

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Background

Refractory rheumatoid arthritis (RRA) refers to rheumatoid arthritis (RA) that is resistant (due to ineffectiveness or toxicity) to several drugs, including methotrexate and at least 2 bDMARDs with different mechanisms of action.

Methods

The anamnestic data of 40 adult patients with RRA, observed from 2010 to 2018. The study did not include patients who were sequentially treated with bDMARDs from the TNF-a inhibitor group as the first and second drugs.

Results

The studied group was represented mainly by women (N = 32, 80%), who received from 3 to 6 bDMARDs, median 3 [3-4]. Clinical forms of RA were presented as seropositive for rheumatoid factor (RF) RA - in 17 patients (42.5%), RA with extra-articular manifestations - in 6 (15.0%), RA seronegative for RF - in 16 (40.0%)), Still's disease in adults - in 1 (2.5%). The average age at the time of RA debut in the study group was 31.1±17.0 years. The onset of RA in juvenile age was observed in 10 patients (25.0%). At the time of bDMARD initiation, the average age of patients was 39.8±15.1 years, and the prescription of RA was 8.7±6.3 years. 17 patients (42.5%) received 4 bDMARDs, 5 (12.5%) - 5 bDMARDs, 2 (5%) - 6 bDMARDs. As the first biologic in the study group, the following were prescribed: TNF-inhibitors - 23 patients (57.5%), abatacept - 10 (25.5%), rituximab - 4 (10.0%), tocilizumab - 3 (7, five%). The first bDMARD was discontinued due to ineffectiveness in 29 patients (72.5%), due to the development of serious adverse events - in 11 patients (27.5%). Second bDMARD - in 31 (77.5%) and 9 (22.5%), respectively.

Conclusions

In the study group, patients with RRA were represented mainly by women with seronegative RA in the RF, onset of the disease at a young age and late addition of the first bDMARD.

Keywords

bDMARDs, refractory arthritis, biologics

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Infectious complications as reason for discontinuations of biologics

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Background

To study infectious complications of therapy with biologics, analyze the frequency of withdrawal of bDMARDs due to infectious complications.

Methods

The ambispective analysis included data on 505 cases of prescribing biologics with different mechanism of action in 188 patients with rheumatoid arthritis (160 women, 28 men).

Results

Patients in the study group received from 2 to 5 bDMARDs, mediana (25% -75%) 2 (2-3). Biologics were discontinued 326 times, of which due to the development of serious adverse reactions - 70 times, of which due to the development of infectious complications - 16 times (5% of all cases of discontinuations, 29% of all serious adverse reactions). During treatment with the first bDMARD, infectious complications that required discontinuation of the drug developed in 5.3% of cases (N = 10), with the second bDMARD - in 5.2% of cases (N = 4), no statistical differences were found between these groups. On the background of treatment with the third bDMARD, infectious complications led to the withdrawal of treatment in 14.3% of cases (N = 1), in the fourth - 0%, and in the fifth - 33.4% of cases (N = 1). There was no correlation between the number of sequentially prescribed biologics and the incidence of infectious complications. Most often, serious infections developed during treatment with drugs of the TNF-α inhibitor group (infliximab, etanercept, adalimumab, golimumab, certolizumab pegol) and tofacitinib. Out of 16 cases of infectious complications, 5 were associated with tuberculosis infection.

Conclusions

Infectious complications make up a significant proportion (29%) of all serious adverse reactions leading to the discontinuations of biologics in patients with rheumatoid arthritis. The frequency of discontinuation of bDMARDs due to infectious complications was about 5% and did not change during treatment with both the first and second biologics.

Keywords

bDMARDs, rheumatoid arthritis, serious infections

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P-022

Immunological remission and prognosis of anti-TNF α treatment response among diagnostic biomarkers in rheumatoid arthritis

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Background

In the management of RA,a new concept has attracted the interest of the scientific community, immunological remission,defined as the disappearance of rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA).

As is well known,a significant number of patients are declared non-responders (NR) to biologic treatment in RA,identifying pretreatment those patients who will/not respond remains an important target to achieve.

We proposed to asses the evolution of serum titres of RF type IgM/A,anti-CCP,anti-MCV under anti-TNFα treatment and we analyzed the existence of correlations with the activity scores (DAS28,SDAI,CDAI).We had also tested the prognostic value for anti-TNF treatment response of them.

Methods

prospective and observationl study including 64 patients followed 12 months with active RA, uncontrolled by csDMARDS which required biologic therapy as EULAR recommendations.

Clinical assessment was performed at 0, 6 and 12 months according to ACR criteria approved by OMERACT and evaluation of treatment response according to EULAR criteria (good /moderate /nonresponder).

Results

following the evolution of serum levels, we noticed a reduction almost for all four biomarkers tested, statistically significant at 6 and /or 12 months , as follow RF IgM,(baseline=123.07± 126.330,6months=77.91±105.670,12months=50.25±88.265),IgA (baseline=80.71± 114.849,6mont hs=44.75±71.649,12months=28.78± 65.694),anti-CCP(baseline=101.52± 51.653,6months=85.14± 50.249,12months=64.19±43.669),anti-MCV(baseline=65.66± 132.080,6months=43.12±85.368,12mont hs=17.15±27.856)

Analyzing the possible correlations,between the immunological parameters and the disease activity scores at any visits, they were not observed, but there are strong positive correlations between all these scores (Example Fig.1).

Following baseline immunological parameters titres and the EULAR response at 6 months, general tests have identified significant differences between groups. Lower baseline titres of RF type IgM (51.36±95.359 U/ml,p=0.01629),IgA(22.45±61.256 U/ml,p=0.03336) and anti-CCP(60.82±26.331ng/

ml,p=0.00011) had predictive value for achieving a good response at 6months.Regarding anti-MCV baseline titres,there were no differences between groups(p=0.45914).
For the response at 12 months, lower baseline titres for RF type IgM (92.93±120.22 U/ml, p=0.01032) and IgA (49.96±98.08 U/ml,p=0.00247) had predictive value for achieving a good EULAR response at 12 months .

Conclusions

achieving immunological remission does not appear to be an absolute goal. Predicting treatment response remains a major need and finding a solution can begin with the use of common biomarkers.

Keywords

Rheumatoid arthritis, Immunological remisson, Biomarkers

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P-023

A study of factors affecting long-term persistence of rituximab in patients with RA : Results from the Korean rheumatology biologics registry

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Background

Unlike other biologic agents for rheumatoid arthritis (RA) that are administered at regular intervals even without flare, rituximab can be administered according to the timing of retreatment determined by the physician. Recently, there has been a tendency to prefer on-demand administration for disease flares rather than regular retreatment. We aimed to investigate the retreatment patterns of rituximab in patients with RA and to identify factors associated with extension of the time interval between retreatment courses.

Methods

This study included RA patients on rituximab treatment who were enrolled in the Korean Rheumatology Biologics registry (KOBIO) or treated at Ajou University Hospital. The persistent rates of rituximab and predictors associated with extending the time interval between retreatment courses were analysed.

Results

We enrolled 82 patient with RA receiving rituximab. The mean age at the first rituximab cycle was 55.2 years, and mean follow-up period from the first cycle of rituximab was 46.1 months. The mean interval between the retreatment courses was 16.3 months. The persistent rates of rituximab after 5 years was 72.4%. Concomitant use of at least two conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) and concomitant use of corticosteroids were independent factors for extending the time interval between the retreatment courses. The failure rate of rituximab treatment was 18.3%, and anti-citrullinated protein antibody negative was the only factor associated with the treatment failure.

Conclusions

The concomitant use of at least two csDMARDs and the concomitant use of corticosteroids are significant influencing factors of extension of the retreatment time interval in rituximab. To our best knowledge, this is the first analysis to identify the influencing factors that extend the time interval during on-demand retreatment in RA patients with good clinical responses to rituximab.

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P-024

Switching from TNF α inhibitor to tacrolimus as maintenance therapy in rheumatoid arthritis after achieving low disease activity with TNF α inhibitors and methotrexate : 24-week result from a non-randomized, active-controlled trial

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Background
Tapering or stopping biological disease-modifying anti-rheumatic drugs has been proposed for patients with rheumatoid arthritis (RA) in remission, but it frequently results in high rates of recurrence. This study evaluates the efficacy and safety of tacrolimus (TAC) as maintenance therapy in patients with established RA in remission after receiving combination therapy with tumor necrosis factor inhibitor (TNFi) and methotrexate (MTX).

Methods
This 24-week, prospective, open-label trial included patients who received TNFi and MTX at stable doses for ≥ 24 weeks and had low disease activity (LDA), measured by Disease Activity Score-28 for ≥ 12 weeks. Patients selected one of two arms: maintenance (TNFi plus MTX) or switched (TAC plus MTX). The primary outcome was the difference in the proportion of patients maintaining LDA at week 24, which was assessed using a logistic regression model. Adverse events were monitored throughout the study period.

Results
In efficacy analysis, 80 and 34 patients were included in the maintenance and switched arms, respectively. At week 24, LDA was maintained in 99% and 91% of patients in the maintenance and switched arms, respectively (odds ratio, 0.14; 95% confidence interval, 0.01–1.59). Drug-related adverse effects tended to be more common in the switched arm than in the maintenance arm (20.9% versus 7.1% respectively), but were well-tolerated.

Conclusions
This controlled study tested a novel treatment strategy of switching from TNFi to TAC in RA patients with sustained LDA, and the findings suggested that TNFi can be replaced with TAC in most patients without the patients experiencing flare-ups for at least 24 weeks.

Keywords
rheumatoid arthritis, tacrolimus, tumor necrosis factor inhibitors

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P-025

Radiographic progression of structural joint damage over 5 years of baricitinib treatment in patients with rheumatoid arthritis : Results from RA-BEYOND

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Background
We evaluate radiographic progression(RP) of structural joint damage in RA patients(pts) over 5yr of BARI treatment.

Methods
This included pts completing RA-BEGIN(DMARD-naïve)/RA-BUILD(csDMARD-IR)/RA-BEAM (MTX-IR) enrolled in RA-BEYOND. Those receiving blinded BARI at end of trials remained on that dose(2/4mg once daily)in RA-BEYOND. At 52wk, DMARD-naïve pts receiving MTX/combination therapy(BARI4mg+MTX) were switched to BARI4mg monotherapy; MTX-IR pts receiving adalimumab(ADA)were switched to BARI4mg on background MTX. At 24wk, csDMARD-IR pts receiving PBO were switched to BARI4mg on background csDMARD. Analysis population:pts with baseline and at least 1radiograph after 2yr. RP of structural joint damage(Yr3-5)was determined by changes from baseline in van der Heijde modified Total Sharp Score(ΔmTSS), erosion score, joint space narrowing. Proportion of pts with no progression was assessed on change from baseline mTSS(ΔmTSS)from originating study using thresholds of 0.5/smallest detectable change(SDC). Mixed model repeated measures and logistic regression models analyzed continuous and categorical variables, respectively; linear extrapolation was used for imputation of missing data(max 1year).

Results
82.6%(2125/2573)pts entered RA-BEYOND. Among DMARD-naïve pts, those on initial BARI monotherapy/ in combination with MTX had significantly slower RP(ΔmTSS)than those on initial MTX at yr3,4,5($p \leq 0.05$) and significantly fewer erosions at these timepoints($p \leq 0.05$). A greater proportion of pts who received initial BARI and BARI-MTX had no RP compared to initial MTX monotherapy using thresholds of 0.5($p \leq 0.05$). Among MTX-IR pts, those on initial BARI had slower RP than PBO and results were comparable to those on initial ADA treatment at yr3,4,5. A greater proportion of pts who received initial BARI therapy had no RP compared to initial PBO using thresholds of SDC($p \leq 0.05$). Among csDMARD-IR pts, though differences between groups were small, pts on initial BARI4mg had slowest RP compared to initial PBO and initial BARI2mg. ≥74% of structure data are based on observed data.

Conclusions
Treatment with once-daily oral BARI maintained low RP rates for up to 5yr in different RA patient populations.
Presented:ACR/ARP2020.

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P-026

Signal detection of adverse drug reactions of biologic and target synthetic DMARDs used in rheumatoid arthritis patients on real-world data in South Korea

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Background

Biologic disease-modifying antirheumatic drugs(bDMARDs) and target synthetic DMARDs(tsDMARDs) are relatively newer categories of treatment in the rheumatologic field and their use them are steadily growing. We aimed to detect signals of adverse drug reactions(ADRs) of these agents from real-world data; single center's electronic medical record(EMR)-driven common data model(CDM) data and Korean College of Rheumatology Biologics & Targeted Therapy Registry, KOBIO registry data.

Methods

Data were extracted from January 2012 to December 2019 for CDM, and from November 2012 to June 2020 for the KOBIO registry. Cases with one of bDMARDs or tsDMARDs including etanercept, infliximab, adalimumab, golimumab, rituximab, abatacept, tocilizumab, tofacitinib, and baricitinib for RA were enrolled. We applied CDM-based MetaLAB algorithm for detecting ADR signals, where the algorithm used laboratory test results as supplementary information on ADRs with statistical approaches. And, we performed disproportionality analysis (e.g., proportional reporting ratio, reporting odds ratio) to KOBIO registry data.

Results

Using the MetaLAB algorithm, we extracted 1411 patients and 28 significant drug-ADR pairs(ROR >1.0 and $p< 0.05$). Significant ADRs were 'Hypochloraemia' for abatacept; 'Blood urea increased' for adalimumab; 'Hyperglycaemia' for golimumab; 'White blood cell disorder' in infliximab; 'hepatic enzyme elevation' in rituximab; 'Anaemia' for tocilizumab; 'Hepatic enzyme elevation', 'Thrombocytosis' in tofacitinib. For the KOBIO registry, 2279 patients were initially registered, then 6908 follow-ups were included and considered as independent cases. Detected signals with disproportionality analysis with ROR or PRR >2 and $p< 0.05$ by PhViD package in R(4.0.5) and not reported in the FDA labels were 'Gastroesophageal reflux disease', 'Hypercholesterolaemia', 'Asthma', and so forth, for abatacept. Other drugs are listed in more detail in Table 1.

Conclusions

Detection of ADR signals for biologic DMARDs prescribed for RA patients from real-world data was performed. Further cross-validation of results with other databases such as adverse event reporting system(AERS) data and continuous pharmacovigilance is needed.

Keywords

Biologicals, Adverse drug reaction, Rheumatoid arthritis

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Immunological remission and prognosis of anti-TNF α treatment response among diagnostic biomarkers in rheumatoid arthritis

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Background

In the age of biologic therapies, at least 2 needs are still being debated to find an answer:
-is immunological remisson a target that should be aimed?
-the need to identify pre-treatment of patients who will respond or not to a certain biological agent.
For this,we proposed to evaluate two new RA diagnostic biomarkers:14-3-3eta protein and cartilage oligomeric matrix protein(COMP).
We assesed the evolution of serum titres under anti-TNFα treatment and we analyzed the existence of correlations with the activity scores (DAS28,SDAI,CDAI).We had also tested their predictive value for treatment response.

Methods

prospective and observational study including 64 patients followed 12 months with active RA,uncontrolled by csDMARDs.Clinical assessment was performed at 0,6,12 months according to ACR criteria and evaluation of treatment response according to EULAR criteria (good/moderate/nonresponder).

Results

following the evolution of serum levels,we noticed a reduction of biomarkers tested as follow:14-3-3eta (baseline=0.43± 0.591,6months=0.32±0.452,12months=0.28± 0.499ng/ml) and COMP (baseline=948.75±215.683,6months =1044.2±674.674,12 months=740.88±227.04 ng/ml)
Analyzing the possible correlations,between the immunological parameters and the disease activity scores at any visits,they were not observed,but there are strong positive correlations between all these scores (Example Fig.1).
Following baseline immunological parameters titres and the EULAR response at 6 months, general tests have identified significant differences between groups.Lower baseline titres of 14-3-3 eta (0.51±0.580, p=0.045178) and for COMP (746.04±130.095, p=0.00000) had predictive value for achieving a good response at 6 months
Grouping patients in 2 categories (responders/nonresponders) for 6 months response, we identified significant differences between groups just for baseline titres of 14-3-3eta (responders 0.36±0.515ng/ml, 0.99±0.888 nonresponders ng/ml, p=0.04041)

For the response at 12 months,we didn't find significant differences between basline titres and a good EULAR response (14-3-3eta p=0.376,COMP,p=0.143)

Conclusions

achieving immunological remission does not appear to be an absolute goal. Predicting treatment response remains a major need and new diagnostic biomarkers could help us in the future.

Keywords

Rheumatoid arthritis, Immunological remisson, Biomarkers

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P-028

Flare after switching from intravenous tocilizumab to subcutaneous formulation in patients with rheumatoid arthritis

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Background

Tocilizumab (TCZ) is a recombinant humanized monoclonal antibody of the IL-6 receptor which inhibits IL-6-mediated signaling. TCZ is available as an intravenous (IV) formulation (TCZ-IV) and a subcutaneous (SC) formulation (TCZ-SC). The present study aimed to evaluate the incidence and risk factors for RA flares after switching to TCZ-SC in stable RA patients as TCZ-IV.

Methods

We retrospectively evaluated the incidence of RA flares in patients who switched from TCZ-IV to TCZ-SC. Patients were divided into two groups based on RA disease activity as assessed by Disease Activity Score in 28 joints (DAS28) after switching from TCZ-IV to TCZ-SC ("SC inefficacy group" versus "SC efficacy group"). Factors associated with RA flares were evaluated by multivariate analysis.

Results

Among 147 patients who were treated initially with TCZ-IV, 37 patients were switched to TCZ-SC after the acquisition of remission or low disease activity. The SC inefficacy and SC efficacy groups included 11 (29.7%) and 26 (70.3%) patients, respectively. At the time of switching, mean DAS28 was not different between the two groups. However, doses of TCZ-IV per weight and methotrexate were higher in the SC inefficacy group. In the multivariate analysis, the use of a high dose (more than 8 mg/kg) TCZ (odds ratio [OR] 33.441, 95% confidence interval [CI], 1.573–710.833, p=0.024), methotrexate non-user (OR 41.416, 95% CI, 1.529–1121.731, p=0.027), and history of prior abatacept use (OR 29.817, 95% CI, 1.069–831.442, p=0.046) were associated with the risk of RA flares after switching to TCZ-SC.

Conclusions

Methotrexate non-use and TCZ-IV overdose per weight were associated with a higher risk of RA flare after switching to TCZ-SC. Thus, we recommend checking these factors before switching from TCZ-IV to TCZ-SC to prevent RA flares.

Keywords

Tocilizumab, Rheumatoid arthritis

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P-029

Therapeutic outcomes of patients with rheumatoid arthritis based on DAS-28 at different clinical settings of Pakistan

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Background

Globally Rheumatoid arthritis (RA) is the most common inflammatory arthropathy. Among autoimmune problems, RA was one of frequently problem. Worlwide 1% of the cases are reported. Current study was designed to analyze the treatment outcomes by using various antirheumatic medications at various clinical setups of Hyderabad, Pakistan.

Methods

Clinical observational study was conducted in RA patients at five different clinical settings of Hyderabad, Sindh, Pakistan from Jan 2020 to December 2020. By using Rao-Soft formula, total sample was 272 based on prevalence. Therapeutic outcomes were assessed for a period of one year by designing follow up protocols. Informed consent were also taken before inclusion in the study. Therapeutic outcome were assessed by using Disease activity score-28. Data was analyzed descriptively.

Results

Out of total 272 patients, 93 (34.19%) are male and 179 (65.81) of female. Based on mean value, the age of patients was 45.32 ±16.27 and disease duration was 4.78 + 6.03 years. Further based on DAS-28 score after applying DMARD therapy, baseline score was 4.92 + 0.74. After six months and 12 months, the overall DAS-28 score was reduced to 3.89+ 1.02. At the end of 12 months, under the category of remission it was 173(63.6%), under low disease activity, it was 63(23.16%) and 36 (13.23%) had moderate disease activity.

Conclusions

It was clearly revealed that Female gender had a higher rate of occurrence of rheumatoid arthritis as compared to male gender while DMARD therapy was effectively used and improvement of DAS-28 had noted.

Keywords

Rheumatoid, Arthritis, Pakistan, Therapeutic

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P-030

Long-term safety of a single infusion of human umbilical cord blood-derived mesenchymal stem cell therapy in rheumatoid arthritis : The 5-year follow-up of the phase I clinical trial

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Background

Mesenchymal stem cell (MSC) therapy represents a promise for the treatment of autoimmune diseases due to its potent immunomodulatory effect. We investigated the long-term safety of a single treatment of human umbilical cord blood-derived (hUCB)-MSCs in patients with rheumatoid arthritis (RA).

Methods

Patients with RA who met the 2010 ACR/EULAR classification criteria and received a single intravenous infusion of hUCB-MSCs (3 groups; 2.5 x 107, 5.0 x 107, 1.0 x 108 cells) in a phase I trial (NCT02221258) entered this 5-year observational study. Safety assessments were carried out at 3, 6, and 12 months for the first year after the hUCB-MSC administration and annually thereafter for the remaining period. Key safety endpoints included overall adverse events (AEs), serious adverse events (SAEs) and AEs of special interest including infection, thromboembolism, and benign/malignant tumor. Physical examination, laboratory tests and electrocardiograms were also performed.

Results

A total of nine patients were treated after the phase I trial at a single center. The most frequent AEs (Table) over 5 years were osteoarthritis (66.7%), nasopharyngitis (44.4%), abdominal pain (33.3%), osteopenia or osteoporosis (33.3%), lumbar spinal stenosis (22.2%), and hypertension (22.2%). SAEs occurred in 5 patients (55.6%); a serious infection (cellulitis) happened in one patient in the 1.0 x 108 group that resolved after treatment. Three years after administration of MSCs, a benign ovarian tumor and a breast adenoma were reported in the 2.5 x 107 and 5.0 x 107 groups, respectively. However, no death, thromboembolism or malignancy occurred during the follow up period. The incidence of AEs increased over time after administration of MSCs, but similar across the dose groups. There were no clinically significant laboratory finding, except for a case of hypertriglyceridemia and a case of anemia.

Conclusions

The long-term safety profile of a single dose of intravenous hUCB-MSC in patients with RA was reasonable and acceptable.

Keywords

Rheumatoid arthritis, Mesenchymal stem cell, Safety

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P-031

Risk of herpes zoster infection in Korean patients with rheumatoid arthritis treated with JAK inhibitors

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Background

Various clinical studies have been conducted to assess the safety of targeted therapy with a focus on infections, and herpes zoster (HZ) is a growing concern with Janus kinase inhibitor (JAKi) therapy. We aimed to determine the risk of HZ in Korean patients with rheumatoid arthritis (RA) using JAKis.

Methods

We conducted a nested case-control study with prospective cohorts of RA patients receiving targeted therapy in an academic referral hospital in Korea. The crude incidence rate ratio (IRR) for HZ in JAKi users versus biologic disease-modifying antirheumatic drug (bDMARD) users was calculated. Logistic regression analyses were performed to determine the risk of HZ and risk factors for HZ development among JAKi users.

Results

Of 1147 patients (223 JAKi users and 924 bDMARD users), 61 patients were diagnosed with HZ during the observation period (3263.1 person-years). The crude IRR for HZ in JAKi users versus bDMARD users was 5.78 (95% CI 3.30–10.11); however, JAKi use did not increase the risk of HZ development in the multivariable analysis (odds ratio (OR) 1.39, 95% CI 0.73–2.66). The ages of 50s and 60s (OR 3.41 and 3.40, 95% CI 1.49–7.82 and 1.52–7.63) and three or more previous bDMARD use (OR 4.89, 95% CI 1.45–16.48) were risk factors for HZ in patients with RA. Among JAKi users, higher disease activity (OR 1.50, 95% CI 1.07–2.12) was identified as an additional risk factor, and vaccination against HZ did not show a protective effect in this study.

Conclusions

Although the crude IRR for HZ in JAKi users versus bDMARD users was increased, JAKi use did not increase the risk of HZ in large Korean prospective cohorts. However, further studies with larger sample sizes and longer follow-up periods are required to investigate the relationship between the JAKi use and HZ development.

Keywords

herpes zoster, rheumatoid arthritis, Janus kinase inhibitor

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P-032

Treatment response to the second JAK inhibitor in patients with rheumatoid arthritis

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Background

Rheumatoid arthritis (RA) patients refractory to a first Janus kinase inhibitor (JAKi) because of inefficacy/adverse events (AEs) are often switched to a second JAKi, although without known benefits. Therefore, we evaluated the treatment response of such patients to the second JAKi.

Methods

This retrospective observational study involved RA patients who received the second JAKi at a single tertiary referral center from August 2015 to March 2021. Clinical information, including age, sex, laboratory data, and medications, was collected from electronic medical records. Clinical responses at baseline and 6 months after the second JAKi were assessed using Disease Activity Score-28 (DAS28) with erythrocyte sedimentation rate (ESR).

Results

We enrolled 25 patients (23 women, 2 men) with a mean age of 54.9 ± 8.2 years. For most patients (96%, 24/25), the first and second JAKis were tofacitinib and baricitinib, respectively. The mean baseline DAS28-ESR score was 5.9 ± 1.1. The median duration for the first JAKi was 8 (interquartile range [IQR], 5–17) months, and reasons for termination were inefficacy and AEs in 72% and 28% patients, respectively. The median number of biologics between two JAKis was 1 (IQR, 1–2), and median duration was 11 (IQR, 5–22) months. Reasons for early discontinuation (<6 months) of the second JAKi were inefficacy and AEs in three (12%) and two (8%) patients, respectively. Six months after second JAKi administration, of the 20 patients (80%, 20/25) evaluated for treatment efficacy, 10 (40%) reached low disease activity/remission, with mean reduction in the DAS28-ESR score of 2.9± 0.9. Among patients who discontinued the first JAKi because of AEs, none discontinued the second JAKi because of AEs.

Conclusions

For RA patients refractory to the first JAKi, another JAKi was effective in reducing disease activity. Further studies are warranted to determine the efficacy of this switching.

Keywords

Rheumatoid arthritis, JAK inhibitor, switch

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P-035

Real-world comparative effectiveness of tofacitinib versus tumor necrosis factor inhibitor in patients with rheumatoid arthritis: A prospective observational study

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Background

To evaluate the effectiveness of tofacitinib compared with tumor necrosis factor inhibitor (TNFi) in Korean patients with rheumatoid arthritis (RA)

Methods

Data were extracted from each registry of biologic disease modifying anti-rheumatic drugs (bDMARDs) (between Jan. 2014 and Mar 2021) or tofacitinib (between Mar. 2017 and Mar. 2021) of a single academic referral hospital in Seoul, Korea. The analysis included RA patients with moderate or high disease activity at baseline and completed a 6-month follow-up visit. Outcomes was assessed at 6 and 12 months after initiation of tofacitinib or TNFi (adalimumab, etanercept, golimumab, infliximab) and included the rate of achieving remission based on disease activity score (DAS) 28 erythrocyte sedimentation rate (ESR), DAS 28 C reactive protein (CRP), clinical disease activity index (CDAI), and simplified disease activity index (SDAI). Multivariable conditional logistic regression based on the stratification with age, gender, and previous use of bDMARDs was performed to account for potential confounding factors.

Results

A total of 527 patients (168 tofacitinib-treated and 359 TNF inhibitor-treated patients) were included. Tofacitinib-treated patients were older (53.4 vs 50.3); they had longer disease duration (11.0 vs 7.8 years), higher comorbidity index (0.4 vs 0.2), and higher disease activity at baseline (DAS 28 ESR 6.6 vs 6.2), and a greater proportion had previously received bDMARDs (50.0% vs 10.0%) than TNFi-treated patients. Other baseline characteristics were comparable. There were no statistically significant differences observed between the treatment groups in the rate of achieving remission based on DAS 28 ESR (OR 0.67, 95% CI 0.29-1.58, p=0.36) at 6 months, and this result persisted at 12 months (OR 0.72, 95% CI 0.37-1.37, p=0.31).

Conclusions

In clinical practice, tofacitinib- and TNFi-treated patients differed in baseline characteristics. However, tofacitinib and TNFi were found to have similar effectiveness after adjusting for confounders.

Keywords

Tofacitinib, TNF inhibitor, effectiveness

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P-036

Construction of numerous classifiers to prognosis rheumatoid arthritis in patients by data mining approach

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Background

Rheumatoid arthritis is a autoimmune with chronic inflammatory diseases. The mechanism of RA is still not clear and occurred due to problem related with autoimmume produced via infection caused by pathogen or predisposing of genetic factors. On the basis of diseases severity, selection of therapy in clinical practice for RA is prerequisite. Moreover unclear, ambiguous and uncertain treatment in patients with RA cause makes the quality healthcare worsen. The present study performed to merge the physicians opinions for constructing numerous classifiers of data mining approach to examine among the group of patients prognosis.

Methods

We collect the clinical data of patients to construct numerous classifier and scrutinize the accuracy rate of prediction for every classifier. From these classifier the prediction model was chosen to measure the RA prognosis for patient among theses treatment approach and all finding were analyzed. We predicted that inflammatory biomarker (ESR) among both patients groups are in the normal value range upon treatment with various medication plan.

Results

Finding indicates prediction model accuracy rate via DT (decision tree), logistic regression (LGR) and SVM (support vector machines) module which was 0.9324, 0.7567 and 0.7629. During the complication of RA the dataset were generated with accuracy rate of 0.9921, 0.9452 and 0.9267 respectively. Moreover, obtained ratio gain was again utilized in analyzing rules & branch nodes was discovered, an important parameter.

Conclusions

It was concluded from the results that execution of decision support system by the help of prediction model aids healthcare profession to craft a right decions in the early stage of RA and also assist in developing guidelines for the correct treatment in RA.

Keywords

Data mining, Decision tree, Rheumatoid arthritis

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P-037

Comparison of retention rate and efficacy between tocilizumab monotherapy and MTX combination therapy from KOBIO registry

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Background

It has been known that tocilizumab monotherapy is not inferior to tocilizumab and methotrexate (MTX) combination therapy in patients with rheumatoid arthritis (RA). However, the data from real world setting is lacking, so we compared the drug retention rate and efficacy between tocilizumab monotherapy and MTX combination therapy.

Methods

From the Korean College of Rheumatology Biologics (KOBIO) registry, 342 patients with RA treated with tocilizumab were enrolled this study. The drug retention rate was compared using the Kaplan-Meier method, and efficacy was analyzed by comparing the ACR20, 50, 70 and EULAR response criteria of the two groups.

Results

The median follow-up time after initiating tocilizumab was 23 [11-36] months. 258 patients (75.4%) were received tocilizumab combined with MTX and 84 patients (24.6%) were received tocilizumab monotherapy. Kaplan-Meier analysis estimated that 83.0% of combination therapy group and 79.2% of monotherapy group continued to receive tocilizumab at 1 year, and each of 66.6% and 62.3% at 3 years (log-rank p=0.581). At 1 year, the combination therapy group showed better response regarding ACR 20 (84.1% and 67.6%, p=0.003) and ACR 50 (63.6% and 38.0%, p<0.001). But when comparing ACR 70 and EULAR response, there was no difference between two groups. At final follow-up, there was no difference in ACR 20, 50, and 70 responses between two groups, but combination therapy group showed better EULAR response than monotherapy group (72.5% and 60.5% in good response, p=0.004). There was no significant difference in adverse effect leading to drug switching or discontinuation between two groups.

Conclusions

In the real practice in Korea, the combination of MTX seemed to be more effective in controlling disease activity when treating RA patients with tocilizumab.

Keywords

Rheumatoid arthritis, Tocilizumab, Methotrexate

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P-038

Quality assessment of health care of rheumatoid arthritis in Korea based on multicenter medical record reviews

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Background

Quality indicators (QIs) for evaluating the health care for patients with rheumatoid arthritis (RA) were developed by the experts in Korea [1]. We investigated the quality of health care for RA by these QIs.

Methods

We established denominators and numerators for measuring RA QIs. A total of 26 centers, in which a rheumatologist is placed (tertiary teaching hospital 15, general hospital 7, others 4), participated the study and they provided quality measurements through the reviews of medical records of randomly assigned RA patients who visited the hospitals in 2019.

Results

Visit to a rheumatologist, assessment of disease activity and screening for latent tuberculosis when starting biologics or tsDMARDs, laboratory test before DMARD therapy, and folate supplementation for MTX-treated patients were excellently performed (in over 90% of the patients). Examination by a rheumatologist, hand radiographs for newly diagnosed or suspected RA patients, DMARD therapy initiation during the early stage were taken well (more than 80% of the patients). Feet radiographs in early stage and assessment for comorbidities and drug safety before starting biologic or tsDMARDs were achieved in 64% and 73% of the patients, respectively. Specialized rheumatology nurses for patient counseling and education were 15.4% in rheumatology clinics. Programmed patient education and periodic measurement of standardized disease activity indices were given in 31% of the RA patients.

Screening for hepatitis B virus surface antigen (HBsAg) and hepatitis C testing (HCV antibody) prior to initiation of biologics or tsDMARDs were performed in 60% and 50% of the patients, respectively. However, hepatitis B core antibody (HBcAb) testing was not prevalent (24% of the patients).

Conclusions

Most of the QIs measurements were well in the hospitals with rheumatologists, except for rheumatology nurse personnel, patient education, periodic measurements of standardized disease activity, and HBV and HCV screening prior to initiation of biologics or tsDMARDs.

Keywords

Quality, Health care, Rheumatoid arthritis

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Clinical efficacy of cevidoplenib (SKI-O-703), a selective SYK inhibitor, in early rheumatoid arthritis patients in phase II a clinical trial

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Background

SYK is a non-receptor tyrosine kinase that mediates B cell receptor and Fc receptor signaling and thereby is presumed to play critical roles in antibody-driven inflammatory immune responses. As such, it has been hypothesized that SYK inhibition might be an effective way to ameliorate auto-antibody-induced inflammatory autoimmune diseases including rheumatoid arthritis (RA). Cevidoplenib is a highly potent and specific SYK inhibitor best suited to interrogate the role of SYK in various diseases. Its exquisite specificity had proven to result in an excellent safety profile throughout Phase I studies.

Methods

International multi-center randomized double-blind placebo-controlled Phase IIa clinical trial was conducted, enrolling 163 active RA patients who had previously shown inadequate response to csDMARDs or anti-TNFalpha drugs. Participants were randomly assigned to 3 dose levels of cevidoplenib (100, 200, and 400 mg bid) or placebo for 12 weeks, with mean changes in DAS28-CRP as the primary efficacy endpoint.

Results

While cevidoplenib did not meet the primary endpoint, a subgroup analysis revealed that there was an early, significant improvement among patients with a moderate disease activity (DAS28-CRP < 5.1) at the baseline. Improvements in secondary endpoints, ACR50 and ACR70, were also evident in this 'early RA' patient subgroup. In addition, interestingly, cevidoplenib appeared more effective in patients who were not on any other concomitant medications (csDMARDs), although the differences were not statistically significant.

Conclusions

Although cevidoplenib proved to be ineffective in the heterogeneous population of refractory RA patients, it exhibited promising efficacy in 'early RA' patients with moderate baseline disease activity. This result illuminates the mechanism of action of SYK in the progression of RA pathology and warrants further investigations in, for example, patient stratification strategy or combination regimen.

Keywords

Cevidoplenib, SYK, Ph2 Clinical Trial

E-poster Presentation

SLE-clinical aspects, APS

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Myocardial involvement with pericarditis presenting as decompensated congestive cardiac failure at lupus onset

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Description

Myopericardial involvement as first manifestation of systemic lupus erythematosus is rather rare. The resultant global hypokinesia and severe congestive cardiomyopathy in a young female lupus patient at its onset is presented here.

A middle-aged previously healthy lady with initial two-week history of malaise and constitutional symptoms, presented with reduced effort tolerance with left sided pleuritic chest pain. She was initially treated as pneumonia with left exudative parapneumonic effusion. Cultures including tuberculosis workup were negative. However, symptoms not improved and inflammatory markers were persistently raised. Further imaging with computed tomography revealed pericardial effusion, pleural effusion and ascites. Poor ejection fraction of 25% with global hypokinesia was noted from echocardiography. No clots were found and lipid profiles as well as cardiac enzymes were normal except for high brain natriuretic peptide of 495 pg/ml. Her dyspnoea at exertion and orthopnoea did not improve requiring oxygenation support, despite diuretic, beta blocker and ACE inhibitor. Both her ANA and dsDNA were positive with low complements and negative infective screening. At the same time, proteinuria >0.5 g/24 hours (0.8g) was present. She was diagnosed to have systemic lupus erythematosus based on 2019 EULAR/ACR criteria, with the presence of ANA, pleural and pericardial effusion, heavy proteinuria (>0.5g/24 hour), low complements (C3,C4) and positive antidsDNA. IV methylprednisolone was initiated with marked improvement of symptoms (no orthopnoea, oxygen free, normalization of systolic function). She was then maintained with 2-weekly of intravenous cyclophosphamide (EuroLupus regime). She was well at last follow-up.

Conclusions

Early diagnosis and timely intervention with high dose steroid become a cornerstone for mortality prevention of such major organ involvement in early lupus stage.

Keywords

congestive heart failure, systemic lupus erythematosus, young lady

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P-041

Outcome of transient proteinuria in systemic lupus erythematosus

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Background

Current guidelines recommend performing a kidney biopsy in systemic lupus erythematosus (SLE) patients with overt proteinuria(urine protein/creatinine ratio≥500 mg/g). However, some of these patients show significant improvement in proteinuria shortly after corticosteroid therapy to the point of no biopsy indication. Thus, this study aimed to investigate the characteristics and long-term outcomes of patients who showed an improvement in proteinuria after treatment with corticosteroid alone prior to biopsy.

Methods

The medical records of SLE patients who showed improvement of proteinuria(urine protein/creatinine ratio<500mg/g) after receiving corticosteroid therapy without immunosuppressants were reviewed.

Results

A total of 38 patients with a mean age of 44.6years(IQR,16–73) were analyzed. The mean value of creatinine was 0.75±0.33mg/dl. After receiving corticosteroid therapy alone for a median of 62 days(IQR,9–55), the patients showed decreases in the urine protein/creatinine ratio from 1353±1053mg/g to 289±125mg/g. After further follow-up (median 54 months [IQR, 6–55]), 25(67%) patients maintained the resolution of proteinuria (279±122mg/g) without renal dysfunction, and the remaining 13(32%) patients experienced a relapse of proteinuria (1208±709mg/g). There was no significant difference in the levels of creatinine and proteinuria at baseline between patients with deterioration and those without. Of the 21(55%) patients who underwent renal biopsy, class II(38%) and class III(19%) were the most frequently observed kidney pathologies. After treatment with immunosuppressants for patients(n=9) with proliferative form of lupus nephritis, they showed favorable outcomes including the achievement of complete response, and none of them progressed to end-stage renal disease during a long-term follow-up of 74 months(IQR,20–91).

Conclusions

Two-thirds of SLE patients who showed improvement in proteinuria after corticosteroid therapy alone maintained the non-proteinuria state without renal dysfunction. Thus, performing a kidney biopsy at the time of the first onset of proteinuria may not be necessary in all SLE cases with proteinuria, in particular those showing an improvement in proteinuria after treatment with corticosteroid.

Keywords

lupus nephritis

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P-042

Risk of bleeding-related complications after kidney biopsy in patients with systemic lupus erythematosus

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Background

Kidney biopsy is essential for the diagnosis and classification of lupus nephritis. Even though the risk of bleeding-related complications is not low in such patients, data on the risk of kidney biopsy in SLE patients are limited. Thus, we investigated the rate of bleeding-related complications and examined the risk factors for complications of kidney biopsy in patients with SLE.

Methods

We retrospectively reviewed the medical records of SLE patients who underwent ultrasound-guided percutaneous kidney biopsy between 2002 and 2020 at a tertiary referral center. Major complications included bleeding events that required interventions (e.g., blood transfusion, angiographic embolization, surgery) after biopsy. Minor complications included hematoma, oozing, or hematuria without intervention. Statistical analysis with a multivariate logistic regression model was performed to identify the risk factors associated with

Results

In a total of 165 SLE patients, the rate of overall bleeding-related complication after kidney biopsy was 25% (major: 8%, minor: 17%). In terms of the details of major complications, 86% (12/14) needed a blood transfusion alone without embolization, and the remaining two patients needed embolization for bleeding control. Patients with any kind of complication had a significantly lower platelet level than did those without complications ($p<0.001$). Univariate analysis showed that the levels of hemoglobin (OR 0.81; 95% CI, 0.66–0.99), platelet (OR 0.99; 95% CI, 0.99–1.00), aPTT (OR 1.05; 95% CI, 1.00–1.11), and proteinuria (OR 1.00; 95% CI, 1.00–1.00) were significantly associated with the risk of complications. Multivariate analysis revealed that low platelet count (OR 0.99; 95% CI, 0.98–0.99) was significantly associated with the risk of bleeding-related complications after kidney biopsy.

Conclusions

Percutaneous kidney biopsy was accompanied by the risk of bleeding-related complications, although the majority of events did not require vascular intervention for bleeding control. Low levels of platelet counts had a significantly increased risk of complications after kidney biopsy in patients with SLE.

Keywords

Lupus nephritis, Systemic Lupus Erythematosus, risk factor

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P-043

Radiological imaging findings and outcome of stroke in patients with systemic lupus erythematosus

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Background

This study aimed to evaluate imaging findings and outcome of stroke in patients with systemic lupus erythematosus (SLE)

Methods

Patients who fulfilled ≥4 ACR criteria for SLE and had a history of stroke from 2013-2021 were identified. The non-contrast computed tomography findings, magnetic resonance findings , functional outcome of stroke (assessed by the modified Rankin Scale) at 90 days, mortality, stroke complications and recurrence were retrospectively studied and compared with matched non-SLE patients with stroke.

Results

20 SLE patients and 60 non-SLE patients with stroke (age at stroke 46.8±12.5 years; 76% women) were studied. Ischemic type of stroke (90% versus 85%; p=0.21) and extensive infarction (52% versus 42%; p=0.08) was more common in SLE than non-SLE patients. CT and MRI findings were not significantly different between groups. Patients with SLE were more functionally dependent than controls at 90 days' post-stroke. Stroke mortality at 30 days was non-significantly higher in SLE than non-SLE patients but all-cause mortality (41.5% compared to 16.2%; p<0.001) were significantly more common in SLE patients after an observation of 4.2±3.8 years. SLE was independently associated with all-cause mortality and stroke recurrence over time.

Conclusions

Stroke in SLE patients is associated with a poorer outcome than matched
controls in terms of functional recovery, recurrence and mortality. However radiologic imaging findings are similar each groups.

Keywords

systemic lupus erythematosus, imaging findings, stroke

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P-044

Magnetic resonance imaging in the assessment of shoulder involvement in systemic lupus erythematosus

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Background

Systemic lupus erythematosus (SLE) patients could suffer shoulder function limitations even in the absence of symptoms related to joint or tendon disorders. We aimed to evaluate shoulder involvement in SLE patients with magnetic resonance imaging (MRI) findings.

Methods

We retrospectively reviewed 30 SLE patients with shoulder pain and motion limitation who underwent shoulder MRI between 2018 and 2021. 5 of 30 patients were excluded due to motion artifacts. Remaining 25 patients were included the study to assess shoulder MRI patterns in SLE patients. All MRI findings were recorded.

Results

We assessed 25 SLE patients with shoulder pain and motion limitation (28 shoulders, bilateral in 3 patients) using MRI; 23 (92%) patients had joint effusions, 22 (88%) had bone erosions, 20 (80%) had subacromial-subdeltiod bursitis, 19 (76%) had tendonitis, 18 (72%) had synovitis, 16 (64%) had rotator cuff tendon tears, 15 (60%) had myositis, 15 (60%) had subacromial impingement, 14 (56%) acromioclavicular joint hypertrophy, 11 (44%) had biceps tendon instability, 10 (40%) had labral tears, 8 (32%) had subcoracoid bursitis, 6 (24%) had Hill-Sachs deformity. The most common shoulder MRI findings were joint effusion, bone erosion and bursitis. The supraspinatus tendon full-thickness tear was the most common MRI finding in 16 patients with rotator cuff tears.

Conclusions

SLE patients may have higher subclinical synovitis, erosions and tendon involvement than expected in shoulder MRI studies. MRI represents a valuable imaging tool for the assessment of shoulder involvement in patients with SLE. Thus, MRI examinations should be performed in SLE patients with shoulder pain

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P-045

Adjusted global antiphospholipid syndrome score (aGAPSS) based nomogram for predicting avascular necrosis in SLE

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Background

The aim of this study was to describe the prevalence and distribution of avascular necrosis (AVN) in Systemic Lupus Erythematosus (SLE) and to see the performance of adjusted GAPSS based nomogram in predicating AVN.

Methods

This was a retrospective case-control tertiary care hospital based study. AVN diagnosed based on imaging evidence in symptomatic patients were considered as cases. Individuals with SLE without AVN matched for gender, age and follow up duration till AVN onset were controls. Multivariable logistic regression was used to analyse the association of each variable with the likelihood of AVN, and a nomogram was created with the variables in aGAPSS score for probable likelihood of developing AVN. The discrimination of the nomogram was measured by using the area under the receiver operating characteristic (ROC) curve.

Results

Out of the 900 patients screened, 52 (5.7%) had AVN in 171 sites. Femoral head (n=50; 96.1%) was the commonest site followed by femoral condyles (n=35;67.3%) Figure 1A.. Hyperlipidaemia, positive Lupus anticoagulant (LAC), clinical SLEDAI (cSLEDAI) score at baseline, cumulative steroid in the 6 months preceding AVN were associated with AVN ($p<0.005$). The median adjusted GAPSS in cases and controls was similar ($p=0.08$).Upon multivariable logistic regression, hyperlipidaemia (OR-18.4 95% CI 7.1-47.5,$p<0.005$), positive LAC (OR-3.7 95% CI 1.4-9.6,$p<0.005$) and baseline SLEDAI (OR - 1.1 95% CI 1.03-1.17,$p<0.005$) were associated with AVN. The nomogram (Figure 1B) with the components of aGAPSS score for prediction of AVN in at risk patients demonstrated an AUC of 0.812 (sensitivity 80%; specificity 74%).

Conclusions

Over 5% of patients with SLE had AVN with femoral head being the most common site. Hyperlipidaemia is the major factor associated with AVN. Steroids had no association with AVN. The novel nomogram uses information from aGAPSS and performs well in predicting AVN in our cohort.

Keywords

Osteonecrosis, SLE, GAPSS

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P-046

Clinicopathological correlation at baseline and its impact on one year renal outcome in lupus nephritis

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Background

Diagnosis of Lupus Nephritis(LN) is currently based on laboratory tests and renal histopathology. Though biopsy can determine the severity of LN, it is still unclear if histopathology findings correctly determine long term outcomes. The objectives were to see if clinical and biochemical parameters at baseline could identify renal histopathological class and to assess the impact of baseline biochemical and histopathological factors in determining renal outcomes at one year

Methods

This retrospective study involved 221 biopsy proven lupus nephritis. Histological class assigned as per ISN/RPS classification along with clinical and biochemical parameters at the time of biopsy were noted. Those with class III/IV LN were further grouped as mild, moderate and severe. Histopathological features were correlated with demographic, clinical, biochemical and serological parameters at the time of diagnosis. Renal outcome [complete, partial or no response (CR, PR, NR)] at the end of one year was assessed for 196 patients and their determinants were assessed.

Results

Class III/IV was the commonest 187(84.6%) subset of LN. Majority (57.2%) of class III/IV had hypertension as opposed to <25% each with class II and V($p<0.001$). Class III/IV had lower eGFR [85.7(69.5-113.5)] ($p<0.001$) and higher nephrotic range proteinuria (54%) compared to others ($p<0.03$). Higher proportions of patients with moderate and severe class III/IV had impaired eGFR values ($p<0.03$) and higher uPCR ($p<0.001$) (Table 1). At the end of one year more males (12.5%, $p<0.02$) had poorer outcome. Higher proportion with eGFR<90 (30.6% vs 22%, $p<0.001$) was associated with PR/NR. Those who attained CR had lesser proteinuria at baseline [1.3(0.7-2.75)} versus [1.95(1.07-3.81);$p<0.02$] in non-CR. Higher histopathological activity score($p<0.001$), chronicity score($p<0.001$) and crescents($p<0.003$) were associated with NR/PR.(Table 2).

Conclusions

Clinical and biochemical parameters can predict the biopsy class to a fair extent. Conducting a renal biopsy is important to prognosticate and may allow clinicians to predict outcomes at 1 year.

Keywords

Lupus nephritis, Renal biopsy, Treatment response

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P-047

Clinical significance of frailty to cumulative organ damage and quality of life in patients with systemic lupus erythematosus: A 5-year longitudinal cohort study

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Background

Because frailty in systemic lupus erythematosus (SLE) may occur due to the effects of the disease, its treatment, comorbidities, or aging, we investigated the impact of frailty on organ damage and quality of life in the Korean SLE cohort using the Systemic Lupus International Collaborating Clinics Frailty Index (SLICC-FI) during a 5-year follow-up period.

Methods

We enrolled 199 SLE patients from the KORNET registry. Demographics, clinical, laboratory findings, PGA, SLEDAI-2K, SLICC damage index (SDI), SF-36, and BDI scores were obtained at enrollment, and then annually for 5 consecutive years. We divided the patients into four groups according to their baseline SLICC-FI [robust (SLICC-FI < 0.03), relatively unfit (SLICC-FI 0.03–0.1), unfit (SLICC-FI 0.1–0.21), and frail (SLICC-FI > 0.21) groups]. Univariate and multivariate analyses were performed to assess the impact of baseline SLICC-FI on clinical outcomes in SLE patients.

Results

Of the 199 patients, 7 (3.5%), 83 (41.7%), 96 (48.2%), and 13 (6.5%) were in the robust, relatively unfit, unfit, and frail groups, respectively, at enrollment. The higher SLICC-FI group was older (p=0.036), and had higher rates of serositis (p=0.024) and osteoporosis (p=0.009), than the lower SLICC-FI group. The mean SDI scores, and changes therein, during follow-up were significantly higher in the higher than lower SLICC-FI group in all 5 years (both p<0.001). The mean SF-36 Physical Component Summary (PCS) and Mental Component Summary (MCS) scores during follow-up were significantly lower in the higher SLICC-FI group (both p<0.001). In the multivariate analysis, frailty was significantly associated with age (OR = 1.071, 95% CI: 1.013–1.134, p=0.016), SDI (OR = 1.949, 95% CI: 1.089–3.489, p=0.025), and SF-36 PCS (OR = 0.731, 95% CI: 0.629–0.8550, p=0.001) after adjustment.

Conclusions

Frailty was associated with organ damage and lower quality of life during the 5-year follow-up, suggesting that the SLICC-FI could serve as an outcome measure in SLE patients.

Keywords

frailty, organ damage, quality of life

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The correlations among renal SLEDAI with pro-inflammatory biomarkers and serum urea to creatinne ratio in SLE patients

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Background

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune inflammatory disease. Several indexes can measure SLE activity, and Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) is one of them. A biomarker with predictive appeal could be used in conjunction with SLEDAI. The role of serum urea to creatinine ratio as a possible biomarker of renal injury, in SLE is suggested. The aim was to associate renal SLEDAI with inflammatory biomarkers present in serum and urea to creatinine ratio in SLE patients.

Methods

This study used a retrospective analytic observational design at Dr. Sardjito Central Hospital, Yogyakarta Indonesia. This study included SLE patients who were arranged in two groups according to the value of renal SLEDAI. Renal SLEDAI ranges from 0 to 16, and its calculation is performed through the following tests: Proteinuria, hematuria, pyuria, and haematic or hyaline cylinders. Levels of serum urea and creatinine were quantified by enzymatic colorimetric assay. The data were analyzed with correlation, bivariate, and the ROC curve to determine cut-off. using SPSSv25.

Results

There were 55 SLE patients with renal SLEDAI $\leq$ 8 (n=37), and the other group, renal SLEDAI >8 (n=18). Levels of anti-dsDNA, serum urea and urea to creatinine ratio were significantly higher in the group renal SLEDAI >8. There was a significant positive correlation with renal SLEDAI scores on ANA test (r=0,300; p=0,026), serum urea (r= 0,272; p=0,045) and urea to creatinine ratio (r=0,732; p<0,001). In the ROC curve, a cut-off serum urea to creatinine ratio $\geq$38,75 was obtained with a sensitivity of 77,8%, specificity of 75,7%, likelihood ratio=3,20 (AUC = 0.821 with p-value <0.001) to detect high renal injury, in SLE.

Conclusions

Serum urea to creatinine ratio is a potential predictor biomarker of renal involvement in patients with SLE. It could be used in conjunction with SLEDAI for evaluating SLE activity.

Keywords

Serum urea to creatinine ratio, renal SLEDAI Score, Systemic Lupus Erythematosus (SLE)

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P-049

Distinct clinical characteristics of initial onset macrophage activation syndrome in systemic lupus erythematosus

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Background

Hemophagocytic syndrome(HPS) is a life-threatening disease and when it occurs in autoimmune disease, it is termed Macrophage Activation Syndrome(MAS). The aim of this study was to identify specific clinical characteristics and risk factors for MAS in SLE patients. Furthermore, clinical profiles of SLE patients presented with initial onset and delayed onset MAS were compared.

Methods

We reviewed the medical records of 1384 patients with SLE who admitted to Seoul St. Mary's hospital of the catholic university of Korea from January 1990 to December 2020 and identified 54 patients who had developed MAS. 150 age and sex matched SLE patients admitted for other manifestations were included as disease controls. Features of MAS in these patients were analyzed.

Results

Among 54 SLE patients with MAS, 21 patients had initial onset MAS and 33 had delayed onset MAS. Longer SLE duration (P<0.001), the presence of fever (P<0.001) and high serum LDH levels (P=0.002) were the risk factors for the development of MAS. Among the 21 patients with initial onset MAS, 2 patient died while 5 out of 33 delayed onset MAS patients died. Initial onset MAS patients had shorter SLE duration (P=0.005) and higher incidence of lymphadenopathy (P<0.001), cardiac involvement (P=0.035), pleural effusion (P=0.010), and nephritis (P<0.001) than delayed onset MAS patients. Furthermore, initial onset patients had lower ESR (P=0.002), fibrinogen (P=0.032), C4 (P=0.028) and higher SLEDAI score (P=0.008). The survival rate between the two groups had no significant difference.

Conclusions

The longer disease duration, fever and high serum LDH levels are the risk factors for MAS in SLE patients. As for the difference in the clinical characteristics between initial and delayed onset MAS patients, shorter disease duration, higher incidence of lymphadenopathy, cardiac involvement, pleural effusion and nephritis were more frequently found in patients who developed MAS at the time of SLE diagnosis.

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P-050

A clinical and histopathological characteristics and one year responses in lupus nephritis : Prospective cohort study

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Background

This prospective study aimed to investigate the baseline characteristics and one year outcomes in Korean patients with lupus nephritis (LN).

Methods

Sixty patients with LN underwent biopsy were included from a single rheumatology center in Korea from 2018 to 2020. The data of LN were collected every 0, 3, 6 ,12 months from the date of biopsy. Outcomes were evaluated as a complete (CR), partial (PR), and non-response (NR) at 6 and 12 months, respectively. Multivariable Poisson regression analysis was performed to evaluate factors associated with CR.

Results

The mean age of diagnosis of LN was 29.0 (± 9.70) years and 25 (41.7%) patients were underwent first renal biopsy. The proportion of class III, III+V, IV, IV+V, V was 15 (25%), 10 (17%), 26 (43%), 8 (13%), 1 (2%), respectively. As an induction therapy, mycophenolate mofetil was the most commonly used (83%). The 12 months responses of CR, PR, NR were 55%, 23%, 22%, respectively (table 1) and those of first and repeated-biopsy were 60%, 24%, 16% and 51%, 23%, 26%, respectively. There were no significant differences in the responses of the first and repeated-biopsy. In multivariate Poisson regression analysis, Anti-Ro (odds ratio (OR) 0.60, 95% confidential interval (CI) 0.4158 – 0.789, p-value = 0.0084) and LN class III (OR 0.69, CI 0.5016 – 0.9613, p-value = 0.0280) were factors associated with CR at one year.

Conclusions

Anti-Ro and LN class III were predictive factors for CR at one year. Despite advanced in the treatment of LN, the proportion of PR or NR was still high. Efforts to search for more promising therapeutics as well as biomarkers for renal outcomes are needed.

Keywords

systemic lupus erythematosus, lupus nephritis, clinical outcomes

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P-051

A case report of sqamous cell carcinoma arising within a lesion of discoid lupus erythematosus

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Background

Discoid lupus erythematosus is the most common form of chronic cutaneous lupus erythematosus. Around 5-20% progress to SLE. DLE lesions are associated with increased risk of Squamous cell carcinoma. Decrease in melanin, immunosuppressive therapy, frequent ultraviolet exposure, human papillomavirus infection, chronic scarring, and inflammatory processes are factors associated with the development of SCC1

Objectives: A case report to highlight the occurance of Sqamous cell carcinoma in a DLE lesion.

Methods

A 54 year old female diagnosed as SLE 6 years back who was on immunosuppression presented with a painful progressive ulcer over left preauricular region since 2 months.On examination she had scarring alopecia and discoid lupus erythematosus lesions over cheek,forehead and dorsum of nose (Fig A). Local examination revealed a 6*5 cm ulcer over left preauricular region with necrotic base and everted edges (Fig B).

Histopathology of ulcer showed infiltrated malignant neoplasm with individual cell keratinization and focal keratin pearl formation suggestive of Squamous cell carcinoma (Fig C).CT neck showed the ulceroprolferative mass lesion in left temporal region extending in to temporalis.

Results

She received 5 cycles of cisplatin and 50Gy RT.She underwent wide local excision of tumor with flap cover(Fig D).She is on regular follow up and reported no flares.

Conclusions

Conclusion: Incidence of SCC over DLE in the Indian population is found to be 0.98% to 3.4% with a male-to-female ratio of 1.6:1. The latent period between onset of DLE and development of

SCC was 9.59 ± 5.6 years 2.In our case it was around 6 years.Identifying the risk factors for Sqamous cell carcinoma in DLE and screening for carcinoma in suspicious DLE lesions can reduce morbidity and mortality.

Keywords

Squamous cell carcinoma, Discoid lupus erythematosus, SLE

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P-052

A rare case of simultaneous subarachnoid hemorrhage and superficial vein thrombosis in systemic lupus erythematosus without anti-phospholipid antibody syndrome

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Description

Systemic lupus erythematosus (SLE) is a complex heterogeneous autoimmune disease with a wide variety of clinical and serological manifestations that may affect any organ. Vasculitis prevalence in SLE is reported to be between 11% and 36%. A diverse clinical spectrum, due to inflammatory involvement of vessels of all sizes, is present. A 30-year-old male was presented with a diagnosis of SLE, multiple arthritis, oral ulcer, low complement, ANA 1:160 positive , anti Ro & La Ab , Ds DNA Ab high titer positive. His arthralgia improved after intravenous methylprednisolone (60 mg/d) and hydroxychloroquine therapy. On #10 HD, he complain severe headache, brain MR & CT showed small amount of subarachnoid hemorrahge, but angiography negative. On # 17 HD, he complain Lt. wrist pain, wrist sonography showed suspicious left cephalic vein thrombosis, CT venography showed long segmental acute to subacute thrombosis at cephalic vein of left forearm, and combined mild enhancing thickening of vessel wall, suspicious vasculitis. Antiphospholipid antibody tested twice was all negative.

Conclusions

We would like to share the experience of diagnose and treat a young male lupus patient who showed subarachnoid hemorrhage that had no findings on the cerebral angiography and left cephalic vein thrombosis of forearm at the same time.

Keywords

Male lupus, Subarachnoid hemorrhage, Cephalic vein thrombosis

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P-053

The relationship among serum albumin with disease severity level of systemic lupus erythematosus (SLE) patients in Dr. Sardjito central hospital Yogyakarta

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Background

BACKGROUND

Systemic Lupus Erythematosus (SLE) is an episodic chronic autoimmune inflammatory disease characterized by remission and flare phase. Laboratory parameters are needed to assess the degree/severity of disease activity in SLE include serum albumin. Several studies regarding the laboratory of chemistry on the severity of SLE patients are still inconsistent.

OBJECTIVE

To evaluate of serum albumin with the degree of disease severity in SLE patients in Dr. Sardjito Central Hospital, Yogyakarta.

Methods

This study used a retrospective analytic observational design in SLE patients in January 2016-December 2019 at Dr. Sardjito Central Hospital. Disease severity was assessed by Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score. The laboratory of serum albumin were measured with colorimetric assay. The data were analyzed with correlation, bivariate and multiple regression tests, and the ROC curve to determine cut-off.

Results

There were 55 SLE patients with high activity (SLEDAI 11-19; n=30(54,54%)) and very high activity (SLEDAI≥20; n=25(45,45%)). There was a significant correlation ($p < 0.05$) on the albumin (r=-0,353), blood urea nitrogen (r= 0,282) with SLEDAI scores ($p < 0.05$), but only the serum albumin variable was significant as an independent variable ($p = 0.046$). In the ROC curve, a cut off serum albumin ≤2,83 was obtained with a sensitivity of 80.0%, specificity of 52%, likelihood ratio=1,67 (AUC = 0.640) to detect very high disease activity.

Conclusions

The serum albumin were significantly related to the degree of SLE disease activity.

Keywords

serum Albumin, SLEDAI Score, Systemic Lupus Erythematosus

E-poster Presentation

SLE-pathogenesis and animal model

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P-054

HLA profiling in Malay female patients with systemic lupus erythematosus

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Background

Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease, in terms of clinical presentation, incidence, and severity across diverse ethnic populations. Some studies have reported common SLE-related human leukocyte antigen (HLA) risk factors, mainly the HLA-DRB1 and DQB1 genes, to be observed in multiple ethnic populations worldwide. Nevertheless, others also demonstrated population-specific risk signals associated with SLE. We investigated the HLA profile (i.e. HLA-A, -B, and -C, -DRB1, -DQA1, -DQB1, -DPA1, and -DPB1) in Malaysian Malay female patients with SLE.

Methods

One hundred Malay female patients with SLE were recruited between January 2016 and October 2017 from a nephrology clinic. All patients were genotyped for HLA-A, -B, -C, -DRB1, -DQA1, -DQB1, -DPA1, and -DPB1 alleles using the polymerase chain reaction sequence-specific oligonucleotides method on the Luminex platform. A total of 951 HLA genotyped population-based Malay control subjects was used for association testing by mean of odd ratio (OR) with 95% confidence intervals (95% CI).

Results

Our findings convincingly validated common associations between HLA-A*11:01 (OR=1.54, $p<0.05$), -DRB1*15:02 (OR=1.54, $p<0.01$), and -DQB1*05:01 (OR=1.56, $p<0.05$) and SLE susceptibility in the Malay population. In contrast, HLA-DRB1*12:02 (OR=0.50, $p<0.05$), and DQB1*03:01 (OR=0.51, $p<0.001$) were associated with decreased risk of SLE in Malay population. Additionally, we also detected novel associations of susceptibility HLA genes (i.e., HLA-B*38:02, DRB1*04:05, DRB1*16:02, DPA1*02:02) and protective HLA genes (i.e., HLA-DRB1-12:02 and DPA1*01:03).

Conclusions

This study describes the HLA profiling in Malaysian Malay female patients with SLE. We convincingly replicated the well-established HLA class II genes associated with SLE risk globally. In addition, our data suggest hitherto novel susceptibility and protective HLA class I and class II gene to be observed in Malay female SLE patients of Southeast Asian origins

Keywords

Systemic Lupus Erythematosus, HLA Profile, Malay Population

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P-055

Serum and saliva S100A8 are potential biomarkers for patients with systemic lupus erythematosus

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Background

S100A8 is recognized as a special protein that can activate macrophages through binding and activation of the Toll-like receptor 4-dependent signaling cascade, and is used as a biomarker for inflammation. The clinical significance of circulating S100A8 in patients with SLE is poorly understood. Therefore, this aimed to elucidate the potential of serum or saliva S100A8 as a biomarker of SLE.

Methods

Serum and saliva samples were obtained from 100 patients with SLE from Ajou Lupus Cohort and 50 age and sex matched healthy controls (HC). The concentrations of S100A8 in serum and saliva were quantified using enzyme-linked immunosorbent assay (ELISA) and determined whether they were performed as a biomarker for diagnosing SLE. The correlation between disease activity and S100A8 in serum and saliva levels of patients with SLE with various activity was analyzed using systemic lupus erythematosus disease activity index (SLEDAI).

Results

We measured S100A8 protein expression in the serum and saliva of 100 patients with SLE and 50 HCs. Patients with SLE showed a 2.4-fold increase in serum S100A8 levels compared to HCs (SLE vs. HCs = 1,709 pg/ml vs. 709 pg/ml, $p < 0.001$). In saliva, the average levels of S100A8 were significantly higher in patients with SLE (38,971.6 pg/ml) compared to HCs (30,846.6 pg/ml, $p = 0.034$). Serum S100A8 was significantly associated with anti-double stranded DNA ($r = 0.197$, $p = 0.04$) and saliva S100A8 was significantly correlated with complement 3 ($r = -0.238$, $p = 0.044$) and SLEDAI ($r = 0.289$, $p = 0.015$).

Conclusions

The S100A8 protein was highly expressed in serum and saliva of SLE patients compared to HCs. Thus, we suggest that S100A8 protein could be a potential biomarker for SLE.

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P-056

CTLA-4 gene polymorphisms promotor-1661A/G with risk of systemic lupus erythematosus: Update metaanalysis

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Background

Polymorphisms gene CTLA4 promotor -1661A/G variants have a crucial function in controlling the negative selection and suppression of T lymphocytes. Numerous reports studied the association of CTLA4 variants with different autoimmune disorders. Some study about these gene were conduct, but the result of the study were inconsistent.

Methods

This Metaanalysis is accordance with the PRISMA guidelines. Literature search from Pubmed and EMBASE are conducted until December 2020. Literature are limited to English. 4 publications were considered to be relevant for this review and analyze with Review Manager 5.4.

Results

4 studies were included criteria. From the analyze, promotor -1661A/G correlated with increase of SLE risk (A vs G, OR 95%CI = 1.32 [1.04-1.67] p= 0.54; AA vs GG+AG, OR 95%CI = 1.60 [1.22-2.12] p= 0.36; AG vs AA+AG, OR 95%CI = 2.34[1.22-4.49] p=0.003) and decrease of SLE risk (G vs A, OR 95%CI = 0.76[0.60-0.96] p= 0.54; GG vs AA+AG, OR 95%CI =0.57[0.39-0.84] p= 0.3)

Conclusions

There were correlation CTLA4 Promotor -1661A/G gene polymorphisms with Systemic Lupus Erythematosus risk

Keywords

CTLA4,, Promotor-1661A/G, Systemic Lupus Erythematosus

E-poster Presentation

SLE-treatment

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P-057

Clinical response of tacrolimus treatment for patients with lupus nephritis

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Background

Lupus nephritis (LN) is a severe manifestation of systemic lupus erythematosus (SLE), however, current treatment for LN is still associated with severe adverse effects, treatment failures, and relapse rates. Tacrolimus (TAC), a novel calcineurin inhibitor with immunosuppressive effects, has recently become increasingly interested in its role as a potential therapeutic agent in SLE. The aim of this study was to evaluate the efficacy of TAC as a treatment for LN.

Methods

We retrospectively reviewed the medical records of patients with LN from January 1999 to September 2020. Sixty-nine biopsy proven cases of LN were enrolled, with 35 in the TAC group and 34 in the non-TAC group. The clinical response of TAC treatment in patients with LN was evaluated by proteinuria, estimated glomerular filtration rate (eGFR), anti -double-stranded DNA antibody, complement 3 (C3), complement 4 (C4), and renal SLE disease activity index (SLEDAI).

Results

We analyzed data from 69 patients who were treated with/without TAC over a 3-year period. The baseline mean proteinuria was significantly higher in the TAC group, with 4.73 $\pm$ 4.53 g in the TAC group and 2.45 $\pm$ 1.51 g in the non-TAC group ($p < 0.001$). After 3 years, there was a difference in mean proteinuria between two groups, however, there were no statistically significant differences in eGFR levels, C3/C4 and renal SLEDAI. The overall (complete and partial) renal response rate was not significantly different: 78.3 % of patients receiving TAC and 84.7 % of patients not receiving TAC ($p = 0.129$). The poor outcomes including renal flares, end stage renal disease or death were similar in both groups.

Conclusions

Our results indicate that TAC is potentially effective in treating LN, and may be a reasonable option for patients with LN. TAC can help patients with LN achieve a renal response and slow progression.

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P-058

A case of successful treatment of hemophagocytic lymphohistiocytosis with ruxolitinib in the patient with systemic lupus erythematosus

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Description

A 64-year-old woman visited our hospital with complaints of fever, myalgia and proteinuria which lasted for 6 months and was diagnosed with SLE. She received the steroid pulse therapy as an induction treatment for her lupus nephritis.

After 5 days, sudden onset of fever up to 39.0'C, stupor, splenomegaly and hypotension occurred. Laboratory examination showed the elevation of transaminase, ferritin (209324ng/mL), and fasting triglyceride (493mg/dL). She also showed oliguria and her renal function was also deteriorated. Based on these clinical features, she was diagnosed as HLH according to the established criteria on hospital day14 .(1) Level of soluble interleukin 2-receptor at that time was 4831U/mL (reference range 158~623U/mL).

After the diagnosis of HLH, she received additional steroid pulse and cyclosporine treatment. However, recurrent episodes of stupor persisted and ferritin level was continuously increased, suggesting a progression of HLH. After consultation with hematology department, we started ruxolitinib with the dose of 10mg orally twice daily on hospital day 20. After the treatment, the patient's level of consciousness, hypotension, acute kidney injury and fever improved. Dose of ruxolitinib was escalated to 15mg twice day but leukopenia and thrombocytopenia progressed on hospital day 20 (after 7 days of ruxolitinib). These adverse events improved after tapering its dose to 10mg twice day. The patient was discharged in a stable condition on hospital day 44 and serum level of soluble interleukin-2 receptor was normalized to 487U/mL. Five days after the discharge, she visited outpatient clinic with a complaint of epigastric soreness. Gastric endoscopy revealed an ulcerative lesion on distal antrum and CMV gastritis was confirmed by tissue examination. It was probably attributable to the previous immunosuppressive treatment. No other significant safety issues related to ruxolitinib occurred thereafter.

Conclusions

Ruxolitinib can be an effective and tolerable treatment option for refractory HLH in patients with SLE.

Keywords

Hemophagocytic lymphohistiocytosis, Systemic lupus erythematosus, Ruxolitinib

E-poster Presentation

Spondyloarthropathies and psoriatic arthritis

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Expanded IL-22+ group 3 innate lymphoid cells and role of oxidized LDL-C in the pathogenesis of axial spondyloarthritis with dyslipidaemia

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Background

Group 3 innate lymphoid cells (ILC3), which express interleukin (IL)-22 and IL-17A, play a critical role in axial spondyloarthritis (axSpA) pathogenesis. Dyslipidaemia should be managed in axSpA patients to reduce cardiovascular disease, and dyslipidaemia promotes inflammation. This study aimed to reveal the role of circulating ILC3 in axSpA patients and the impact of dyslipidaemia on axSpA pathogenesis.

Methods

AxSpA patients with or without dyslipidaemia were recruited. Peripheral blood samples were collected, and flow cytometry analysis of circulating ILC3 and CD4+ T cells was performed. The correlation between Ankylosing Spondylitis Disease Activity Score (ASDAS)-C-reactive protein (CRP) and circulating immune cells was evaluated. The effect of oxidised low-density lipoprotein cholesterol (oxLDL-C) on immune cell differentiation was confirmed. AxSpA human PBMC were cultured with ox-LDL-C, IL-22, or ox-LDL-C plus IL-22 to evaluate osteoclastogenesis using TRAP staining and RT-qPCR of osteoclast-related gene expression.

Results

A total of 34 axSpA patients (13 with dyslipidaemia and 21 without) were included in the analysis. Circulating IL-22+ ILC3 and Th17 were significantly elevated in axSpA patients with dyslipidaemia (P=0.001 and P=0.034, respectively), and circulating IL-22+ ILC3 significantly correlated with ASDAS-CRP (Rho=0.4198 and P=0.0367). Stimulation with oxLDL-C significantly increased IL-22+ ILC3, NKp44- ILC3, and Th17 cells. IL-22 and oxLDL-C increased TRAP+ cells and osteoclast-related gene expression.

Conclusions

This study demonstrated a potent pathological role of circulating IL-22+ ILC3 in axSpA. Furthermore, dyslipidaemia augmented IL-22+ ILC3 differentiation, and oxLDL-C and IL-22 markedly increased osteoclastogenesis of axSpA. In axSpA patients, controlling dyslipidaemia and IL-22+ ILC3 may be potential therapeutic targets.

Keywords

spondyloarthritis, group 3 innate lymphoid cells, interleukin-22

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P-060

Biologic retention rate and efficacy in patients with cluster-based phenotypes of ankylosing spondylitis: data from a Korean biologics registry

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Background

Patients with ankylosing spondylitis (AS) have a heterogenic disease course and treatment response. Cluster-based phenotypes are useful for predicting disease course. Here, we compared drug retention time and clinical efficacy of biologic disease-modifying antirheumatic drugs in AS patients with cluster A and cluster B phenotypes.

Methods

AS patients enrolled in the Korean College of Rheumatology BIOlogics registry (KOBIO) were divided into cluster A (axial symptoms only) and cluster B (both axial and peripheral symptoms). Retention of bDMARDs was measured using Kaplan-Meier curve and Cox regression analyses. Clinical efficacy (BASDAI50, ASAS20, ASAS40, ASDAS low disease activity, and clinically important improvement/major improvement of ASDAS) at 1-year follow-up was measured by logistic regression analyses. Also, propensity score (PS)-matched analyses were conducted.

Results

1600 AS patients (1468 for cluster A, 132 for cluster B) were included. Kaplan-Meier analyses revealed that the drug retention time was lower in cluster B patients (P = 0.03). PS-matched and multivariate Cox regression analyses showed that hazard ratio (HR) for drug discontinuation was significantly higher in cluster B patients (HR = 1.568; HR = 1.333, respectively). The odds ratio for assessing BASDAI50 at 1-year was comparable between cluster A and cluster B patients in PS-matched and multivariate regression analyses. A similar result was obtained in other clinical efficacy assessments.

Conclusions

The drug retention rate was lower in cluster B than in cluster A patients; clinical efficacy was comparable between the two groups at 1-year follow-up. These results may help predict drug retention and clinical efficacy in AS patients.

Keywords

ankylosing spondylitis, cluster-based phenotype, biologic disease-modifying antirheumatic drug

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Retention rate and effectiveness of secukinumab vs TNF inhibitor in ankylosing spondylitis patients with prior TNF inhibitor exposure

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Background

The choice of second-line biologics for ankylosing spondylitis (AS) patients previously treated with a tumour necrosis factor inhibitor (TNFi) remains unclear. Here, we compared drug retention and clinical efficacy between AS patients who switched biologics to secukinumab and those who switched to a different TNFi.

Methods

AS patients enrolled in the Korean College of Rheumatology BIOlogics registry were included, and patients with non-radiographic axial spondyloarthritis were excluded. Patients with previous TNFi exposure were divided into the secukinumab group and the TNFi switching group. Drug retention and clinical efficacy (BASDAI50, ASAS20, ASAS40, ASDAS <2.1, ASDAS clinically important improvement, and ASDAS major improvement) were assessed at the 1 year follow-up. Propensity score (PS)-matched and covariate-adjusted logistic regression analyses were performed.

Results

246 had available 1 year follow-up data. Secukinumab as third- or later-line biologics was more frequent than alternative TNFi (54% vs. 14%). PS-matched and multiple covariate-adjusted analyses showed that the odds ratio (OR) for drug discontinuation was comparable between the secukinumab and TNFi switching groups (OR=1.136; 95% CI, 0.843–1.531 and OR=1.000; 95% CI, 0.433–2.308, respectively). The proportion of patients who achieved BASDAI50 was also comparable between the two groups (OR=0.833; 95% CI, 0.481–1.441 in PS-matched analysis). Other clinical efficacy parameters were also comparable. In the subgroup analysis of AS patients with previous TNFi discontinuation due to ineffectiveness, all clinical efficacy parameters were comparable between the two groups.

Conclusions

In AS patients with previous exposure to a TNFi, switching biologics to secukinumab and switching to an alternative TNFi resulted in comparable drug retention and clinical efficacy.

Keywords

ankylosing spondylitis, tumour necrosis factor inhibitor, secukinumab

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P-062

Clinical efficacy of alternative TNF inhibitor and secukinumab between primary non-responder and secondary non-responder of prior TNF inhibitor in ankylosing spondylitis

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Background

To compare the drug retention times and clinical efficacy of alternative tumor necrosis factor inhibitors (TNFi) and secukinumab in primary and secondary non-responders with ankylosing spondylitis (AS).

Methods

AS patients treated with biologics and enrolled in the Korean College of Rheumatology BIOlogics registry were examined. Patients who did not respond to previous TNFi treatment were defined as primary and secondary non-responders. Data regarding drug discontinuation and clinical efficacy (BASDAI50, ASDAS < 2.1, clinical important/major improvement in ASDAS, and ASAS20/40) were collected after 1 year. Kaplan-Meier and cox regression analyses were performed to compare drug survival and associated factors. Logistic regression analyses were conducted to compare the clinical efficacy secukinumab with that of alternative TNFi.

Results

In total, 124 patients (83 receiving alternative TNFi and 41 receiving secukinumab) had biologic changed due to clinical inefficacy. Drug retention rates in the alternative TNFi and secukinumab groups were similar ($p = 0.096$). Subgroup analyses of non-responders to previous anti-TNF monoclonal antibodies or a TNF receptor fusion protein (etanercept) revealed no difference between the alternative TNFi and secukinumab groups. However, subgroup analyses including only secondary non-responders revealed that secukinumab users showed a higher hazard ratio (HR) for drug discontinuation ($HR = 3.91$, $P = 0.041$). In addition, secukinumab was negatively associated with achieving BASDAI50 or a major improvement in the ASDAS.

Conclusions

Alternative TNFi showed better drug retention and clinical efficacy in AS patients experiencing previous TNFi failure, in secondary non-responder. Therefore, alterative TNFi may be a more suitable treatment for secondary non-responders.

Keywords

ankylosing spondylitis, tumor necrosis factor inhibitor, non-responder

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Effectiveness and drug retention of biologic disease-modifying antirheumatic drugs in Korean patients with late-onset ankylosing spondylitis

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Background

The clinical data on the biologic disease-modifying antirheumatic drug (bDMARD) use in late-onset ankylosing spondylitis (LOAS) is limited. Thus, this study aimed to evaluate the drug efficacy and retention rate of bDMARDs in LOAS and compare it to young-onset ankylosing spondylitis (YOAS).

Methods

Data of patients with AS receiving bDMARDs were extracted from the Korean College of Rheumatology Biologics and Targeted Therapy registry. Patients whose age of onset was ≥ 50 years and < 50 years were classified as having LOAS and YOAS, respectively. Their baseline characteristics and disease-associated parameters were evaluated. Drug efficacy (ASDAS-clinically important improvement [CII], ASDAS-major improvement [MI], ASAS 20, and ASAS 40) at 1-year follow-up and drug retention rates were assessed.

Results

A total of 1708 patients (comprising 1472 patients with YOAS and 236 patients with LOAS) were included. The LOAS group had a lower prevalence among males, lower HLA-B27 positivity and a higher prevalence of peripheral arthritis. Patients with LOAS were more likely to have higher disease-associated parameters (inflammatory reactants, patient global assessment, ASDAS-ESR, and ASDAS-CRP). LOAS was negatively associated with achieving ASDAS-CII, ASAS 20, and ASAS 40. The drug retention rate was lower in LOAS; however, the propensity score-matched and covariate-adjusted hazard ratios for bDMARD discontinuation were comparable to YOAS. There were no differences in the drug retention rates based on the type of bDMARD used in LOAS.

Conclusions

Inferior clinical efficacy and drug retention rates were found in patients with LOAS receiving bDMARDs using real-world nationwide data.

Keywords

ankylosing spondylitis, biologics, drug efficacy

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P-064

Development of machine learning model to predict radiographic progression in patients with ankylosing spondylitis

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Background

The purpose of this study is to develop machine learning model for predicting radiographic progression in patients with ankylosing spondylitis (AS) using electric medical records (EMR).

Methods

Of the 1,123 patients with AS who were followed-up for 18 years in a single center, EMR data such as baseline characteristics, laboratory finding, drug administration, and modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) were obtained at the time point (T) of 4 consecutive follow-ups (T1, T2, T3, and T4). The radiographic progression (Pn+1 = Tn+1mSASSS - TnmSASSS) / (Tn+1-Tn) $\geq$ 1) was predicted using follow up data from T1 to Tn (Figure 1). Machine learning methods (e.g., logistic regression with a least absolute shrinkage and selection operation (LASSO), random forest, and Extreme Gradient Boosting (XGBoost) algorithms) with 3-folds cross validation were used.

Results

Results: Among machine learning models with follow-up data, predicting the radiographic progression of P2 using random forest model with the EMR data of first follow-up (T1) was the most accurate. The mean sensitivity, specificity, accuracy, AUROC of 3-folds cross validation were 73.72%, 73.73%, 73.73%, and 0.79, respectively (Figure 2A). Among the variables of T1, it was the most important variable for prediction of radiographic progression in the order of total mSASSS, age, and alkaline phosphatase (Figure 2B). However, when 2 or more follow-up EMR data (T1+T2 and T1+T2+T3) were used for prediction of radiographic progression (P3 and P4), their models showed poor performance than the model using first follow-up EMR data (predicting P2 using T1 data).

Conclusions

We developed a machine learning model that predicts radiographic progression using EMR data. This model may need more data such as image or life-log for better performance.

Keywords

Ankylosiing spondylitis, Machine learning, radiographic progression

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P-065

Body mass composition, adipokines, disease factors and their relationship in determining atherosclerotic cardiovascular risk in spondyloarthritis

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Background

Assess prevalence of high risk cardiovascular status in spondyloarthritis (SpA) by using carotid intima medial thickness and QRISK3. To identify the factors associated with subclinical atherosclerosis in SpA.

Methods

This was a cross-sectional study involving age and BMI matched adults with Psoriatic arthritis (PsA) (n=56) and non-psoriatic Spondyloarthritis (SA) (n=58). Body composition using whole body Dual Energy X-ray Absorptiometry, anthropometric measurements, adipokines, and disease characteristics along with cardiovascular risk scoring using QRISK3 and USG based carotid intimal medial thickness (CIMT) were collected. Individuals with a QRISK3 ≥10% or CIMT of ≥75 percentile of general population were categorised as high risk cardiovascular (HRCVS). Predictors of HRCVS were determined by logistic regression.

Results

Characteristics of the patients enrolled are (PsA and SA) in table 1. There were more females in the PsA [28(50%) vs 14(24.1%)]. PsA males had higher quantities of total fat and visceral fat (229.97 ± 81.55) as compared to SA-males (199.15 ± 81.94;p=0.047). PsA had higher CIMT [0.58 (0.52,0.67) vs 0.52 (0.48,0.58);p<0.001] opposed to SA, but QRISK3 scores were comparable. PsA had elevated levels of leptin, adiponectin and MCP-1(p<0.001). Thirty nine(34.2%) patients had high risk cardiovascular profile. The differences between those with and without HRCVS are in table 2. Higher age, PsA subtype and higher visceral and trunk adipose tissue were associated with HRCVS. The variables that were univariately associated with HRCVS and those with (P < 0.15) were used to construct predictive models. Upon multiple logistic regression sarcopenia [appendicular lean mass(ALM)/height 2](p=0.006) was significant in the resulting model despite having low hsCRP(p=0.038).

Conclusions

Subclinical atherosclerosis is seen in ~35% of patients with SpA and is more in Psoriatic arthritis. Sarcopenia is an often neglected but important determinant of HRCVS. Focused physical therapy to avoid muscle loss may help in preventing atherosclerosis.

Keywords

Spondyloarthritis, Sarcopenia, Visceral adiposity

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P-066

Signal detection of adverse drug reactions of biologic DMARDs used in ankylosing spondylitis patients on real-world data in South Korea

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Background

Biologic disease-modifying antirheumatic drugs(bDMARDs) are a relatively newer category of treatment in the rheumatologic field and their use is steadily growing. We aimed to detect signals of adverse drug reactions(ADRs) of these agents from real-world data; single center's electronic medical record(EMR)-driven common data model(CDM) data and Korean College of Rheumatology Biologics & Targeted Therapy Registry, KOBIO registry data.

Methods

Data were extracted from January 2012 to December 2019 for CDM, and from November 2012 to June 2020 for the KOBIO registry. Cases with one of the target bDMARDs including etanercept, infliximab, adalimumab, golimumab, certolizumab pegol, secukinumab, and ustekinumab for ankylosing spondylitis(AS) were enrolled. We applied CDM-based MetaLAB algorithm for detecting ADR signals, where the algorithm used laboratory test results as supplementary information on ADRs with statistical approaches. And we performed disproportionality analysis (e.g., proportional reporting ratio, reporting odds ratio) to KOBIO registry data.

Results

Using the MetaLAB algorithm, we extracted 656 patients and 28 significant drug-ADR pairs(ROR >1.0 and p< 0.05). Significant ADRs were 'Blood alkaline phosphatase increased', 'Hyperkalaemia', 'Thrombocytopenia' for adalimumab; 'Alanine aminotransferase increased', 'Hypoalbuminaemia', 'Hypoproteinaemia', 'Thrombocytosis' for etanercept; 'Acidosis', 'Alkalosis' for infliximab. For the KOBIO registry, 1940 patients were initially registered, then 5199 follow-ups were included and considered as independent cases. Detected signals with disproportionality analysis with ROR or PRR >2 and p< 0.05 by PhViD package in R(4.0.5) and not reported in the FDA labels were 'LDL decreased', 'Benign prostatic hyperplasia, and so forth, for adalimumab. Other drugs are listed in more detail in Table 1.

Conclusions

Detection of ADR signals for biologic DMARDs prescribed for AS patients from real-world data were performed. Further cross-validation of results with other databases such as adverse event reporting system(AERS) data and continuous pharmacovigilance is needed.

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Correlation of whole spinal inflammatory activity on MRI with radiographic progression and systemic inflammatory burden in axial spondyloarthritis

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Background

Investigate the predictive value of axial spondyloarthritis (axSpA)-relevant lesions on whole spine magnetic resonance imaging (MRI) for radiographic progression and systemic inflammation of axSpA.

Methods

We reviewed the medical records of 452 axSpA patients who were serially monitored in a single center. Whole spine MRI at the time of diagnosis were available in 70 axSpA patients. The Spondyloarthritis Research Consortium of Canada (SPARCC) spine score and count of discovertebral units (DVUs) affected by ASAS/OMERACT group defining lesions were measured. Radiographic progression of the spine was defined as the increase of 2 or more in the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) over 2 or 3 years. Cumulative values of ESR and CRP were calculated using the trapezoidal rule. Logistic regression and linear regression analyses were performed for the determination of radiographic progression and cumulative ESR/CRP, respectively.

Results

Radiographic progression developed in 19 of 70 axSpA patients (27%) at the second year and 22 of 52 patients (42%) at the third year. At baseline, mSASSS correlated positively with the number of inflammatory lesions in facet joints, costovertebral (CV) / costotransverse (CT) joints, and whole spine on MRI (r=0.245, 0.439, and 0.530). In multivariate analysis, counts of inflammatory lesions on MRI and baseline mSASSS were independent predictors for radiographic progression at 2 and 3 years. Receiver operating characteristic (ROC) curve analysis showed that 6 or more inflammatory lesions on MRI (AUC 0.829, 95%CI: 0.72-0.937) predicted radiographic progression at the second year. Moreover, 3-year cumulative values of ESR and/or CRP increased in proportion to the number of inflammatory lesions in facet joints, CV/CT joints, and whole spine on baseline MRI.

Conclusions

Our data suggest that whole spinal inflammatory activity on MRI at presentation predicted radiographic progression and systemic inflammatory burden. We also presented the clinical significance of inflammation on facet and CV/CT joints.

Keywords

Spondyloarthritis, Spondylitis, Ankylosing

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P-068

ERAP1/ERAP2 and IL23R gene variations and the risk of developing ankylosing spondylitis in multi-ethnic Malaysian population with different HLA-B*27 allele subtypes

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Background

The HLA-B*27 alleles confer the greatest risk to ankylosing spondylitis (AS) susceptibility across different populations worldwide. Several other non-major histocompatibility complex genes were associated with risk for AS, but the findings were inconsistent between Caucasians and Asians. We investigated the associations of endoplasmic reticulum-related aminopeptidase (ERAP1/ERAP2) and Interleukin-23 receptor (IL23R) genes in AS patients with different HLA-B*27 allele subtypes from the multi-ethnic Malaysian population.

Methods

A total of 302 clinically-diagnosed AS patients (75 Malays, 172 Chinese, 24 Indians, and 31 mixed-ethnicities) were enrolled between 2014 and 2016. One hundred and ninety healthy subjects were included for association testing with odds ratio (OR) and 95% confidence interval (CI). The HLA-B*27 subtype alleles were genotyped using the PCR-SSO method on Luminex platform. The ERAP1_rs30333A/G, ERAP2_rs2247650G/T, IL23R_rs11209032A/G, IL23R_rs56928441A/G and IL23R_rs10889676A/C SNP variants were genotyped using TaqMan Allelic Discrimination SNP genotyping assay for all participants.

Results

Our data demonstrated preponderance of male AS patients (83%, n=250). The risk for AS was strongly associated with HLA-B*27 alleles (AS versus controls, 81.1% versus 2.6%; OR=159.0, 95% CI= 65.5-404.6, $\chi 2$=287.37, p<0.0001) irrespective of ethnic groups. Stratification by HLA-B*27 allele subtypes showed that 66.9% AS patients were HLA-B*27:04 positive followed by HLA-B*27:05 positive (10.9%). The single-point analyses of SNPs variants revealed that genotypes for ERAP1_rs30333_AG (OR=1.78, p=0.03), ERAP2_rs2247650_GT (OR=1.53, p=0.04) and IL23R_rs56928441_GG (OR=2.89, p=0.02) were associated with increased risk in AS patients with HLA-B*27:04, but not with HLA-B*27:05. The IL23R_rs10889676_CC genotype were significantly associated with the AS risk in patients with positive HLA-B*27:04 (OR=3.73, p=0.001) and HLA-B*27:05 (OR=3.97, p=0.03). No association was observed between IL23R_rs11209032 variants and AS risk in the Malaysian population.

Conclusions

The risk of developing AS is associated with ERAP1_rs30333, ERAP2_rs2247650, IL23R_rs56928441 in particular with the HLA-B*27:04 subtype, which is common in Asian populations, but not in Caucasians.

Keywords

ankylosing spondylitis, HLA-B*27 subtypes, ERAP1/ERAP2/IL23R

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P-069

Clinical features and drug survival of tumor necrosis factor inhibitor in elderly patients with ankylosing spondylitis: Results from the nationwide KOrean college of rheumatology BIOlogics (KOBIO) registry

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Background

Tumor necrosis factor inhibitor (TNFi) therapy was well recognized for efficacy and safety profiles as chronic autoimmune diseases, such as rheumatoid arthritis, ankylosing spondylitis (AS), and psoriatic arthritis. But, the limited data have been studied about the use of TNFi in elderly patients, especially for ankylosing spondylitis. We evaluate the clinical features, outcomes, and drug retention rate of TNFi compared with elderly and younger groups in patients with AS.

Methods

Data was extracted from a nationwide rheumatologic database, the Korean College of Rheumatology Biologics registry, which had been registered from 2012-2019. Clinical variables and outcomes were compared and drug retention rate was evaluated using Kaplan-Meier analysis.

Results

Three hundred six patients were same or older than 50 years old, and 1218 patients were not among AS patients. The comorbidities, hypertension (38.6 vs 9.0%) and diabetes (10.5 vs 2.5%) were more frequent in older patients compared in those not (all $p < 0.001$). Peripheral arthritis was more frequent (35.6 vs 27.1%, $p = 0.004$), ASDAS-ESR were higher (4.0 ± 1.1 vs 3.6 ± 1.0, $p < 0.001$), and BASFI was higher (4.2 ± 2.6 vs 3.3 ± 2.5, $p < 0.001$), while BASDAI was not different ($p = 0.83$) in older patients than those not. The proportion of NSAID use was smaller (79.4 vs 86.0%, $p = 0.005$), and the proportion of DMARD use was higher (16.0 vs 8.0%, $p < 0.001$) in older patients than those not. The drug retention rate were not different between older patients and those not (log rank $p = 0.064$).

Conclusions

The characteristic of AS patients with TNF inhibitor use were different in comorbidities, sex, the presence of peripheral arthritis, inflammatory marker levels between older patients and those not. But, the drug retention rate were not different after adjusting for disease activity.

Keywords

Ankylosing spondylitis, elderly, Tumor necrosis factor inhibitor

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P-070

Achievement of low disease activity according to BASDAI with Ixekizumab in patients with axial spondyloarthritis: 16-week results from the COAST trials

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Background

The efficacy of ixekizumab (IXE), a selective interleukin-17A antagonist, was assessed in patients (pts) with axial SpA (axSpA) in three Phase 3, randomized, double-blind, placebo (PBO)-controlled trials, COAST-V, COAST-W and COAST-X. The BASDAI is the 'gold standard' for measuring disease activity in axSpA clinical trials and BASDAI≥4 is one of the criteria used to define active disease. Clinically meaningful improvement is defined as a 50% reduction in BASDAI (BASDAI50) or change from baseline of at least 2 units. We present 16-week outcomes for BASDAI<4, BASDAI50, BASDAI change of ≥2 points and quality of life (QoL) in pts achieving BASDAI<4 from the COAST trials.

Methods

COAST-V (NCT02696785) and COAST-W (NCT02696798) assessed pts with radiographic axSpA (radiographic sacroiliitis centrally defined by modified New York criteria), and COAST-X (NCT02757352) assessed pts with nonradiographic axSpA. All pts fulfilled Assessment of Spondyloarthritis International Society (ASAS) classification criteria for axSpA. Pts were either biologic-naive (COAST-V, COAST-X) or TNFα inhibitor-experienced (COAST-W) and were randomized to IXE (80 or 160 mg at week 0 then 80 mg every 2 or 4 weeks [Q2W, Q4W]) or PBO or adalimumab (ADA, 40 mg Q2W; COAST-V only). QoL was assessed by the Short Form (SF)-36 Physical Component Summary (PCS). Missing data were imputed using non-responder imputation and efficacy outcomes were analyzed by logistic regression.

Results

In total, 341 pts from COAST-V, 316 from COAST-W, and 303 from COAST-X were included in this analysis. At week 16, a greater proportion of pts treated with IXE achieved BASDAI<4, BASDAI50, and change from baseline of ≥2 points (Figure) compared to PBO across all three trials. In addition, a greater proportion of IXE-treated patients achieved the BASDAI endpoints compared with ADA in COAST-V (Figure).

Conclusions

In the COAST trials, IXE produced clinically meaningful improvements in pts with axSpA after 16 weeks of treatment.

Keywords

Ixekizumab, Axial spondyloarthritis, COAST trials

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P-071

Evaluation of spinal radiographic progression in patients with radiographic axial spondyloarthritis receiving Ixekizumab therapy over 2 Years

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Background

We examined radiographic progression in the spine among patients with active radiographic axial spondyloarthritis (r-axSpA) treated with ixekizumab (IXE) for 2years, and potential predictors of spinal radiographic progression.

Methods

Active r-axSpA, biologic-naive (COAST-V, NCT02696785), or TNF inhibitors (TNFi)-experienced (COAST-W, NCT02696798) patients received 80mg IXE every 2 or 4weeks for 2years (of which 56weeks were the COAST-Y extension study, NCT03129100). Mean change from baseline of modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) for patients treated with IXE for 2years with data at both baseline and Year2 is presented (N=230; 54% of total randomized patients). Non progression is presented for all patients and subgroups based on TNFi-experience. Predictors were identified in multivariate logistic regression models with stepwise selection criteria of p-value <0.1.

Results

At baseline, patients (N=230) were predominately male (82%) with an average age of 43years, mean symptom duration of 16years, 52% were TNFi-experienced, mean (SD) ASDAS score was 4.0 (0.7), most were HLA-B27 positive (87%) and 40% had syndesmophytes. Baseline mSASSS (SD) was 11.0 (16.3) and change from baseline at Year2 of treatment was 0.3 (1.8) (Table). Proportion of non-progressors (mSASSS change from baseline <2) over 2years was 89.6% (total IXE [all patients]), 90.9% (biologic-naive) and 88.3% (TNFi-experienced), and, if defined as mSASSS change from baseline ≤0, 75.7% (total IXE [all patients]), 78.2% (biologic naive) and 73.3% (TNFi-experienced) (Table). Predictors of structural progression at Year2 (mSASSS change >0) were age, baseline syndesmophytes, HLA-B27 status, and gender (Table). Week52 inflammation in MRI SPARCC spine was a predictor for structural progression at Year2 for patients where MRI measures were available at baseline and Week52 (N=109).

Conclusions

The majority of patients treated with IXE for 2years did not show radiographic progression, and the overall mean progression was low. Similar levels of non-progression were observed in biologic-naive patients and patients previously exposed to TNFis.

Keywords

Ixekizumab, Axial spondyloarthritis, Spine

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P-072

Efficacy and safety of Ixekizumab versus adalimumab (SPIRIT-H2H) with and without concomitant conventional synthetic disease-modifying antirheumatic drugs (DMARD) in biologic DMARD-naïve patients with psoriatic arthritis: 52-week results

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Background

Ixekizumab (IXE) was superior to adalimumab (ADA) at Week (Wk)24 for simultaneous achievement of ACR50 and PASI100 in patients with active PsA from SPIRIT-H2H. To determine how concomitant csDMARD use affects safety and efficacy of IXE and ADA in prespecified subgroups (biologic monotherapy, concomitant csDMARD).

Methods

SPIRIT-H2H (NCT03151551) was a 52-week, multicentre, randomised, open-label, assessor-blinded, parallel-group study evaluating efficacy and safety of IXE vs. ADA in adults with PsA naïve to biologic DMARDs, predominantly MTX. Efficacy outcomes (by presence/ absence of csDMARDs) through Wk52 were compared between IXE and ADA using logistic regression models and Fisher's exact tests. Nine patients with active PsO and BSA≥3% were assessed as PASI=0 at baseline, a medical inconsistency that was resolved using medical judgement. These patients were considered PASI100 responders if PASI=0 and BSA=0 at post baseline visits.

Results

At baseline, 193/283 IXE-treated patients and 199/283 ADA-treated patients had concomitant csDMARD use. A significantly greater proportion of patients on IXE vs. ADA achieved the primary endpoint of simultaneous ACR50 and PASI100 when used as monotherapy (38% vs. 19%, $p<0.01$) or with csDMARD (40% vs. 29%, $p\leq0.05$) at Wk52, respectively. Significantly more patients achieved PASI100 with IXE vs. ADA when used a monotherapy (66% vs. 35%, $p \leq0.001$) or with csDMARD (64% vs. 44%, $p<0.01$) at Wk52. No difference was seen in ACR50 response at Wk52 between IXE and ADA subgroups. A significantly higher proportion of patients achieved MDA on IXE vs. ADA in the monotherapy subgroup (49% vs. 33%, $p\leq0.05$), while response rates were similar in the combination subgroups (47% vs. 44%). Adverse event frequencies were similar across subgroups for IXE and ADA, with infections and nasopharyngitis most common.

Conclusions

Consistent efficacy across multiple PsA domains was observed with IXE regardless of whether IXE was taken with/without csDMARD or MTX therapy.

Keywords

Ixekizumab, csDMARD, SPIRIT-H2H

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P-073

Challenges of referral, diagnosis and management of axial spondyloarthritis

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Background

There are many challenges in the referral, diagnosis, and management of patients with suspected (AxSpA) worldwide. Gulf-REDMAS comprises a group of expert rheumatologists from the Gulf countries who convened to create and disseminate a survey to understand the aforementioned challenges with the main aim to fill the evidence gap.

Methods

An anonymous online survey consisting of 35 multiple choice closed questions that lasted for 1 month was circulated among practicing rheumatologists in the Gulf countries (calculated sample size was 101).

Results

132 rheumatologists completed the survey from 371 rheumatologists in the region.

The majority of responders (88%) noted that they faced delays in the referral of AxSpA patients to their clinic, with the main reason being a 'lack of disease awareness by primary care physicians' (56%) (Table).

The survey respondents surmised that the leading reasons for non-rheumatology specialists' reluctance to refer patients with suspected AxSpA included 'lack of awareness of long-term complications of spondyloarthritis' (34%), and 'some non-rheumatology specialists think they can treat and diagnose AxSpA without the need to refer to a rheumatologist' (28%).

Two-thirds of survey respondents (66%) highlighted that the greatest challenge being 'patients who present with atypical symptoms e.g., with <3 months back pain, chronic back pain occurring >45 years of age, or chronic back pain with ≥1 spondyloarthritis features but without sacroiliitis on imaging' (51% of responders who highlighted they faced a challenge).

The main patient-related challenges to management of axial spondyloarthritis were: 'patients cannot access the medication as it is unavailable in my hospital/clinic pharmacy' (31%, first reason) and 'patients may have fears of drug side effects (39.6%, second reason).

Conclusions

Responses to this survey highlighted several challenges in the referral, diagnosis, and management of AxSpA patients. Future recommendations that should be implemented to address these challenges.

Keywords

Spondyloarthritis, survey, challenges

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P-074

Spinal mobility impairment among patients with axial spondyloarthritis stratified by HLA-B*27 status

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Background

Axial spondyloarthritis is a chronic spinal inflammatory disorder which leads to progressive fusion and deformity. The Bath Ankylosing Spondylitis Metrology Index (BASMI) is a combined tool for assessing spinal mobility and hip function. We aimed to assess the severity of axial status impairment among axial spondyloarthritis patients as stratified by HLA-B*27 positivity.

Methods

Three hundred and forty-five axial spondyloarthritis patients (i.e., radiographic axial spondyloarthritis = 302, non-radiographic axial spondyloarthritis = 43) were recruited from Malaysian government hospitals between 2014 and 2017. Five BASMI measurements i.e., lateral lumbar flexion, tragus-to-wall distance, lumbar flexion (modified Schober's), maximal intermalleolar distance and cervical rotation were performed by the rheumatologists and trained researchers following a designated protocol. BASMI measurement data was available for 98% of the recruited subjects. The classification of BASMI data into three groups, i.e., mild, moderate, severe was based on the guidelines set by The BATH indices. We analysed each BASMI measurement by HLA-B*27 status.

Results

The proportion of HLA-B*27 positivity among the axial spondyloarthritis patients was 76.2% (n=263). Our data demonstrated that more than one third of patients have reported mild impairment of spinal mobility measurements except for cervical rotation (3.8%). Interestingly, cervical rotation was the commonest measurement to be moderately impaired compared to other spinal mobility measurements (n=232) which was significantly dominated by patients with HLA-B*27 positive ($p<0.0001$). Our data revealed lumbar flexion (modified Schober's) to be the most common severely impaired measurement (n=122, 35.4%) of which 86% was HLA-B*27 positive compared to HLA-B*27 negative (14%) ($p<0.0001$). Notably, lateral lumbar flexion, tragus-to-wall distance and maximal intermalleolar distance measurements were observed to be mildly impaired BASMI component among axial spondyloarthritis patients in Malaysia.

Conclusions

Axial spondyloarthritis patients with HLA-B*27 positive experience more severe impairment than HLA-B*27 negative patients across the different BASMI spinal mobility measurements.

Keywords

axial SpA, BASMI, HLA-B*27

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Comparison of comorbidity profiles between HLA-B*27 positive and HLA-B*27 negative patients with axial spondyloarthritis

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Background

Axial spondyloarthritis (axSpA) is a chronic inflammatory disease of the spine and sacroiliac joints which can cause severe disability. Patients with axSpA suffer from multiple comorbidities (CM) which may be linked to the presence or absence of HLA-B*27 gene. We investigated the profile of different CM subgroups observed in axSpA patients, stratified by HLA-B*27 status.

Methods

Three hundred and forty-five axSpA patients (i.e. radiographic axSpA = 302, non-radiographic axSpA = 43) were recruited from Malaysian government hospitals between 2014 and 2017. All subjects were genotyped for HLA-B alleles using the PCR-SSO method. We retrieved the CM data from medical records and classified them into four subgroups with presence of one-comorbidity (SCM), two-comorbidities (DCM), three-comorbidities (TCM) and four-comorbidities (FCM). We analysed the profile of CM present in each subgroup by HLA-B*27 status.

Results

More than two-thirds of axSpA patients were HLA-B*27 positive (76.2%). We analysed the captured CM data from 235 individuals, of these, 107 reported at least one CM (45.5%). Hypertension (42.4%), diabetes mellitus (33.3%) and dyslipidaemia (43.1%) were the most common CM in the DCM subgroup. Cardiovascular diseases (54.5%) were highest among patients in the FCM subgroup. Interestingly, osteoporosis was most frequently observed in the SCM subgroup (75%). Our data showed that more than two-thirds of axSpA patients with hypertension (63.1%), dyslipidaemia (69%), osteoporosis (83.3%) and cardiovascular diseases (63.6%) were HLA-B*27 positive. Of all five common CM, diabetes mellitus is the least frequent CM in HLA-B*27 positive patients (52.8%). Notably, that among HLA-B*27 negative patients, the occurrence of hypertension, diabetes mellitus and dyslipidaemia were evident with the increasing number of CM.

Conclusions

Our data suggest varied CM profiles defined by the reported number of CM in axSpA patients. Higher occurrence of CM was observed among axSpA patients with HLA-B*27 positive, compared to those with HLA-B*27 negative.

Keywords

axial SpA, comorbidities, HLA-B*27

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P-076

Incidence and risk of overall infections in patients with ankylosing spondylitis receiving biologic therapies: A real-world prospective observational study using KOBIO registry

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Background

The aim of this study was to characterize infection events in patients with ankylosing spondylitis (AS) and to identify the risk factors associated with the development of infections in a real-world setting.

Methods

This was a prospective observational cohort study including AS patients in the KOBIO registry. Infections were evaluated by types or organ during the follow-up period. Infection incidence rates (IR) per 1,000 person-years (PY) were calculated with 95% CI based on Poisson distribution method. Cox proportional hazard regression models with adjustment of confounding factors was used to estimate hazard ratios (HRs) with 95% CIs for occurrence of infection.

Results

A total of 1610 AS patients were included in the analysis. Most (76.8%) were men and the median age was 37 years with 5.73 median AS duration. 129 infection events occurred during 5020.5 PY. The most frequent infections were upper and lower respiratory tract, followed by herpes zoster. The overall incidence of any infection was 25.7/1000 PY of follow-up (95% CI, 21.5 - 30.5) : 29.5/1000 PY among those treated with infliximab and biosimilar ; 26.8/1000 PY among those treated with adalimumab ; 21.5/1000 PY among those treated with golimumab ; 17.8/1000 PY among those treated with etanercept and biosimilar. ; 81.1/1000 PY) among those treated with secukinumab. Significant univariate risk factors for infection were age, ischemic heart disease, complicated diabetes, solid tumor, abnormal chest x-ray, anemia, and biologics user. In multivariate Cox regression model, ischemic heart disease, complicated diabetes, abnormal chest x-ray and current biologics users remained significant.

Conclusions

The total incidence rate of infections was 26 events/1000 PY and respiratory infection was the most frequent in the KOBIO-AS registry. Ischemic heart disease, complicated diabetes, abnormal chest x-ray and current biologics user were risk factors for any infection in this large cohort of patients with AS.

Keywords

Ankylosing spondylitis, Infection, real-world data

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P-077

Elevated WNT16 expression induced cell senescence of osteoblasts in ankylosing spondylitis

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Background

WNT16 has been reported to be critical for bone homeostasis, but effect of WNT16 in Ankylosing spondylitis (AS) is still unknown. Here, we investigated whether WNT16 influences bone formation and pathophysiological changes of AS in vitro model.

Methods

Bone tissues of facet joints were obtained from 5 disease control (Control) and 6 AS patients. Primary osteoprogenitor cells of the facet joints were isolated using outgrowth method. Isolated osteoprogenitor cells of both Control and AS were analyzed by microarray, RT-qPCR, immunoblotting, and immunohistochemistry. Bone-forming activity of osteoprogenitor cells was assessed by various in vitro assay. β-galactosidase staining and senescence-associated secretory phenotype (SASP) using RT-qPCR were used for measuring cell senescence.

Results

In microarray analysis, WNT16 expression was significantly elevated in AS-osteoprogenitor cells compared to control. We also confmd that WNT16 expression was elevated in AS-osteoprogenitor and human AS-bone tissues. WNT16 treatment inhibited bone formation in AS-osteoprogenitor cells but not in control. Intriguingly, β-galactosidase playing a role in cell senescence showed strong signal in AS-osteoprogenitor cells treated with WNT16. Furthermore, in H2O2 stress-induced premature senescence condition, WNT16 treatment increased senescence in AS-osteoprogenitor cells compared to vehicle. This WNT16 treatment under H2O2 stress condition showed an increase of p21 protein and senescence-associated secretory phenotype (SASP) mRNA expression in AS-osteoprogenitor cells. The WNT16-induced SASP expression in AS-osteoprogenitor cells were reduced by knockdown of WNT16.

Conclusions

We here exhibited that WNT16 was highly expressed in AS and WNT16 treatment facilitated cell senescence in AS-osteoprogenitor cells during osteoblasts differentiation accompanied by suppression of bone formation. The identified role of WNT16 could reflect the bone loss in AS patients.

Keywords

ankylosing spondylitis, WNT16, bone loss

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Clinical and genetic factors associated with severe radiographic damage in ankylosing spondylitis

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Background

Ankylosing spondylitis (AS) is a heritable inflammatory disease eventually leading to spinal fusion. Severity of structural damage is highly variable, some patients develop no change in spinal structure for long disease duration, whereas others have total ankylosis even in the early stage of disease. This study was aimed to identify clinical and genetic factors associated with severe radiographic damage in patients with AS.

Methods

We newly generated genome-wide variant data (833K, KoreanChip) of 444 AS patients. Clinical data were collected and the severity of radiographic damage was assessed using the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). To identify clinical and genetic factors associated with severe radiographic damage, multiple linear regression analyses were performed. Human AS osteoprogenitor cells were used for functional validation. Pathway analysis was also conducted.

Results

The median mSASSS at baseline was 7.7 (5.5-16.8). The patients were observed for 9.6 (7.9-11.3) years. Within this period, the median mSASSS score increased to 14.0 (7.0-36.8). The most influential clinical factor of final mSASSS was baseline mSASSS ($p < 0.001$). Eye involvement, longer follow up duration, and older age at enrollment were associated with increased final mSASSS ($p < 0.001$, $p < 0.001$, and $p = 0.002$, respectively). Peripheral joint involvement was associated with decreased possibility of severe radiographic damage ($p < 0.001$). After adjusting clinical factors, Ryanodine receptor 3 (RYR3) gene was associated with severe radiographic damage ($p = 1.97x10-06$). Treatment with Rhodamine B, a ligand of RYR3, dose-dependently induced extracellular matrix mineralization of AS osteoprogenitors in vitro. For the pathway analysis, PI3K-Akt signaling pathway and focal adhesion pathway were associated with severe radiographic damage in AS.

Conclusions

This study identified clinical and genetic factors that contributed to better understanding of the pathogenesis and biology associated with severe radiographic damage in AS.

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Age-stratified trend of spinal radiographic damage progression in patients with ankylosing spondylitis

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Background
To estimate the course of spinal radiographic progression for specific age range categories in patients with ankylosing spondylitis (AS) using a longitudinal dataset in a real-life setting.

Methods
In total, 4016 radiographic intervals from 1125 AS patients with spinal radiographs available at a single hospital were stratified into five groups based on the age at each radiograph: age <20 (n=122); 20–29 (n=1124); 30–39 (n=690); 40–49 (n=794); and ≥50 years (n=286). Radiographic progression rate was defined as the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) change per year. Age-stratified mSASSS change per year was estimated using the generalized estimating equations (GEE) after adjusting for predictors of radiographic progression. A subgroup analysis was performed to estimate the course of radiographic progression, stratified for identified risk factors.

Results
The mean (SD) follow-up duration was 8.4 (2.9) years and the mean number of radiographs was 4.6 (1.2) per patient. The mean radiographic progression rate of the overall intervals was 0.8 (1.9). In the GEE multivariable analysis, smoking, peripheral joint involvement, eye involvement, log-transformed C-reactive protein (CRP) values at each radiograph, and preexisting syndesmophytes were significant and independent factors for predicting structural damage progression.
GEE-estimated radiographic progression was highest at age group 30–39 (estimated mean mSASSS change per year was 1.148), followed by 40–49 (1.003), 20–29 (0.868), ≥50 (0.779), and <20 (0.643). However, radiographic damage scores rapidly increased among younger age groups with risk factors. The estimated mean mSASSS change per year for the age group 20–29 was 1.244 with elevated CRP levels and 2.505 with preexisting syndesmophytes, respectively.

Conclusions
In AS, spinal structural damage with age progresses in an increasing trend where periods of relatively rapid increase and slow increase may alternate, and it seems to progress the most in the 30s. However, patients with risk factors show a rapid progression from under the 30s.

Keywords
Ankylosing spondylitis, Age, modified Stoke Ankylosing Spondylitis Spinal Score

E-poster Presentation

Behcet's disease & Vasculitis

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Aortic valve surgery in patients with Takayasu's arteritis: A nationwide analysis of 1,197 patients during a 9-year period

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Background

Takayasu arteritis (TA) is associated with an elevated risk of valvular heart disease, especially in the aortic valve. This study aimed to evaluate the rate and risk factors of AVS in patients with TA.

Methods

The clinical data of 1,197 patients were identified in the Korean National Health Insurance Claims database between 2010 and 2018. Case ascertainment was done by using the ICD-10 code of TA and inclusion in the Rare Intractable Diseases registry. The incidence rate/1,000 person-years was calculated to compare the age- and sex- adjusted incidence rate ratio (IRR) of AVS according to the time period between TA diagnosis and AVS: < 1 year, 1-2 years, 2-3 years, and after 3 years. Evaluation of factors associated with AVS was performed using a time-dependent Cox regression analysis.

Results

Forty-five patients (3.8%) underwent AVS during the follow-up. The mean follow-up duration of patients with AVS was 1.2 years, and two-thirds of the patients (66.7%) underwent AVS within 1 year. The adjusted IRR was significantly higher among patients who underwent AVS < 1 year after the diagnosis of TA than among those who underwent AVS 3 years after diagnosis (adjusted IRR: 10.31; 95% confidence interval [CI]: 4.29-24.81). A history of hypertension before the diagnosis of TA was an independent risk factor for AVS (adjusted hazard ratio: 2.18; 95% CI: 1.12-4.24).

Conclusions

Approximately 4% of patients with TA undergo AVS, usually within the first year of TA diagnosis. Previous history of hypertension is a risk factor for AVS.

Keywords

Takayasu arteritis, aortic valve surgery, risk factor

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P-081

Incidence, prevalence, and risk of stroke in patients with Takayasu arteritis: A nationwide population-based study in South Korea

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Background

Takayasu arteritis (TAK) is a disease associated with increased risk of cardiovascular complications. We aimed to evaluate the incidence, prevalence, and risk of stroke in patients with TAK.

Methods

Data from 1065 patients were obtained from a national database (2010-2018). The annual incidence and prevalence per 100,000 persons were estimated using the registration population at the midst of every year, and the standardized incidence ratio (SIR) of stroke was compared to the general population based on the data from the 2006 national report for cardiovascular and cerebrovascular diseases. Age-adjusted incidence rate ratio (IRR) of stroke based on the time interval after diagnosis was also calculated. A time-dependent Cox regression was conducted to investigate predictive factors of stroke.

Results

The overall incidence rate of TAK ranged between 0.2 and 0.3/100,000 person-year annually; the prevalence of TAK gradually increased, reaching 3.25/100,000 person-year in 2018. Seventy-three (6.9%) patients experienced stroke during follow-up, and the risk of developing stroke was higher than the general population (overall SIR 7.39, 95% confidence interval [CI] 5.79-9.29; Men: SIR 5.70, 95% CI 2.84-10.20; Women: SIR 7.06, 95% CI 5.41-9.05). Most stroke events (90.9%) were cerebral infarction for men, whereas the proportion of cerebral infarction was lower (62.9%) in women. Over half of stroke events occurred within 6 months after diagnosis, and stroke was more common within 6 months of diagnosis compared to after 3 years in women (IRR 13.46, 95% CI 6.86-26.40). In Cox regression analysis, age was the sole predictor of stroke (adjusted hazard ratio 1.02, 95% CI 1.00-1.04, p=0.043).

Conclusions

The annual incidence of TAK was similar to the previous studies from Asia, and the risk of stroke increased in TAK. Different pattern of subtype and incidence of stroke were found according to sex, although age was the only predictor.

Keywords

Takayasu arteritis, stroke, incidence

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P-082

The relationship of brain plaques with radiological severity after COVID-19 as a cause of vasculitis

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Background

We aimed to examine the relationship between disease severity and brain plaque formation in a healthy population with Covid-19 disease.

Methods

123 patients who had Covid-19 disease and had cranial MRI in the last one year and had a cranial MRI scan between 3-12 months after Covid were examined. Patients who had a history of chronic disease and had other cranial pathologies in the process were excluded from the study. 52 patients with no known comorbidity were included in the study. The first and second cranial MRIs of 52 patients were examined by a radiologist for the formation of new parenchymal plaques. Covid radiological severity classification was made according to the radiological involvement percentages on CT imaging. Mild radiological findings were classified as = 0-50%, severe radiological findings = 51-100%.

Results

23 of 52 patients had new parenchymal plaque formation. While 11 of the 19 patients with newly formed plaques had severe radiological findings, 8 had mild radiological findings. Of the 33 patients without plaque formation, 25 had mild radiological findings, while 8 had severe radiological findings. No significant difference was observed in terms of age and gender between those with radiological new plaques in the brain parenchyma and those without. A significant and high level of correlation was observed between Covid disease severity and brain parenchymal plaque formation. (P= 0.0004, r = 0.7273)

Conclusions

As the radiological severity increases in Covid infection, an increase in plaque formation can be seen in the brain parenchyma.

Keywords

Brain Plaques, Covid-19, Vasculitis

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P-083

Pulmonary involvement evaluation with high resolution computed tomography in aortic arch syndrome patients

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Background

This study aimed to evaluate and describe pulmonary high-resolution CT (HRCT) findings in Aortic Arch Syndrome (AAS) Patients

Methods

A total of 62 AAS patients were evaluated retrospectively after excluding patients with other pulmonary disorders or incomplete data. Patients were divided into two groups: those with normal lung HRCT and those with abnormal lung HRCT. Clinical characteristics were compared between groups and binary logistic regression analysis was applied to identify possible causes of the lung lesions.

Results

Of the 62 patients, 41 (66.0%) had normal lung HRCT while 21 (34.0%) had abnormal lung HRCT, including stripe opacity (61.9%), nodules (42.8%), patchy opacity (28.5%), pleural thickening (19.4%), pleural effusion (14.2%), ground-glass opacity (9.5%), pulmonary infarction (9.5%), mosaic attenuation (4.7%) and bronchiectasis (4.7%) and. Patients with abnormal HRCT were significantly more likely to have pulmonary arterial involvement (PAI; 38 % vs 12.1%, P<0.001. Logistic regression analysis demonstrated that PAI and age were associated with the presence of pulmonary lesions.

Conclusions

Pulmonary lesions are not rare in patients with AAS. Age and PAI are potential risk factors for the presence of pulmonary lesions in AAS.

Keywords

Aortic Arch Syndrome, Takayasu arteritis, high-resolution computed tomography

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P-084

Chest MRI findings of Behcet's disease

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Background

There is no study about Behcet's disease's chest MRI findings in the literature. The aim of the study was to evaluate chest MRI findings in patients with Behcet's disease by 3-T magnetic resonance imaging (MRI).

Methods

Twenty-four patients with Behcet's disease (mean age 32 years, range 22–48) were retrospectively assessed with 3-T MRI of the Chest. MRI findings were evaluated.

Results

Of the 24 patients, 15 (62.5%) had normal chest MRI while 9 (37.5%) had abnormal chest MRI, including Pulmonary artery aneurysm (44.4%), pulmonary artery thrombosis (33.3%), pericardial effusion (33.3%), pulmonary infarction (22.2%) and pleural effusion (11.1%).

Conclusions

Pulmonary lesions are not rare in patients with Behcet's disease. MRI is a reliable method that does not involve radiation in the evaluation of pulmonary involvement.

Keywords

Behcet disease, MRI, vasculitis

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P-086

Novel mortality-predicting index at diagnosis can effectively predict all- cause mortality in patients with antineutrophil cytoplasmic antibody-associated vasculitis

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Background

Active treatment is required from the time of diagnosis of AAV, and indicators at diagnosis that can predict a poor prognosis during follow-up may be clinically useful.

We developed a novel index, the mortality-predicting index (MPI) which is calculated as NLR × CAR × monocyte counts at diagnosis. This study investigated whether IPI, and MPI at diagnosis could predict all-cause mortality during follow-up.

Methods

The medical records of 223 patients with AAV were retrospectively reviewed.

Indices for predicting prognosis

(i) NLR = neutrophil counts (/μL) / lymphocyte counts (/μL);5 (ii) CAR = CRP (mg/L) / serum albumin (g/dL);6 (iii) IPI = NLR × CAR;10 (iv) MPI = NLR × CAR × monocyte counts (/μL).

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 25. (IBM Corp., Armonk, NY, USA).

Results

Regarding the ROC curves of the four indices for all-cause mortality, MPI exhibited the highest area under the curve (AUC) value (0.691, 95% confidence interval [CI] 0589, 0.792), followed by IPI (0.686, 95% CI 0.587, 0.786).

The cumulative patients' survival rates were significantly lower in patients with NLR ≥ 3.22 (P = 0.001), CAR ≥ 3.25 (P = 0.004), IPI ≥ 18.53 (P < 0.001), and MPI ≥ 8367.82 (P = 0.001) than those without.

. In the multivariable analysis with MPI ≥ 8367.82 (HR 3.356, 95% CI 1.290, 8.735), smoking history and FFS at diagnosis were significantly associated with all-cause mortality.

Conclusions

We conducted a multivariable Cox hazards model analysis using the candidate indices with the conventional risk factors for mortality. We developed and proposed new indices with higher predictability compared to previously reported mortality-predicting indices. To overcome the ethnic and geographical differences, we suggested a method of determining a cut-off for predicting mortality for each index.

Keywords

Mortality-predicting index, inflammation prognostic index, antineutrophil cytoplasmic antibody

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Three cases of Takayasu's arteritis with Crohn's disease in young female patients

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Description

Takayasu's arteritis (TA) and Crohn's disease (CD) are chronic inflammatory diseases that involve different major organs. Although literature reports have increased, it is very rare that TA and CD coexist.

Case 1: A 19-year-old female was referred for fever, myalgia and arthralgia. She was first diagnosed with CD four months ago and is taking azathioprine and 5-aminosalicylic acid. Gastrointestinal symptoms and colonoscopy were improved. The neck computed tomography (CT) showed multifocal stenosis in both common carotid artery (CCA) and increased Fluorodeoxyglucose (FDG) uptake along both CCA, thoracic to suprarenal abdominal aorta in positron emission tomography (PET) CT. Her symptoms improved after using methotrexate (MTX), azathioprine, and steroids.

Case 2: A 20-year-old female patient was diagnosed with CD 6 months ago and came to our clinic with fever and myalgia while taking infliximab. CT findings confirmed concentric wall thickening of both CCA. PET CT showed FDG uptake along the wall of both CCA, subclavian, aorta and both superficial femoral artery. Currently, MTX, leflunomide, and steroid are co-administered while maintaining infliximab and her symptoms have improved.

Case 3: A 22-year-old female who was diagnosed with CD 6 years ago and was being treated with adalimumab was referred for fever. Severe stenosis of the long region of Right CCA was observed on CT, and FDG uptake was observed in the same region on PET CT. We switched from adalimumab to infliximab due to persistently high levels of inflammatory marker despite the use of immunosuppressants and steroids.

Conclusions

Our patients were younger at diagnosis and tended to have systemic symptoms such as fever and myalgia more frequently. Clinicians should have a suspicion for TA in CD patients who have well controlled gastrointestinal symptoms, if they have systemic symptoms such as fever and myalgia or have high levels of inflammatory marker.

Keywords

Takayasu's arteritis, Crohn's disease

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P-088

Risk of ocular comorbidities and blindness among patients with Behçet's disease : A nationwide population-based cohort study in Korea

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Background

This study aimed to evaluate and describe pulmonary high-resolution CT (HRCT) findings in Aortic Arch Syndrome (AAS) Patients

Methods

A total of 62 AAS patients were evaluated retrospectively after excluding patients with other pulmonary disorders or incomplete data. Patients were divided into two groups: those with normal lung HRCT and those with abnormal lung HRCT. Clinical characteristics were compared between groups and binary logistic regression analysis was applied to identify possible causes of the lung lesions.

Results

Of the 62 patients, 41 (66.0%) had normal lung HRCT while 21 (34.0%) had abnormal lung HRCT, including stripe opacity (61.9%), nodules (42.8%), patchy opacity (28.5%), pleural thickening (19.4%), pleural effusion (14.2%), ground-glass opacity (9.5%), pulmonary infarction (9.5%), mosaic attenuation (4.7%) and bronchiectasis (4.7%) and. Patients with abnormal HRCT were significantly more likely to have pulmonary arterial involvement (PAI; 38 % vs 12.1%, P<0.001. Logistic regression analysis demonstrated that PAI and age were associated with the presence of pulmonary lesions.

Conclusions

Pulmonary lesions are not rare in patients with AAS. Age and PAI are potential risk factors for the presence of pulmonary lesions in AAS.

Keywords

Aortic Arch Syndrome, Takayasu arteritis, high-resolution computed tomography

E-poster Presentation

Metabolic and crystal arthropathies

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P-089

Development of a plain radiographic scoring system for new bone formation in gout

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Background

The aim of this project was to develop a plain radiographic scoring system for new bone formation (NBF) in patients with gout.

Methods

Following a systematic review of scoring systems for NBF in other bone and joint diseases, and a structured review of plain radiographs, a range of published scoring systems were tested in 80 individual joints (40 1st MTP joints and 40 5th MTP joints) from 20 patients with gout. Two readers scored the plain radiographs for sclerosis and spur using these scoring systems. In addition, construct validity was assessed by comparing plain radiography scores with gold standard computed tomography (CT) measurements of sclerosis and spur of the same joints. The best-performing scoring system was then tested in sets of hand and foot radiographs from an additional 25 patients with gout (n=52 sites/set, scores summed for each individual patient). Inter-reader intra-class correlation coefficients (ICCs) were calculated, and NBF scores were correlated with plain radiographic erosion scores (using the gout-modified Sharp-van der Heijde system).

Results

A semi-quantitative scoring system for spur and sclerosis (Table) was found to have high feasibility and face validity. In the individual joint analysis, the inter-observer ICC (95% CI) using this system was 0.84 (0.76-0.89) for sclerosis and 0.81 (0.72-0.87) for spur. Plain radiographic sclerosis and spur scores correlated with CT measurements ($r = 0.65$-0.71, $P < 0.001$ for all analyses). For the hand and foot radiograph sets, the inter-observer ICC (95% CI) was 0.94 (0.90-0.97) for sclerosis score, 0.77 (0.62-0.86) for spur score, and 0.92 (0.86-0.95) for combined sclerosis and spur score. The sclerosis and spur scores correlated highly with plain radiographic erosion scores ($r = 0.81$-0.94, $P < 0.001$ for all analyses).

Conclusions

A semi-quantitative plain radiographic scoring method is feasible and reproducible for assessment of NBF in gout. This method may facilitate consistent measurement of NBF in gout.

Keywords

gout, new bone formation, radiography

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P-090

The association between hyperuricemia and oral health : A cross sectional study using KNHANES data

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Background

Hyperuricemia plays an important role in the development of gout. Hyperuricemia has been reported to have an incidence rate of 4.8% in Korea, and a prevalence rate of 12.7% in the United states [1][2]. Despite clinical importance of hyperuricemia, a relationship between oral health and hyperuricemia has not been clearly established [3]. In this study, the correlation between oral health and hyperuricemia in the general population was investigated.

Methods

The Korea National Health And Nutrition Examination Survey (KNHANES) is a cross-sectional survey and a nationally representative database of the Korean population controlled by the Korea Centers for Disease Control and Prevention (KCDC). In this study, data from the KNHANES 2016–2019 was utilized. this study included 17,584 subjects (7,831 males and 9,753 females). The number of dental caries was categorized as 0, 1–2, and ≥3. Oral health-related questionnaires including the time of day when subjects brushed their teeth, used secondary oral products, and regular dental examination, were recorded as oral health behaviors.

Results

In all subjects, oral health status with dental caries and oral health behaviors including tooth brushing, secondary oral products, and regular dental examination were significantly associated with hyperuricemia. The adjusted OR and 95% CIs for hyperuricemia comparing more than three dental caries with no dental caries were 1.28 (1.08–1.51). The adjusted OR and 95% CIs for hyperuricemia comparing more than three tooth brushing with under one tooth brushing were 0.78 (0.67–0.91). The adjusted OR and 95 CIs for hyperuricemia in secondary oral products and regular dental examination were 0.91 (0.82–1.00) and 0.86 (0.78–0.95), respectively. The tendency between oral health and hyperuricemia was more pronounced in the male group.

Conclusions

We found that the number of dental caries, the number of tooth brushing in a day, the use of secondary oral product and regular dental examination were associated with hyperuricemia.

Keywords

Hyperuricemia, Oral health

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P-091

Patient perspectives and preferences regarding gout and gout management : Impact on adherence

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Background

Patient-centered management is becoming increasingly important in gout, but there are limited studies exploring patients' perspectives and preferences. We aimed to investigate patients' perspectives and preferences regarding gout and gout management, and their impacts on adherence to urate lowering therapy (ULT).

Methods

A paper-based survey was performed in patients with gout seen at the rheumatology outpatient clinics of 16 tertiary hospitals. The survey included questions regarding demographics, comorbidities, gout attacks, current treatment and adherence, and patients' perspectives and preferences regarding gout and gout management. Multivariate regression analysis was performed to determine the factors associated with ULT adherence.

Results

Of 809 surveyed patients with gout, 755 (94.5%) were using ULT. Among those using ULT, 89.1% had ≥

80% adherence to ULT. Majority of the patients knew management strategies to some extent (94.8%), perceived gout as a life-long disease (91.2%), and were making efforts toward practicing at least one lifestyle modification (89.2%). Most patients (71.9%) obtained information about gout management during their clinic visits. Approximately half of the patients (53.6%) preferred managing their disease with both ULT and lifestyle modification, 28.4% preferred ULT only, and 17.4% preferred lifestyle modification only. Adherence was better in patients with older age (odds ratio [OR] 1.03), those with better knowledge of gout management strategies (OR 3.56), and those who had preference for ULT (OR 2.07).

Conclusions

Patients' perspectives and management preferences had high impacts on adherence to ULT in gout. Consideration of patients' perspectives and preferences is important for achieving the desired clinical outcome in gout.

Keywords

Gout, Perspective, Patient preference

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P-092

The impact of gout on the risk of dementia according to age group : A nationwide population-based cohort study

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Background

Dementia is a common mental illness associated with aging. Alzheimer's disease (AD) and Vascular dementia (VaD) are the most common causes of dementia in the elderly. Hyperuricemia was suggested to have antioxidant effects and possible neuroprotective effects. Hyperuricemia is the most important factor in the pathogenesis of gout. This study aims to investigate association between gout and dementia using a retrospective cohort study in Korean.

Methods

total of 5,496 gout patients and 27,480 age- and sex-matched control cohorts were selected from National Health Insurance Service–National Sample Cohort (NHIS-NSC) database. Dementia incidence was followed through NHIS record for healthcare utilization and prescriptions. Cox proportional hazards model was used to evaluate the influence of gout on dementia incidence.

Results

During follow-up period, 88 and 620 subjects were developed dementia in gout patients and control cohorts, respectively. Gout patients had a lower risk of overall dementia [hazard ratio (HR): 0.79; 95% confidence interval (CI): 0.63-0.99] and AD (HR: 0.74; 95% CI: 0.56-0.98) after adjusted for age, sex, household income, comorbidities. However, gout was not associated with the risk of VaD (HR: 0.97; 95% CI: 0.58-1.63) or mixed dementia type (HR: 0.81; 95% CI: 0.44-1.51). In stratified analysis by age and sex of gout patients, the inverse association between gout and the risk of dementia was observed only in the elderly male group. However, HR of VaD significantly increased in the younger male group (HR:2.54, 95% CI 1.10-5.85).

Conclusions

Gout decreased the risk of incident AD type dementia, especially in elderly patients. Our study results suggested that the association between gout and dementia risk may differ by gout-onset age and disease duration by different mechanisms

Keywords

gout, Alzheimer disease, vascular dementia

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Reliability and quality of Korean youtube videos for patient education regarding gout

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Background

YouTube has become an increasingly popular educational tool and an important source of healthcare information. However, dissemination of inaccurate medical information can be misleading and may even result in serious consequences among YouTube users. We investigated the reliability and quality of YouTube videos for gout in Korean.

Methods

We performed a comprehensive electronic search on April 2, 2021, using the following key words: 'gout', 'acute gout', 'gouty arthritis', 'gout treatment', and 'gout attack' and identified 140 Korean videos. Two rheumatologists categorized the videos into 'useful', 'misleading', and 'personal experience' groups. Reliability was determined using a 5-item questionnaire modified from the DISCERN validation tool and overall quality scores based on the Global Quality Scale (GQS). The inter-class correlation coefficient (ICC) was determined as a measure of agreement.

Results

The ICCs of the DISCERN tool and GQS were 0.89 (95% confidence interval [CI] 0.85–0.92) and 0.85 (95% CI 0.79–0.89), respectively. Among the 140 videos identified, 105 (75.0%), 29 (20.7%), and 6 (4.3%) were categorized as 'useful', 'misleading', and 'personal experience', respectively. Videos in the 'useful' group were mainly created by rheumatologists (70.5%). The mean DISCERN and GQS scores in the 'useful' group (3.3 ±1.0 and 3.8 ± 0.7) were higher than those in the 'misleading' (0.9 ± 1.0 and 1.9 ± 0.6) and 'personal experience' groups (0.8 ± 1.2 and 2.0 ± 0.8) ($p < 0.001$ for both the DISCERN and GQS tools).

Conclusions

Approximately 75% of YouTube videos that contain educational material regarding gout were useful; however, we observed some inaccuracies in the medical information provided. Therefore, healthcare professionals should closely monitor media content and actively participate in the development of videos that provide accurate medical information.

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P-094

Diagnostic value of ultrasound versus dual-energy computed tomography in patients with gouty acute gouty arthritis

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Background

Previous studies of the diagnostic accuracy of ultrasound (US) and dual-energy computed tomography (DECT) in patients with gout have reported different results. The aim of this study is to compare the diagnostic value of US and DECT in patients with acute gouty arthritis.

Methods

Based on the presence of monosodium urate (MSU) crystals in the synovial fluid, patients (n = 18) were divided into three groups according to gout duration: early-stage (within 1 year, n = 8), middle stage (1 to 3 years, n = 6), and late-stage (more than 3 years, n = 4). All the affected joints were examined by US and DECT.

Results

In the early-stage group, the sensitivity of US was higher than DECT in identifying MSU deposition (62.5% vs 50 %, p: 0.08), while in the middle- and late-stage groups, the sensitivity of US and DECT was similar. In the early-stage group, the US results in five joints were positive (two with double contour sign, three with snowstorm sign, and one with both double contour sign and snowstorm sign), while DECT did not show any urate crystal deposits.

Conclusions

In conclusion, the US should be the first choice for acute gouty arthritis

Keywords

Acute gouty arthritis, Dual-energy computed tomography (DECT), Ultrasound (US)

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P-095

Gout as an independent risk factor for major adverse cardiac events

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Background

In the pathogenesis of cardiovascular (CV) disease, gout have been suggested as causative mechanisms such as endothelial dysfunction, oxidative metabolism, platelet adhesiveness, and aggregation. In addition, traditional CV risk profiles and development of gout can simultaneously affect the development or change of CV risk profiles during the progression from asymptomatic hyperuricemia to gout over a long time. These long-term interaction between the CV risk profile and gout may influence CV event. As a result, it is unclear that gout is an independent risk factor for CV event.

Methods

This was a retrospective cohort study using data from the Korean National Health Insurance claims database, including data from the National Health Screening Program. Patients aged 20 to 89 years who were newly diagnosed with gout in 2012, and controls without gout matched by age and sex were enrolled. After adjusting for traditional CV risk profiles that existed 10 years before the diagnosis of gout and their long-term changes, the relative risks of incident CV events (myocardial infarction, cerebral infarction, and cerebral hemorrhage) and death in the incident gout patients were assessed.

Results

The study consisted of 113,853 patients with gout and 1,138,530 matched general population. After adjusting for traditional CV risk profiles and their long-term changes, multivariable analysis showed that gout patients had an increased risk for myocardial infarction [hazard ratios (HRs): 1.37, 95% CI: 1.27–1.47, P<0.01 confidence interval (CI)], cerebral infarction (HRs: 1.39, 95% CI: 1.27–1.53, P<0.01), cerebral hemorrhage (HRs: 1.49, 95% CI: 1.31–1.69, P<0.01), and all-cause death (HRs: 1.05, 95% CI: 1.01–1.10, P=0.02).

Conclusions

The risk of incident CV events and all-cause death was increased in incident gout patients, even after adjusting for traditional CV risk profiles and their long-term changes. Gout may play an important role in the development of CV diseases.

Keywords

Gout, Cardiovascular diseases

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P-096

Gender differences in associations between the serum level of uric acid and metabolic disorders in Russian overweight patients

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Background

In this study, we aimed to assess gender differences in associations between the serum level of uric acid and metabolic disorders in Russian overweight patients.

Methods

We investigated 146 overweight adults (body mass index≥25.0). The checkup included evaluation of clinical history, serum levels of uric acid, lipid fractions, leptin, insulin, thyroid-stimulating hormone, C-reactive protein, creatinine, liver function tests, 25-hydroxyvitamin D, homocysteine, and calculation of glomerular filtration rate (CKD-EPI), SCORE index, HOMA-IR index, and visceral adiposity index. Pearson's correlation coefficient (r) and chi-squared test were used for statistical analysis.

Results

Hyperuricemia was found in 52.0% overweight women and 73.8% overweight men (p=0.024). When analyzing the female group we found that serum levels of uric acid were correlated with age (r=0.303, p=0.018), SCORE index (r=0.416, p=0.006), serum triglycerides (r=0.266, p=0.043), and homocysteine (r=0.307, p=0.030). However, in the male group serum levels of uric acid were interconnected with body mass index (r=0.319, p=0.003), waist-to-hip ratio (r=0.313, p=0.005), serum leptin (r=0.294, p=0.009), triglycerides (r=0.303, p=0.005), insulin (r=0.232, p=0.038), HOMA-IR index (r=0.226, p=0.036), visceral adiposity index (r=0.245, p=0.029) and serum gamma-glutamyl transferase (r=0.289, p=0.009). In both groups, hyperuricemia had no correlations with total, HDL and LDL cholesterol, thyroid-stimulating hormone, C-reactive protein, creatinine and glomerular filtration rate, AST, ALT, bilirubin, and 25-hydroxyvitamin D.

Conclusions

The results of the study demonstrate that hyperuricemia is highly prevalent in overweight Russian patients. The observed gender differences suggest that men and women with hyperuricemia and gout require different approaches to screening for associated metabolic disorders and their correction.

Keywords

uric acid, overweight, metabolic disorders

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P-097

Association between female reproductive factors and gout : A nationwide population-based cohort study of 1 million postmenopausal women

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Background

Previous studies have shown that the incidence and risk factors of gout differs according to sex. However, little research has been done on the association between reproductive factors and gout. We conducted an analysis of a large nationwide population-based cohort of postmenopausal women to determine whether there is an association between reproductive factors and the incidence of gout.

Methods

A total of 1,076,378 postmenopausal women aged 40–69 years who participated in national health screenings in 2009 were included in the study. The outcome was the occurrence of incident gout, which was defined using the ICD-10 code of gout (M10) in the claim database. Cox proportional hazard models were used for the analyses and stratified analyses according to body mass index (BMI) and the presence/absence of chronic kidney disease (CKD) were performed.

Results

The mean follow-up duration was 8.1 years, and incident cases of gout were 64,052 (incidence rate, 7.31 per 1,000 person-years). Later menarche, earlier menopause, and a shorter reproductive span were associated with a high risk of gout. No association between parity and gout incidence was observed. Use of oral contraceptives (OC) and hormone replacement therapy (HRT) were associated with an increased risk of gout. The association between reproductive factors and gout was not statistical significant in the high BMI group. The effects of OC and HRT usage on gout were not significant in the CKD group.

Conclusions

Shorter exposure to endogenous estrogen was associated with a high risk of gout. Conversely, exposure to exogenous estrogen such as OC and HRT was associated with an increased risk of gout.

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P-098

The risk of hyperuricemia associated with metabolic syndrome and smoking is more pronounced in women than in men

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Background

Hyperuricemia is a relatively common metabolic disorder and there is growing interest in the relationship between serum uric acid and cardiovascular risk. The burden of hyperuricemia in women is also increasing, but there are still some areas that are overlooked. This study aimed to investigate risk factors associated with hyperuricemia with particular focus on sex differences.

Methods

Multivariate logistic regression analysis was performed using data from the 2016-2018 Korean National Health and Nutrition Examination Survey. Hyperuricemia was defined as a serum uric acid level of ≥7.0 mg/dL in men and ≥6.0 mg/dL in women.

Results

A total of 16,288 Korean adults were enrolled. Among those, 21% of male and 7% of female subjects had hyperuricemia. Hyperuricemia was significantly associated with metabolic syndrome (MetS) in both sex (OR: 1.80, 95% CI: 1.47-2.21 in men, OR: 2.40, 95% CI: 1.78-3.23 in women). In particular, in women, the risk increased substantially when three or more of the MetS items were satisfied (OR: 4.35, 95% CI: 2.52-7.50). The risk of hyperuricemia among female smokers was 1.6 times higher than that of non-smokers. Female current smokers with MetS showed increased risk of hyperuricemia by more than four times (OR: 4.27, 95% CI: 2.47- 7.35) while male current smoker with MetS had lower risk (OR: 2.23, 95% CI: 1.51-3.30). To a similar degree, the risk of hyperuricemia was high in women with MetS when they consumed 30g/day or more of alcohol (OR: 4.13, 95% CI: 1.68-10.16). The ORs of hyperuricemia related to obesity was 1.42 (95% CI: 1.15-1.75) in man and 2.24 (95% CI: 1.73-2.90) in women.

Conclusions

Traditional cardiovascular risk factors such as MetS, smoking and obesity are associated with a higher risk of hyperuricemia in women compared to men. More attention should be paid to hyperuricemia in women and further investigation is required.

Keywords

Hyperuricemia, Metabolic syndrome, Women

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Cardiovascular risk associated with treatment of allopurinol and benzbromaronein patients with gout

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Background

There are many studies on the effect of uric acid lowering therapy on CV risk in gout patients, but few studies have compared allopurinol and benzbromarone. A nationwide population-based cohort study is designed to compare cardiovascular risk according to the treatment of allopurinol and benzbromarone in Korean gout patients.

Methods

We used South Korea's database of the Health Insurance Review and Assessment service (HIRA) to identify gout patients 18 years of age or older who newly started allopurinol or benzbromarone between 2009 and 2015. The primary outcome of the study was the occurrence of a composite cardiovascular endpoint, which included coronary revascularization, hospitalization due to MI, ischemic stroke, and transient ischemic attack.

Results

257,097 allopurinol initiators and 7,868 benzbromarone initiators were included in the study. In baseline, the benzbromarone initiator had more cardiovascular comorbidities and related drug administration than the allopurinol initiator. In allopurinol and benzbromarone initiators, the adjusted hazard ratio (aHR) of the composite CV endpoint was 1.01 (95% CI 0.83-1.21), which was not significantly different. No significant difference was found between the two groups in each of the items of the composite CV endpoint and hospitalization for heart failure. The results did not change even when 1:3 propensity score matching was performed for baseline characteristics. In subgroup analysis of high risk patients with cardiovascular disease, there was no significant difference between allopurinol and benzbromarone initiators. When the analysis was limited to the group taking allopurinol ≥200mg and benzbromarone ≥50mg, there was no difference in primary outcome, but the risk of coronary revascularization was higher in benzbromarone initiator (aHR 1.58, 95% CI 1.16-2.14).

Conclusions

In our study, there was no significant difference in cardiovascular risk between allopurinol initiator and benzbromarone initiator. In the high risk group of cardiovascular disease, there was no difference in risk between the two drugs.

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Altered risk of gout according to change of metabolic syndrome status in young male

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Background

Many studies have shown a link between gout and metabolic syndrome (MetS). The purpose of this study was to investigate the relationship between gout risk and MetS in a nationwide population based young male cohort, and to determine whether changes in MetS status affect gout risk changes.

Methods

Among male aged 20-39 years who participated in national health check-up programs from 2009 to 2012, a total of 3,564,877 subjects were included in the study, excluding subjects who were previously diagnosed with gout. To determine the effect of changes in metabolic parameters on gout incidence, 1,621,963 subjects who participated in the health examination once more 2 years later were used for the analysis. Outcome was defined as the occurrence of gout, when the ICD-10 code (M10) was registered twice in the claim database.

Results

The incidence rate of gout was higher in male with MetS compared to those without (10.7 vs. 5.0 per 1,000 person-years). The risk of gout in male with MetS was 2-fold higher. Each component of MetS was also associated with increased gout risk, and abdominal obesity had the highest adjusted HR. The greater the number of MetS components, the higher the gout risk. The risk of gout was 2.5-fold higher in those who had MetS consistently and 1.8-fold higher in those with newly developed MetS than those who did not have MetS at the two health examinations. The development of MetS increased the risk of gout by 70%, and recovery of MetS lowered the risk of gout by 30%.

Conclusions

In young male, MetS was associated with a higher risk of gout, especially with more components, the higher the risk. Since the occurrence of MetS is associated with an increased risk of gout, prevention of MetS would be important to reduce gout incidence.

E-poster Presentation

Pediatric rheumatology

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P-101

Childhood SLE with isolated mycobacterium tuberculous spinal epidural abscess: A case report and review of unusual presentations

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Description

Introduction: Mycobacterium tuberculosis (Tbc)-caused Tbc spine with/without epidural abscess is rare. Herein we report the case of a systemic lupus erythematosus (SLE) girl with a Tbc spinal epidural abscess.

Case Report: A 14-year-old girl presented for a neuropsychiatric SLE follow up 6 months after the original diagnosis. She had complained of back pain for one month, followed by difficulty walking for one week. The physical examination found BT 36.8oC, back tenderness at thoracic level 2-4, and muscle power grades III and IV on right and left lower extremities, respectively. Her sensory test found impairment from thoracic level 4 right side and absent abdominal reflexes. An MRI of the thoracic spine showed a thick rim enhancing posterior epidural lesion size 1.1x2.2x7.5 cm in the axial, anteroposterior and vertical diameters, respectively, from the T3-6 levels without evidence of spondylodiscits. A mass effect was causing severe spinal stenosis, cord compression and myelopathy from the T3-5 levels.
She was diagnosed as spinal epidural abscess with cord compression and underwent a thoracic 4-6 laminectomy with a 10 cc abscess removal. Her muscle power and sensation dramatically improved after the surgery. Pus sent for an acid-fast bacilli (AFB) smear was positive 3+, and Tbc Polymerase Chain Reaction (PCR) was also positive. She was treated with 12-month isoniazid rifampicin, pyrazinamide and levofloxacin.

Conclusions

Isolated Tbc spinal epidural abscess is rare. Manifestations may mimic neuropsychiatric SLE. Early diagnosis and treatment can prevent long-term neurological complications.

Keywords

Epidural abscess, SLE, Tuberculosis

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Clinical outcomes of juvenile idiopathic arthritis and predictors of joint damage

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Background

Juvenile Idiopathic Arthritis is a heterogeneous disease with varying manifestations and outcomes. Epidemiological studies from India showed enthesitis-related arthritis and polyarticular JIA as the commoner subtypes than oligoarticular JIA. Outcome studies from the western world had shown remission in 7% to 47% of JIA patients at 18 months to 10 years of diagnosis. Remission was least in Rf positive polyarticular arthritis and extended oligoarthritis. Data from the Indian population is scarce.

Methods

A cross-sectional study of JIA patients who attended OPD of the Immunology department from January 2020 to April 2021 was done. The activity and damage scores were calculated using Wallace criteria and JADI respectively. The baseline and the follow-up data were obtained from the medical records. Chi-square tests and logistic regression analysis were done to find out the predictors of clinical remission and damage.

Results

135 JIA patients were recruited out of which 79(58.5%) were ERA, 18(13.33%) were RF+ polyarticular JIA, 9(6.67%) were RF negative polyarticular JIA, 15(11.11%) systemic JIA, 9(6.67%) persistent oligoarticular JIA, 2(1.48%) extended oligoarticular JIA, and 3(2.22%) juvenile psoriatic arthritis. The median duration of follow-up was 19(12-43) months. 55(40.74%) had active disease, 70(51.85%) were in remission on treatment, and 10(7.4%) were in complete remission (without treatment). 22(16.30%) had articular damage and 10(7.40%) had extraarticular damage. Predictors of joint damage were duration of the disease OR 1.24(1.02-1.51), ACPA positivity OR23.89 (3.39-168.59), and predictors of clinical remission were the age of onset of the disease OR 1.815(1.174-2.806).

Conclusions

Clinical remission in JIA is very low in the Indian population compared to the western world. This could be due to the predominance of enthesitis-related arthritis and polyarticular JIA in our population, the delay in diagnosis as well as socioeconomic factors. Longitudinal studies, as well as national registries, are needed to analyze the short-term and long-term outcomes of JIA.

Keywords

JIA, arthritis, outcome

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Systemic juvenile idiopathic arthritis flare after ChAdOx1 nCoV-19 vaccine

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Description

A number of publications emphasize the possibility of SARS-CoV-2 virus infection as a trigger to autoimmune rheumatic diseases [1]. Few de-novo cases of rheumatic diseases and few cases of flares of rheumatic disease following SARS-CoV-2 virus infection have been reported [2–4]. A similar uncertainty prevails with the vaccine for the COVID-19 being a trigger to these rheumatic diseases, with the underlying common theme of immune activation in a host susceptible to autoimmunity. We report a frontline worker who developed a flare of systemic juvenile idiopathic arthritis (SJIA) after the second dose of ChAdOx1 nCoV-19 vaccine. Our patient, who is a 33 years old male, had an onset of SJIA at the age of six years with a polycyclic course. After treatment of his last flare in the year 2016, he was in remission off medications. After eight days of the second dose of the vaccine in March 2021, he started having fever, arthralgia, myalgia and throat pain. When he presented to us, he had fever and tachycardia with normal blood pressure and respiratory rate. He had generalized lymphadenopathy, salmon-pink rash over the abdomen (Figure 1), and systemic examination was normal. His investigation showed neutrophilic leukocytosis with high c-reactive protein (CRP), transaminitis and elevated serum ferritin. Treatment was initiated with prednisolone 0.5 milligrams per kilogram (bodyweight) per day and methotrexate 15 milligrams per week. He had transient improvement, but the fever recurred with worsening hyperferritinemia, transaminitis and persistent leukocytosis. We could not give tocilizumab due to financial constraint, and steroid dose was hiked, and cyclosporine was added to the treatment. After an improvement in clinical status and investigations, he was advised to continue treatment with steroids, methotrexate and

Conclusions

Prompt preparedness is needed considering the possibility of the post-COVID-19 vaccination flare of autoimmune rheumatic disease, especially those affecting the paediatric population.

Keywords

Sytemic JIA FLARE, COVID-19, Post vaccine flare

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Idiopathic intracranial hypertension (IIH) with papilledema developed in juvenile idiopathic arthritis (JIA) during the biologic therapy

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Description

A 10-year-old JIA girl, who complained headache with visual disturbance for 2 months. These symptoms have become worse in recent when she running. She was on adalimumab SC every 2 weeks for 10 months. With concomitant MTX therapy over 6 years.

The neurological and systemic examinations were unremarkable. The Laboratory data showed normal CBC, renal and liver function test.

Brain MRI showed rather flattened posterior optic globe. Suspicious bulging of the optic nerve heads. Slightly flattened pituitary gland along sella floor. The papilledema is a legitimate finding.

Lumbar puncture revealed CSF pressure was 320 mgH2O.

Fundus showed multiple whitish retinal infiltration disc swelling. The tentative diagnosis were papilledema and panuveitis.

She has stopped taking the adalimumab injection and received oral prednisolone with acetazolamide. After discontinued adalimumab for 1 month, the whitish retinal infiltration with disc swelling lesions are much improved.

Conclusions

Idiopathic Intracranial Hypertension (IIH) is a rare disorder in children. It is characterized by raised intracranial pressure (ICP) in the absence of brain parenchymal lesion, vascular malformation, hydrocephalus, or CNS infection. The diagnosis is usually confirmed by high pressure of CSF. If not treated properly, it may lead to severe visual dysfunction. According to the AbbVie clinical data, the AEs of papilledema were not reported coincident with Humira in JIA. We exprienced a case of IIH with papilledema in JIA during the adalimumab therapy. In summary, beacuse adalimumab is commonly used drug for JIA, children treated with biologics should be warned against these potential adverse effects. To our knowledge, this is the first case of adalimumab induced IIH in JIA.

Keywords

Idiopathic Intracranial Hypertension, Juvenile Idiopathic Arthritis, Adalimumab

E-poster Presentation

Idiopathic inflammatory myositis and muscle biology

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Reevaluation of the prognostic significance of oropharyngeal dysphagia in idiopathic inflammatory myopathies

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Background

To investigate the prognostic significance of videofluorographic swallowing study (VFSS)-confirmed oropharyngeal dysphagia in idiopathic inflammatory myopathies (IIMs).

Methods

We reviewed the medical records of patients who were diagnosed with IIM between 2009 and 2020 at Seoul St. Mary's Hospital. All oropharyngeal dysphagia cases were limited to VFSS-confirmed dysphagia found during the initial diagnostic workup for IIM. We described the findings on VFSS and the course of the dysphagic symptoms. Logistic regression and survival analysis were performed to evaluate the risk of pneumonia and mortality, respectively.

Results

We found 88 patients with IIM who met the criteria. Among them, 17 (19%) patients had oropharyngeal dysphagia. Except for 2 cases lost to follow-up and 1 deceased case, all of the patients with dysphagia (14 of 14) had swallowing function restored within 6 months. The risk of pneumonia within 3 months from the diagnosis of IIM was significant (OR = 4.49, 95% CI: 1.07 – 18.88). The median follow-up duration was 34 and 27 months for the groups without and with dysphagia, respectively. The survival analysis failed to demonstrate that the presence of oropharyngeal dysphagia increased the risk of death (HR = 0.77, 95% CI: 0.085 – 7.00).

Conclusions

Oropharyngeal dysphagia found at the initial diagnosis of IIM improved within 3 to 6 months in nearly all cases. Furthermore, IIM patients who had oropharyngeal dysphagia at the initial diagnosis of IIM were not likely to have shorter survival, even if the risk of pneumonia was increased in the short-term.

Keywords

Dermatomyositis, Polymyositis, Deglutition Disorders

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P-106

Timed function tests as measures of disease activity and functional outcome in inflammatory myositis

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Background

Manual muscle testing (MMT) and Functional index 2(FI-2) are used in assessing disease activity in IIM1. They have several limitations. Several Timed function tests (TFTs) namely 2-minute walk test (2MWT), 30s raise from a chair test and 30s 1kg arm rise test have potential to measure both muscle strength and endurance 2 and needs to be evaluated in IIM. Our objective was to evaluate the performance of TFT in assessing muscle diseases at baseline and to evaluate the performance of TFTs to detect the longitudinal change in muscle power and endurance at 3 and 6 months.

Methods

This was an observational cohort study which included 42 patients with polymyositis and dermatomyositis satisfying EULAR/ACR classification criteria. MMT8, FI-2, FI-3 and TFTs were done at baseline, 3 months and 6 months.

Results

All 42 [11 (27%) polymyositis, and 31 (73%) dermatomyositis] completed three month follow-up assessment and 39 underwent evaluation at 6 months. The 3 TFTs had moderate to high correlation with MMT8 and FI-2 and FI-3 at baseline ($p<0.05$). The change in TFTs showed a moderate to strong correlation with the change in FI-2 as well as FI-3 among the study population at three months and six months (Table 1). Among the TFTs 2MWD had the best performance with moderate correlation with both MMT8, FI-2 and FI-3 in active disease suggesting a role in assessing both disease activity and endurance.

Conclusions

Using timed function tests can be an excellent alternative to FI-2/3 in assessing muscle endurance. 2-minute walk distance could be a better alternative to conventional muscle testing as it measures both power and endurance, is simple to perform and could be a valid patient reported outcome measure.

Keywords

Outcome measures, Myositis, Muscle strength

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Inverse and ulcerative Gottron's : Sinister sign in case of dermatomyositis

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Description

Despite the enormous advancement in the science of precision medicine, clinical medicine never fails to make its significance. Some clinical signs stand out to predict the course of the disease. Here we describe an ominous clinical sign, inverse Gottron, in a patient with amyopathic dermatomyositis patient with anti-MDA-5 antibody positivity (1). A 43 years old gentleman presented to us with symptoms of worsening dyspnea (mmrc grade 3) over the last four months associated with dry cough. He also reported constitutional symptoms such as fever, fatigue, and arthralgia and had a history suggestive of Raynaud's phenomenon. On examination, he was tachypneic and respiratory examination signified the presence of end-inspiratory crepitations. He did not have any muscle weakness. General examination was remarkable for tender erythematous palmar macules suggestive of inverse Gottron's sign (Image 1A) and Gottron's papule over bilateral MCP (Image 1B). There was evidence of healed ulcerative Gottron's on the left-hand dorsum (Image 1B). The clinical presentation was sufficient to quench the diagnosis of amyopathic dermatomyositis. The evidence of ulcerative and inverse Gottron pointed to the association with antibody against MDA-5, carrying a grim prognosis. After counselling the diagnosis and prognosis, management was started with prednisolone 1 mg/kg per day, cyclosporine and cyclophosphamide. As his symptoms were progressing, limiting his daily activities, therapy with rituximab (1 gram, two doses 14 days apart) was considered. Nevertheless, as predicted with the natural history of this disease, he had further deterioration in the clinical course and the option. Respecting the financial constraint and lack of comparative data, tofacitinib at 10 mg per days was considered over tocilizumab. Unfortunately, the patient did not respond to all tried immunosuppressant and succumbed to death after developing bacterial pneumonia with a compromised lung.

Conclusions

Inverse and ulcerative Gottron's are poor prognostic signs.

Keywords

Inverse and ulcerative Gottron's, anti-MDA-5 antibody, amyopathic dermatomyositis

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Anti-synthetase syndrome masquerading as COVID-19

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Description

A 31-year-old gentleman presented with eight months of exertional dyspnea, fever, inflammatory polyarthritis and myalgia. Three months into the illness, COVID-19 pneumonia was suspected based on bilateral basal ground-glass opacities (GGOs) on thoracic imaging with CT score of 9/25. However, COVID-19 RT-PCR tested negative on several occasions. With initiation of steroids, some improvement in shortness of breath was noted, with reappearance of symptoms on discontinuation (Figure 1A). Repeat CT at this juncture suggested worsened ground glassing, with CT score of 12/25 though COVID-19 RTPCR still tested negative (Fig 1B, C).

He reported to rheumatology department eight months into the illness when on examination, fine inspiratory crackles were evident in lower lung fields. Small hand joints were tender, and manual muscle testing score was 76/80. A diagnosis of anti-synthetase syndrome was suspected. Muscle enzymes (creatinine kinase 114 U/L and lactate dehydrogenase 502 U/L) were elevated. Anti-nuclear antibodies were positive (4+ cytoplasmic), and myositis specific antibodies tested positive for Ro52 and PL-12. Pulmonary function tests showed restrictive pattern of lung function (FVC: 39%, FEV1: 43%).

GGOs of autoimmune origin may be confused with COVID-19 pneumonia amidst pandemic. Insidious onset and other rheumatic manifestations may be salient pointers to alternative diagnosis. This patient did not exhibit classic cutaneous features like gottron's, heliotrope rashes, mechanic's hands. Subpleural sparing and progression of CT-findings over three-months favoured nonspecific interstitial pneumonia (NSIP) interstitial lung disease (Figure 1B, C) in this case.

Conclusions

COVID-19 manifests as peripheral GGOs that may progress into patchy areas of consolidation and fibrosis. GGO may occur in ASSD-related NSIP with sparing of subpleural lung zones and absence of consolidation. Symptoms of dyspnea, fever, myalgia during COVID-19 pandemic may pose diagnostic challenge. Therefore, it is imperative to educate practitioners about discriminating features between viral pneumonia and autoimmune NSIP.

Keywords

Anti-synthetase syndrome, COVID-19, Interstitial lung disease

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Systematic review of mycobacterial infections in patients with idiopathic inflammatory myopathies

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Background

Infections like Tuberculosis (TB) are a leading cause of morbidity and mortality in Idiopathic Inflammatory Myopathies (IIM). We systematically reviewed the prevalence of Mycobacterial infections in patients with IIM.

Methods

We screened MEDLINE, EMBASE and SCOPUS databases for original articles. Conference abstracts (2015-2020) were screened separately. We used Covidence to find relevant studies and collate estimates of prevalence. TB prevalence in IIM was mapped against reported prevalence rates in the general population.

Results

Of 83 studies, 28 were cohort-based, 2 case-control in design and 53 were case reports. Of these, 19 focused exclusively on IIM. Among 14,109 IIM patients, 217 cases of Mycobacterial infections were reported and most were in Dermatomyositis (57.60%). Most studies of TB in IIM were from Asia (52.63%), within the past 2 decades. Largest studies were from England (n=7033), followed by Taiwan (n= 4985). Prevalence of TB varied widely across studies (0.43% - 21.05%). M. Tuberculosis was the most common pathogen followed by Mycobacterium Avium Complex, while Non-tuberculous Mycobacteria were less common overall (4.61%). Disseminated and extrapulmonary forms (33.18%) were as common as pulmonary forms (39.63%). Tubercular muscle involvement was frequently seen in case reports (30.2%). TB was diagnosed during different points in the course of IIM, from diagnosis to 21-years after disease onset, often in those with comorbidities. In most cases TB occurred in absence of past exposure or family history. While death due to TB was occasionally reported (4.61%), successful anti-tubercular treatment (ATT) was fairly common (13.82%). Hepatitis was the most common ATT related ADR. Data on duration of ATT and follow up period was limited.

Conclusions

Tuberculosis is common in IIM, particularly in endemic regions. Extra-pulmonary forms and atypical sites such as skeletal muscle may be frequently involved. Limited data suggests fair outcomes, although larger prospective studies are needed for better understanding in this area.

Keywords

Idiopathic Inflammatory Myopathies, Tuberculosis, Mycobacteria

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P-110

Successful treatment of calcinosis universalis with infliximab in juvenile dermatomyositis

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Description

A 12-year-old girl with juvenile dermatomyositis who developed calcinosis Universalis of both shoulder and forearm. She had been in continuous remission of dermatomyositis as receiving treatment with multiple medications, including glucocorticoids, intravenous immunoglobulin, methotrexate, and mycophenolate mofetil over 6 years since the age of 5. She complained of swelling and limitation of the motion of both elbow joints. On physical examination, she presented with diffuse palpable subcutaneous nodules in both the axilla and the upper extremities. A radiograph of the humerus revealed extensive calcification in both axillary areas, extending downwards. , treatment with infliximab, intravenous bisphosphate, and aluminum hydroxide was initiated. 14 months after treatment, repeat radiograph showed that calcinosis Universalis has been markedly decreased.

Conclusions

This is the first report of successful treatment of calcinosis Universalis complicating JDM in Korea.

Keywords

Calcinosis Universalis, Juvenile dermatomyositis, Infliximab

E-poster Presentation

Sjögren's syndrome

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P-111

Ultrasonographic characteristics of major salivary glands in anti-centromere antibody-positive primary Sjögren's syndrome : A retrospective case-control study

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Background

To investigate salivary gland ultrasonography (SGUS) findings in primary Sjögren's syndrome (pSS) patients positive for the anti-centromere antibody (ACA) and compare these with those in ACA-negative pSS patients.

Methods

We analyzed demographic, clinical, laboratory, and SGUS data of pSS patients who fulfilled the 2002 American-European Consensus Group, 2012 American College of Rheumatology (ACR) or 2016 ACR/European League Against Rheumatism classification criteria for pSS. SGUS findings of four major salivary glands (bilateral parotid and submandibular glands) were scored in five categories and compared between ACA-positive and ACA-negative pSS patients. Linear regression analysis was performed to elucidate the factors associated with SGUS score.

Results

In total, 116 pSS patients were enrolled (14, ACA-positive). The ACA-positive patients were older (65.1 vs 54.2 years, P = 0.002), whereas anti-Ro/SSA and anti-La/SSB positivity was more prevalent in the ACA-negative group (89.2% vs 21.4%, P < 0.001, and 47.1% vs 7.1%, P = 0.011, respectively). The total SGUS and hypoechoic area scores were lower in ACA-positive patients (13.5 vs 23.0, P = 0.010, and 4.0 vs 7.0, P = 0.007, respectively). In univariate regression analysis, being positive for unstimulated salivary flow rate (USFR < 1.5 ml/15 min), anti-Ro/SSA, and rheumatoid factor were positively associated whereas ACA positivity was negatively associated with the SGUS score. In multivariate regression analysis, being positive for USFR, anti-Ro/SSA, and rheumatoid factor showed significant association with the SGUS score.

Conclusions

ACA-positive pSS patients showed a lower SGUS score than ACA-negative patients, which was especially prominent in the hypoechoic area component.

Keywords

primary Sjögren's syndrome, salivary gland ultrasonography, anti-centromere antibody

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P-112

Sjögren's syndrome initially diagnosed with tubulointerstitial nephritis and thymoma

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Description

A 60-year-old female was referred with acute renal dysfunction. There was no history of arthritis, dry eye syndrome and Raynaud's phenomenon. Antinuclear antibody (Ab) was a cytoplasmic speckled pattern with titer of 1:1280 and rheumatoid factor was 2389 IU/mL. Anti-Ro Ab was 3+, anti-La Ab was 1+, anti mitochondrial Ab was 3+ ; anti-dsDNA Ab, anti-Sm ab, anti-cardiolipin Ab, anti-phospholipid Ab, anti-CCP Ab and ANCA were all negative. The serum IgG level was elevated to 1848 mg/dL (normal range: 700-1,600mg/dL), the levels of C3 was decreased to 51 mg/dL (normal ragne 90-180), and cryglobulin was negative. Renal biopsy showed marked acute immune mediated tubulointerstitial nephritis without significant glomerular immunofluorescence (IF) staining. Positive granular IF staining of immunoglobulins and complements in the interstitium is compatible with immune mediated interstitial nephritis. Minor salivary gland biopsy found focal lymphocytic sialadenitis and focus score of 4 / 4 mm2. After confirmation of pSS with initially diagnosed with TIN, treatment commenced with the prednisolone (1 mg/kg) for 2 weeks; the dose was tapered gradually. Following the renal function was restored, a computed tomography (CT) was performed to check whether other organs were invaded. Chest CT showed about 5x2x3.7 cm sized lobulated well defined poorly enhancing mass in prevascular area of the left anterior mediastinum. It suggested the thymic epithelial tumor such as thymoma. And, although current scientific evidence compiled the various interactions between thymoma and autoimmune diseases, co-exist with pSS is a very rare condition.

Conclusions

The most frequent form of nephropathy of pSS is a monolymphocytic TIN having similarity to the lymphoplasmacytic infiltration of the salivary glands. Although the wide spectrum of clinical manifestations extends from secretory dysfunction to systemic involvement with pSS, it is very uncommon that TIN and thymoma appear as the first clinical features at diagnosis.

Keywords

Sjögren's syndrome, tubulointerstitial nephritis, thymoma

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Autoimmune hepatic involvement in patients with Sjögren's syndrome in Korea : An analysis of single-center, retrospective data

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Background

Sjogren's syndrome (SS) is a chronic autoimmune disease characterized by exocrine glandular dysfunctions mainly presenting as xerostomia and xerophthalmia. Autoimmune-mediated inflammation could involve not only glandular tissues but also other various internal organs. Liver is one of the most important extraglandular organs which could be affected in SS. This study aimed to delineate epidemiology and clinical characteristics of SS patients with hepatic involvement in Korea.

Methods

Clinical information of SS patients who visited the rheumatology department of Seoul St. Mary's hospital, a tertiary referral hospital in Korea, between January 2015 and December 2020 was retrospectively gathered. Subjects with abnormal liver functions potentially originated from other etiologies such as viral hepatitis and steatohepatitis, were excluded in analysis. Demographic data, disease activity markers, laboratory values including autoimmune profiles potentially related to SS, and pathologic information of biopsy, if available, were included as clinical variables.

Results

Of total 1116 patients with SS, 50 subjects presented autoimmune hepatic involvement, which was diagnosed clinically or confirmed by histologic assessment. Among them, 33 patients showed autoimmune hepatitis (AIH), 14 were primary biliary cholangitis (PBC), and three were cases with combined features. All cases with AIH were confirmed by histologic assessment. 42% of patients with liver involvement presented positivity for anti-mitochondrial antibodies. SS patients with autoimmune hepatic involvement were significantly older at the time of diagnosis for SS, and presented lower platelet counts and higher serum prevalence of anti-centromere antibodies compared to patients without.

The severity of inflammatory infiltration in glandular tissues and disease activity scores for SS showed no significant differences.

Conclusions

Some of SS patients could have mainly two types of liver diseases, AIH and PBC, caused by autoimmunity. We shoulder consider liver biopsy in SS patients with elevated liver enzymes suspicious for autoimmune hepatic involvement.

Keywords

Sjogren's syndrome, extraglandular manifestations, Hepatic involvement

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Acute renal failure as the initial presentation of Sjögren's syndrome

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Description

A 52-year-old female presented with generalized weakness, easy fatigability, anorexia, low grade fever along with sudden onset oliguria of 1 month duration. On examination, she had no features of fluid overload, however had hypertension along with oral sicca with no other features of connective tissue disorder. Schirmer's test was positive in B/L (right:3mm, Left:2mm) eyes. Her baseline BUN and creatinine were 75mg/dl and 8.6mg/dl respectively requiring haemodialysis. Her 24 hr urinary protein was 777mg/dl and renal biopsy revealed acute on chronic tubulointerstitial nephritis (Figure 1A,B). USG parotids was normal, ANA/ENA were negative. Minor salivary gland biopsy was consistent with Sjogren's syndrome with a focus score of >1 (Figure 1C,D). She was started on 1mg/kg steroids and showed remarkable improvement with normalisation of creatinine (0.79mg/dl) with clinical improvement over three months; currently on prednisolone 7.5mg/day and doing well.

About 30% of patients with Sjogren's syndrome have renal involvement, typically manifesting as renal tubular acidosis or interstitial nephritis.(1) Most of these cases are mild and often missed initially. Significant renal involvement occurs in about 10% cases mostly as chronic disease not requiring renal replacement therapy. It is one of the diseases which is often misdiagnosed or not thought of initially. Our case also had acute renal failure as first manifestation of disease, highlighting the importance of proper clinical history and evaluation of sicca symptoms. In cases with high index of suspicion despite negative autoantibodies or hypergammaglobinemia, USG parotids or minor salivary gland biopsy should be performed.

Conclusions

Renal involvement may precede sicca symptoms, but Sjogren's syndrome should always be kept in mind.

Keywords

Sjogren syndrome, Acute renal failure, Presentation

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P-115

Disease-specific antigen presentation on MHC class II can be inhibited by small molecules in Sjögren's syndrome

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Background

Sjogren's syndrome (SjS) is an autoimmune disease that possesses a strong genetic linkage. To date, there is no vaccine or therapeutic agent to cure SjS taking the genetic predisposition into account. Patients rely on lifelong therapies to treat symptoms for primary SjS. Human leukocyte antigens (HLA) are one of the primary susceptibility loci that form the genetic basis for many autoimmune diseases including SjS.
In this study, we sought to determine whether blocking I-Ag7 antigen presentation in the NOD mouse would impair the development of SjS by preventing recognition of autoantigens by pathogenic T cells.

Methods

Molecular modeling and Docking, measurement of saliva and tear flow rate, ELISA for detecting the antibodies against Ro52, Ro60 and La, Histological examination of the salivary and lacrimal glands, Immunofluorescent staining for CD3+T cells and B220+B cells, Detection of antinuclear antibodies (ANA) in the sera, Examination of salivary gland T helper cells, cytotoxic T cells and B cells by flow cytometry.

Results

We used two previously identified small molecules, tetraazatricyclo-dodecane (TATD) and 8-Azaguanine, that have been shown to bind to I-Ag7. The results demonstrated that Ro60 autoantigen was predicted to bind to I-Ag7 with high affinity. Treatment of NOD mice with TATD or 8-Azaguanine alleviated SjS symptoms by improving salivary and lacrimal secretory function, decreasing the levels of autoantibodies, reducing the severity of lymphocytic infiltration in the salivary and lacrimal glands.

Conclusions

This study presents a novel therapy method for SjS by identifying small molecules capable of inhibiting T cell response via antigen-specific presentation.

Keywords

Sjogren's syndrome, Human Leukocyte Antigen, Major Histocompatibility Complex

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Increased syndecan-1 expression in the salivary gland of NOD mouse, a model for primary Sjögren's syndrome

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Background

Syndecan-1 (SDC-1), a transmembrane heparin sulfate proteoglycan predominantly expressed on epithelial cells, also exists in a soluble form by ectodomain shedding and expression and shedding of SDC-1 is modulated in the inflammatory milieu. SDC-1 binds to and regulates heparan sulfate-binding molecules, such as chemokines. In this study, we investigated the expression of SDC-1 and homeostatic chemokines in mouse model of primary Sjögren's syndrome (SS) to define the role of SDC-1 in early stage of disease.

Methods

Female NOD/ShiLtJ of 6-week-old and 8-week-old were used. Salivary flow rates (SFRs), histopathologic findings, and chemokines expression were evaluated. SDC-1 levels in submandibular glands (SMGs) and blood were analyzed using dot blot assay.

Results

SFRs between NOD mice and age-matched BL10 mice were similar (6 week, p=0.46; 8 week, p=0.98). Periductal inflammatory foci were observed in the SMGs in 2 of 6 6-week-old NOD mice and in 4 of 6 8-week-old NOD mice. Mean focus scores (FSs) were 0.7 and 5.9 in the 6-week-old and 8-week-old NOD mice, respectively. SDC-1 expression was detected on the surface of ductal epithelial cells and SDC-1 levels of SMGs and plasma were increased in NOD mice (SMG, 6 week, p=0.131, 8 week, p=0.041; plasma, 6 week, p=0.108, 8 week, p=0.031).

SDC-1 levels between SMGs and plasma showed a significant correlation (6 week, r=0.933, p<0.001; 8 week, r=0.867, p=0.001) but SDC-1 levels of SMGs or plasma were not correlated with FSs. Expression of CXCL13 and CXCL12 in SMGs dramatically increased in 6-week-old and 8-week-old NOD mice, compared to controls, while that of IL-7 and CCL21 were not different between two groups. CXCL13 expression was upregulated on the ductal epithelial cells in NOD mice.

Conclusions

These results suggested that increased SDC-1 expression in SMGs plays a role in early inflammatory mechanisms through interaction with inflammatory chemokines in SS.

Keywords

Sjogren's syndrome, Syndecan-1, Chemokine

E-poster Presentation

Systemic sclerosis and Raynaud's phenomenon

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Macrovascular Dysfunction and its Clinical Implication in Systemic Sclerosis

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Background

Microvascular dysfunction is a key and determining feature of scleroderma (SSc). But contrary to earlier belief there is emerging evidence to suggest co-occurrence of macrovascular dysfunction. The clinical implications of macrovascular dysfunction in SSc are unknown and its correlation with microvascular dysfunction is inconclusive [1,2]. Objective of study were - to assess the prevalence and clinical impact of macrovascular dysfunction in a cohort of SSc. To study the correlation between macrovascular dysfunction as assessed by percent change in flow mediated vasodilation (FMD) of brachial artery and microvascular dysfunction as assessed by nail fold capillaroscopy (NFC) findings in

Methods

Cross-sectional comparative study enrolled SSc patients (n=59) and age & gender matched healthy controls (n=64). FMD change was calculated using standard USG probe (6 MHz) in right brachial diameter from the average of 3 consecutive end diastolic frames. NFC was performed using portable nail fold capillary microscope at 800X magnification. Clinical features of SSc were compared between SSc patients with and without macrovascular dysfunction.

Results

SSc had significantly ($p < 0.001$) lower FMD change (median-4.54, IQR 3.13-8.82) compared to healthy controls (median – 10.30, IQR 8.33-13.16). Two out of every three SSc patients 43/59 (66.2%) had impaired FMD. We replicated significantly (p-value< 0.0001) lower capillary density (median – 3.19, IQR 2.38-3.94) in SSc compared to healthy controls (median – 7.56, IQR 7.06-8.0). Impairment in FMD was not associated with Raynaud's phenomenon, digital gangrene, digital ulcer, acro-osteolysis or pulmonary hypertension suggesting need for a prospective study to identify the implications (Table 01). Magnitude of NFC findings and FMD changes did not corelate with the impairment in FMD among SSc patients.

Conclusions

About 2/3rd of patients with SSc have macrovascular complications but their clinical implications may need long term prospective follow up. Macrovascular and microvascular dysfunction appears to be independent of each other in SSc.

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Low trabecular bone score is associated with high C-reactive protein levels in systemic sclerosis

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Background

To evaluate trabecular bone score (TBS) in patients with systemic sclerosis (SSc) and to identify risk factors related to low TBS in SSc.

Methods

TBS and areal bone mineral density (aBMD) were assessed in patients with SSc (n=57), rheumatoid arthritis (RA) (n=47), and hand osteoarthritis (OA) (n=37) using DXA. Osteoporosis risk factors, laboratory findings, SSc-specific organ involvement, and patterns of nailfold capillaroscopy (NFC) were also assessed. Multivariate linear regression analysis was performed to identify the risk factors associated with TBS in SSc patients.

Results

The median TBS (Q1, Q3) value was 1.378 (1.322, 1.425) in SSc patients, 1.336 (1.261, 1.396) for RA patients, and 1.430 (1.387, 1.438) for controls ($p<0.001$). No significant differences were observed in the median lumbar spine TBS and aBMD at the lumbar spine, femoral neck, and total hip between the SSc and RA groups. The TBS was negatively correlated with the erythrocyte sedimentation rate ($p=0.042$) and C-reactive protein (CRP) ($p=0.005$) in the SSc group only and with cumulative glucocorticoid doses in the RA group only ($p=0.031$). We found no association between TBS and SSc cutaneous subtype, internal organ involvement, autoantibody profile, NFC patterns, and use of immunosuppressive agents, such as cyclophosphamide. In the multivariate analyses, age, female sex, current, and average CRP were significantly associated with TBS.

Conclusions

TBS assessment revealed poor bone quality in patients with SSc, similar to those with RA. CRP levels were negatively correlated with TBS in patients with SSc, and higher CRP levels were independently associated with low TBS.

Keywords

Systemic sclerosis, Osteoporosis, Inflammation

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A refractory case of juvenile systemic sclerosis with myocardial dysfunction

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Description

We report a case of juvenile systemic sclerosis (JSSc) with stormy clinical course and myocardial dysfunction. Index child was symptomatic from the age of 7 years with progressive skin tightening and difficulty in getting up from sitting posture (due to stiffness of lower limbs). There was associated polyarthritis and Raynaud phenomenon. Clinical examination showed diffuse skin thickening with modified Rodnan score of 38. Investigations revealed positive antinuclear antibodies (ANA) and positive anti Scl70 antibodies. The child also had esophageal involvement in the form dilated distal esophagus on computed tomography (CT) of chest. So, the child was diagnosed as juvenile systemic sclerosis and was administered tapering doses of oral prednisolone (starting dose-1 mg/kg/day), nifedipine, hydroxychloroquin and weekly subcutaneous methotrexate (15 mg/m2).

In the next 5 years, child had worsened with features of interstitial lung disease and pulmonary arterial hypertension resulting in administration of 9 pulses of inj cyclophosphamide. Mycophenolate mofetil and sildenafil were given as maintenance therapy. Subsequently, the child developed severe dyspnea. High resolution CT chest showed progressive interstitial lung disease. There was evidence of myocardial dysfunction like elevated pro-BNP and troponin, and 2D echocardiography showing decreased ejection fraction with left ventricular dysfunction. In view of severity, 2 doses of rituximab (500mg/m2) were given at an interval of 2 weeks. At 2 months follow-up, child is doing well with no further worsening.

Conclusions

Juvenile systemic sclerosis is a disease with variable prognosis. Sometimes, it can be aggressive and refractory to initial lines of treatment as in our case. [1] Therefore, timely diagnosis and aggressive multidisciplinary treatment are required. Biologics like rituximab may be useful in refractory cases. [1]

Keywords

juvenile systemic sclerosis, myocardial dysfunction, rituximab

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Establishment of a humanized animal model for systemic sclerosis by injection of human peripheral blood leukocytes from patients with systemic sclerosis

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Background

Systemic sclerosis (SSc) is a chronic autoimmune disease characterized by inflammation, microangiopathy, and progressive fibrosis in skin and other internal organs. In order to understand pathophysiologic mechanisms, and evaluate efficacies of potential therapeutics for SSc, a pre-clinical model recapitulating the disease phenotypes properly is in need. Here, we introduce a new mouse model for SSc using immunodeficient mice injected with peripheral blood mononuclear cells (PBMCs) from SSc patients.

Methods

Human PBMCs isolated from SSc patients or healthy controls were transferred into eight-week old NSG mice (5.0 x 10^6 cells per mouse). After 4 weeks from injection, blood, skin, and lung tissues from each NSG mouse were acquired and evaluated about human immune cells engraftment and SSc-mimicking pathologies. In addition, it was also investigated whether compound x could suppress pathologic fibrosis of skin and lung in this humanized murine model.

Results

Human PBMCs, especially CD4+ and CD8+ T cells and B cells, from SSc patients and healthy controls were well engrafted in NSG mice according to the results of flow cytometric analysis. Histopathologic staining results of skin and lung tissues showed significant inflammation and fibrosis combined with human immune cells infiltration in humanized mice injected by PBMCs from SSc patients than controls. Inflammatory and pro-fibrotic cytokines and chemokines such as IL-17, TGF-β, CCL2, CCL3, and CXCL9 were highly expressed in skin and lung tissues from SSc PBMCs-engrafted NSG mice. Treatment with compound x significantly reduced tissue fibrosis in this murine model for SSc.

Conclusions

The present study suggests that humanized mice induced by injection of PBMCs from SSc patients could be a novel animal model for SSc.

Keywords

Systemic sclerosis, animal model, peripheral blood leukocytes

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Butyrate ameliorates skin and lung fibrosis in bleomycin-induced fibrotic mouse models

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Background

Systemic sclerosis (SSc) is an autoimmune rheumatic disease characterized by vasculopathy, inflammation, and fibrosis in the skin and internal organs. Recent studies have showed the potential of gut microbiota in autoimmune diseases. Intestinal dysbiosis, such as reduction of butyrate-producing bacteria has been observed in SSc patients. Since evidences suggest a relationship between SSc and gut microbiota, we investigated the therapeutic effects of sodium butyrate (SB) on skin and lung fibrosis using a bleomycin-induced fibrosis mouse model and human dermal fibroblasts (HDFs).

Methods

Bleomycin (BLM) was injected subcutaneously or intratracheally to mice for induction of skin or lung fibrosis. Sodium butyrate (SB) was orally administered five times a week over four weeks starting from two weeks before BLM injection. Histological and molecular fibrotic changes were evaluated in skin and lung tissues. Bacterial 16S rRNA sequencing and flow cytometric analysis was performed to analyze fecal microbiota composition and immune cell population of mesenteric lymph node (MLN), spleen, and bronchoalveolar lavage (BAL) fluid. TGF (transforming growth factor)-β1-stimulated expression of profibrotic mediators and H3 acetylation were investigated in HDFs.

Results

SB attenuated bleomycin-induced skin and lung fibrosis in mouse by preventing myofibroblast differentiation. SB supplementation influenced fecal microbiota composition altered in BLM-induced fibrosis mice. Infiltration of inflammatory monocyte or macrophage differentiation was inhibited by SB in MLN, spleen, skin, and BAL fluid of BLM-induced skin fibrosis model. SB prevented upregulation of profibrotic/proinflammatory gene expression in BLM-treated skin. Furthermore, SB suppressed TGF-β1-induced fibrotic responses with increased acetylation of histone 3 in HDFs.

Conclusions

Sodium butyrate attenuated dermal and pulmonary fibrosis by suppressing proinflammation in SSc mouse model. Butyrate may exhibit anti-fibrogenic efficacy on fibroblasts through regulation of macrophage differentiation and inhibition of histone deacetylase 3. SB is considered as a potential candidate for SSc treatment.

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Development of digital ulcers on fingertips of patient with systemic sclerosis after capillary glucometer monitoring

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Description

A 66-year-old woman was consulted for the abnormal findings of the autoantibody profile during admission to the neurology department. The ANA titer was 1:1280, and anti-centromere antibody was 63 U/ml, and other antibody titers were within the normal range. She has a history of Raynaud's phenomenon and physical examination showed early ulcers on several fingertips and cyanosis of the distal tip of the right fingers with diminished capillary refill and exquisite tenderness to palpation. Nailfold capillaroscopy revealed giant capillaries and avascular areas. The diagnosis of limited cutaneous systemic sclerosis was established through her lab findings and clinical manifestation. She complained of pain in the fingertips of the right hand which showed early ulceration. The early ulceration of her fingertips and color changes were presented after the serial capillary glucometer monitoring. After the occurrence of the ulceration, the capillary glucometer monitoring was stopped. She was prescribed medications including sufficient analgesia, vasodilator therapy, and topical antibiotics. However, her digital ulceration of the 4th and 5th finger got aggravated by tissue necrosis, and she undertook surgical amputation due to intractable pain.

Conclusions

The development of digital vascular disease in SSc is believed to be multifactorial and mechanical factors such as microtrauma and increased skin tension can initiate and promote ulceration in the silent phase of digital ulcer development. Therefore, it is required for the clinicians to be aware of the possibility of the development of digital ulceration initiated by microtrauma such as capillary glucometer monitoring in systemic sclerosis and to educate patients regarding the importance of avoiding trauma to digits.

Keywords

Systemic sclerosis, Digital ulcers, Capillary glucometer monitoring

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P-123

Significance of antineutrophil cytoplasmic antibody positivity in patients with systemic sclerosis : A single-centre pilot study in Korea

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Background

We investigated whether antineutrophil cytoplasmic antibody (ANCA) positivity at diagnosis may be associated with the cross-sectional clinical features at diagnosis and predicting all-cause mortality during follow-up in Korean patients with systemic sclerosis (SSc). In addition, we assessed the incidence of SSc and ANCA-associated vasculitis (AAV) overlap syndrome in patients with ANCA positivity.

Methods

We retrospectively reviewed the clinical and laboratory features through the medical records of 177 SSc patients who fulfilled the inclusion and exclusion criteria. SSc was classified by the 2013 American College of Rheumatology/European League Against Rheumatism classification criteria. AAV was classified by the 2007 European Medicine Agency algorithms and the 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides.

Results

The median age was 52 years, and 23 patients were males. The detection rate of ANCA in Korean patients with SSc was 20.3%. Unlike a previous study, ANCA positivity at diagnosis was significantly associated with neither the cross-sectional clinical and laboratory variables at diagnosis nor the rate of all-cause mortality during follow-up in Korean patients with SSc. However, three female patients (8.3%) with ANCA could be classified as having microscopic polyangiitis (MPA) during follow-up.

Conclusions

No significant associations of ANCA positivity with the crosssection clinical features or all-cause mortality during follow-up were observed in this study. But, given that 3 of 36 SSc patients with ANCA were classified as having AAV based on the histological confirmation, we suggest that physicians should consider recommending a biopsy when AAV is strongly suspected in SSc patients with ANCA.

Keywords

antineutrophil cytoplasmic antibody, systemic sclerosis

E-poster Presentation

Miscellaneous rheumatic and inflammatory diseases

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Impact of hospitalization on clinical outcomes in patients with connective tissue disease associated interstitial lung disease (CTD-ILD)- A single center observational study

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Background

Interstitial lung disease (ILD) is major cause of morbidity and mortality in patients with connective tissue disease (CTD).The objective of our study was to assess the impact of hospitalization on clinical outcomes in patients with CTD-ILD.

Methods

We conducted a retrospective chart review of patients with CTD-ILD who were seen at Montefiore Medical Center between January 2007 and December 2018. Patients with age>18 years who had either 2 CT scans of the chest and/or 2 sets of pulmonary function tests (PFT) atleast 6 months apart were included in the study. Clinical demographics, cause of hospitalization, length of hospital stay and mortality were identified. Patients were stratified into 2 cohorts; non-hospitalized and hospitalized patients. The latter cohort was further sub-stratified into patients with cardiopulmonary vs. non-cardiopulmonary hospitalization. Kaplan-Meier method was used for calculating the survival probabilities, and log-rank tests were used to compare differences between the groups.

Results

213 patients were identified but only 96 met our inclusion criteria. Both groups were similar in baseline clinical characteristics but transplant referrals were significantly higher in the hospitalized group(23.9%) vs. non-hospitalized group(0%)(Table 1). Seventy-three patients(76%) had at least 1 hospitalization with 51 patients(70%) admitted with cardiopulmonary issues. Median time from diagnosis of ILD to first hospitalization was 1.42 years.

The patients hospitalized for cardiopulmonary cause were significantly older(Mean+SD)(57.2 +13.1 years) than those admitted with non-cardiopulmonary cause(Mean+SD)(49.2+14.8 years). Older age (HR 1.95, p=0.02) and length of stay greater than 7 days for cardiopulmonary cause(HR 4.82,p=0.01) was associated with higher risk of mortality.

Kaplan Meier curve analysis showed that hospitalization (p-value=0.02) was associated with statistically significant increased risk of death.

Conclusions

-Hospitalization in CTD-ILD patients especially length of stay more than 7 days due to cardiopulmonary causes was associated with statistically significant increased risk of death.

Keywords

Connective tissue disease, Interstitial lung disease, Clinical outcomes

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Risk of hepatitis B virus reactivation according to the timing of starting anti-viral agents in patients receving biologics

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Background

Patients with hepatitis B virus (HBV) infection have a high risk of HBV reactivation. Therefore, prophylactic antiviral therapy is required for patients receiving biologics. However, it is not clear when biologics should be started after antiviral prophylaxis. We investigated the risk of HBV reactivation according to the timing of biologics initiation after anti-HBV prophylaxis in Immune-Mediated Inflammatory Disease (IMID) patients with HBV infection.

Methods

We retrospectively evaluated the incidence of HBV reactivation in IMID patients who received biologics between July 2005 and April 2020. The patients were divided into two groups ("within 1-week " vs. "after 1-week") according to when biologics were initiated after anti-HBV treatment. We evaluated the cumulative probabilities and factors associated with HBV reactivation.

Results

A total of 60 hepatitis B surface antigen-positive patients with IMID received biologics (within 1-week group, n = 23 [38%]; after 1-week group, n = 37 [62%]). During a median follow-up of 34 months (interquartile range, 20–74), three (5%) patients developed HBV reactivation. In the univariate analysis, the timing of biologics after HBV prophylaxis was not significantly associated with the risk of HBV reactivation (hazard ratio, 0.657; 95% confidence interval, 0.059–7.327; p = 0.733). The cumulative probabilities of HBV reactivation did not significantly differ according to the timing of biologics as well (p = 0.731).

Conclusions

The risk of HBV reactivation was not significantly associated with the timing of biologics administration after anti-HBV prophylaxis. Therefore, biologics can be started early in IMID patients who are being treated for HBV.

Keywords

Hepatitis B virus, Biologics, Immune-mediated inflammatory disease

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Macrophage activation syndrome in rheumatic disease : Clinical characteristics and prognosis of 20 patients

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Background

Macrophage activation syndrome (MAS) is a hyperinflammatory condition that is known to be secondary hemophagocytic lymphohistiocytosis (HLH) in patients with rheumatic disease. The aim of study was to evaluate the clinical manifestations and outcomes in patients with MAS with rheumatic disease.

Methods

We performed a retrospective study of 20 adult patients who were diagnosed with MAS from 2012 to 2020. MAS was classified according to the HLH-2004 criteria. Patients' information, including clinical features, laboratory findings, and treatment regimens, was collected, and the overall survival rate was estimated by the Kaplan–Meier method.

Results

Twenty patients (18 women, 35.6 ± 18.3 years) who met the HLH-2004 criteria also fulfilled the 2016 EULAR/ACR/PRINTO classification criteria for MAS, and HScore was higher than 169 (median, 238.5). Fourteen patients with systemic lupus erythematosus and 6 patients with adult-onset Still's disease were included. All patients were treated initially with corticosteroids, and 16 patients required additional immunosuppressants. The overall survival at 3 and 6 months was 75.2% and 64.3%. In survivors, renal impairment was less common (23.1% versus 42.9%, p = 0.007), the levels of AST (202.0 versus 72.0 IU/L, p = 0.006) and LDH (1144.0 versus 343.0IU/L, p = 0.001), and platelet count (90.0 versus 46.0 × 109/L, p = 0.016) were higher in compared to non-survivors. Nine patients had opportunistic infections, five of whom died during admission.

Conclusions

The mortality of patients with MAS remains high. Renal impairment, levels of AST and LDH, and platelet count might be associated with prognosis.

Keywords

macrophage activation syndrome, systemic lupus erythematosus, adult-onset Still's disease

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Involvement of white matter fiber tracts in patients with seropositive inflammatory arthritis in magnetic resonance diffusion tensor tractography

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Background

White matter involvement can be encountered in patients with seropositive arthritis and, detection of white matter lesions in magnetic resonance imaging (MRI) is crucial for the identification of the affection of the central nervous system (1). MR tractography is used for the estimation of the major fiber tracts in the brain using anisotropic diffusion. In this study, our goal is to delineate the distribution of white matter lesions of patients with seropositive arthritis on the basis of fiber tracts in the cerebral white matter.

Methods

57 patients with a diagnosis of seropositive inflammatory arthritis (n= 23 for SLE, n= 21 for RA, n=4 for Sjogren's, n=6 for vasculitis, and n=3 for scleroderma) were underwent brain MRI imaging with tensor tractography between 2019 and 2021. Lesions detected in conventional MR images were matched with the fiber tracts using MRIcroGL (https://www.nitrc.org/projects/mricrogl). Involvement of the fiber tract along with the imaging findings of the white matter lesion was recorded on a lesion basis.

Results

Of the 57 patients, 39 were female (68.4%), and the mean age of the study population was 43.4 ± 8.6 years. A total of 295 white matter lesions were detected in MR imaging. 57 lesions (21.2%) were showed enhancement after contrast administration. Majority of the lesions were localized in the superior longitudinal fasciculus (n= 124, 42.0%) followed by arcuate fasciculus (n=85,28.8%) and cingulum (n= 56, 19.0%). Lesser lesion accumulation was observed in corpus callosum (n=16, 5.4%), internal capsule (n=8, 2.8%) and optic radiations (n=6, 2%).

Conclusions

Our results showed that lesion accumulation due to seropositive arthritis in the brain involves major fiber tracts in the cerebral white matter. Identification of specific tract involvement of this disease spectrum may improve our understanding of specific or non-specific neurological symptoms of the patients.

Keywords

Magnetic Resonance Tractography, Seropositive arthritis, White matter

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Combined pulmonary fibrosis and emphysema syndrome in interstitial pneumonia with autoimmune features : A case report and literature review

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Description

Combined pulmonary fibrosis and emphysema (CPFE) is a novel entity characterized with the coexistence of upper lobe emphysema, lower lobe fibrosis, and abnormalities of gas exchange. CPFE associated pulmonary arterial hypertension contributes to high mortality and morbidity. Cigarettes smoking has been identified as an independent risk for CPFE. Additionally, increasing evidence, mostly from rheumatoid arthritis and systemic sclerosis, indicated that immune dysregulation and inflammation play an important role in the pathogenesis of connective tissue disease related CPFE. Herein, we describe a patient diagnosed with interstitial pneumonia with autoimmune features (IPAF) complicated CPFE.

Conclusions

Although little is know about the relationship between IPAF and CPFE, our case indicates that IPAF might be an underlying condition in patient with CPFE.

Keywords

Combined pulmonary fibrosis and emphysema, Interstitial pneumonia with autoimmune features, Pulmonary arterial hypertension

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Performance of the 2019 ACR/EULAR classification criteria for IgG4-related disease in Seoul St. Mary's hospital cohort

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Background

Immunoglobulin G4-related disease (IgG4-RD) is a chronic inflammatory condition characterized by tissue infiltration of lymphocytes and IgG4-secreting plasma cells, various degrees of fibrosis (scarring) and a usually prompt response to oral steroids. IgG4-RD mimics malignant, infectious, and inflammatory disorders, and can affect the lacrimal glands, orbits, major salivary glands, pancreas, bile ducts, retro-peritoneum, lungs, kidneys, aorta, pachy-meninges and thyroid gland. So early detection is important to avoid wrong diagnosis, organ damage, and potentially serious complications. Finally, ACR/EULAR classification criteria for IgG4-RD have been developed and validated in a large cohort of patients in 2019.

Methods

To confirm the rate of agreement between the comprehensive criteria and the 2019 ACR/EULAR criteria, 27 patients with definitive IgG4-RD according to the comprehensive criteria were applied the 2019 ACR/EULAR criteria and their medical records were reviewed retrospectively. Our retrospective cohort study was anonymized information from all patients in the Seoul St. Mary's hospital clinical administrative database who were 18 years of age or older since 2010.

Results

Finally, 4 of 27 definite IgG4-RD patients (14.8 %) were not reclassified as IgG4-RD patients according to the 2019 ACR/EULAR criteria. So compared with our data, the threshold of 20 points had a sensitivity of 85.2%. The 4 cases did not fulfill the classification criteria. Although serum IgG4 concentration level was high, they could not get any points in immunostaining, so they did not get more than 20 points. The four patients were clinically diagnosed with IgG4-RD and were treated with steroids and improved.

Conclusions

According to the IgG4-RD criteria, some patients with clinical diagnoses of IgG4-RD will not fulfill these ACR / EULAR classification criteria. So if the appropriate clinical diagnosis for the patient is IgG4-RD, the patient's condition should be managed accordingly, even if the ACR / EULAR classification criteria are not met.

Keywords

IgG4-RD, ACR / EULAR classification criteria

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A case with immunoglobulin G4 related hypertrophic pachymeningitis mimicking brain tumor

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Description

63 male with right frontal scalp mass visited to neurosurgery department. Brain magnetic resonance imaging (MRI) revealed 1.5 cm enhancing mass with adjacent subgaleal tissue thickening/enhancement and bony destruction in the right frontal area. Dural thickening/enhancement and leptomeningeal enhancement along the right cerebral convexity were shown. Differential diagnosis recommended for malignant bone tumor or bone metastasis with combined pachymeningeal and leptomeningeal metastasis. Operation was done for diagnose and remove mass. Biopsy showed hypertrophic pachymeningitis with marked lymphoplasmacytic, neutrophilic and histiocytic infiltration, dense fibrosis, destruction of skull. There were increased Immunoglobulin G4 (IgG4)-positive cells (up to 68/HPF). Consultation to rheumatology was done and patient was transferred to rheumatology department for further workup and management. He had dry eye and hearing difficulty on both ears for several years. However, there was no further immunoglobulin infiltration in other organ systems. Plasma IgG was 1094.4 mg/dL (680-1620) and IgG4 testing 9.6 mg/dL (3.9-86.4). Antinuclear antibody, antineutrophil cytoplasmic antibody, rheumatoid factor, anti-cyclic citrullinated peptide, angiotensin converting enzyme level were all normal. Erythrocyte sedimentation rate (ESR) and C- reactive protein (CRP) were 13 mm/hr (0-10) and 1.5 mg/dL (0-0.5) respectively before the operation, and they decreased to 0.68 mm/hr, and 0.06 mg/dL at the 4 days after operation (POD 4). Although naproxen and antibiotics had been done after operation, they increased 21 mm/hr and 3.99 mg/dL at the consultation day. ESR and CRP decreased dramatically just one day after starting prednisolone (0.5 mg/kg). They became to be normalized at the 5 days after steroid therapy. Now we are tapering oral prednisolone. Followed-up brain MRI finding was no mass redeveloped except mild dural thickening/enhancement along the right convexity.

Conclusions

Here we report a case with IgG4 related- hypertrophic pachymeningitis mimicking brain tumor, which was successfully treated with oral steroid.

Keywords

Immunoglobulin G4, Pachymeningitis, Tumor

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Soluble programmed death-1 is a useful indicator for mortality in patients with adult-onset still's disease

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Background

Adult-onset Still's disease (AOSD) is a systemic inflammatory disease, characterized by fever with an evanescent rash, arthritis, sore throat, organomegaly, leukocytosis and an elevated serum ferritin level, and can sometimes be fatal. Currently, there are no validated biomarkers of AOSD available for predicting prognosis. Soluble form of programmed death-1 (sPD-1), which can be shed from activated T cells, plays an important role in a variety of autoimmune diseases. However, the clinical significance of sPD-1 has not been explored yet in AOSD. This study aimed to evaluate the correlation with disease activity and prognostic values of sPD-1 in AOSD.

Methods

Serum levels of sPD-1 were measured by enzyme-linked immunosorbent assays in 69 patients with AOSD and 33 age- and sex- matched healthy controls. Comprehensive disease activity of AOSD was determined by a modified Pouchot score. To identify factors associated with mortality, the Cox proportional hazard model was performed.

Results

The serum levels of sPD-1 did not differ between AOSD patients and healthy control and between active AOSD and inactive AOSD. The levels of sPD-1 did not correlate with markers reflecting disease activity such as erythrocyte sedimentation rate, C-reactive protein, lactate dehydrogenase, ferritin, and the modified Pouchot score. sPD-1 values were significantly higher in the non-survivors than in survivors (p=0.047). Upon univariate analyses, fever (p=0.046), elevated liver enzymes (p=0.034), the highest quartile of sPD-1 (p=<0.01), and ferritin level > 3000 μg/l (p=0.026) were identified as associated factors responsible for the death. In the multivariate Cox hazard model analysis, the highest quartile of sPD-1 was an only independent risk factor for mortality (HR 14.818, p=0.026, 95% CI 1.68-130.19)

Conclusions

Our findings suggest that sPD-1 level could be used as a biomarker for predictor of mortality rather than disease activity in AOSD.

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Clinical pattern and risk factors of IgG4-RD patients with new organ involvement onset : A study of 125 relapsed IgG4-RD patients in up to 10 years follow-up

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Background

High frequency of relapse is a critical characteristic for IgG4-related disease (IgG4-RD). According to the types of involved organs at relapse, the relapse patterns were divided into recurrent organ involvement (ROI) and new organ onset (NOI). The aim of this study is to investigate the difference in clinical relapse patterns and find risk factors of patients with NOI.

Methods

We retrospectively enrolled 125 patients from a prospective IgG4-RD cohort, who suffered a relapse during follow-up. Patients were classified into two groups: with NOI (including NOI and NOI+ROI) and without NOI (ROI). We compared the demographic features, clinical manifestations, organ involvement, laboratory tests and treatment outcomes between two groups. The most common organs of ROI and NOI also be defined. Univariate and multivariate logistics regression analyses were used to assess risk factors for NOI.

Results

There were 81(64.8%) and 44 (35.2%) patients in without NOI and with NOI. Patients without NOI showed a higher frequency of allergy history, IgG4-RD responder index, IgG and IgG4, lower levels of C3 and C4 at baseline. The most common ROI were lacrimal gland and submandibular gland, while lung and urinary system were most involved in NOI. Serum IgG4 re-elevated to 74.31% of baseline was associated with NOI relapse. Experienced multiple relapses and only involvement of superficial organs at baseline were independent risk factors for NOI, conversely, receiving GC combines IM treatment in maintenance period was an independent protective factor for NOI.

Conclusions

About one-third of IgG4-RD relapse patients suffer from NOI. Lung and kidney are the most common new organs of IgG4-RD. Serum IgG4 re-elevated to 74.31% of baseline, superficial organ involvement and experienced multiple relapses were associated with NOI. To avoid NOI, GC and IM combined treatment at maintenance is recommended.

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Risk of metabolic syndrome and its components in fibromyalgia

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Background

Fibromyalgia is a chronic widespread pain syndrome that accompanies chronic fatigue and sleep disturbance. Patients of fibromyalgia experience lack of activity due to physical pain and fatigue, which can lead to weight gain and cardiovascular complications. The purpose of this study is to confirm the association of metabolic syndrome in patients with fibromyalgia.

Methods

This study was conducted at a single institution from January 1, 2018 to March 2020. Based on the 1990 American College of Rheumatology classification criteria, 49 women diagnosed with fibromyalgia and 143 women without inflammatory diseases were enrolled. Metabolic syndrome was confirmed by measurement of BMI, waist circumference, triglyceride, cholesterol, fasting blood glucose and blood pressure based on the NCEP-ATP III presented in 2001. The association between fibromyalgia and metabolic syndrome was confirmed using multivariable-adjusted logistic analysis that adjusted for age, alcohol consumption, smoking status, and C-reactive protein(CRP) level.

Results

The odds ratio for waist circumference satisfying the criteria for metabolic syndrome in fibromyalgia patients was 2.99 (p-value 0.002), and the odds ratio for hypertension was 1.50 (p-value 0.238). The odds ratio for triglycerides was 2.95 (p-value 0.005), the odds ratio for low HDL was 1.77 (p-value 0.137), and the odds ratio for fasting glucose was 4.47 (p-value <0.001). The odds ratio of fibromyalgia patients corresponding to metabolic syndrome, which can be diagnosed when three or more of the metabolic syndrome factors is met, was 3.16 (p-value 0.002). This association was also significant in the adjusted analysis of alcohol consumption, smoking and log-transformed crp.

Conclusions

The patients with fibromyalgia had a higher risk of metabolic syndrome and its components. Strategies for managing components of metabolic syndrome in patients with fibromyalgia should be accompanied.

Keywords

fibromyalgia, metabolic syndrome

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Serum B cell activating factor and lung ultrasound B-lines in connective tissue disease related interstitial lung disease

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Background

To investigate the role of serum B cell activating factor (BAFF) and lung ultrasound (LUS) B-lines in connective tissue disease related interstitial lung disease (CTD-ILD), and their association with ILD phenotypes.

Methods

We measured the levels of BAFF and Krebs von den Lungen-6 Antigen (KL-6) in the sera of 66 CTD-ILD patients [22 in the fibrotic ILD (F-ILD) group and 44 in the non-fibrotic ILD (NF-ILD) group), 36 CTD patients without ILD (non-ILD group), and 26 healthy controls, using the ELISA method. All patients underwent chest high resolution computed tomography (HRCT) and LUS (independently performed within 1 week) examination. To assess severity and extent of ILD at HRCT, the Warrick score was used. The B-lines score denoting the extension of ILD was calculated by summing the number of B-lines on a total of 50 scanning sites. The correlation among serum BAFF levels, KL-6 levels, Warrick score, and B-lines number was analyzed.

Results

Serum levels of BAFF were significantly higher in CTD-ILD patients compared to healthy subjects ($p<0.01$). In patients with CTD-ILD, BAFF concentrations was significantly correlated with B-lines number ($r=0.33$, $p<0.01$) and Warrick score ($r=0.44$, $p<0.01$). A positive correlation between B-lines number and the Warrick score ($r=0.67$, $p<0.01$), and KL-6 levels ($r=0.47$, $p<0.01$) was confirmed. Subgroup analysis showed that patients with F-ILD higher BAFF concentrations ($p<0.05$), KL-6 levels ($p<0.05$), B-lines numbers ($p<0.01$), and Warrick score ($p<0.01$) compared to patients with NF-ILD.

Conclusions

Our findings indicated that BAFF and LUS B-lines could be useful biomarkers for detecting and evaluating the severity of CTD-ILD. In the future, combining serological and sonographic biomarkers should play an important role in screening, assessing, and follow-up of CTD-ILD.

Keywords

B cell activating factor, lung ultrasound, connective tissue diseases related interstitial lung disease

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Risk of serious infection in patients with rheumatic diseases exposed to prolonged high-dose glucocorticoids

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Background

To investigate the incidence and risk factors of serious infection in patients with rheumatic disease receiving prolonged high dose steroid treatment.

Methods

This retrospective study included 1,696 rheumatic disease patients who received high-dose steroid treatment (≥ 30 mg/day of prednisolone or equivalent dose) more than 4 weeks between 2004 and 2019. The primary outcome was 1-year incidence of serious infection after exposure to prolonged, high-dose steroids. Serious infections were defined as those led to hospitalization. Incidence rate of the primary outcome was analyzed according to the underlying rheumatic diseases. Risk factors for serious infection were investigated using Cox proportional hazard regression analysis.

Results

During a 1681.4 person-years (PYs), 195 (11.5%) patients developed serious infection with an incidence rate of 11.6 (95% CI 10.1 to 13.3) per 100 person-years. Among the individual rheumatic diseases, ANCA-associated vasculitis (IR 21.0 per 100 PYs, 95% CI 15.1 to 28.6) showed the highest incidence rate. In the multivariate analysis, older age (> 65 years) (adjusted HR 1.92, 95% CI 1.34 to 2.75), baseline lymphopenia (aHR 1.68, 95% CI 1.23 to 2.28), baseline azotemia (aHR 2.18, 95% CI 1.55 to 3.05), and concomitant cyclophosphamide pulse therapy (HR 1.55, 95% CI 1.01 to 2.37) were significantly associated with the development of serious infection. Initial steroid dosage at baseline, concomitant steroid pulse therapy, and other immunosuppressive agents such as calcineurin inhibitors, mycophenolate mofetil, methotrexate, and azathioprine were not significantly associated with the outcome.

Conclusions

More than 10% of patients with rheumatic diseases receiving prolonged, high-dose steroids experience serious infection within 1-year of the treatment. Old age, lymphopenia, azotemia, concomitant cyclophosphamide pulse therapy further increased the risk.

Keywords

Steroid, Infection, Rheumatic disease

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Risk factors of acute rheumatic fever

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Background

It is proven nowadays that occurrence of Acute Rheumatic Fever (ARF) and its relapses are associated with Group A ß-hemolytic streptococcus (GAS). Currently the group of ARF risk factors includes diffuse connective tissue diseases, as well as congenital inferiority of connective tissue in the family, i.e., first-degree relatives, family; heart connective tissue dysplasia (HCTD); female gender.

Methods

We have studied the influence of various factors on ARF development risk, which was evaluated by the odds ratio (OR) with calculation of 95% confidence interval (CI), i.e., in respect of events (i.e., presence / absence of risk factor) in the groups of patients with/without ARF. At the same time, based on the results of collected history data of patients, it found out that acute rheumatic fever occurred predominantly in the age periods of 6- 25 years.

Results

In presence of HCTD, the ARF risk was increasing by more than 8 times (OR- 8,2; 95% CI 4,1-60,4; p <0,005). As the results of our research prove, tonsillopharyngitis was associated with almost 6-fold increase in RF risk (OR – 5,8; 95% CI 3,26-10,33; p <0,01). Important role in RF development was played by the presence of chronic foci of infection (sinusitis, otitis), the detection of which increased the risk of rheumatic fever (RF) by 1,92 times (OR -1,92; 95% CI 1,18-3 24; p <0,05). Women are more than 1.5 times more likely to get sick with rheumatic fever versus (OR 1.55; 95% CI 1,05-2,47; p <0,05). Influence of family history of RHD did not show a significant impact on RF risk in the studied patients (p> 0,05).

Conclusions

The highest increase in ARF risk noted in patients with the HCTD syndrome.

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A case of hyper-immunoglobulin E syndromes mistaken for IgG4-related disease

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Description

Hyper-immunoglobulin E syndrome (HIES) is a primary immunodeficiency disease, characterized by eczemoid dermatitis, recurrent bacterial infection and elevated IgE levels. IgG4 related disease (IgG4-RD) is systemic disease, which causes fibroinflammatory lesions involving multi organs. Here, we report a case of 32 year old woman who thought to have an IgG4-related disease, but was finally diagnosed with HIES. Seven years ago, she had a tongue mass, which excisional biopsy pathology revealed an IgG4 count of 156/HPF and IgG4/IgG Ratio 44%, and she was diagnosed with IgG4-RD, initially. However, she did not demonstrate typical organ involvement (major salivary glands, pancreas, biliary tree, the kidneys, the aorta and retroperitoneum), and thereafter she had recurrent multiple lymph nodes (LNs) enlargements in neck, supraclavicular fossa, subcarina, and right external iliac area. We obtained multiple LN biopsy pathologies from neck, supraclavicular fossa, and subcarina, which showed increased number of IgG4 count (up to 157/HPF) and elevated IgG4/IgG ratio (74.8%). However, the patient's pathology was done mostly on LNs, which must be cautious to conclude the disease as IgG4 RD and the patient did not demonstrate typical organ involvement of IgG4 RD. Furthermore, subsequently, she presented with right lower leg pain, which confirmed as Intramuscular abscess, and underwent incision and drainage. Since the patient had atypical manifestations, we performed next generation sequencing (NGS), which showed pathologic mutation on STAT3, which is the HEIS' genetic mutation. While waiting for the results of the NGS results, she had ICU care due to severe pneumonia requiring mechanical ventilation, and her serum IgE level was > 5000. Based on the history of recurrent infections, STAT3 mutation, and elevated serum IgE level, she was finally diagnosed with HIES.

Conclusions

Typical organ involvement and specific pathologic findings are essential to diagnose IgG4-RD, and elevated IgG4 count in LN requires special caution.

Keywords

IgG4-realted disease, Hyper-immunoglobulin E syndrome

E-poster Presentation

Epidemiology & Public health
COVID-19 & Rheumatic diseases

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Impact of lifestyle and comorbidities on seropositive rheumatoid arthritis and ankylosing spondylitis risk from Korean health insurance data

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Background

Rheumatoid arthritis (RA) and ankylosing spondylitis (AS) are forms of systemic inflammatory arthritis in which primary prevention is key. However, the impact of lifestyle and comorbidities on their development is unknown.

Methods

Data from the Korean National Health Insurance Service (NHIS)-national sample cohort from 2002 to 2016 were used. At baseline, demographic characteristics, socioeconomic status, type of residential area, lifestyle behaviours (including exercise), and comorbidities (including the Charlson Comorbidity Index, CCI) were included. Cox regression analysis and Kaplan–Meier curves were used to evaluate the impact of lifestyle and comorbidities on disease occurrence.

Results

A total of 517,053 and 515,347 participants were included in the analysis for seropositive RA and AS occurrence, respectively. Seropositive RA was diagnosed in 1,948 participants (0.37%), and AS in 4,455 participants (0.86%), during follow-up. Cox regression analysis revealed that being aged between 40 and 79, a higher CCI, and hyperlipidaemia resulted in elevated hazard ratios (HRs) for RA, whereas male gender, city residence, moderate alcohol consumption, high regular exercise and a BMI between 23 and 34.9 kg/m2 resulted in lower HRs. For AS, being over 50 years old, a higher CCI, diabetes mellitus, hypertension and hyperlipidaemia resulted in elevated HRs, whereas city residence, moderate alcohol consumption and any intensity of regular exercise resulted in lower HRs.

Conclusions

Using Korean NHIS data, the present study demonstrates that regular physical exercise and moderate alcohol consumption resulted in decreased risk of seropositive RA and AS occurrence, which are modifiable lifestyle habits that could aid the primary prevention of seropositive RA and AS.

Keywords

Rheumatoid arthritis, ankylosing spondylitis, environmental factors

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Relationship with lung radiological involvement caused by COVID-19 in patients with chronic sacroileitis

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Background

We aimed to investigate the sacroiliac joint MRI findings related to infection in patients with Covid-19 infection and to examine its relationship with disease severity.

Methods

124 patients who were followed up for chronic sacroileitis and had Covid-19 infection were examined. Among these patients, 46 patients whose sacroiliac joint complaints increased after Covid infection and who had sacroiliac MRI scan in the last year before Covid infection were included in the study. After Covid, control sacroiliac MRI was performed in these patients and the activity data occurred in the sacroiliac joint were evaluated. Covid radiological severity classification was made according to the radiological involvement percentages on CT imaging. Mild radiological findings were classified as = 0-50%, severe radiological findings = 51-100%.

Results

Fifteen (32%) of 46 patients who underwent control sacroiliac MRI had signs of acute sacroiliitis. No significant difference was observed in terms of age and gender between those with and without radiological findings in the sacroiliac joint. According to the radiological severity classification, 6 of 15 patients had mild radiological findings, while 9 had severe radiological findings. Of the 31 patients without signs of acute sacroileitis, 21 had mild radiological findings and 10 had severe radiological findings. There was a significant, moderate correlation between radiological severity and sacroiliac joint changes ($P = 0.0038$, $r = 0.6299$).

Conclusions

The severity of radiological involvement in Covid infection may cause acute findings and exacerbations in patients with chronic sacroileitis.

Keywords

Covid-19, Sacroileitis, MRI

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Lung damage in COVID-19 in patients with rheumatic diseases (register data)

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Background

To analyze changes in the lungs according to computed tomography(CT) data in patients with COVID-19 and rheumatic and musculoskeletal diseases(RMD).

Methods

the Russian NIIR/ARR database-COVID-19.

Results

132 patients (100 women-75%), age: 51,8±14,4, 21,9% - over 65 years old. the following RMD were studied: rheumatoid arthritis(RA)43.2%, ankylosing spondylitis(AS)15.9%, Sjogren's syndrome-9.1%, systemic sclerosis 8.3%, systemic lupus erythematosus(SLE)6.8%, psoriatic arthritis 6.8%, dermatomyositis 3%, systemic vasculitis(SV)3%, gout 1.5%, osteoarthritis 0.8%, Still's disease in adults(SDA) 0.8%, undifferentiated arthritis(NDA) 0.8%. RMD activity at the time of COVID-19 disease in 122 patients: high - 19(15.7%), moderate - 43(35.2%), low – 43(35.2%), remission - 17(13.9%). Assessment of CT of the chest organs of 119 patients on an "empirical" visual scale: stage 0 in 38 patients(31.9%), stage 1-in 32(26.9%), stage 2 - in 31(26.1%), stage 3-in 18(15.1%), stage 4 - 0. Patients with stage 0 (without lung damage) had the following diagnoses: RA -36.8%, AS-26.3%, Sjogren's syndrome - 13.2%, psoriatic arthritis(PSA)-13.2%, SLE - 5.3%, systemic sclerosis and SV - 2.6% each. Patients with CT-1 had the following diagnoses: RA-56.2%, SLE-12.4%, AS and systemic sclerosis -9.4% each, Sjogren's syndrome, gout, SV and NDA-3.2% each. Patients with CT-2 had the following diagnoses: RA-45.1%, systemic sclerosis -19.4%, dermatomyositis-9.7%, Sjogren's syndrome and SV-6.5% each, SLE, AS, PSA, BSV-3.2% each. Patients with CT-3:RA 27.7%, Sjogren's syndrome -22.2%, AS-16.6%, SLE, gout, systemic sclerosis, dermatomyositis, PSA, OA-5.5% each.

Changes in the lungs showed a positive correlation with age($r=0.21$, $P<0.05$), duration of COVID-19($r=0.21$, $P<0.05$), presence of fever($r=0.3$, $P<0.05$), cough($r=0.35$, $P<0.05$), shortness of breath($r=0.23$, $P<0.05$) and CRP from 5 to 75 mg/l($r=0.20$, $P<0.05$). Patients with lung damage were significantly($P<0.05$) more often treated with medication: antibiotics, intravenous glucocorticoids, tocilizumab, anticoagulants, and hydroxychloroquine.

Conclusions

In the study group, COVID-19 occurred with moderate lung involvement. The severity of CT changes correlated with age, typical pulmonary manifestations, duration of the disease, and

Keywords

COVID-19 , rheumatic and musculoskeletal diseases

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Interchanging biologics and JAK inhibitors in targeted therapy-naïve patients with rheumatoid arthritis : A nationwide retrospective cohort study

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Background

To investigate the frequency of switching between biologics and JAK inhibitors (JAKis) in targeted therapy-naïve Korean patients with rheumatoid arthritis (RA).

Methods

Patients newly diagnosed with RA (index period Jan–Dec 2014) in the Korean National Health Insurance Database were selected and followed up until 2018. The initial line of therapy (LOT1) included patients treated with conventional DMARDs. Patients in LOT2 were treated with targeted therapy (either a biologic DMARD (bDMARD) or JAKi), and patients who switched from a bDMARD to a JAKi, or vice versa, were allocated to LOT3. Treatment changes within LOT2 were analyzed, along with frequency of hospitalizations and healthcare utilization. We analyzed the most common treatment regimens covering at least 75% of the population in each treatment category (initial, last and treatment change).

Results

Of 662 patients in LOT2, 614 (92.7%) patients first received a bDMARD (group A) (51.5% for TNF inhibitor and 13.8% for tocilizumab), whereas 48 (7.3%) were first treated with a JAKi (group B). By the end of LOT2, TNF inhibitors (245/614, 39.9%) remained the most frequently used bDMARD, but the proportion of tocilizumab users (120/614, 19.5%) increased. Adding or switching to another bDMARD within LOT2 was identified in 349/457 (76.4%) and 19/44 (43.2%) patients in group A and group B, respectively. After entering LOT2, 45/614 (7.3%) patients in group A switched to a JAKi (LOT3), while 2/48 (4.2%) patients in group B switched to a bDMARD (LOT3) (Figure). The mean (SD) number of hospitalizations per person in a year during LOT2 period was 1.76 (2.44) for group A and 1.57 (0.58) for group B.

Conclusions

Interchanging between bDMARDs and JAKi was infrequent during the 5-year observation period in Korean patients with RA. Overall changes in therapy while maintaining the LOT were more common in first-line bDMARD users than in first-line JAKi users.

Keywords

Rheumatoid arthritis, DMARD, Treatment pattern

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Patterns of treatment and healthcare utilization in patients with newly diagnosed rheumatoid arthritis in South Korea

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Background

To investigate the patterns of initial treatment and healthcare utilization in patients newly diagnosed with rheumatoid arthritis (RA) in South Korea.

Methods

This study utilized Claims data from the Korean Health Insurance Review and Assessment, which covers all healthcare claims related to diagnosis and treatment of 98% of the Korean population. Patients with seropositive RA (ICD-10 code M05) or other RA (M06) who were first prescribed a conventional synthetic DMARD (csDMARD) in 2014 were included. Line of therapy (LOT) 1 was defined as the period in which csDMARDs were the mainstay drug of the patient's treatment regimen, while patients in LOT2 started a biologic DMARD (bDMARD) or JAK inhibitor (JAKi) during the observational period. Treatment patterns and healthcare utilization in both patient groups were analyzed.

Results

A total of 21,136 patients were included; 6,565 (31.1%) were identified as seropositive. During the follow up (mean 500 days), 17,438 (82.5%) patients discontinued csDMARDs; 77.8% of discontinuations (13,571/17,438) occurred within one year of starting treatment (Figure). The discontinuation rate was significantly higher in seronegative patients (13,150/14,571; 90.2%) than in seropositive patients (4,288/6565; 65.3%) ($P < 0.001$). Only 662 (3.1%) patients in LOT1 switched to a bDMARD (n=614) or JAKi (n=48). Regarding healthcare utilization, nearly all patients (21,118/21,136; 99.9%) had at least one visit to an outpatient clinic. However, only 7,851 (37.1%) patients ever visited a rheumatology clinic during the LOT1 period, with an overall rate of 0.54 per person-month. In contrast, 597 (90.2%) patients visited a rheumatology clinic, with rates of 1.02 (bDMARD group) and 1.06 (JAKi group) per person-month during the LOT2 period.

Conclusions

A significant number of patients with newly diagnosed RA, especially those who are seronegative, generally discontinue csDMARDs in the early stage of treatment. This reflects that RA is yet frequently misdiagnosed among physicians, for which continuing medical education is needed.

Keywords

Rheumatoid arthritis, Treatment pattern

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The effect of COVID-19 infection on joint findings in patients with rheumatoid arthritis

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Background

We aimed to investigate the joint MRI findings of rheumatoid arthritis related to infection in patients with Covid-19 infection and to examine its relationship with disease severity.

Methods

32 patients who were followed up for rheumatoid arthritis and had Covid-19 infection were examined. Pre- and post-infection MRI was available for a total of 50 joints in 32 patients. 32 knee joints, 12 wrist joints and 6 ankle joints were evaluated with MRI. Radiological changes in the joints (increased fluid, bone oedema/osteitis, synovitis) were examined by a single radiologist. Covid radiological severity classification was made according to the radiological involvement percentages on CT imaging. Mild radiological findings were classified as = 0-50%, severe radiological findings = 51-100%.

Results

There was an increase in joint fluid in 14 joints. An increase in joint enhancement due to synovitis was observed in 12 joints. Bone edema/osteoitis increase was observed in 3 joints. Severe pulmonary involvement was accompanied in 4 of the joints with increased joint fluid. 10 joints were accompanied by mild lung involvement. While 4 joints with increased joint enhancement due to synovitis were accompanied by severe lung involvement, 8 joint synovitis was accompanied by mild pulmonary involvement. 3 joints with bone edema/osteoitis were accompanied by severe lung involvement.There was a significant, moderate correlation between radiological severity and joint changes ($P = 0.0042$, $r = 0.6012$).

Conclusions

As the lung involvement in Covid-19 disease increases, changes due to inflammation in the joint may increase.

Keywords

Covid-19, rheumatoid arthritis, MRI

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The assessment of positive and negative affect in patients with arthritis. The role differential item functioning.

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Background

Positive affect and negative affect has been shown to influence the severity of and sensitivity to pain in patients with arthritis. Research has also indicated that the association between pain and affect may be moderated by sex and other demographic variables. Despite a broad body of substantive research, little is known about the validity of research instruments examining affect in patients with arthritis. The present study investigates the factorial validity of the Positive and Negative Affect Schedule (PANAS) – a frequently used instrument for the assessment of affect consisting of 20 items – in a random sample of patients with arthritis over the age of 40 residing in Germany.

Methods

Data from a representative population-based survey conducted in Germany in 2017 (n=1080) was used. The factorial validity and differential item functioning was examined by means of confirmatory factor analysis (CFA) and multiple indicators multiple causes (MIMIC) models, respectively.

Results

After addition of four residual covariances, the baseline model of the PANAS showed a satisfactory fit (RMSEA = 0.05, TLI=0.90, CFI = 0.91, SRMR = 0.05). Gender-related DIF was observed in 7 items. Disparities between women and men in positive and negative affect differed between analyses adjusted and not adjusted for DIF (beta = 0.090 and beta = 0.137, respectively, vs. beta = 0.109, beta=0.157, respectively). DIF was also observed with respect to age and educational level.

Conclusions

While the PANAS shows high validity in the assessment of positive and negative affect in patients with arthritis, comparisons between sociodemographic categories may be biased as a result of DIF. This may result in the under- or overestimation of true group differences. Appropriate approaches such as latent variable modeling need to be employed to obtain valid estimates.

Keywords

arthritis, differential item functioning, PANAS

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Henoch–Schönlein purpura relapse after infected by COVID-19 : A Case Study

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Description

Henoch–Schönlein Purpura (HSP) is a disease characterized by inflammation of small blood vessels in the skin, joints, intestines, and kidneys. This disorder can cause symptoms of a red or purple rash (purpura) on the skin in the lower leg area or buttocks. Not much is known about the relationship between this disease and COVID-19 infection. Here we present a case of controlled HSP that relapsed after being infected with COVID-19.

A 33-year-old woman is a patient with stable HSP who was diagnosed at the age of 30 years. The patient routinely received Mycophenolate Sodium and was stable for the last 3 years. The patient was planning to become pregnant so the drug was changed to Azathioprine and Methyl Prednisolone 4 mg. When the gestational age was 35 weeks, the patient underwent antenatal examination including PCR examination. The results of the examination showed that the patient was infected with COVID-19 with symptoms of fever and anosmia without other common signs for COVID-19. Thus categorized as mild symptomatic COVID-19. Patients then experience symptoms of diarrhea 8-15 times per day pale in color. Body and eyes look yellow and puffy cheeks. Urination is colored like tea.

The pregnancy was then terminated because of Pre Eclampsia condition at 36 weeks of gestation. The patient's medication was again adjusted for HSP to Methyl Prednisolone 16 mg 2 times a day. For the treatment of COVID-19, Oseltamivir 75 mg 2 times a day is given. The results of the PCR examination on the 10th day showed negative results. The patient is now stable and controlled.

Conclusions

This case presents the relapse of HSP that occurred after COVID-19 infection that showed some relationship. Some case reports showed another type of autoimmune condition affected by COVID-19 infection, although the mechanism didn't clear yet.

Keywords

Henoch–Schönlein Purpura, Autoimmune, COVID-19

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The effect of cytokines storm on the severity of COVID-19

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Background

covid19 is not over yet, every time there are additional cases in various countries. The total number of COVID-19 cases in the world as of June 17 was 177,781,626, a total of 162,279,376 have recovered and 3,847,982 died, so the total active cases in the world are 11,654,268 cases. Some people with COVID-19 have severe symptoms of acute respiratory syndrome, which can lead to death. This high level of severity depends on the cytokines storm. This cytokine storm needs to be studied further to find a solution in the current pandemic era. Therefore, this paper aims to explain the effect of cytokines storm on the severity of covid19, how can this happen? and how to overcome it?. To answer this question, it is necessary to conduct a literature review from previous research.

Methods

Literature review

Results

Cytokines storm is used by clinicians as a sign to identify the level of disease, because COVID-19 patients admitted to the ICU have higher CXCL10, CCL 2, and TNF-a than patients with mild symptoms. The coronavirus that has infected humans targets the ACE2 receptor on lung cells, and destroys human lungs through a storm of cytokines, causing hyperinflammation and forcing immune cells to destroy healthy cells. when this condition happens, the cytokines storm by covid19 will produce immunopathogenic damage. There are several strategies for handling cytokines storm by covid19 including, Chloroquine, IFN-λ, Stem Cell Therapy, The Artificial Liver Technology, Immunototherapy (given at the time of cytokines storm diagnosis).

Conclusions

Cytokines storm by covid19 needs to be handled properly so as not to cause more severe organ damage. There are several solutions or handling strategies that can be done so that the cytokine storm does not aggravate covid19.

Keywords

cytokines storm, covid19, immunopathogenic

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Quality assessment of health care of rheumatoid arthritis in Korea using national sample cohort database

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Background

Quality indicators (QIs) for evaluating the health care for patients with rheumatoid arthritis (RA) were developed by experts in Korea [1]. We assessed the quality of health care for RA by these QIs.

Methods

We analysed the National Health Insurance Service-National Sample Cohort Database from 2002 to 2015 [2]. RA patients were defined as having the Korean Classification of Diseases codes M053, M058, M059, M060, M069, and M069 as a principal diagnosis.

Results

The patients with RA were 4.2% (seropositive RA 0.7%). Among them, 13.2% of the patients had visited a rheumatologist once and more. The RA patients to see the rheumatologist within 90 days after initial diagnosis were 6.0%. The patients who had radiographs of the hands or feet within 90 days before or after initial diagnosis was 30.9%. DMARDs were prescribed in 19.5% of patients and started within 90 days after initial diagnosis in 13.9% of patients. Early DMARD therapy was higher in patients who had seen rheumatologists compared with non-rheumatologists (39.2 vs. 10.0%). Among patients treated with DMARDs for more than one year, 11.1% of patients did laboratory tests twice and more per year. 69.3% of methotrexate-treated patients were adequately supplemented with folic acid. Approximately 50% and 13% of patients were tested for hepatitis B and hepatitis C within 1 year prior to use of biologics, respectively. Chest radiograph was undertaken in 74.3% of patients and interferon gamma release assays or tuberculin skin test in 62.7% of patients within 3 months prior to biologic therapy. 23.2% of patients had cervical spine radiographs within 1 year before surgery with general anesthesia.

Conclusions

Most of the patients with (suspected) RA did not see rheumatologists during the study period. The results of this study raised concerns about whether appropriate diagnosis, treatment and monitoring are being conducted in patients with RA in Korea.

Keywords

Quality, Health care, Rheumatoid arthritis

E-poster Presentation

Osteoporosis and metabolic bone diseases

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A study on knowledge, attitude and practices on osteoporosis among college students in Laguna, Philippines

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Background

Osteoporosis has been known to affect the elderly but measures to prevent its development are linked to important lifestyle choices that are made at an early age. This study described the level of knowledge, attitudes toward osteoporosis and practices related to the prevention of osteoporosis of 160 college students, enrolled in both allied health and non-allied health courses in Laguna, Philippines.

Methods

A self-administered online questionnaire was distributed to college students through social media forums from April 12-16, 2021 and 160 students, who fit the inclusion criteria were included in the study.

Results

The study showed that among the participants, 57% have low to very low knowledge about osteoporosis and only 12.5% have high level of knowledge considering that 81.25% (n=130) of the participants were enrolled in an allied health course. Six out of ten participants cannot identify risks associated with osteoporosis; while 46% were not able to identify complications. Four out of ten participants believed that a DEXA scan is used to measure serum calcium levels. Furthermore, about 45% of the participants showed highly positive attitude towards osteoporosis describing it as a “serious disease” and “desires to know more about osteoporosis.” 30% of the students believed that they do not have enough resources to prevent the illness. Poor practices were noted in 68% of the sample population. High knowledge is significantly associated with taking an allied health course, being enrolled in a private school, and having parents with educational attainment of college and higher, with p-value less than 0.001. Good preventive practice is significantly associated with high knowledge about osteoporosis; while low attitude is associated with poor preventive practices.

Conclusions

Based on the results of the study, there is a need to increase the awareness of college students about osteoporosis and to clarify misconceptions about the disease. Increasing the students’ knowledge can increase the preventive measures that they would take against osteoporosis thus, could potentially reduce the prevalence of the disease.

Keywords

KAP on osteoporosis, Philippines osteoporosis, knowledge level on osteoporosis

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Effects of Moringa oleifera leaf extract on bone turnover and resorption induced in ovariectomized rats

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Background

To evaluate the therapeutic role of Moringa oleifera leaves (MOL) against bone turnover, resorption and osteoporosis induced in ovariectomized rats as a postmenopausal model and comparing the results with those from Generic CycloProgynova drug (D).

Methods

The study used western albino rats undergo bilaterally ovariectomization as a model for postmenopausal. Forty female western albino rats (age: 3-4 months) weighing 150-180 gm. Rats were divided into four groups, 10 rats each; SC-group: Sham control = untreated and unovariectomized rats; OVX-group = ovariectomized rats; (OVX-MOL) and (OVX-D) groups = OVX rats were treated with MOL and D, respectively. Bone markers (BMs) especially osteocalcin (BGP), alkaline phosphatase (ALP), tartarate resistance acid phosphatase (TRAcP), bone weight, bone calcium concentrationl and histopathological examination of bones were determined.

Results

In OVX group the activities of ALP and TRAcP and the levels of BGP, serum calcium, sodium and body weight were significantly higher ($p \leq 0.05$) than SC-group, while bone calcium concentration, bone mass, serum E2 and potassium level as well as uterus mass were significantly lower ($p \leq 0.05$). Also histopathological results revealed that the outer cortical bone became thinner, while the cancellous bone trabeculae lost their normal architecture. Treatment of OVX rats with MOL or D for 12 weeks improved both the architecture of bones as shown from the histopathological results and BMs, serum electrolytes and E2 levels ($p \leq 0.05$) which approached SC-group. Moreover after treatment of OVX rats with SOE the levels of lipid profile and uric acid were improved and approached

Conclusions

The results of this study show that MOL offers a promising alternative in the design of new strategies in nutritional management of age-related bone complications.

Keywords

Bone Turnover, Ovariectomized Rats., Moringa oleifera leaf extract

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Associations of neutrophil-to-lymphocyte ratio, monocyte-to-lymphocyte ratio with osteoporosis and incident vertebral fractures in postmenopausal women with rheumatoid arthritis : A single - center retrospective cohort study

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Background

We aimed to investigate whether neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR) are associated with the presence of osteoporosis (OP) and vertebral fractures in patients with rheumatoid arthritis (RA).

Methods

This retrospective cohort study included 413 consecutive postmenopausal patients with RA and age-matched (±2 years) postmenopausal healthy controls who underwent dual energy X-ray absorptiometry (DEXA) between January 2005 and December 2017. The date of DEXA examination was defined as index date. OP was defined as a T-score <-2.5 and incident vertebral fractures were defined at the first occurrence of non-traumatic fracture after the index date. NLR, PLR and MLR were each dichotomized by a median split (low vs. high).

Results

The median NLR, PLR and MLR in RA patients were significantly higher than those in controls. The frequency of OP of the lumbar spine, hip and either site in postmenopausal patients with RA were 24.7%, 15.5% and 32%, respectively and were significantly higher than those in controls. After adjusting for confounding factors, a high baseline NLR was significantly associated with OP of the either hip or lumbar spine (OR=1.61, 95% CI=1.03-2.58) and OP of the hip (OR=2.11, 95% CI=1.1-4.2), but not with OP of the lumbar spine. RA patients with a high baseline PLR had an increased risk of lumbar spine OP (OR=2.3, 95% CI=1.21-4.36) in multivariable logistic regression model. During the median follow-up duration of 61 months, 53 (12.8%) RA patients developed incidental vertebral fractures. In multivariable Cox regression models, a high baseline NLR (HR=4.04, 95% CI=1.99-8.21) and a high baseline MLR (HR=2.28, 95% CI=1.26-4.15) were independently associated with a higher risk of incidental vertebral fractures in patients with RA.

Conclusions

Our data suggests that NLR, PLR and MLR may be used as potential markers for systemic bone loss in RA.

Keywords

Rheumatoid Arthritis, Osteoporosis, Vertebral Fracture

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Low-dose glucocorticoids on bone mineral density in patients with rheumatoid arthritis

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Background

This study aimed to provide reliable information on the impact of low-dose glucocorticoids (GCs) on the bone mineral density (BMD) of patients with rheumatoid arthritis (RA).

Methods

In this retrospective study, 933 patients with RA who continued the consumption of GCs (GC group) and 100 patients who had discontinued its consumption >1 year (no-GC group) at Ajou University Hospital were enrolled. The BMD values were measured at baseline and follow-up, and the annual rate of changes in BMD between the groups was compared using dual-energy X-ray absorptiometry. We used multiple linear regression analysis to identify the factors associated with changes in BMD.

Results

The demographic characteristics and use of medical treatments affecting bone metabolism were similar between the two groups. Furthermore, there were no significant differences in the annual rate of changes in BMD and incidence of newly developed osteoporosis and incidental fractures between the two groups. Multiple linear regression analysis revealed that the disease activity score for 28 joints with erythrocyte sedimentation rate was the only factor affecting the annual rate of changes in BMD, and it was inversely proportional to changes in BMD.

Conclusions

The benefits of GC therapy in attenuating inflammation compensate for the risk of osteoporosis if adequate bone loss is prevented in patients with RA.

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Case series report : Adult-onset hypophosphatemic osteomalacia

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Description

Osteomalacia (OM) is a disease characterized by the softening of bones caused by impaired bone metabolism. Two main mechanism of osteomalacia are 1) insufficient calcium absorption from the diet of a deficiency of or resistance to the action of vitamin D, 2) phosphate deficiency due to reduced absorption and increased excretion (wasting at renal tubule) or increased utilization of phosphate in cells. Hypophosphatemic OM is important cause of Adult onset OM. Adult OM patients usually complain of diffuse body pain including multiple bone pain and arthralgia, muscle weakness and fragility of the bones leading to height loss. Because clinical features are non-specific, OM is often confused with various rheumatic or other musculoskeletal diseases. This study assessed the clinical, laboratory, imaging findings of patients with adult-onset hypophosphatemic OM to ease early diagnosis. We included adult patients presenting with multiple bone pain, hypophosphatemia, high serum bone-specific alkaline phosphatase levels, and at least one of the imaging findings suggestive of OM: Looser zone/pseudo-fracture or codfish vertebrae on radiography, and costochondral junction beadings (adult rachitic rosary appearance) on bone scintigraphy.Seven patients were diagnosed with adefovir-induced Fanconi syndrome, and other two patients were diagnosed with tumor-induced OM and light chain nephropathy, respectively. After phosphorus and vitamin D supplementation, and treatment for underlying etiologies, improvement in pain, muscle strength, and gait was observed in all patients.

Conclusions

Physicians should always consider the possibility of OM as a cause of multiple bone pain in adult patients. Mechanical pain, hypophosphatemia and a distinctive pattern on bone scintigraphy can be the initial diagnostic indicators. Drugs such as antiviral agents for hepatitis B may be the most common etiology of OM in adult patients with normal nutritional status.

Keywords

adult onset osteomalacia, Hypophosphatemic OM

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Pitavastatin prevents ovariectomy-induced osteoporosis by regulating osteoclastic resorption and osteoblastic formation

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Background

Excessive osteoclast activity, along with relatively weak osteoblast function, is strongly associated with bone disease. Therefore, studies to identify novel anti-osteoporosis candidates with dual actions of inhibiting osteoclastogenesis and increasing osteoblastogenesis may provide an ideal approach for treating osteoporosis. Pitavastatin, an inhibitor of 3-hydroxy-3 methyl-glutaryl coenzyme A reductase, has demonstrated various pharmacological activities, including anti-inflammation, bone anabolic effects, vasodilation, and inhibition of revascularization; however, the precise effects and mechanisms of pitavastatin on the regulation of osteoblast and osteoclast activity need to be comprehensively elucidated.

Methods

The sham or OVX operated mice were randomly assigned to four groups. Primary BMMs were isolated from the femurs and tibias. Primary osteoblasts were obtained from neonatal (1-day-old) ICR mouse calvaria. Resorption pit areas were captured using a microscope. The total area of resorption pits was analyzed. Quantitative real-time RT-PCR (qRT-PCR) and Western bolt analysis were done.

Results

Pitavastatin exerted dose-dependent inhibitory effects on receptor activator of nuclear factor kappa-B ligand-induced osteoclast formation, bone resorption, and osteoclast-specific marker gene expression. These inhibitory effects were achieved by inhibiting the Akt, NF-κB, and mitogen-activated protein kinase (p38, ERK, and JNK) signaling pathways, resulting in the downregulation of major transcription factors c-Fos and NFATc1. Furthermore, pitavastatin potentially stimulated osteoblast differentiation by activating alkaline phosphatase (ALP), enhancing mineralization by Alizarin Red S, and increasing the expression of osteoblastogenic marker genes such as runt-related transcription factor 2, ALP, osteocalcin, and collagen type 1 alpha.

Conclusions

Our findings demonstrated a new function and mechanism for pitavastatin in bone remodeling, indicating its potential as a therapeutic candidate in treating osteoporosis by inhibiting osteoclastic resorption and promoting osteoblastic formation.

E-poster Presentation

Osteoarthritis and biology of bone and joint

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Lingzhi and San-Miao-San with hyaluronic acid gel mitigate cartilage degeneration in anterior cruciate ligament transection induced osteoarthritis

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Background

Osteoarthritis (OA) is one of the most common types of arthritis characterized by inflammation, abnormal remodeling of subchondral bone (SCB), chronic degeneration of articular cartilage (AC) and osteophyte formation. This study aims to investigate the mitigate efficacy of Chinese medicine Lingzhi (LZ) and San-Miao-San (SMS) combined with hyaluronic acid (HA)-gel in attenuating cartilage degeneration in traumatic osteoarthritis (OA).

Methods

The standardized surgery of anterior cruciate ligament transection (ACLT) was made from the medial compartment of right hind limbs of 8-week-old female SD rats and resulted in a traumatic OA. Rats (n=5/group) were treated once intra-articular injection of 50 μl HA-gel, 50 μl HA-gel+50 μg LZ-SMS, 50 μl of saline+50 μg LZ-SMS and null (ACLT group) respectively, except sham group. Gene Ontology and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis was adopted to predict the potential targets and signaling pathway of LZ-SMS in OA through the tool of DAVID Bioinformatics.

Results

In vivo, HA-gel + LZ-SMS treatment resulted in a higher volume ratio of hyaline cartilage (HC)/calcified cartilage (CC) and HC/Sum (total volume of cartilage), compared to ACLT and HA-gel groups. Furthermore, there was also a down-regulated inflammatory cytokines and upregulated anti-inflammatory cytokine IL-10 in HA+LZ-SMS group. Finally, 64 shared targets from 37 active compounds in LZ-SMS related to the core genes for the development of OA. LZ-SMS has a putative role in regulating inflammatory circumstance through influencing the MAPK signaling pathway.

Conclusions

In conclusion, LZ-SMS can directly attenuate AC degeneration through activating the chondrogenic signaling pathway in a traumatic OA model. Meanwhile, the indirect effect on maintaining the integrity of SCB microstructure offers a stabilized physiological environment which is favorable to the cartilage recovery.

Keywords

LZ-SMS, Osteoarthritis, Subchondral trabecular bone

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A meta-analysis of adipose tissue derived mesenchymal stem cell therapy for the treatment of knee osteoarthritis

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Background

Background: Osteoarthritis (OA) is a degenerative disorder associated with cartilage loss and is a leading cause of disability around the world. In old age, the capacity of cartilage to regenerate is diminished. With an aging population, the burden of OA is set to rise. Currently, there is no definitive treatment for OA. However, mesenchymal stem cell (MSCs) therapy derived from adipose tissue is promising.

Methods

Methods: A PRISMA systematic review was conducted employing four databases (MEDLINE, EMBASE, Cochrane, Web of Science) to identify all clinical studies which utilized adipose tissue derived MSCs (AMSCs) or stromal vascular fraction (SVF) for the treatment of knee OA.

Results

Results: Eighteen studies were included which met the inclusion criteria. Meta-analyses were conducted on fourteen of these studies, which all documented WOMAC scores after administration of AMSCs. Pooled analysis revealed that AMSC treatments definitively improve WOMAC scores, post treatment. These improvements increased with time.

Conclusions

Conclusions: The studies in this metanalysis have established the safety and efficacy of both AMSC therapy and SVF therapy for knee OA in old adults and show that they reduce pain and improve knee function in symptomatic knee OA. Suggesting that they may be effective therapies to improve mobility in an aging population.

Keywords

Meta analysis, Osteoarthritis, Mesenchymal Stem Cells

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Barriers to effectiveness of non-surgical treatments for knee osteoarthritis in a diverse racial/ethnic population : A nominal group qualitative study

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Background

Knee osteoarthritis (OA) has worse outcome in racial/ethnic minorities, who also have more severe pain, disability and worse outcomes. However, most qualitative studies include primarily Caucasian people with knee OA. Therefore, our objective was to examine patient experience, views and opinions of reasons for why the current knee OA treatments are not working for them in a diverse racial/ethnic group of people.

Methods

Nominal groups were conducted with consecutive clinic patients with knee OA at a medical center, oversampling African Americans. Patients discussed and rank-ordered their concerns.

Results

Fourteen nominal groups with 48 knee OA patients were conducted with mean age, 60.6 years (standard deviation, 9.8) and knee OA duration, 7.8 years (sd, 5.4); 25% were men, and 46% were African American. The most frequently cited highly-ranked concerns, divided into 3 categories as follows:

A. Medication-related: (1) side effects (9 groups); (2) limited efficacy (9 groups); (3) medication not targeting underlying disease; (4) lack of personalized medication use; and (5) temporary benefit;

B. Exercise/Physical therapy related: (1) exacerbation of joint pain (8 groups); (2) difficulty in doing exercises (6 groups); (3) lack of motivation (8 groups); (4) technical challenges/lack of personalized exercise regimens (1 group); (5) cost (3 groups); and

C. Weight loss related (1) difficulty in achieving weight loss (7 groups); (2) motivation (2 groups); and (3) limited efficacy for symptom improvement (1 group).

Conclusions

Participants with knee osteoarthritis, consisting of a diverse racial/ethnic representation, identified several barriers to the effectiveness of current knee OA treatments. This new knowledge provides insights for making the current treatment options potentially more usable and/or more effective. Given the significant consequences of knee OA, limited/no disease-modifying drugs this strategy can potentially improve clinical care and patient outcomes.

Keywords

osteoarthritis, qualitative research, Barriers to treatment effectiveness

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Effects of education, income, and occupation on prevalence and symptoms of knee osteoarthritis

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Background

To examine the effect of socioeconomic status (SES) as measured by three components of education level, income level, and occupation on prevalence and symptom severity of knee osteoarthritis (OA) and to determine which of these factors has the strongest association.

Methods

We conducted a cross-sectional study using data from the Fifth Korean National Health and Nutrition Examination Survey that were collected between 2010 and 2012. Male and female participants 50 years or older were included. Analyses to examine the associations of the three SES components with prevalence and symptom severity of knee OA were performed.

Results

A total 9,071 participants was included in the study. As expected, lower education, lower income level, and non-managerial or no job were associated with higher prevalence of knee OA and knee symptoms. Among the three SES components, lower education was most strongly associated with knee pain and radiographic knee OA after adjusting for the other two.

Conclusions

Lower education level is the component of SES that most strongly relates to higher prevalence of knee OA and knee symptoms. Improving societal education level might decrease the socioeconomic burden of knee OA.

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Correlation of the low back pain and degenerative changes of miners

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Background

Low back pain is a prevalent musculoskeletal condition and represents a substantial socioeconomic burden in the world, as well as in Mongolia. MRI is a commonly used imaging technique. Disc herniations and other degenerative manifestations, however, frequently occur in asymptomatic individuals. The purpose of this study was to analyze for associations between back pain intensity and degenerative manifestations of MRI findings in Mongolian miners.

Methods

Included were 82 miners (29-60 years) with and without low back pain between January 2019 and January 2020 were examined retrospectively by a specialist in this cross-sectional study. All participants examined by MRI of the lumbar spine. The Odd Ratio and its 95% CI are investigated on the basis of the evaluation of differences of back pain score, MRI features.

Results

Low back pain was present in 58 % of the participants. Back pain intensity was higher in patients with type 1 Modic endplate changes. In patients with radiculopathy, nerve root touch caused as much leg pain as nerve root displacement or compression.

A significant, positive association was found between severe disc extrusion, Modic type I endplate change and back pain (OR = 1.52, 95% CI: 1.23-1.72 & OR = 1.32, 95% CI: 1.16-1.42) that differed significantly ($p < 0.01$). The association between other MRI features was non significant.

Conclusions

A significant association was found between severe disc extrusion, Modic type I endplate changes and back pain in miners.

Keywords

Disc herniation, Low back pain, Magnetic resonance imaging

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Association between resting heart rate and osteoarthritis in the knee and hand joints: The Dong-Gu study

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Background

Although the resting heart rate (RHR) predicts the clinical outcome of cardiovascular disease, its role in degenerative musculoskeletal diseases, such as osteoarthritis (OA), is not clear. This study investigated the association of RHR with the extent of radiographic changes in the knees and hands of OA patients.

Methods

We enrolled 2,377 subjects from the Dong-gu Study. Radiographic findings for the hand and knee joints were examined with a semi-quantitative grading system for OA, to calculate the total hand and knee joint scores. Multiple linear regression was performed to examine the associations between RHR and the radiographic characteristics of the hand and knee joints in the OA patients.

Results

Regarding the radiographic findings for the knee joints, RHR was positively associated with the total ($p=0.001$), osteophyte ($p=0.002$), joint space narrowing (JSN) ($p<0.001$), and tibial attrition ($p=0.002$) scores after adjusting for age, gender, body mass index, smoking, alcohol consumption, education, and physical activity. In the hand joints, RHR was positively associated with the JSN ($p=0.010$) and subchondral cyst ($p=0.002$) scores after adjustment. However, no association was found between RHR and the total, osteophyte, sclerosis, erosion, and malalignment scores in the hand joints.

Conclusions

This is the first study to demonstrate an association between RHR and the radiographic severity of knee OA, but not hand OA. This suggests that RHR might be a biomarker of the radiographic severity of OA, and not merely a physical sign.

Keywords

resting heart rate, osteoarthritis

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Mitigation of osteoarthritis progression by SIRT1-mediatd inhibition of NLRP3 inflammasome

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Background

Various inflammatory mediators, such as interleukin-1 beta (IL-1β), are associated with osteoarthritis (OA) progression. However, the molecular mechanism of IL-1β in OA pathogenesis is not clarified. Here, we investigated the mechanism of IL-1β using human OA synoviocyte in vitro model and OA mice in vivo model.

Methods

OA synoviocytes were isolated from synovium of OA knee patients and control synoviocytes were extracted from traumatic knee patients who had no history of OA. IL-1β, NLRP3, ASC, and caspase-1expression was analyzed using immunohistochemistry, immunofluorescence, and immunoblot. IL-1β secretion was measured by ELISA assay. Experiment were also conducted in OA mice model.

Results

OA synoviocytes secreted IL-1β when induced with LPS and ATP in a NLRP3 inflammasome-dependent manner. Treatment with SRT1720, a SIRT1 activator, increased the phosphorylated levels of adenosine monophosphate-activated protein kinase (AMPK) α/acetyl-CoA carboxylase (ACC) in OA synoviocytes. Further, activated SIRT1 inhibited NLRP3 inflammasome activation by blocking ASC oligomerization and reduced IL-1β secretion. These effects were inhibited by EX527 (inhibitor of SIRT1) and compound C (inhibitor of AMPK) treatment. SIRT1-knockdown synoviocytes showed attenuation of the inhibitory effect of SIRT1720 on IL-1β secretion. In OA mice model, IL-1β expression in synovium was reduced in SIRT1-Tg mice compared with that in wild-type mice. The SIRT1-Tg mice showed less degenerative change in articular cartilage and adjacent bone.

Conclusions

SIRT1 suppressed NLRP3 inflammasome-dependent secretion of IL-1β in inflammation and SIRT1-Tg mice showed less bone degeneration, which indicates that blocking OA inflammation may be helpful to mitigate OA progression.

Keywords

Osteoarthritis, NLRP3 inflammasome, IL-1β

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Patient with acromegaly presented with Vaughan-Jackson syndrome : A case report

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Description

Vaughan-Jackson syndrome was originally described as rupture of extensor tendons of little and ring fingers due to degenerative arthritis. Arthropathy is prevalent in acromegaly with distinct structural osteoarthritis abnormalities. We described a case of acromegaly presented with Vaughan-Jackson syndrome, which to our knowledge has not been reported before.

A 68-year-old female experienced progressive deformity of her left hands over several months with mechanical pain over metacarpal joints without inflammatory symptoms. Clinical evaluation revealed ulnar deviation of metacarpal joints of the left third, fourth and fifth digit with limited extension, most prominent over the left fifth digit. These were suggestive of progressive disruption of extensor digitorum with plausible sequential involvement from fifth digit, fourth and third digit, consistent with Vaughan-Jackson syndrome. There were Bouchard and Heberden nodes suggestive degenerative arthritis, but no active synovitis. As hand deformities were significantly affecting activities of daily living, hand reconstructive surgery including tendon transfer was undertaken to improve function. Of note, she also had osteoarthritis affecting elbow, knee and hip. Over the subsequent 4 years, acromegalic features became more apparent. She had coarse facial features: prominent frontal bone, supraorbital ridge, jaw and nose, acral enlargement and multiple skin tags. Investigations revealed elevated insulin-like growth factor 1 (IGF-1) level at 496 ug/L (normal range: 35-216 ug/L), and non-suppressible serum growth hormone on two-hour 75-g oral glucose tolerance test. Rest of anterior pituitary function was otherwise intact. MRI scan localised a macroadenoma in the pituitary gland and she was referred to a pituitary surgeon for consideration of surgery.

Conclusions

Given the insidious nature of the clinical manifestations, it was nearly four years later before diagnosis of acromegaly was made. Acromegalic arthropathy could lead to significant motor disability, hence timely recognition of the disease coupled with effective treatment are key in the management of acromegaly arthropathy.

Keywords

osteoarthritis, acromegaly, Vaughan-Jackson syndrome

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Feasibility and validity of wearable tracking devices to measure various parameter associated with joint pains in osteoarthritis

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Background

Now adays wearable activity trackers are utilized to examine the individual physical activity having musculoskeletal ailments .i.e spondyloarthritis, rheumatoid arthritis, and osteoarthritis (OA). The present study explored the wearable activity trackers (Samsung, fitbit, Garmin) feasibility and validity to measure the effects of OA on sleep and physical measure for 6 months. In short, a pilot investigation (prospective) was intended to measures feasibility and preference of patient with OA.

Methods

112 patients were enrolled in the present study which comprises of healthcare detected OA, swelling, joint pain and tenderness. Wearable activity trackers were used to measure various parameters such as heart rate, sleep data and physical activity. Accessibility of fully activity data received from all participants with 85 % of the day is termed as patient data compliance. OA related joints pain and swelling were estimated with physical activity and sleep profile and correlated with pain related data to step count and sleep every day. To record the repeated result a mixed linear models was utilized

Results

Out of 112 participants 98 follows the criteria wear time and pains reports after wearing wearable device, so the result was available of all total work days with 62.6%. Age with 47.3±12.4years (Mean±SD), 82% were male and 178 % were female, 76 % were take corticosteroids and 25% showed ≥5 joint pain and swelling in the last 6 months. Devices were showed 41% with pains and 59% participants with pain. Daily step count was markedly decreases over the week with pain and swelling 5437±4011 in comparison with non swelling and pains times (6745+5367), NO significant difference were observe in sleep activity

Conclusions

In short, the pattern of wear explains the feasibility and validity of wearble devices in patient with OA. More research are required to measures various parameter with more advanced technology for OA.

Keywords

wearable devices, osteoarthritis, joint pain

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Depressive symptoms among patients with osteoarthritis. Results from a representative survey on 2,680 patients in Germany

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Background

Osteoarthritis is one of the most frequent musculoskeletal diseases and is particularly prevalent among middle-aged and older individuals [1]. Osteoarthritis often leads to pain and is associated with restrictions in everyday life and may affect quality of life [2]. It may also be associated with depressive symptoms which may significantly limit the ability of patients to cope with the condition. Little is known about the contributing factors for depressive symptoms among osteoarthritis patients. The aim of the present study was to examine factors associated with depression in patients with osteoarthritis residing in Germany.

Methods

The study is based on survey data from of the German Ageing Survey, a nationwide representative cross-sectional and longitudinal survey of the middle-aged and older population in Germany. For the analysis, 2017 data from the sixth wave of the survey is used providing information on 6,626 individuals of whom 2,759 reported suffering from osteoarthritis. Depression was assessed by the Center for Epidemiological Studies Depression (CES-D) inventory, with a cutoff of 16 considered to indicate depressive symptoms [3, 4]. Only cases with no missing values were included into the analysis, resulting in a sample of 2,680 patients. Multivariable logistic regression was used to examine factors associated with depressive symptoms.

Results

Of the 2,680 individuals with osteoarthritis, 11.5% had a CES-D score of 16 or higher. Depressive symptoms were significantly associated with being female (OR=1.39, 95%-CI=1.06, 1.82), not living in a relationship with a partner (OR=1.60, 95%-CI= 1.21, 2.10), and having a low socioeconomic status (OR=2.19, 95%-CI=1.39, 3.43). Furthermore, depressive symptoms were associated with pain and younger age.

Conclusions

The findings can inform the development of targeted support measures for patients with osteoarthritis and could support affected individuals in their coping strategies. These measures should also include adequate pain management to reduce the burden of depressive symptoms.

Keywords

depression, osteoarthritis, Germany

E-poster Presentation

Orthopedics & Rehabilitation

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Clinical and radiological outcomes in robotic-assisted total knee arthroplasty : A systematic review and meta-analysis

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Background
The aim of this systematic review is to determine if robotic-assisted total knee arthroplasty (RATKA) results in improved clinical and radiological outcomes, and to elucidate the breadth and depth of studies conducted on this topic.

Methods
A Preferred Reporting Items for Systematic Reviews and Meta-Analyses systematic review was conducted using 4 databases (MEDLINE, EMBASE, Cochrane, and Web of Science) to identify all clinical studies that investigate clinical or radiological outcomes using RATKA. The Critical Appraisal Skills Program checklist for cohort studies was employed for critical appraisal and evaluation of all 22 studies that met the inclusion criteria.

Results
All studies reviewed determined that knee arthroplasty improved clinical outcomes. Twelve studies found statistically better clinical outcomes with RATKA compared with conventional TKA, whereas 9 studies found no difference. One study did not assess clinical outcomes. When assessing radiological outcomes, 14 studies reported that RATKA resulted in more consistent and accurate postoperative mechanical alignment, whereas 2 studies reported no difference. Six studies did not assess radiological outcomes.

Conclusions
Although knee arthroplasty is one of the most commonly performed orthopedic operations (1-3), the level of patient satisfaction varies (4-5). The meta-analyses conducted in our systematic review shows that RATKA results in greater improvements in postoperative Hospital for Special Surgery score and Western Ontario and McMaster Universities scores compared to conventional TKA. Furthermore, it shows that RATKA results in more accurate postoperative alignment of prostheses. These together can explain the improved postoperative outcomes. More randomized controlled trials must be conducted before this technique is integrated into routine clinical practice.

Keywords
Meta analysis, Robotics, Total Knee Arthroplasty

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Wearable technology and geo-fencing device is a boon for rheumatoid arthritis patients

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Background

To study role of wearable (MI Band) and Geo-Fencing technology to monitor daily life routine activities on movement and memory data in rheumatoid arthritis (RA) patients.

Methods

Total of 62 RA patients were taken as subject with an equal ratio of male and female and age group between 68 to 80 years in New Delhi. Wearable monitoring devices like MI band and Geo-Fencing device were put on the wrist of RA patients for 30 days and a questionnaire was filled out by each patient. In all subjects, blood pressure, blood glucose was measured on daily basis with day to day data of their monitoring of step count, calorie burnt, motion time, sleep monitoring, calorie consumption, monitoring heart rate to know daily routines and recording them for health purpose. Wearable bands, automatically provides a cueing sound with sensing alert when RA patients move out of the geo-fenced area and which stays until the subject resumes walking in virtual boundary.

Results

Present results shown that both wearable device reading showed there was a normal heart rate, more calorie burnt with better control of sugar control and average good sleep count in more physically workout, include walking in RA patients compared to less physically workout RA patients, identified by professional physiotherapists. Both device reading showed that after changing lifestyle routine among less physically active RA patients, their memory loss and wandering

Conclusions

By using, these wearable devices ensured their health awareness with more concerned towards exercising and demonstrate the benefit of such a context-aware system and motivate further studies. Wearable devices and technology have introduced a new way for caregivers and families to prevent the dangers of wandering in senior loved ones with RA.

Keywords

wearable devices, rheumatoid arthritis (RA) patients, Geo-Fencing device

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Effects of light-emitting diode therapy on hand stiffness and pain in patients with tenosynovitis

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Background

This study aimed to investigate the efficacy and safety of Light-Emitting Diodes therapy (LEDT) as a non-pharmacologic treatment for pain and stiffness in patients with hand tenosynovitis.

Methods

We enrolled 12 patients with hand tenosynovitis who were not responding to maximal doses of non-steroidal anti-inflammatory drugs (NSAIDs) for two weeks. We performed 20-minute LEDT twice per week for four weeks and collected sociodemographic, clinical, and laboratory data. We assessed the Visual Analog Scale (VAS) pain and stiffness scores of each hand every two weeks and evaluated the thickness of the flexor tendon in the patients' hands by ultrasonography. Additionally, to determine the effect of LEDT on different types of molecules in tenocytes from four patients were obtained and stimulated by LPS with or without LEDT.

Results

After LEDT, all the patients showed clinical improvements in the pain VAS scores in weeks 2, 4, and 8 as compared with the baseline ($p = 0.036$, 0.015 and 0.003, respectively). The stiffness VAS scores improved in weeks 4 and 8 ($p = 0.036$ and 0.033, respectively). Tendon thickness of left second finger showed a significant decrease as compared to the baseline and week 8 values ($p = 0.030$). No adverse events were documented. After LEDT, levels of aggrecan RNA, COL1, COL2, and COL3 were significantly higher in LPS with LEDT group than in LPS only group ($p = 0.0164$, 0.0356, 0.0231, and 0.0028, respectively).

Conclusions

LEDT significantly reduced the pain and stiffness in the hands of tenosynovitis patients who were refractory to treatment with NSAIDs. Our results suggest that LEDT has significant potential as an alternative non-pharmacologic treatment in the future due to its non-invasive, technically simple, and effective method of administration.

Keywords

Light-Emitting Diodes, hand pain, tenosynovitis

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