Volume 192 Supplement 1 March 2024 ISSN 0167-8140

ELSEVIER

Radiotherapy & Oncology

Journal of the European SocieTy for Radiotherapy and Oncology

ICHNO 2024

21-23 March 2024
Barcelona, Spain

ESTRO

Radiotherapy &Oncology

Journal of the European SocieTy for
Radiotherapy and Oncology

Volume 192 Supplement 1 (2024)

ESTRO

ECCO
FOUNDING
MEMBER

Radiotherapy & Oncology is available online:
For ESTRO members: http://www.thegreenjournal.com
For institutional libraries: http://www.sciencedirect.com

ELSEVIER

Amsterdam • Boston • London • New York • Oxford • Paris • Philadelphia • San Diego • St. Louis

International Standard Serial Number 0167-8140

Orders, claims, and journal inquiries: Please visit our Support Hub page https://service.elsevier.com for assistance.

Funding Body Agreements and Policies

Elsevier has established agreements and developed policies to allow authors whose articles appear in journals published by Elsevier, to comply with potential manuscript archiving requirements as specified as conditions of their grant awards. To learn more about existing agreements and policies please visit https://www.elsevier.com/fundingbodies

Available online at www.sciencedirect.com

ScienceDirect

ICHNO 2024

21-23 March 2024
Barcelona, Spain

Table of contents

SPEAKER ABSTRACTS ..... **Page 8**

PROFFERED PAPERS ..... **Page 20**

POSTERS..... **Page 78**

SPEAKER ABSTRACTS

62

What is the functional gain?

Katherine Hutcheson

The University of Texas, MD Anderson Cancer Center, Houston, USA

Abstract

Swallow optimized IMRT is now supported by level 1 evidence from the phase III DARS trial (CRUK/14/014). By avoiding non-target RT dose to the pharyngeal constrictors, dysphagia optimized IMRT achieved mean MDADI score 7.2 points lower than conventional IMRT as 12 months. What does this mean? Is this a meaningful difference in swallowing function? Will the functional gain be durable into the second decade of survivorship?

After a primer on radiation-associated dysphagia in oropharyngeal cancer, the presenter will pragmatically interpret the DARS results from the perspective of a dysphagia specialist - including implications for supportive care. DARS results will be put into context of contemporary function-sparing trials in oropharynx cancer.

63

Techniques and outcomes from trials of dysphagia-optimised IMRT

Christopher Nutting

Royal Marsden Hospital, London, United Kingdom

Abstract

Dysphagia remains one of the most common complications of chemoradiotherapy in patients with head neck cancer.

The pathophysiology is thought to be due to atrophy and fibrosis or possibly neuromuscular damage to the pharyngeal muscles which control swallowing function.

Radiotherapy techniques have been developed to reduce the dose to the pharyngeal muscles in an attempt to ameliorate this long-term side effect for patients.

Techniques of dysphagia optimised radiotherapy will be discussed and the results of clinical trials will be presented.

Conclusions regarding mechanism of action of dysphagia optimise IMRT will be discussed and future directions for research will be presented.

64

Does dysphagia optimised radiation matter in the adjuvant setting

Pierre Blanchard

Gustave Roussy Cancer Center, Radiation Oncology, Villejuif, France

Abstract

Although the issue has been relatively under-studied, the relationship between swallowing outcomes and radiotherapy dose to dysphagia and aspiration-related structures (DARS) may be different following definitive versus postoperative radiotherapy (PORT) for mucosal head and neck cancer (HNC). It also likely different across the head and neck subsites, given the variety of swallowing structures involved and surgical interventions performed. The goal of the presentation will be to provide an overview of swallowing outcomes and trajectories after surgery or surgery plus adjuvant radiotherapy for head and neck cancers, the potential organs at risk involved and the ability to spare them during radiotherapy planning, as well as the results of the interventions published to date and future directions.

65

Recent developments in antibody-drug conjugates (ADC) in the treatment of head & neck cancer

Christophe Le Tourneau

Institut Curie, Department of Drug Development and Innovation (D3i), Paris, France

Abstract

Chemotherapy, targeted therapy and immunotherapy represent standard of care treatment options in patients with head and neck squamous cell carcinoma (HNSCC). Despite this armamentarium, the prognosis of patients with recurrent and/or metastatic disease remains poor.

Antibody drug conjugates (ADC) are a novel class of anticancer drugs that are composed by an antibody, a linker and a payload consisting of anticancer drug. Additional important features include the Drug Antibody Ratio (DAR) and the stability of the linker. The aim of ADCs is to deliver conjugated drugs selectively to cancer cells while sparing normal cells.

First ADCs were approved for clinical use more than two decades ago, initially for the treatment of hematological malignancies followed by metastatic breast cancer.

The most obvious target for ADCs in HNSCC is EGFR, but other targets were investigated as well. Results of clinical trials investigating the safety and efficacy of ADCs in HNSCC will be presented.

68

Changing paradigm in the treatment of nasopharyngeal carcinoma

Brigette Ma

The Chinese University of Hong Kong, Clinical Oncology, Shatin, Hong Kong

Abstract

Nasopharyngeal cancer (NPC) is a deadly disease where over 50% of people are diagnosed at advanced stage, of whom a third dies from cancer recurring after radiotherapy. It is endemic to Southeast Asia, Southern China and North Africa, with an age-standardized global incidence rate of over 2 per 100,000 in 2019. Over the last two decades, the treatment paradigm of advanced NPC has changed substantially. These advances include the use of concurrent chemotherapy during radiotherapy, the use of immunotherapy in combination with chemotherapy, and also the clinical application of 'liquid biopsy' with plasma Epstein-Barr virus DNA blood test in monitoring response to treatment. The mutational and immune landscape of NPC has also been extensively elucidated since 2014, leading to the discovery of new biomarkers and potential therapeutic targets. This lecture will outline the practice-changing in the treatment of advanced NPC over the last two decades and their impact on patient's survival.

69

Innovating multidisciplinary rehabilitation after head & neck cancer treatment

Michiel W van den Brekel[1,2], Lisette van der Molen[1]

[1]Netherlands Cancer Institute, Head and Neck Surgery, Amsterdam, Netherlands. [2]University of Amsterdam, ACLC, Amsterdam, Netherlands

Abstract

Head and neck cancer treatment is associated with toxicity and long-term morbidity. Especially in advanced cases, these long term consequences can have a serious impact on quality of life and functioning of the patients. In the Netherlands Cancer institute, since long we have focussed on reducing toxicity and limiting long term sequels of the tumor and treatment. Apart from focussing on organ and function preservation, programs on prehabilitation as well as post-treatment rehabilitation have been implemented and studied in our institute. Using focussed screening protocols, patients in need of rehabilitation support are selected for targeted interventions. In this key-note lecture, an overview will be presented on our research efforts in laryngectomy rehabilitation, development of medical devices in this field, dysphagia and lymphedema studies as well as our multidisciplinary rehabilitation program.

70

Next generation robotic systems

Christian Simon

CHUV, ORL, Lausanne, Switzerland

Abstract

This presentation will focus on currently available robotic systems for head and neck surgery, how to exploit them beyond trans-oral surgery, i.e hybrid approaches, and address future concepts, i.e. „soft" robots, all in the context of optimizing surgical margins.

73

Long-term psychosocial impact of head & neck cancer treatment

Irma Verdonck- de Leeuw

AmsterdamUMC, ENT, Amsterdam, Netherlands

Abstract

Advancing insights into QOL of long-term survivors

In this presentation, the following topics will be addressed:

- Changes in health related quality of life over time from time of diagnosis to 2 years after treatment
- Health related quality of life in relation to survival
- What is the role of personal, clinical, biological, physical, psychological, social, lifestyle, and HNC-related factors?

Data was used of The NETherlands QUality of life and BIomedical Cohort study in head and neck cancer (HNC) (NET-QUBIC) a prospective cohort study including 739 HNC patients and 262 informal caregivers. NET-QUBIC comprises a Data Warehouse and Biobank integrating detailed clinical information and data derived from patient reported outcomes, interviews, and functional tests, and samples of tumour tissue, blood, oral rinse, and saliva. Data and samples are available to researchers worldwide via data releases that are announced on www.kubusproject.nl.

In the present study, we used NET-QUBIC data and samples to investigate the course of health related quality of life of HNC patients from diagnosis to 3, 6, 12 and 24 months after treatment. Health related quality of life was operationalised by the EORTC QLQ-C30 global quality of life subscale (2 items) and the summary score.

75

Inflammation and post-tx sickness syndrome as an explanation for late effects

Paolo Bossi

Humanitas University, Medical Oncology, Milan, Italy

Abstract

The changing epidemiology of head and neck cancer, with an increase in HPV-positive oropharyngeal cancers and the refinement of a multidisciplinary approach, has led to an increase in the prevalence of long-term survivors after treatment. Consequently, a higher proportion of patients are suffering from late effects of the treatments, temporally defined as effects occurring or persisting more than 3 months after the end of the treatments. These late toxicities consist both of locoregional problems and systemic syndromes, with an impact on patients' quality of life.

There is still limited knowledge about the precise causes of these late toxicities, and at the same level, we lack predictive factors able to identify patients at higher risk of late effects. Treatment combinations with surgery followed by (chemo)radiation or with chemotherapy added to radiation with a radiosensitizing effect increase the probability of suffering from the late consequences of the same therapies. Pain, swallowing difficulties, trismus, osteonecrosis, dental disorders, mucositis, xerostomia or sticky saliva, hoarseness, lymphedema, and fibrosis are the most reported symptoms and signs, while fatigue, anxiety, depression, and cognitive impairment are the counterparts at the systemic level.

There is growing evidence for the role of inflammation in the progression of cancer and treatment-related side effects. However, for head and neck cancer patients, there are still a lot of unanswered questions related to the role of inflammation as being both related to cancer disease and to the consequences of the intensive treatments carried out for this disease. In particular, it is well known that pro-inflammatory cytokines have been shown to be activated by malignant tumors and cancer treatment, and that their level during treatment is linked to higher acute toxicities. Also, the level of pro-inflammatory cytokines such as interleukin (IL)-1 beta (IL-1β), IL-6, IL-8, and tumor necrosis factor (TNF) has been correlated to higher mucositis, dysphagia, and pain due to the acute toxic effect of chemoradiation. However, researchers have not yet proven the association between the level of pro-inflammatory cytokines in the acute phase of the treatment and the development of late toxicities. Even the role of the same pro-inflammatory mediators in the follow-up period has a conflicting correlation with the late toxicities reported by the patients. Chronic inflammation may cause fibrosis, one of the key pathological features of radiation-induced late effects such as dysphagia and transforming growth factor beta (TGF-β) and TNF are involved in the formation of fibrosis in irradiated tissue. There is even more debate about the cause of systemic symptoms after cancer treatment. Head and neck cancer patients may develop the post-treatment sickness syndrome, consisting of chronic fatigue, mood alteration, cognitive impairment, and sleep problems, among the most frequently reported symptoms. The neuro-behavioral sickness model recapitulates all these symptoms as being related to the stress induced by the treatment, causing alterations in mood, cognition, nutritional intake, and the neurovegetative system. One of the hypotheses is that activation of peripheral pro-inflammatory cytokine networks transmits signals to the brain, which promote sickness behavior. The tissue damage induced by the oncological treatments would result in a self-perpetuating activation of biological processes, leading to a persistent inflammation condition that results in worsening systemic late effects over time. However, this theory needs to be carefully validated with prospective studies exploring patient-reported outcomes and their correlation with inflammatory mediators. According to this model, if inflammation recapitulates the locoregional and systemic late toxicities induced by the treatments, research should lead efforts to find ways to counteract it. From one side, it is possible to define de-escalating treatments that could offer the same level of cancer control with a reduced burden of acute

and late toxicities. This is particularly awaited in HPV-positive cancer patients, who are usually younger patients, obtaining higher survival rates and thus a higher impact of toxicities on quality of life. On the other hand, it is important to define specific protocols to reduce the impact of inflammation in the long-term. In this regard, the role of physical exercise has been clearly underestimated, and recent research has shown benefits for the survival and quality of life of head and neck cancer patients. Also, even with less scientific evidence, nutrition could offer a less inflamed systemic status that could help minimize the late effects of cancer treatment. It is clear that research in this field is in its infancy, and we need to put more efforts into defining the translational correlates of late toxicities and exploring new ways to counteract the post-treatment sickness syndrome.

77

Emerging strategies for head & neck cancer prevention

Pierre Saintigny

Centre Léon Bérard, Medical Oncology, Lyon, France

Abstract

Head and neck squamous cell carcinoma (HNSCC) is a group of malignancies mostly involving the oral cavity, oropharynx, hypopharynx, and larynx. All together they represent the seventh most common cancer diagnosis worldwide. With 890,000 new cases and 450,000 deaths annually per GLOBOCAN estimates, HNSCC accounts for roughly 4.5% of cancer diagnoses and deaths. In the developing world, the incidence of HNSCC is growing with increasing consumption of tobacco (smoked or chewed), alcohol, and areca nut (betel quid). Alcohol and tobacco have a synergistic effect, with the heavy consumption of both increasing HNSCC risk 40-fold. In this context, the risk of second primary tumors in the field of cancerization is high. In developed nations, HPV-related HNSCC surpasses tobacco- and alcohol-related disease. HPV-related HNSCC more commonly affects the oropharynx, hypopharynx, and larynx than the oral cavity, and is associated with a significantly longer survival.

Based on this epidemiological facts, different strategies involving primary, secondary and tertiary prevention will be discussed. For prevention of HPV-positive HNSCC, emphasis will be given to vaccination strategies and novel diagnostic biomarkers for early detection. HPV-negative HNSCC are mostly represented by oral cavity cancers. In this particular context, a Working Group of international experts was convened by the International Agency for Research on Cancer (IARC) to review and assess all available evidence on the effectiveness of primary and secondary preventive interventions in reducing the incidence of and mortality from oral cancer. Available evidence will be summarized. Finally, we will address the challenge of unmet oral cancer prevention in the context of oral potentially malignant disorders (OPMD) in terms of oral cancer risk assessment and pharmacological interception approachs.

In conclusion, a lot remains to be done to improve the prevention of HNSCC but significant opportunities exist that will hopefully allow in the near future to significantly decrease its morbidity, mortality, and profound impact on patient's quality of life.

78

Targeting tumor-promoting myeloid cell functions in head & neck cancer

Jadwiga Jablonska

University Hospital Essen, Otorhinolaryngology (ENT), Essen, Germany

Abstract

Myeloid cells are a major component of immune cells infiltrating tumors, interacting with each other, with tumor cells and other stromal cells, and demonstrating a prominent plasticity. Tumor-associated myeloid cells, such as neutrophils (or so-called MDSCs: suppressory neutrophils) contribute to cancer progression via multiple mechanisms. Neutrophils are the most abundant myeloid blood cells, which have been shown to exert heterogeneous phenotypic and functional states: reaching from anti- to pro-tumoral. On the one hand these cells can suppress anti-tumor immune responses, support tumor angiogenesis or metastatic dissemination. On the other hand, neutrophils actively kill tumor cells, or activate T-cell dependent immune responses.

There is still little information on tumor-infiltrating neutrophils and their clinical relevance. Nevertheless, neutrophils were demonstrated to be associated with poor clinical outcome in patients with different kinds of cancer, including renal cancer, non-small-cell lung carcinoma, melanoma and head and neck cancer. Enrichment of neutrophils was also associated with metastases in various tumor entities. The recruitment of neutrophils within the tumor microenvironment is strictly regulated by chemokines, such as CXCL2 or CXCL8/IL-8.

Neutrophil activity strongly depends on the stimulus present in the microenvironment. Since these cells are highly plastic and can easily alter their functionality, they are an ideal target for designing anti-tumor therapies. However, most of therapeutic strategies to target neutrophils in tumor-bearing hosts are dealing with the blocking of their migration into the tumor site. The efficiency of such approaches is, however, limited, as it does not address heterogeneity of these cells, and thus depletes as well anti-tumoral cells, leading to cancer progression and infectious complications.

Given a critical role of neutrophils in tumor progression, we tested several alternative strategies to neutralize pro-tumoral activity of these cells, including reprogramming and inhibition of their immunosuppressive functions. Our recent data using own designed CCL2 peptide MyeloMIB show promising therapeutic results in head and neck cancer preclinical models. Application of this peptide leads not only to the specific inhibition of neutrophil migration into tumor tissue, but also reprograms these cells into anti-tumoral state. These results suggest a dual-edged role of neutrophils as essential regulators of anti-cancer immune responses and argue for approaches fostering anti-cancer activity of these cells, not only their migration, during cancer immunotherapy.

79

Biomarker of response to immunotherapy

Pablo Nenclares

Barts Cancer Centre, Clinical Oncology, London, United Kingdom. The Institute of Cancer Research, Radiotherapy and Imaging, London, United Kingdom

Abstract

Immunotherapy has revolutionized the treatment in head and neck squamous cell carcinoma (HNSCC). Immune checkpoints inhibitors (ICI) that target the programmed death-1 (PD-1) axis have shown unprecedented rates of durable responses in relapsed and metastatic (R/M) HNSCC. Indeed, pembrolizumab monotherapy or in combination with platinum-based chemotherapy has been approved in the first line setting for R/M HNSCC and nivolumab has received approval in the second line platinum-refractory setting. However, a significant number of treated patients do not respond, and the potential for serious side effects remains. There is a growing imperative to identify biomarkers that can enhance the selection of patients likely to respond optimally to therapy, provide deeper insights into drug mechanisms of action, and facilitate the customization of therapy regimens.

Currently, only combined positivity score (CPS) for PD-L1, a score based on the ratio between tumour cells and immune cells expressing PD-L1 to define tumour PD-L1 positivity, has shown a positive correlation with response to pembrolizumab and survival in the phase III KEYNOTE-048 study. In KEYNOTE-040, the correlation with clinical outcome was also strongly positive when using PD-L1 expression in tumour cells only (TPS 50%), congruent with the experience in non-small cell lung cancer in KEYNOTE-010. In contrast, no correlation was found in the nivolumab CHECKMATE-141 study, where PD-L1 expression was exclusively determined in tumour cells. Furthermore, PD-L1 negative patients may still benefit from ICI in combination with chemotherapy. Crucially, the regulation of PD-L1 expression involves various signalling pathways, including MAPK, PI3K, and Akt/PKB, which are frequently altered in HNSCC. Due to these molecular crosstalks, PD-L1 emerges as a dynamic biomarker, exhibiting temporal variations and spatial heterogeneity. Its expression may undergo changes from initial diagnosis to recurrence or progression and may vary between primary and coexisting metastatic lesions. Indeed, conflicting results regarding the intra-tumoural heterogeneity of PD-L1 expression in HNSCC are evident in published reports. Therefore, additional factors beyond PD-L1 expression might also contribute to treatment response. On this regard, some preliminary studies have shown that tumour mutational burden (TMB), T-cell-inflamed gene expression profile and human papillomavirus (HPV) status may correlate with response to ICI. In addition, somatic mutations with frameshift events in tumour suppressors (i.e. NOTCH1, SMARCA4) appear significantly enriched in among HPV-negative responders. Type I interferons (IFNs) play a crucial role in the mechanism through which the innate immune sensing of tumours leads to recruitment of cytotoxic T cells, a pivotal step in establishing an inflamed tumour microenvironment. In the context of HNSCC, the relationship between IFNs and response to ICI was explored in the KEYNOTE-O12 trial, where the results revealed a statistically significant association between the pre-treatment IFN-γ gene signature (including IDO1, CXCL10, CXCL9, HLA-DRA, STAT1, IFN-γ gene expression) and best overall response and progression-free survival, suggesting its potential as a biomarker for patient exclusion from immunotherapy, given its high negative predictive value.

Although tumour tissue-based biomarkers are extensively employed for identifying patients with enhanced responsiveness to ICI, several challenges persist in clinical practice such as its invasive nature (constrained by tumour accessibility, patient's overall condition and potential procedure-related complications), spatial heterogeneity and low tumour content. Furthermore, the dynamic nature of cancer immunity during immunotherapy makes longitudinal monitoring through repeated biopsies impractical in the clinical setting. Consequently, clinicians typically base decisions on a pre-treatment single-timepoint tumour biopsy, rather than conducting repeated biopsies to track the evolving immunological profiles. The emergence of high throughput multiplexed analytical technologies has made peripheral blood a viable source for more comprehensive immune profiling. Peripheral blood sampling, being readily available, minimally invasive, and repeatable, offers a means to address the aforementioned limitations of tissue-based biomarkers. On this regard, circulating biomarkers such as serum proteins and cytokines, circulating immune and tumour cells, and T-cell receptor repertoire dynamics, are under exploration. Finally, host-related markers have been gradually explored. These include general characteristics (i.e. sex, age and performance status), host germline genetics and

intestinal commensal microbiota. Accumulating evidence suggests that the intestinal microbiota can influence host anti-cancer immune responses and impact the efficacy of anticancer therapies, including immunotherapy. The role of the microbiota in predicting the response to ICI in HNSCC is yet to be fully understood. A single sub-study from CHECKMATE-141 that explored the oral microbiota measured in saliva as a potential predictive biomarker in patients with R/M HNSCC treated with nivolumab showed no significant correlation with treatment efficacy or survival, but it had limitations such as non-uniform sample collection, small number of responses for correlation, and notably and omission of the analysis of the intestinal microbiota. Considering the immunomodulatory effects of the intestinal microbiota and the emerging evidence of the oral microbiota influencing HNSCC tumorigenesis and progression, there is a need to study their role as predictive biomarkers for the response to ICI in HNSCC.

The pursuit of reliable biomarkers is constrained by our incomplete understanding of how immunotherapies modify the intricate immune response to cancer, along with the impact of immuno-editing on a dynamic and inducible tumour microenvironment and immune milieu. Moreover, the limited extension of candidate assays into large, prospective studies and the lack of standardization in measurement and interpretation curtail their validity.

270

Radiologic diagnosis of Extranodal Extension (ENE) in patients with HPV-positive oropharyngeal cancer: consensus diagnosis and influence on prognosis

Shao Hui Huang

Princess Margaret Cancer Centre, Radiation Oncology, Toronto, Canada

Abstract

Tumor often progresses through the weakest part of any surrounding tissues. The extent of tumor invasion depends on: a. Aggressiveness of the tumor cells (e.g. number and invasive character of stem cells), b. robustness of the surrounding tissues and their composition (e.g. vessels), and c. time to allow the tumor to proliferate. The lymph node (LN) capsule comprises dense connective tissue stroma and collagenous fibers, and is a natural barrier that generally prevents further tumor progression. Permeation of tumor through the nodal capsule into surrounding tissues is termed “extranodal extension”. The idiosyncratic and inconsistent mechanism of ENE is imprecisely understood, but it is thought to be due to either tumor cell proliferation that outpaces the capacity of nodal capsular expansion (“ruptures” the LN capsule), or factors within the tumor or tumor microenvironment that facilitate the “breach” of the capsule. The latter might explain ENE in small LNs, or a “neglected” tumor (lengthy intranodal tumor growth with eventual “rupture” through an expanded nodal capsule). Several biomarkers (e.g. podoplanin) that are often associated with tumor aggressiveness have been reported to have a high expression in ENE+ LN. ENE represents a spectrum of tumor nodal invasion. The early sign of ENE can only be visible under the microscope (pathologic ENE); when ENE progresses further, the radiographic signal changes become apparent, making it visible on imaging (iENE). Most advanced ENE causes emergence of clinical surrogates (e.g. *peau d'orange*, or a “fixed” nodal mass), rendering it detectable by regular clinical examination (ENEc). iENE has been reported to be one of the strongest anatomic prognostic factors for overall survival (mainly due to increased risk of distant metastasis) in HPV-positive oropharyngeal carcinoma (HPV+ OPC), and is able to identify a subgroup of stage I disease with poor prognosis. Several deintensification trials (NRG-HN002, ORATOR, ORATOR2, E3311) have excluded HPV+ OPC with some form of iENE from trial enrolment. Several authors have proposed that iENE be included in future clinical N classification for HPV+ OPC. However, adoption of iENE in clinical care remains challenging because it is not a well-defined radiologic feature among the radiology

community. Various definitions / descriptions of iENE have been used in literature. There is also insufficient awareness of the prognostic importance of this parameter in head and neck oncology community. The international iENE Expert Panel was convened under the HNCIG comprised expert internationally renowned neuroradiologists and clinicians. Several rounds of Delphi process were conducted to consolidate iENE definition. The consensus recommendations on the terminology and diagnostic criteria for iENE were generated. The experts in the consensus process recognized the following as criteria for the diagnosis of iENE: clear evidence of irregular or indistinct nodal margin/border; extension into perinodal fat; extension into adjacent structures, and conglomerate/matted/coalescent nodes. These recommendations have been endorsed by 19 national organisations, representing 34 countries. With increased awareness and consolidated definition as well as training, iENE could become an important baseline factor for risk stratification and staging in HPV+ OPC.

PROFFERED PAPERS

25

Utilizing H&E Images and Digital Pathology to Predict Response to Buparlisib in SCCHN

Denis Soulières[1], Justin Lucas[2], Antoine Desilets[1], Orit Matcovitch-Natan[3], Amit Bart[3], Shir Rosen Zvi[3], Amit Gutwillig[3], Kevin Dreyer[4], Tom Tang[4], Lars Birgerson[4], Jochen Lorch[5], Lisa Licitra[6]

[1]CHUM, Hématologue et Oncologue Médical, Montreal, Canada. [2]Adlai Nortye, Translational Research, New Jersey, USA. [3]Nucleai, Translational Research, Tel Aviv-Yafo, Israel. [4]Adlai Nortye, Clinical Research, New Jersey, USA. [5]Northwestern Medical Group, Hematology and Medical Oncology, Chicago, USA. [6]National Cancer Institute of Milan, Head and Neck Tumors, Milan, Italy

Topic

Biology and molecular targeting

Keywords

H&E, Image Analysis, Therapeutic Improvement

Purpose/Objective

This study aimed to evaluate a novel methodology to identify subjects that could derive benefit from Buparlisib treatment in metastatic SCCHN patients. The analysis was focused on image analysis of H&E images to select features associated with improved clinical benefit from paclitaxel+buparlisib.

Material/Methods

BERIL-1 (NCT01852292) was a multicenter, randomized, double-blind, placebo-controlled phase II study evaluating treatment with either buparlisib + paclitaxel or placebo + paclitaxel in adult patients with histologically or cytologically confirmed recurrent or metastatic SCCHN. H&E stained whole slide images (WSI) were scanned at 40x and a model was developed to identify features of the tumor and the tumor immune microenvironment through digital pathology. We then evaluated spatial histological biomarkers from 145 subjects (73 in treatment & 72 in placebo arms) associated with improvement in efficacy endpoints of Progression Free Survival (PFS) and Overall Survival (OS) within and between the treatment and control arms.

Results

A deep learning model was developed that can accurately identify and classify tumor, necrotic and stromal areas as well as fibroblast, endothelial and immune cells (plasma, lymphocyte, granulocyte), from H&E images. The accuracy of this model was developed against the ground truth of human pathology analysis of the same images. This analysis demonstrated that a >10% infiltration of TILs ($p=0.00058$, HR=0.195) as well the heterogeneity of cells in the TME ($p=0.015$, HR=0.53) are both associated with a survival advantage in patients receiving the combination treatment when compared to placebo. Moreover, we discovered that the proximity of granulocytes to tumor cells ($p=0.00006$, HR=0.32) is associated with improved survival in patients treated with buparlisib + paclitaxel combination therapy.

Conclusion

This analysis highlights a novel approach, utilizing the common and cost-effective biomarker of H&E to identify metastatic SCCHN subjects that could derive therapeutic benefit from the combination of

Buparlisib + paclitaxel. Further analysis will be conducted to determine if this method provides a better prediction of clinical benefit than regular pathology evaluation. This approach also highlights interesting and novel biological observations that underscore the mechanisms of this therapeutic combination that could lead to studies evaluating novel therapeutic combinations. The results of this analysis can be expanded to the ongoing Phase III BURAN study to further optimize and validate this method of identifying subjects for therapeutic intervention; providing a fast and cost effective method for clinicians to understand which subject would benefit from treatment with Buparlisib.

44

Refining cN classification for HPV-positive oropharyngeal carcinoma: a multi-center study

Shao Hui Huang[1], Jie Su[2], Shlomo A Koyfman[3], David Routman[4], Frank Hoebers[5], Eugene Yu[6], Eric Bartlett[6], Anna Spreafico[7], Jonathan Lee[8], Sarah Stock[8], Robin Davis[3], Neil M Woody[3], Alex A Nagelschneider[9], Daniel Ma[4], Kathryn M Van Abel[4], Alida A Postma[10], Walter M Palm[10], Ann Hoeben[11], William Lydiatt[12], Snehal Patel[13], Wei Xu[2], Brian O'Sullivan[1]

[1]Princess Margaret Cancer Centre, Radiation Oncology, Toronto, Canada. [2]Princess Margaret Cancer Centre, Biostatistics, Toronto, Canada. [3]Cleveland Clinic Taussig Cancer Institute, Radiation Oncology, Cleveland, USA. [4]Mayo Clinic, Radiation Oncology, Rochester, USA. [5]Maastricht University Medical Centre, Radiation Oncology, Maastricht, Netherlands. [6]Princess Margaret Cancer Centre, Radiology, Toronto, Canada. [7]Princess Margaret Cancer Centre, Division of Medical Oncology, Toronto, Canada. [8]Cleveland Clinic Taussig Cancer Institute, Radiology, Cleveland, USA. [9]Mayo Clinic, Radiology, Rochester, USA. [10]Maastricht University Medical Centre, Radiology, Maastricht, Netherlands. [11]Maastricht University Medical Centre, nt of Medical Oncology, Maastricht, Netherlands. [12]Nebraska Methodist Hospital, Department of Surgery, Omaha, USA. [13]Memorial Sloan Kettering Cancer Center, Department of Surgery, New York, USA

Topic

HPV or EBV related cancers

Keywords

HPV; Oropharngeal carcinoma; extranodal extension,

Purpose/Objective

Although, the 8th edition TNM (TNM8) significantly improved risk stratification of HPV-positive oropharyngeal carcinoma (HPV+ OPC) compared to the 7th edition TNM (TNM7) which was agnostic to tumor HPV status, undesirable heterogeneity still exists within each N category of the TNM8 classification, especially in cN1 disease. Compelling evidence suggests that image-identified extranodal extension (iENE) is prognostic in HPV+ OPC. The International Collaboration of Oropharyngeal cancer Network evaluated its role in refining the TNM8 cN classification in HPV+ OPC (ICON-N-HPV+).

Material/Methods

Curative-intent HPV+ OPC from 4 institutions in Canada, USA, and the Netherlands were included. cN+ patients were randomly allocated to Training (60%) and Validation (40%) datasets. All cases were staged according to TNM8. Pre-treatment (within 8 weeks of treatment commencement) CT/MRI were

reviewed by radiologists for presence/absence of iENE (iENE+/iENE–) and other nodal features, including total lymph node (LN) number, laterality of neck nodes, presence of retropharyngeal LN [RPLN]) using a priori definition. Multivariable analysis (MVA) employing a step-wise approach evaluated the prognostic value of iENE and other nodal features for overall survival (OS) in cN+ patients in both Training and Validation datasets, adjusted for age, smoking, T-categories, N-categories, and treatment. We used the adjusted hazard ratio (AHR) and recursive-partitioning analysis (RPA) methods to derive cN-classifications that included nodal features that were significant in MVA. We evaluated the performance of stage schemas using the refined cN-classifications (including cN0) against TNM8 for hazard consistency, hazard discrimination, outcome prediction, and sample size balance.

Results

A total of 1898 cN+ (1139 Training; 759 Validation) and 155 cN0 patients were included. iENE+ patients accounted for 37% (710/1898) of cN+ patients. The Training dataset contained 435 (38%) iENE+ and 704 (62%) iENE– cases. iENE positivity increased with higher cN categories: 33% in N1, 43% in N2, and 82% in N3 diseases. Median follow-up was 5.1 years. The iENE+ cohort (vs iENE–) had inferior 5-year OS (69% vs 86%) vs iENE–. MVA confirmed that iENE was prognostic for both Training (Hazard ratio [HR] 2.72) and Validation (HR 1.90) datasets ($p<0.001$). RPLN and LN number (5+ vs 1-4) were also significant in univariable analysis but non-significant in MVA. We proposed to reclassify iENE+ cases one-stratum higher than that of the existing TNM8 cN, while iENE– either remained as TNM8 cN categories based on AHR model. To evaluate the performance of the stage schemas on OS and DFS, we reassembled cN+ and cN0 patients to create various stage groupings combining the T-categories with TNM8-N, AHR_N, and RPA_N schemas, respectively. The performance of stage grouping with AHR_N and RPA_N were similarly better than that of TNM8 for OS in both Training (1.23 and 1.17 vs 3.03) and Validation (0.85 and 0.37 vs 4.06) datasets. The 5-year OS for the entire cohort by TNM8 stage I/II/III were 89%/80%/62%, by AHR stage I/II/III were 92% vs 83% vs 64%, and by RPA stage I/II/III were 91%/81%/63%. These survival changes are evident in the relocation of higher risk disease with iENE to the higher stage groupings defined by the AHR_N and RPA_N models.

Conclusion

This ICON-N-HPV+ study confirms the prognostic importance of iENE. We propose that iENE+ patients be reclassified one-stratum higher in the N categorization (similar to pN classification in HPV-negative head and neck cancer) while iENE– cases could either remain as per TNM-8 cN (AHR cN schema) or be amalgamated to form a new N1 (RPA cN schema) with consequent modification of the TNM stage groups. Since the AHR2 cN schema retains the TNM8 cN framework and is also consistent with current pN classification for non-viral head and neck cancer, it may be a more practical and less complicated proposal. T1-2_cN+_iENE– patients are potentially more appropriate candidates for deintensification trials while new strategies are needed to address the high risk of disease progression in iENE+ patients.

45

Experience of long-term fatigue and neurocognitive changes in oropharyngeal cancer survivors

Zsuzsanna Iyizoba-Ebozue[1,2], Emma Nicklin[2], James Price[3], Robin Prestwich[1], Sarah Brown[4], Emma Hall[5], John Lilley[1], Matthew Lowe[3], David Thomson[3], Finbar Slevin[1,2], Louise Murray[2,1], Florien Boele[2]

[1]Leeds Cancer Centre, Clinical Oncology, Leeds, United Kingdom. [2]University of Leeds, Leeds Institute of Medical Research, Leeds, United Kingdom. [3]The Christie NHS Foundation Trust, Manchester, UK, Clinical Oncology, Manchester, United Kingdom. [4]Leeds Cancer Research UK Clinical Trials Unit, Leeds

Institute of Clinical Trials Research, Leeds, United Kingdom. [5]The Institute of Cancer Research, London, UK, Institute of Cancer Research, London, United Kingdom

Topic

Quality of life and outcomes

Keywords

Neurocognition, Fatigue, Oropharyngeal Cancer

Purpose/Objective

Late effects of cancer treatment, such as neurocognitive deficits and fatigue, can be debilitating. Yet other than head and neck cancer (HNC) specific functional deficits such as impairments in swallowing and speech, little is known about survivorship after oropharyngeal cancer(OPC).

The National Comprehensive Cancer Network (NCCN) defines fatigue as "a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning" [1]. It is one of the most prevalent and distressing late effects of cancer treatment [2,3]. Chronic fatigue is fatigue lasting for six months or more [4,5]. In a cross-sectional study of patients with HNC, a moderate-to-severe fatigue rate of 18% at least 1 year after radiotherapy was reported [6]. This is high in comparison to a prevalence rate in the general population of approximately 0.5-1% [7,8].

During head and neck radiotherapy normal brain tissues may receive a low radiation dose, and this could have a detrimental effect on neurocognitive function[9-11]. Several small retrospective HNC series report neurocognitive dysfunction within 2 years of treatment[12-14]. Observed cognitive decline appears to persist >5 years post-treatment[15-16] and memory problems, fatigue, anxiety and reduced QoL are reported in HNC survivors[17-22]. These studies are limited by small sample sizes, heterogeneity of HNC patients sampled or having a sole focus on nasopharyngeal cancer. In addition, neurocognition has often been assessed using screening tools which lack sensitivity and domain-specific information. In addition, previous studies have mostly had quantitative methodology[23], which although valuable, lacks contextual information on how late effects may impact on patients' everyday lives.

In view of the typical profile of patients with HPV OPC the need to preserve QoL is highly relevant. Therefore, we undertook the ROC-oN study (Radiotherapy for Oropharyngeal Cancer and impact on Neurocognition reference 22/WM/0207), a mixed method cross sectional study evaluating fatigue and neurocognitive function in patients following RT +/- chemotherapy for OPC and impact on QoL.

Material/Methods

This work is part of the multicentre study ROC-oN which was approved by the West Midlands Research Ethics Committee in October 2022 (22/WM/0207), evaluating fatigue and neurocognitive function in adult patients following radiotherapy +/- chemotherapy) for oropharyngeal cancer >/=24 months post-treatment and impact of these issues on quality of life.

The full study involved patients with OPC being invited to complete a quantitative survey as well as an online, unsupervised cognitive test battery, after which a subset of participants were invited for qualitative interviews to investigate the lived experience of fatigue and neurocognitive deficits in

survivors and impact on their daily lives. Semi-structured interviews were conducted and reflexive thematic analysis was performed.

The NCCN definition of fatigue was adopted [1]. As both fatigue and neurocognition are multidimensional constructs, there is some overlap between the emotional and cognitive aspects of fatigue and neurocognitive function, and fatigue will impact on neurocognitive performance. For the purpose of this study, emotional/cognitive fatigue was considered a psychobiological state caused by demanding neurocognitive tasks, presenting as a feeling of tiredness, lack of energy, decreased motivation and alertness[24,25], while physical fatigue referred to the physical sensation of tiredness and impact of fatigue on physical activity[1,26].

Results

A total of 257 ROC-oN study participants expressed an interest in being interviewed, of whom 33 were approached and 21 were interviewed . 11 men and 10 women participated, median age was 58 years and median time post-treatment was 5 years (inter quartile range 4-8 years). Interviews took on average 52 minutes (range 41-70minutes) and produced six themes with sub-themes

Participants described fatigue that persisted beyond the acute period as well as changes in neurocognitive abilities across several neurocognitive domains with memory and attention commonly affected . This negatively influenced paid and unpaid work, as well as emotions and mood. Participants described navigating the new normal by adopting self-management strategies and accepting external support. They felt there was a lack of recognition of these late effects and expressed being poorly informed and unprepared for these. Follow up services were thought to be inadequate.

Conclusion

Fatigue and neurocognitive impairment were frequently experienced by survivors of oropharyngeal cancer, at least two years after treatment. Emotional and cognitive fatigue were most affected, along with cognitive complaints across several domains, with a likely strong correlation between these late effects. Patients felt ill-prepared for these late sequelae, highlighting opportunities for the improvement of patient information and support services.

References

[1] Berger A, Abernethy A, Atkinson A. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology: Cancer-Related Fatigue. Version 1. 2010.

[2] Bower JE, Bak K, Berger A, Breitbart W, Escalante CP, Ganz PA, et al. Screening, assessment, and management of fatigue in adult survivors of cancer: an American Society of Clinical oncology clinical practice guideline adaptation.

[3] Cella D, Davis K Fau - Breitbart W, Breitbart W Fau - Curt G, Curt G. Cancer-related fatigue: prevalence of proposed diagnostic criteria in a United States sample of cancer survivors.

[4] Reinertsen KV, Engebraaten O, Loge JH, Cvancarova M, Naume B, Wist E, et al. Fatigue During and After Breast Cancer Therapy-A Prospective Study.

[5] Goedendorp MM, Gielissen MFM, Verhagen CAHHVM, Bleijenberg G. Development of Fatigue in Cancer Survivors: A Prospective Follow-Up Study From Diagnosis Into the Year After Treatment. Journal of Pain and Symptom Management. 2013;45:213-22.

[6] Bossi P, Di Pede P, Guglielmo M, Granata R, Alfieri S, Iacovelli NA, et al. Prevalence of Fatigue in Head and Neck Cancer Survivors. Annals of Otology, Rhinology & Laryngology. 2019;128:413-9.

[7] Solomon L, Nisenbaum R, Reyes M, Papanicolaou DA, Reeves WC. Functional status of persons with chronic fatigue syndrome in the Wichita, Kansas, population. Health and quality of life outcomes. 2003;1:1-10.

[8] van't Leven M, Zielhuis GA, van der Meer JW, Verbeek AL, Bleijenberg G. Fatigue and chronic fatigue syndrome-like complaints in the general population*. European Journal of Public Health. 2010;20:251-7

[9] Cheung M, Chan As Fau - Law SC, Law Sc Fau - Chan JH, Chan Jh Fau - Tse VK, Tse VK. Cognitive function of patients with nasopharyngeal carcinoma with and without temporal lobe radionecrosis.

[10] Hsiao KY, Yeh Sa Fau - Chang C-C, Chang Cc Fau - Tsai P-C, Tsai Pc Fau - Wu J-M, Wu Jm Fau - Gau J-S, Gau JS. Cognitive function before and after intensity-modulated radiation therapy in patients with nasopharyngeal carcinoma: a prospective study.

[11] Kiang A, Weinberg VK, Cheung KH, Shugard E, Chen J, Quivey JM, et al. Long-term disease-specific and cognitive quality of life after intensity-modulated radiation therapy: a cross-sectional survey of nasopharyngeal carcinoma survivors.

[12] Hsiao K-Y, Yeh S-A, Chang C-C, Tsai P-C, Wu J-M, Gau J-S. Cognitive function before and after intensity-modulated radiation therapy in patients with nasopharyngeal carcinoma: a prospective study. International journal of radiation oncology, biology, physics. 2010;77:722-6.

[13] Hua MS, Chen ST, Tang LM, Leung WM. Neuropsychological function in patients with nasopharyngeal carcinoma after radiotherapy. Journal of clinical and experimental neuropsychology. 1998;20:684-93.

[14] Lam LCW, Leung SF, Chan YL. Progress of memory function after radiation therapy in patients with nasopharyngeal carcinoma. The Journal of neuropsychiatry and clinical neurosciences. 2003;15:90-7.

[15] Lee PW, Hung BK, Woo EK, Tai PT, Choi DT. Effects of radiation therapy on neuropsychological functioning in patients with nasopharyngeal carcinoma. Journal of neurology, neurosurgery, and psychiatry. 1989;52:488-92.

[16] McDowell LJ, Ringash J, Xu W, Chan B, Lu L, Waldron J, et al. A cross sectional study in cognitive and neurobehavioral impairment in long-term nasopharyngeal cancer survivors treated with intensity-modulated radiotherapy. Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology. 2019;131:179-85.

[17] Wilbers J, Kappelle AC, Versteeg L, Tuladhar AM, Steens SCA, Meijer FJA, et al. Cognitive function, depression, fatigue and quality of life among long-term survivors of head and neck cancer. Neuro-oncology practice. 2015;2:144-50.

[18] Zer A, Pond GR, Razak ARA, Tirona K, Gan HK, Chen EX, et al. Association of Neurocognitive Deficits With Radiotherapy or Chemoradiotherapy for Patients With Head and Neck Cancer. JAMA otolaryngology-- head & neck surgery. 2018;144:71-9.

[19] Bolt S, Baylor C, Burns M, Eadie T. "I would have told you about being forgetful, but I forgot": the experience of cognitive changes and communicative participation after head and neck cancer. Disability and rehabilitation. 2020;42:931-9.

[20] Gan HK, Bernstein LJ, Brown J, Ringash J, Vakilha M, Wang L, et al. Cognitive functioning after radiotherapy or chemoradiotherapy for head-and-neck cancer. International journal of radiation oncology, biology, physics. 2011;81:126-34.

[21] Tang Y, Luo D, Rong X, Shi X, Peng Y. Psychological disorders, cognitive dysfunction and quality of life in nasopharyngeal carcinoma patients with radiation-induced brain injury. PloS one. 2012;7:e36529.

[22] McDowell L, Corry J, Ringash J, Rischin D. Quality of Life, Toxicity and Unmet Needs in Nasopharyngeal Cancer Survivors. Frontiers in oncology. 2020;10:930.

[23] Iyizoba-Ebozue Z, Prestwich R, Brown S, Hall E, Lilley J, Lowe M, et al. Neurocognitive function following (chemo)radiotherapy for nasopharyngeal cancer and other head and neck cancers: A systematic review. Radiother Oncol. 2023;188:109863.

[24] van der Linden D, Massar SAA, Schellekens AFA, Ellenbroek BA, Verkes R-J. Disrupted sensorimotor gating due to mental fatigue: Preliminary evidence. International Journal of Psychophysiology. 2006;62:168-74.

[25] de Raaf PJ, de Klerk C Fau - van der Rijt CCD, van der Rijt CC. Elucidating the behavior of physical fatigue and mental fatigue in cancer patients: a review of the literature.

[26] Low J. A Pragmatic Definition of the Concept of Theoretical Saturation. Sociological Focus. 2019;52:131-9.

49

Development of a Normal Tissue Complication Probability Model for Dysphagia in PATHOS trial patients

Emma Higgins[1], Richard Webster[1], Nachi Palaniappan[1], Chris Hurt[2], Zohal Nabi[3], Kostas Rizos[3], Kate Elliott[3], Elizabeth Miles[3], Joanne Patterson[4], Kate Hutcheson[5], Joanne Canham[6], Lisette Nixon[6], Christie Heiberg[6], Matthew Beasley[7], Terry M Jones[8], Mererid Evans[1,9]

[1]Velindre Cancer Centre, Clinical Oncology, Cardiff, United Kingdom. [2]University of Southampton, Southampton Clinical Trials Unit, Southampton, United Kingdom. [3]Mount Vernon Cancer Centre, RTTQA, London, United Kingdom. [4]University of Liverpool, School of Health Sciences, Institute of Population Health / Liverpool Head and Neck Centre, Liverpool, United Kingdom. [5]M.D Anderson, Department of Head and Neck Surgery, Houston, USA. [6]Cardiff University, Centre for Trials Research, Cardiff, United Kingdom. [7]University Hospitals Bristol NHS Foundation Trust, Clinical Oncology, Bristol, United Kingdom. [8]University of Liverpool, Department of Moelcular and Clinical Cancer Medicine, Liverpool, United Kingdom. [9]Cardiff University, Division of Cancer and Genetics, School of Medicine for Trials Research, Cardiff, United Kingdom

Topic

HPV or EBV related cancers

Keywords

NTCP, MDADI, PATHOS

Purpose/Objective

Normal Tissue Complication Probability (NTCP) models have the potential to enable head and neck (H&N) oncologists to adopt a personalised treatment strategy for their patients by quantifying individual risks to developing specific toxicities. [1] While NCTP models for dysphagia in patients receiving definitive radiotherapy for head and neck cancer are available [1-5], suitable models, that contain the most relevant OAR with reliable dose–response estimates, are lacking in the adjuvant (post-operative) setting. This study aimed to develop a NTCP model for dysphagia, following transoral surgery and adjuvant radiotherapy for patients in the PATHOS trial [NCT: A25317]. This trial examines whether reducing the intensity of adjuvant treatment following minimally invasive transoral surgery in HPV related Oropharyngeal Squamous Cell Cancer (OPSCC) patients, either by lowering radiotherapy (RT) dose or omitting chemotherapy, will result in improved swallowing function, whilst maintaining excellent clinical outcomes.[6]

Material/Methods

The dataset consisted of 116 patients allocated into arms B1 & C2 of PATHOS from Jul 2007 to Feb 2020, who received 60Gy in 30 fractions IMRT following transoral surgery. The model endpoint of dysphagia was defined as MDADI composite score <80 at 12months post treatment (MDADI_12m). Candidate predictors included mean dose in Gy to nine swallowing OARs (SWOARs). SWOARs were outlined as per PATHOS swallowing atlas by a single investigator and checked by 2 senior investigators.

To develop the prediction model, first a univariable analysis was conducted to show the raw uncorrected effects of each candidate variable on MDADI_12m. Next non-linear transformations were evaluated for continuous variables and multicollinearity was assessed. Finally a multivariate logistic regression analysis with stepwise backward elimination was used. Model performance was evaluated using discrimination specified by the area under the receiver operating curve (AUC) and calibration using calibration-in-the-large (CITL) and calibration slope (C-slope). [7] Internal validation was completed using bootstrapping and model performance was subsequently adjusted for optimism.

Statistical analysis was conducted using Stata© software (version 17.0 SE, statacorp).

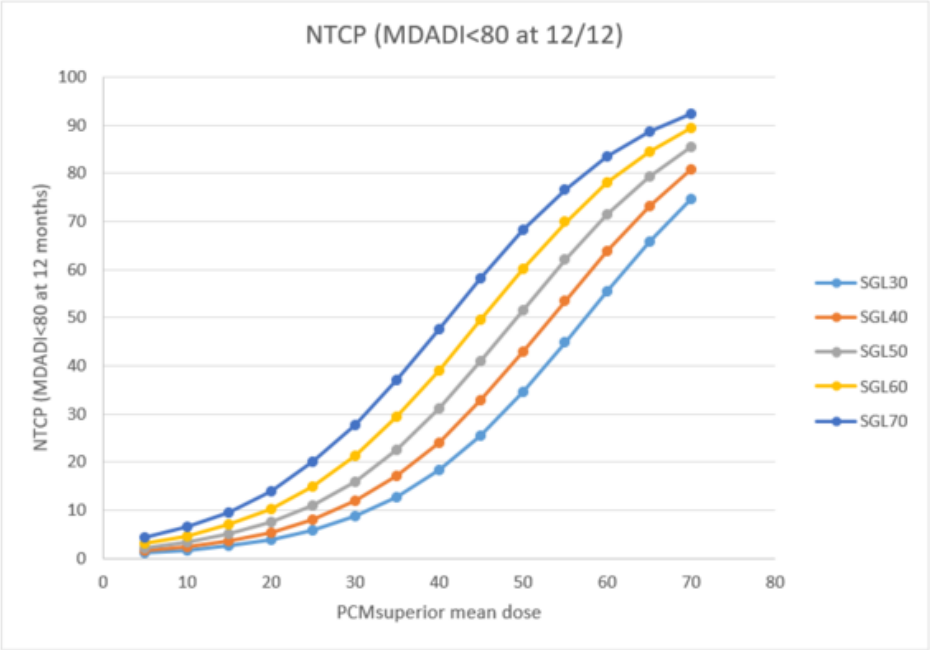
Results

The prevalence of MDADI_12m of <80 was 54%. Following pre-selection based on clinical expertise and prior knowledge, the candidate predictor variables included in the model were as follows; superior, middle and inferior pharyngeal constrictors, crico-oesophgeal inlet, supraglottic and glottic larynx and oral cavity. The multivariable model with the best performance consisted of the superior pharyngeal constrictor muscle (PCM_Superior) and the supraglottic larynx (Larynx_SG). In individual cases the risk of MDADI_12m <80 can be estimated using the following equation: NTCP MDADI_12m = $1/(1+ e^{-S})$, where S= -5.99 + (mean dose PCM Superior x 0.086) + (mean dose Larynx_SG x 0.035). (Figure 1)

Apparent model performance is presented in the calibration plot (Figure2). The AUC was 0.70 (p=0.001) showing good discrimination indicating good potential performance in populations with similar case-mix. The measures of CITL, ratio of expected to observed endpoints and C-slope were 0, 1 and 1 respectively indicating apparent perfect calibration performance as we would expect when we fit the developed model in the development cohort.

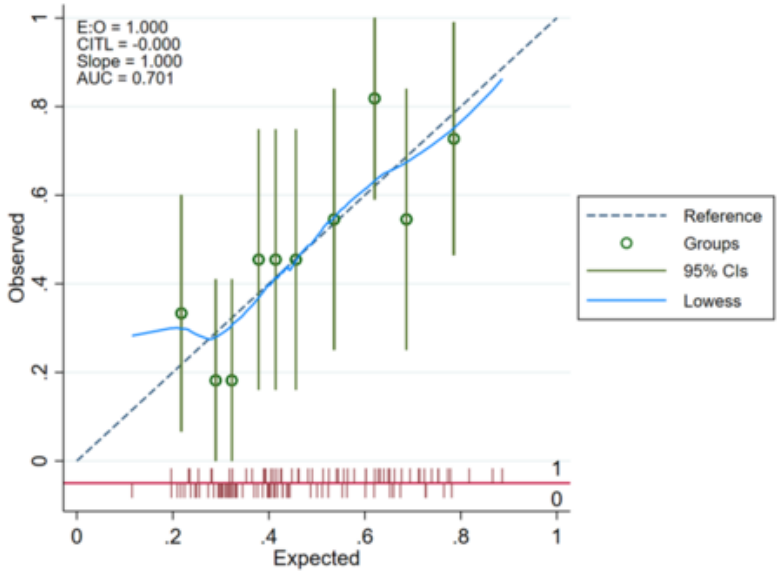
Optimism adjusted AUC, CITL and C-slope were 0.66, -0.003 and 0.73 respectively indicating good internal performance in terms of discrimination and minimal mis-calibration in CITL. However the C-slope of 0.66 suggests a moderate amount of shrinkage is required to adjust the predictor effects in the model for overfitting.

Figure 1: NCTP MDADI_12m



Normal tissue complication probability curves for MDADI_12m with each curve representing a 10 Gy increase in dose to the supraglottic larynx plotted against dose to PCM Superior mean dose. Abbreviations: NTCP = normal tissue complication probability, PCM = pharyngeal constrictor muscle, SGL = mean dose supraglottic larynx

Figure 2: Calibration Plot of Apparent Model Performance.



Calibration plot showing visual calibration across 10 risk groups of individuals. The lowess smoother shows that there is some miscalibration at the individual level in the lower and higher risk patients, though there is less data at these risk probabilities as indicated by the spike plot at the bottom of the graph. Abbreviations: AUC= Area under the curve; E:O= ratio of expected versus observed endpoints; CITL=Calibration in the large.

Conclusion

A novel NTCP model for MDADI_12m was developed to identify patients at risk for dysphagia after transoral surgery and adjuvant radiotherapy in PATHOS. Mean doses to the PCM_Superior and Larynx_SG were most predictive. An NTCP model including these parameters could be used to direct limited resources such as speech and language therapy to patients who are at highest risk of dysphagia, as well as in treatment planning to prioritise SWOAR optimisation. In future this model will need to be further updated in a larger dataset and externally validated before use in clinical practice.

The PATHOS trial is funded by Cancer Research UK (Grant no: A25317) and co-sponsored by Cardiff University and Velindre University NHS Trust.

References

1. Sharabini M, Clementel E, Andratschke N, Hurkmans C. Generalizability assessment of head and neck cancer NTCP models based on the TRIPOD criteria. Radiotherapy and Oncology 146 (2020) 143–150.

2. Van den Bosch, L., et al., Comprehensive toxicity risk profiling in radiation therapy for head and neck cancer: A new concept for individually optimised treatment. Radiother Oncol, 2021. 157: p. 147-154.

3. Wopken, K., et al., Development of a multivariable normal tissue complication probability (NTCP) model for tube feeding dependence after curative radiotherapy/chemo-radiotherapy in head and neck cancer. Radiother Oncol, 2014. 113(1): p. 95-101.

4. Beetz, I., et al., External validation of three dimensional conformal radiotherapy based NTCP models for patient-rated xerostomia and sticky saliva among patients treated with intensity modulated radiotherapy. Radiother Oncol, 2012. 105(1): p. 94-100.

5. Christianen, M.E., et al., Predictive modelling for swallowing dysfunction after primary (chemo)radiation: results of a prospective observational study. Radiother Oncol, 2012. 105(1): p. 107-14.

6. Owadally W, Hurt C, Timmins H, Parsons E, Townsend S, Patterson J, Hutcheson K, Powell N, Beasley M, Palaniappan N, Robinson, Jones T, Evans M. PATHOS: a phase II/III trial of risk-stratified, reduced intensity adjuvant treatment in patients undergoing transoral surgery for Human papillomavirus (HPV) positive oropharyngeal cancer. BMC Cancer 2015; 15: 602 DOI 10.1186/s12885-015-1598-x

7. Steyerberg EW, Vickers AJ, Cook NR, Gerds T, Gonen M, Obuchowski N, Pencina MJ, Kattan MW. Assessing the performance of prediction models: a framework for traditional and novel measures. Epidemiology. 2010 Jan;21(1): p.128-38.

87

Distinctions in Tumor Microenvironment Between PD-L1 Positive versus Negative Head and Neck Squamous Cell Carcinoma (HNSCC)

Kamal S Saini[1,2], Heidi C Ko[3], Zachary D Wallen[3], Michelle F Green[3], Kyle C Strickland[3,4], Rebecca A Previs[3,5], Shengle Zhang[3,6], Jeffrey Conroy[3,6], Taylor J Jensen[3], Brian J Caveney[3], Marcia Eisenberg[3], Laura Vidal[1], Eric A Severson[3], Shakti Ramkissoon[3,7]

[1]Fortrea Inc, Oncology, Durham, USA. [2]Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, Oncology, Cambridge, United Kingdom. [3]Labcorp Oncology, Oncology, Durham, USA. [4]Duke University Medical Center, Duke Cancer Institute, Pathology, Durham, USA. [5]Duke University Medical Center, Duke Cancer Institute, Obstetrics & Gynecology, Durham, USA. [6]Omniseq (Labcorp), Pathology, Buffalo, USA. [7]Wake Forest Comprehensive Cancer Center, Pathology, Winston-Salem, USA

Topic

Immuno-oncology

Keywords

TME, genomic profiling, PD-L1

Purpose/Objective

Background: Although immunotherapy has revolutionized the treatment paradigm of many cancers including HNSCC, only a subset of patients derives meaningful clinical benefit from immune checkpoint inhibitors (ICIs). Currently, PD-L1 protein expression remains the only predictive biomarker for ICI response studied in prospective first line immunotherapy clinical trials in HNSCC. PD-L1 expression level, however, is an imperfect biomarker for ICI response due to several limitations such as the variability in expression level cut-offs defined as positive vs. negative between assays, subjective interobserver variability and clinical sampling bias in acquiring specimens. Research efforts are ongoing to develop other biomarkers that can precisely identify patients who will derive benefits from ICIs. Our objective was to assess the results of comprehensive genomic and immune profiling (CGIP) in patients with HNSCC and describe the immune microenvironment of tumors with different levels of PD-L1 expression.

Material/Methods

Methods: A retrospective analysis of 409 patients with HNSCC tested by CGIP during standard-of-care was performed to compare the immune microenvironment of tumors with high (N=168), moderate-low (N=183), or negative (N=58) PD-L1 expression. Patient tumors were categorized into PD-L1 expression groups using combined positive score (CPS) thresholds of ≥20 (high), 1 to 19 (moderate-low), and <1 (negative). These CPS scores were selected according to the cut-offs used in the Phase III Keynote-048 study that led to the approval of pembrolizumab in HNSCC. DNA-seq of 523 genes analyzed tumor mutational burden (TMB). RNA expression analysis was performed for 395 immune genes. Gene expression-based signatures for tumor immunogenicity score (TIGS), cellular proliferation (CP) and cancer testis antigen burden (CTAB) were calculated from percentile ranks of normalized gene expression values. Expressions of three emerging biomarkers linked to an immune checkpoint mechanism (LAG3, TIGIT and TIM3) were also determined by RNA-seq. PD-L1 expression was assessed using immunohistochemistry. Wilcoxon rank-sum tests were used to detect significant differences between PD-L1 groups in TMB, gene expression signatures, and gene expressions of TIM-3, TIGIT and LAG-3.

Results

Results: Tumors with high PD-L1 demonstrated increased expression of genes associated with tumor immunogenicity compared to moderate-low (median TIGS of 54 vs 41; p<1E-4) and negative (median TIGS of 54 vs 43; p<1E-4) tumors (Fig 1B). PD-L1 high tumors also showed increased expression of other emerging biomarkers involved in immune checkpoint pathways such as LAG-3, TIGIT and TIM-3, compared to moderate-low and negative tumors (Fig 1E-G). We found no significant differences

between PD-L1 groups in TMB and the remaining composite gene expression signatures (p>0.05; Fig 1A,C,D).

Conclusion

Conclusion: Our findings highlight the complex interplay of diverse immune cells and checkpoint markers in the tumor microenvironment (TME) beyond PD-L1 in HNSCC. Tumors with high PD-L1 expression harbored a greater degree of immune infiltration, demonstrating a higher TIGS score as well as other checkpoint markers of emerging clinical importance such as LAG-3, TIGIT and TIM-3. Interestingly, tumors with PD-L1 moderate-low expression did not exhibit significant differences in TIGS, TIGIT and TIM-3, compared to PD-L1 negative tumors. These results suggest that HNSCC tumors with PD-L1 CPS ≥ 20 have the most robust immunogenic profile. Understanding the different components of TME can aid in implementing innovative therapeutic strategies to enhance the immune responses and potentially overcome resistance to ICIs in HNSCC.

References

Figure 1: Comprehensive immune profiling of HNSCC, stratified by different PD-L1 expression levels (CPS ≥ 20, 1 to 19, and <1).

98

An open-source foundation for head and neck radiomics

Katy L. Scott[1], Sejin Kim[1,2,3], Jermiah J. Joseph[1], Matthew Boccalon[1], Mattea Welch[1,3], Umar Yousafzai[4], Ian Smith[1,2], Chris McIntosh[2,5,6], Katrina Rey-McIntyre[6], Shao Hui Huang[6,7], Tirth Patel[3,5,6], Tony Tadic[3,6,7], Brian O'Sullivan[6], Scott V. Bratman[2,6,7], Andrew J. Hope[6,7], Benjamin Haibe-Kains[1,2,3]

[1]Princess Margaret Cancer Centre, Princess Margaret Research, Toronto, Canada. [2]University of Toronto, Department of Medical Biophysics, Toronto, Canada. [3]Princess Margaret Cancer Centre, Cancer Digital Intelligence, Toronto, Canada. [4]University of Waterloo, Cheriton School of Computer Science, Waterloo, Canada. [5]University Health Network, Techna Institute, Toronto, Canada. [6]Princess Margaret Cancer Centre, Radiation Medicine Program, Toronto, Canada. [7]University of Toronto, Department of Radiation Oncology, Toronto, Canada

Topic

Imaging, radiomics and artificial intelligence

Keywords

RADCURE, automated pipelines, FAIR data sharing

Purpose/Objective

With the purported future of oncological care being precision medicine, the hunt for predictive biomarkers has become a focal point. A potential source lies in radiological imaging, which has motivated the field of radiomics for the last decade [1–4]. Radiomics research, however, has been hampered by inconsistent methodology, despite efforts to establish standard features [5]. The release of the open-source PyRadiomics toolkit [6] was a significant and necessary step to standardize

radiomics analysis, but the collation and distribution of publically available radiomics datasets remains poorly organized within the community. As a result, significant overhead remains when dealing with multiple training, testing, and validation datasets from both internal and external sources. Further, a recent study has raised the question of whether radiomic features with high predictive value are surrogates for tumour volume measurements [7]. There is a need for standard methodology for radiomic feature extraction, as well as large, publicly available radiomic datasets that have undergone rigorous processing to benchmark analyses.

In this study, we have developed a reproducible, automated, open-source processing pipeline to generate analysis-ready radiomics data. We showcase the pipeline's capabilities by processing and analyzing the largest publicly available head and neck cancer (HNC) dataset, RADCURE [8], and compare three previously published radiomics models [1,7,9] using the resulting data. Data outputs have been made available via https://www.orcestra.ca/, a web-app that hosts processed 'omics data.

Material/Methods

Our proposed pipeline leverages three main tools: Med-ImageTools [10], PyRadiomics [6], and ORCESTRA [11]. While the former two are imaging-specific, we have modified ORCESTRA to work with clinical radiological data.

The proposed pipeline was developed using the RADCURE [12] dataset. It consists of 3,346 HNC CT image volumes, corresponding radiotherapy structure sets (RTSTRUCT) containing primary gross tumour volume (GTVp) contours, and clinical data. The Med-ImageTools library was used to generate complete file lists for each CT acquisition, associate these with the correct RTSTRUCT, and load both as Simple ITK [13] images.

For each GTVp, preprocessing, quality checking, and radiomic feature extraction was performed using PyRadiomics. Extraction settings from the RADCURE prognostic modelling challenge [8] were applied. Feature extraction was repeated with two negative control samples for each CT, either by shuffling voxel index values or randomly generating voxel values within the range of values in the original CT [7] (Figure 1).

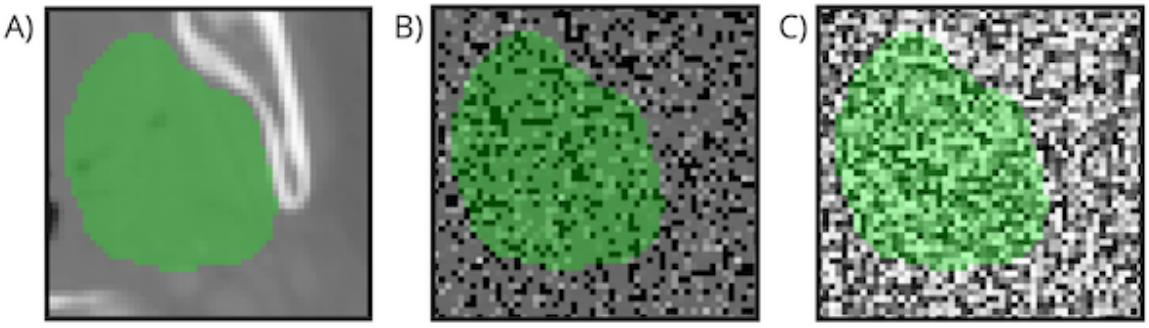


Figure 1. Cropped 2D axial slice extracted from example inputs to the radiomic feature extraction with the corresponding GTV contour (green). (A) The original CT volume; (B) volume with shuffled voxel indices from the original CT; (C) volume with randomly generated voxel values based on the original CT volume values.

The standard for data organization on ORCESTRA [11] is the MultiAssayExperiment R object [14], designed to harmonize multiple experimental assays from an overlapping patient set. To leverage this for radiomics, each set of extracted features becomes an experiment, with clinical data included as the primary metadata describing each patient.

To demonstrate the pipeline's utility, we replicated previously published survival analysis models with the training and test cohorts from the RADCURE challenge subset [8]. Coefficients from the MW2018 [7] and Kwan [9] models were used to calculate prognostic index values for the test cohort. For comparison, we fit a Cox model to the RADCURE training cohort using the same radiomic signature and applied it to the test cohort. A univariate model for GTVp Mesh Volume was also tested. All models were compared using the concordance index.

Results

We processed 2,949 patients with GTVp contours, for a total of 2,988 GTVps from patients with varying primary tumour sites. We extracted 1,317 radiomic features from the CT and the negative control volume for each GTVp. For the 37 patients with multiple GTVps, features were extracted independently for each contour.

The final data object containing all of these features, along with the clinical data and PyRadiomics configuration file, are available at https://www.orcestra.ca/radiomicset/10.5281/zenodo.8332910. The pipeline implementation is published at https://github.com/BHKLAB-DataProcessing/RADCURE_radiomics.

Results from our radiomics analysis are available in Table 1. The subset of 2400 GTVs was split into training and test cohorts based on the 'RADCURE-challenge' label in the clinical data. The Kwan model was tested with the oropharynx patients only. Model performance is similar whether the features were extracted from the CT or negative control samples, signaling that the radiomic signature is likely highly correlated with tumour volume, a known confounder of radiomics analysis. This is confirmed by the comparable performance of the univariable volume model.

Table 1. Concordance index and *p*-values from each of the replicated survival analysis models and a univariate volume model for comparison. 95% CI are shown for point-estimated c-index values. Aerts [1] radiomic signature = Energy, Compactness 1, Gray Level Run Length Matrix Non-Uniformity, Wavelet HLH Gray Level Run Length Matrix Non-Uniformity.

	Features	Image	c-Index (95% CI)	*p*-Value
MW2018 [7]	Aerts signature	Original	0.692 (0.640-0.743)	<0.001
		Shuffled	0.710 (0.660-0.759)	<0.001
		Randomized	0.587 (0.529-0.645)	0.003
Kwan [9]	Aerts signature	Original	0.522 (0.425-0.620)	0.827
		Shuffled	0.711 (0.653-0.770)	<0.001
		Randomized	0.611 (0.536-0.686)	0.004
Aerts RADCURE	Aerts signature	Original	0.726 (0.662-0.764)	<0.001
		Shuffled	0.713 (0.664-0.762)	<0.001
		Randomized	0.587 (0.529-0.645)	0.003
Univariate	Volume	Original	0.708 (0.658-0.757)	<0.001

Conclusion

This standardized architecture framework and the publicly available processed RADCURE dataset can be used to benchmark new datasets or radiomics models semi-automatically. Future work will include organ at risk and nodal targets in the RADCURE dataset and the production of ORCESTRA objects for other publicly available HNC datasets. We anticipate that this pipeline and the RADCURE objects generated could be a standard testing benchmark for future radiomics analyses and publications.

References

1. Aerts HJWL, Velazquez ER, Leijenaar RTH, Parmar C, Grossmann P, Carvalho S, et al. Decoding tumour phenotype by noninvasive imaging using a quantitative radiomics approach. Nat Commun. 2014;5: 4006.

2. Gillies RJ, Kinahan PE, Hricak H. Radiomics: Images Are More than Pictures, They Are Data. Radiology. 2016;278: 563–577.

3. Rogers W, Thulasi Seetha S, Refaee TAG, Lieverse RIY, Granzier RWY, Ibrahim A, et al. Radiomics: from qualitative to quantitative imaging. Br J Radiol. 2020;93: 20190948.

4. Lambin P, Rios-Velazquez E, Leijenaar R, Carvalho S, van Stiphout RGPM, Granton P, et al. Radiomics: extracting more information from medical images using advanced feature analysis. Eur J Cancer. 2012;48: 441–446.

5. Zwanenburg A, Vallières M, Abdalah MA, Aerts HJWL, Andrearczyk V, Apte A, et al. The Image Biomarker Standardization Initiative: Standardized Quantitative Radiomics for High-Throughput Image-based Phenotyping. Radiology. 2020;295: 328–338.

6. van Griethuysen JJM, Fedorov A, Parmar C, Hosny A, Aucoin N, Narayan V, et al. Computational Radiomics System to Decode the Radiographic Phenotype. Cancer Res. 2017;77: e104–e107.

7. Welch ML, McIntosh C, Haibe-Kains B, Milosevic MF, Wee L, Dekker A, et al. Vulnerabilities of radiomic signature development: The need for safeguards. Radiother Oncol. 2019;130: 2–9.

8. Kazmierski M, Welch M, Kim S, McIntosh C, Rey-McIntyre K, Huang SH, et al. Multi-institutional Prognostic Modeling in Head and Neck Cancer: Evaluating Impact and Generalizability of Deep Learning and Radiomics. Cancer Research Communications. 2023;3: 1140–1151.

9. Kwan JYY, Su J, Huang SH, Ghoraie LS, Xu W, Chan B, et al. Radiomic Biomarkers to Refine Risk Models for Distant Metastasis in HPV-related Oropharyngeal Carcinoma. Int J Radiat Oncol Biol Phys. 2018;102: 1107–1116.

10. Kim S, Kazmierski M, Qu K, Peoples J, Nakano M, Ramanathan V, et al. Med-ImageTools: An open-source Python package for robust data processing pipelines and curating medical imaging data. F1000Research. 2023. p. 118. doi:10.12688/f1000research.127142.1

11. Mammoliti A, Smirnov P, Nakano M, Safikhani Z, Eeles C, Seo H, et al. Orchestrating and sharing large multimodal data for transparent and reproducible research. Nat Commun. 2021;12: 5797.

12. Welch, M. L. , Kim, S. , Hope, A. , Huang, S. H. , Lu, Z. , Marsilla, J. , Kazmierski, M. , Rey-McIntyre, K. , Patel, T. , O'Sullivan, B. , Waldron, J. , Kwan, J. , Su, J. , Soltan Ghoraie, L. , Chan, H. B. , Yip, K. , Giuliani, M. , Princess Margaret Head And Neck Site Group, Bratman, S. , … Tadic, T. Computed Tomography Images from Large Head and Neck Cohort (RADCURE) (Version 1) [Data set]. The Cancer Imaging Archive; 2023. doi:10.7937/J47W-NM11

13. Lowekamp BC, Chen DT, Ibáñez L, Blezek D. The Design of SimpleITK. Front Neuroinform. 2013;7: 45.

14. Ramos M, Schiffer L, Re A, Azhar R, Basunia A, Rodriguez C, et al. Software for the Integration of Multiomics Experiments in Bioconductor. Cancer Res. 2017;77: e39–e42.

113

Longitudinal assessment of plasma EBV-DNA in non-endemic EBV-related nasopharyngeal cancers (NPC)

Salvatore Alfieri[1], Sara Marceglia[2], Carolina Sciortino[1], Walter Ferrari Bravo[1], Maria Luigia Piscitelli[3], Monica Zucchini[3], Imperia Nuzzolese[1], Rebecca Romanò[1], Stefano Cavalieri[1], Cristiana Bergamini[1], Elena Colombo[1], Resteghini Carlo[1], Arianna Ottini[1], Giuseppina Calareso[4], Pasquale Quattrone[5], De Cecco Loris[6], Ester Orlandi[7,8], Marzia Franceschini[8], Nicola Alessandro Iacovelli[8], Alberto Deganello[9], Paolo Bossi[10,11,1], Laura Deborah Locati[12,13,1], Flavio Arienti[3], Francesca Taverna[1], Lisa Francesca Licitra[1]

[1]Fondazione IRCCS Istituto Nazionale dei Tumori (INT) di Milano, Head and Neck Medical Oncology 3 Department, Milan, Italy. [2]University of Trieste, Faculty of Clinical Engineering, Trieste, Italy. [3]Fondazione IRCCS Istituto Nazionale dei Tumori (INT) di Milano, Immunohematology and Transfusion Medicine Service, Milan, Italy. [4]Fondazione IRCCS Istituto Nazionale dei Tumori (INT) di Milano, Radiology Department, Milan, Italy. [5]Fondazione IRCCS Istituto Nazionale dei Tumori (INT) di Milano, Pathology Department, Milan, Italy. [6]Fondazione IRCCS Istituto Nazionale dei Tumori (INT) di Milano, Integrated Biology of Rare Tumors, Department of Research, Milan, Italy. [7]CNAO National Center for Oncological Hadrontherapy, Radiotherapy Department, Pavia, Italy. [8]Fondazione IRCCS Istituto Nazionale dei Tumori (INT) di Milano, Radiotherapy Department, Milan, Italy. [9]Fondazione IRCCS Istituto Nazionale dei Tumori (INT) di Milano, Department of Otorhinolaryngology - Head and Neck Surgery, Milan, Italy. [10]Humanitas University, Department of Biomedical Sciences, Milan, Italy. [11]IRCCS Humanitas Research Hospital, Medical Oncology Department, Rozzano, Italy. [12]University of Pavia, Department of Internal Medicine and Therapeutics, Milan, Italy. [13]Istituti Clinici Scientifici Maugeri Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS), Medical Oncology Unit, Pavia, Italy

Topic

HPV or EBV related cancers

Keywords

Nasopharyngeal carcinoma, EBV-DNA, Biomarker

Purpose/Objective

Plasma Epstein Barr virus (EBV)-DNA is employed as a biomarker for EBER (EBV-encoded RNA) positive nasopharyngeal cancer (NPC) patients. In Europe, the use of plasma EBV-DNA is limited by the lack of harmonization among different European Conformity (CE)-marked EBV-DNA detection methods and BamHI-W, the latter being the gold standard assay in endemic areas. Our Institution demonstrated that three CE-marked (i.e., ELITech, Abbott, Artus) and BamHI-W assays significantly agreed in plasma EBV-DNA quantification in non-endemic NPC (1). In this setting, the role of plasma EBV-DNA was better defined only before curative treatment, (2) with undetectable baseline plasma EBV-DNA levels holding a positive prognostic significance in terms of disease-free survival (DFS) and overall survival (OS) (2). However, the value of CE-marked assays in Longitudinal assessment of plasma EBV-DNA (LEA) - alongside the curative management and follow-up of non-endemic NPC - is still lacking (1; 2). Herein, we present the results of the LEA study (Ethics Comittee n. 150/23) concerning the dynamics of plasma EBD-DNA viral load in a single-Institution cohort of non-endemic NPC patients.

Material/Methods

From 2012 to 2023 we retrospectively collected data of all EBER-positive NPC patients treated with curative intent at our Institution. All subjects underwent plasma EBV-DNA quantification at the following time-points: 1) pre-treatment (within 1 month since treatment start); 2) post-treatment (2A, early post-treatment, within 6 weeks after treatment completion and/or 2B, late post-treatment, within 16 weeks after treatment end); 3) follow-up phase. EBV-DNA results were classified as negative (if EBV-DNA was not detected) or positive (if EBV-DNA was detected and quantifiable or detected but not quantifiable) and were expressed as log IU/ml. Descriptive statistics were performed on all available data. The role of pre-treatment EBV-DNA as predictive factor for disease recurrence was assessed by estimating the Receiver Operating Characteristic (ROC) curve at different cut-offs. The predictive value of post-treatment (2A, 2B) EBV-DNA load was assessed considering its ability to forecast recurrence. For patients with both 2A and 2B available samples, the 2B value was considered for post-treatment analyses.

Results

At the data cut-off (Aug, 07th, 2023), 169 EBV-related NPC patients were identified. Median age at diagnosis was 50 years (range: 22-75). Most of them were male (72%) and staged as III/IV (84%) according to AJCC classification (VIII Ed.). Only two patients presented oligo-metastatic disease at distant sites, and they were not included in the final analyses on the predictive value of EBV-DNA. At a median follow-up of 66 months (range: 9-134), 41 patients (24.2%) recurred and 139 (82.2%) were still alive. Out of 167 evaluable patients, median viral load of pre-treatment plasma EBV-DNA was of 2.59 log IU/ml (range: 1.59-5.11), while it was undetectable only in six (3.5%) patients who did not recur. All 41 recurrences occurred in patients with pre-treatment detectable EBV-DNA. In addition, subjects with undetectable baseline EBV-DNA had almost significantly (p=0.07) higher DFS with respect to those who showed detectable baseline values (DFS: 66 vs. 47 months, respectively). For pre-treatment plasma EBV-DNA, the best cut-off in terms of disease recurrence prediction was not identified within total population (area under curve, AUC: 0.56) and in early (at 1-y) recurrent patients (n=20) (AUC: 0.58). Regarding the predictive value of post-treatment EBV-DNA measurement (2A, 2B; within 16 weeks), its accuracy, sensitivity, specificity were 78%, 61%, and 80%, respectively, with regards to recurrence detection at any time-point during the follow-up. Moreover, its negative predictive value (NPV) was 94%, which resulted stable across the first three years of follow-up (93% at 1^{st}-y, 95% at 2^{nd}-y, 95% at 3^{rd}-y). On the other hand, its overall positive predictive value (PPV) was 27%, which progressively decreased during follow-up (40% at 1^{st}-y, 34% at 2^{nd}-y, 30% at 3^{rd}-y).

Conclusion

To our knowledge, this is the largest longitudinal evaluation of plasma EBV-DNA quantification in non-endemic EBV-related NPC patients. Undetectable pre-treatment plasma EBV-DNA confirmed its positive prognostic role. NPV of post-treatment (within 16 weeks since curative therapy end) plasma EBV-DNA was 94%, remaining stable during follow-up time (first 3 years) whereas its sensitivity and PPV were lower - 61% and 27%, respectively. The LEA study provides additional data on the significance of plasma EBV-DNA in non-endemic curable NPC, which can also guide clinicians towards a standardization of the timing of plasma EBV-DNA assessment in this setting.

References

(1) Taverna F et al, Oral Oncology 2022 [doi: 10.1016/j.oraloncology.2022.106229]

(2) Alfieri S et al, Oncotarget 2017 [doi:10.18632/oncotarget.17822]

121

Differential functional outcomes following transoral surgery for oropharyngeal carcinoma – laser versus robot

James T O'Hara[1], Chris Hurt[2], Kate Ingarfield[2], Joanne Patterson[3], Kate Hutcheson[4], Christie Heiberg[5], Mererid Evans[6], Terry Jones[7]

[1]Newcastle University, Population Health Sciences Institute, Newcastle-upon-Tyne, United Kingdom. [2]Cardiff University, Statistics, Cardiff, United Kingdom. [3]Liverpool University, Institute of Population Health, Liverpool, United Kingdom. [4]MD Anderson Centre, Head and Neck, Houston, USA. [5]Cardiff University, Centre for Trials Research, Cardiff, United Kingdom. [6]Velindre Cancer Centre, Clinical Oncology, Cardiff, United Kingdom. [7]Liverpool University, Head and Neck Centre, Liverpool, United Kingdom

Topic

HPV or EBV related cancers

Keywords

robot, laser, HPV

Purpose/Objective

Transoral robotic surgery (TORS) has become a more popular technique than transoral laser microsurgery (TLM) for the treatment of oropharyngeal carcinoma (OPC), in particular for human papilloma virus (HPV) related OPC. The two techniques differ in terms of the energy source used and the resection philosophy. TLM commonly employs transtumoural cuts to assess the depth of a tumour, whereas TORS usually performs an en bloc resection, avoiding breaching the tumour. This could result in differences in post-operative healing and quality of life (QoL). The ongoing PATHOS trial is recruiting participants undergoing transoral surgery (technique is centre choice) for HPV-related OPC with the aim to analyse the oncological effectiveness of de-intensified adjuvant therapies. The trials' QoL and functional data pre- and post-surgery present a unique opportunity to conduct this pre-planned sub-study comparing early post-operative functional and QoL outcomes following TLM and TORS.

Material/Methods

PATHOS trial participants who underwent TLM or TORS without re-resection or later, staged neck dissection, and who had 4 weeks post-surgery data available were included. The MD Anderson Dysphagia Inventory (MDADI), EORTC QLQC30 and H&N35, and 100mls Water Swallow Test (volume, capacity, speed) were administered pre-surgery and 4 weeks post-surgery. Data on length of in-hospital stay is collected post-surgery and nasogastric tube (NGT) use is collected at 12 months post-surgery.

Data were analysed according to a pre-specified plan using mixed effects cox, linear and logistic regression models that included surgery type, age, anatomical site (lateral vs non-lateral), pathological T-stage, gender, smoking status, pre-surgery scores (for QoL/functional outcomes) and centre as a random effect. For the NGT analysis, only NGTs inserted within 4 weeks of surgery were considered as events and patients who had an NGT inserted pre-surgery were excluded.

Results

Between November 2015 and July 2023, 508 eligible patients were recruited from 40 centres in UK, Germany, France, USA, Australia. 313 (62%) underwent TORS, and 195 (38%) underwent TLM. There was no significant difference in length of hospital stay after surgery between patients undergoing TORS and TLM, when centre was taken in consideration (HR=0.89, 95%CI 0.69-1.16, p=0.401). NGT insertion rates were significantly higher after TORS than TLM (85/189 – 45.0% vs 10/126 - 7.9%, respectively, OR=4.41, 95%CI=1.01-19.3, p=0.049) but there was no difference in duration (median 5 (95% CI=0.5-12) days TLM, 6 (95% CI=4-6) days TORS; HR=1.05, 95%CI=0.52-2.12, p=0.897). Mean scores significantly favoured TLM (relative to TORS) in all MDADI domains and the H&N35 swallowing item at 4 weeks post-surgery (see table 1); between group difference (95% CI): MDADI composite -4.89 (8.27,-1.50), p=0.005; MDADI physical -6.37 (-10.15, -2.59), p=0.001; MDADI global -10.02 (-16.50, -3.54), p=0.002; H&N35 swallowing 7.24 (2.17, 12.30), p=0.005. There was a trend (p<0.1) for difference in EORTC H&N 35 pain score (4.58, 95%CI(-0.90, 9.96), p=0.095) and water swallow capacity (mL/second) (-1.51, 95%CI(-3.11, 0.10), p=0.067) favouring TLM. There was no significant difference between the following scores: EORTC C30 global, constipation, and summary; H&N35 opening mouth, pain killers, and weight loss.

Conclusion

PATHOS presents a unique opportunity to compare two different transoral surgical techniques. In this study population, TORS was associated with significantly higher rates of NGT use, worse H&N35 swallowing scores, and worse MDADI scores at 4 weeks post-surgery compared to TLM. There was also a trend (p<0.1) favouring TLM in H&N35 pain score and water swallow capacity. This is the largest comparative study of functional outcomes following TORS vs TLM. The recruiting institutions' practices are likely to impact on length of stay and NGT use and has been accounted for in the analysis. This represents a non-randomised, unpowered sub-study for multiple secondary endpoints across which multiplicity was unadjusted. As such the results should be seen as hypothesis generating rather than confirmatory. Furthermore, the study has focused solely on the post-operative recovery period following surgery. It cannot comment on the impact of surgical philosophy (TORS vs TLM) on margins and how this may relate to the PATHOS randomised groups.

Head and neck surgical oncologists may wish to reconsider the role that laser surgery, both as an energy source and a philosophy, has in the emerging field of robotic surgery.

Funded by Cancer Research UK (Grant no: A25317), co-sponsored by Cardiff University and Velindre University NHS Trust.

122

Objective evaluation of plan quality in the PATHOS clinical trial using automated treatment planning

Salvatore Berenato[1], Mererid Evans[2,3], Richard Webster[2], Nachi Palaniappan[2], Lisette Nixon[4], Emma Higgins[2], Rush Patel[5], Anthony E Millin[1], Christian Hurt[6], Christie Heiberg[4], Joanna Canham[4], Terence M Jones[7], Elizabeth Miles[5], Matthew Beasley[8], Philip A Wheeler[1]

[1]Velindre Cancer Centre, Radiotherapy Physics Department, Cardiff, United Kingdom. [2]Velindre Cancer Centre, Medical Directorate, Cardiff, United Kingdom. [3]Cardiff University, Division of Cancer and Genetics, School of Medicine, Cardiff, United Kingdom. [4]Cardiff University, Centre for Trials Research, Cardiff, United Kingdom. [5]Mont Vernon Cancer Centre, National Radiotherapy Trials Quality Assurance (RTTQA) Group, Northwood, United Kingdom. [6]University of Southampton, Southampton Clinical Trials

Unit, Southampton, United Kingdom. [7]University of Liverpool, Liverpool Head and Neck Centre, Liverpool, United Kingdom. [8]United Hospitals Bristol, Bristol Cancer Institute, Bristol, United Kingdom

Topic

Imaging, radiomics and artificial intelligence

Keywords

Quality Assurance, Automation, Treatment Planning

Purpose/Objective

Radiotherapy (RT) plan quality is critical in ensuring treatment efficacy. Poor quality RT can increase the risks of treatment failure, overall mortality and detrimentally impacting a patient's quality of life [1–4]. This is especially important within RT clinical trials, where standardisation of treatment plan quality is paramount. However, widespread objective quantitative assessment of plan quality within trials is not performed routinely, leading to uncertainty on the magnitude of quality variations. Automated planning enables the possibility to efficiency and objectively assess the quality of individual clinical plans (CP) through comparison with an automatically generated standardised 'baseline' plan. Utilising this innovative auditing methodology within a trial enables full quantitative characterisation of: (i) overall plan quality, (ii) potential outliers and (iii) variation solely due to planning practice. The aim of this study was to use fully automated planning to objectively assess plan quality within the Cancer Research UK funded (A25317) multi-centre international phase III trial PATHOS.

Material/Methods

337 patients enrolled in the PATHOS clinical trial before 1st July 2021 were included in this study. 55 cases were excluded due to incomplete data and 16 for calibrating the automated solution, leaving 264 patients for analysis. 219 (83%) and 45 (17%) cases were treated with unilateral (Unilat) and bilateral (Bilat) volumes respectively. Planning was performed in alignment with the PATHOS protocol, with prescriptions of Bilat66Gy, Bilat60Gy, Unilat66Gy or Unilat60Gy in 30 fractions and Unilat50Gy in 25 fractions. Automated treatment plans (AP) were generated in RayStation using a locally developed 'Protocol Based Automatic Iterative Optimization' automated planning solution [5]. CP were quantitatively compared to AP across all the PATHOS trial metrics (including: Parotid Dmean; SpinalCord/BrainStem PRV D1cc; and PTV D98%, D2% and D50%) together with conformality (CI) and homogeneity (HI) indices. Analysis was performed with data categorised in terms of prescription and also tumour laterality. Statistical significance was assessed via a two-sided Wilcoxon matched-paired signed-rank test.

Results

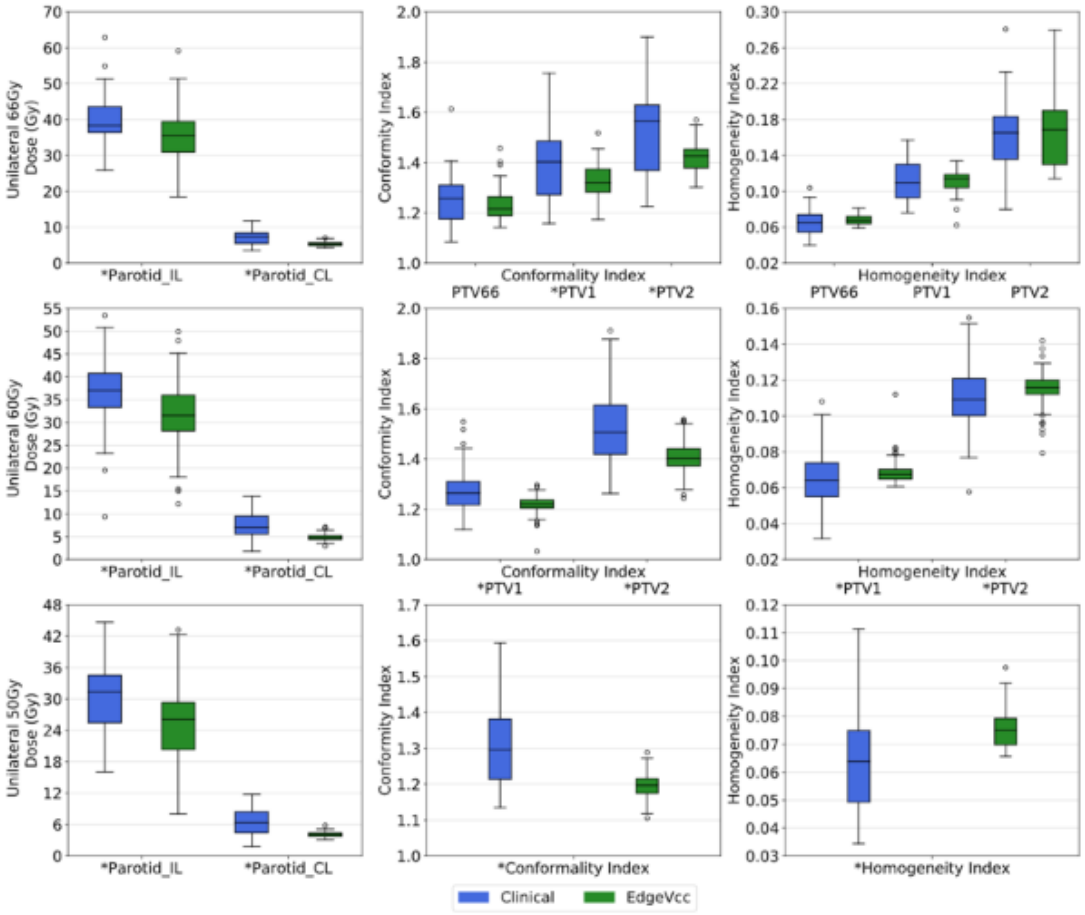


*Figure 1: The boxplots show the dosimetric results for the clinical plan (in blue) and the automated plan (in green) for unilateral cases. Significant differences (p-values ≤0.05) are highlighted with a *symbol.*

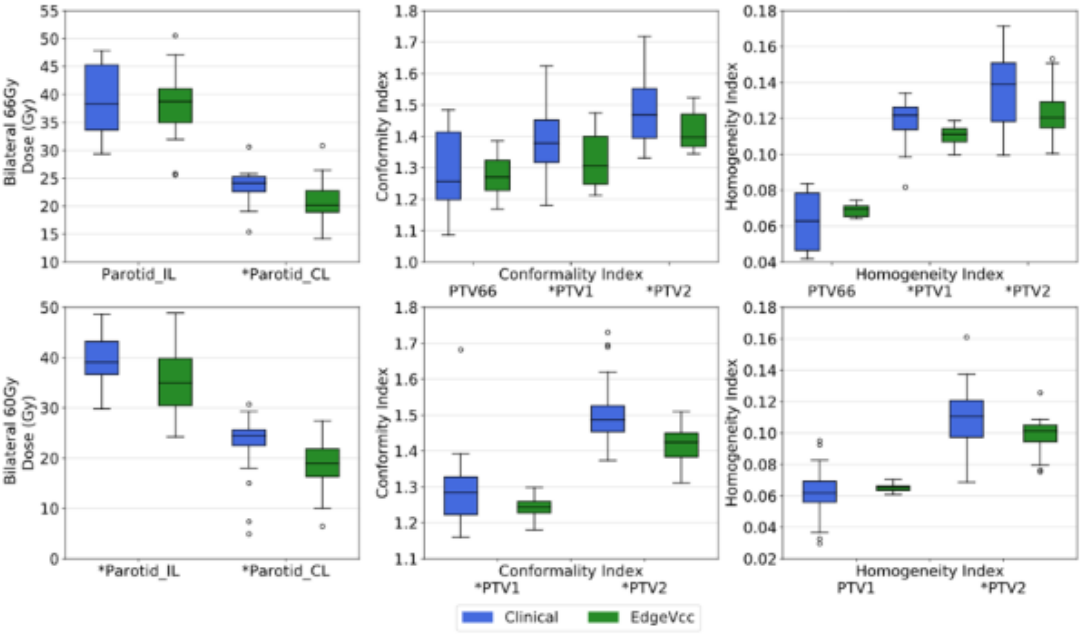


*Figure 2: Dosimetric analysis of the bilateral cases for the clinical plans (in blue) and the automated plans (in green). Significant differences (p-values ≤0.05) are highlighted with a *symbol.*

Fig. 1 and Fig. 2 present a summary of the dosimetric results, categorised in terms of prescription. When comparing CP to the AP baseline (CP-AP), statistically significant ($p \leq 0.05$) differences, Δ, in median values were observed across most key metrics. For HI, small changes across all prescriptions were detected for the primary PTV with the largest Δ equalling (-0.012, $p<0.001$) for Unilat50Gy prescriptions. This indicated CP were marginally more homogeneous that the AP baseline. For CI, significant differences were observed across primary PTVs for three prescriptions (Unilat50Gy, Unilat60Gy and Bilat60Gy) and all secondary PTVs. Median differences were substantial, with a max Δ of +0.110 ($p<0.001$, Unilat66:PTV54), which represented a 10% increase in the volume treated to 54Gy for CP. When categorised in terms of tumour laterality, differences in contralateral Parotid (Parotid_CL) Dmean were small for Unilat (Δ=+2.2Gy, $p<0.001$) and moderate for Bilat cases (Δ=+3.5Gy, $p<0.001$). For ipsilateral Parotids (Parotid_IL), differences were substantial for Unilat cases (Δ=+4.8Gy, $p<0.001$) but nominally equivalent to Parotid_CL for Bilat (Δ=+3.1Gy, $p<0.001$).

At an individual patient level, AP baseline plans highlighted potential quality improvements that could have been realised for CP. For 50% of all patients, AP led to a reduction in Parotid_IL and Parotid_CL Dmean of between 4.4Gy-14.7Gy and 2.5Gy-8.9Gy respectively. In terms of conformality, for 50% of all patients AP reduced CI by between 0.06-0.35 and 0.08-0.28 for PTV60 and PTV54 respectively.

In terms of overall variation with the trial, Fig. 1 and Fig. 2 demonstrate that a high proportion of the variation observed in the majority dose metrics was a direct result of plan quality. For example, a standardised AP planning method would have reduced the inter-quartile range (IQR) for Parotid_CL Dmean from 5.4Gy to 1.4Gy, for HI (PTV54) from 0.031 to 0.015 and for CI (PTV54) from 0.194 to 0.071. Parotid_IL Dmean was a key exception, with similar IQRs for both AP and CP.

Conclusion

Clinics participating in PATHOS undergo a comprehensive quality assurance process prior to patient recruitment, with additional 'on trial' qualitative reviews performed on small subset of patients. Furthermore, all patient plans must, where practicable, meet trial dose metric tolerances. Results of this study demonstrate that despite these procedures, which are common to many high-quality trials, meaningful variations in plan quality remain. Automated planning was found to be an effective tool in objectively assessing plan quality within a large trial. Implementation on a prospective basis could be a powerful QA tool to reduce this observed variation.

References

[1] Fairchild A, Straube W, Laurie F, Followill D. Does quality of radiation therapy predict outcomes of multicenter cooperative group trials? A literature review. Int J Radiat Oncol Biol Phys 2013; 87:246–60. https://doi.org/10.1016/j.ijrobp.2013.03.036.

[2] Ohri N, Shen X, Dicker AP, Doyle LA, Harrison AS, Showalter TN. Radiotherapy protocol deviations and clinical outcomes: A meta-analysis of cooperative group clinical trials. J Natl Cancer Inst 2013; 105:387–93. https://doi.org/10.1093/jnci/djt001.

[3] Weber DC, Tomsej M, Melidis C, Hurkmans CW. QA makes a clinical trial stronger: Evidence-based medicine in radiation therapy. Radiother Oncol 2012;105:4–8. https://doi.org/10.1016/j.radonc.2012.08.008.

[4] Peters LJ, O'Sullivan B, Giralt J, Fitzgerald TJ, Trotti A, Bernier J, et al. Critical impact of radiotherapy protocol compliance and quality in the treatment of advanced head and neck cancer: Results from TROG 02.02. J Clin Oncol 2010;28:2996–3001. https://doi.org/10.1200/JCO.2009.27.4498.

[5] Wheeler PA, Chu M, Holmes R, Smyth M, Maggs R, Spezi E, et al. Utilisation of Pareto navigation techniques to calibrate a fully automated radiotherapy treatment planning solution. Phys Imaging Radiat Oncol 2019;10:41–8. https://doi.org/10.1016/j.phro.2019.04.005.

133

Proton therapy significantly reduces acute and late toxicity in nasopharyngeal cancer

Johannes A. Langendijk[1], Tineke W.H. Meijer[1], Johanna G.M. van den Hoek[1], Stefan Both[1], Edwin Oldehinkel[1], Hans H.G. Verbeek[1], Gyorgy Halmos[2], Sjoukje F. Oosting[3], Roel H.M. Steenbakkers[1]

[1]University Medical Center Groningen, Radiation Oncology, Groningen, Netherlands. [2]University Medical Center Groningen, Otolarygology, Groningen, Netherlands. [3]University Medical Center Groningen, Medical Oncology, Groningen, Netherlands

Topic

Innovative treatments

Keywords

Nasopharyngeal carcinoma; Proton therapy; Toxicity

Purpose/Objective

The aim of the study was to test the hypothesis that Intensity Modulated Proton Therapy (IMPT) reduces acute and late radiation toxicity in nasopharyngeal cancer (NPC) patients compared to photon-based radiation techniques including IMRT and VMAT.

Material/Methods

The study population of this prospective cohort study was composed of 131 NPC patients treated with curative radiotherapy (RT) or chemoradiotherapy. Between July 2007 and December 2017, all patients were treated with IMRT or VMAT. Since January 2018, 97 out of 99 patients (98%) qualified for IMPT according to model-based selection. All patients were included in a prospective data registration program in which acute and late toxicity was prospectively scored weekly during RT and at fixed time points after RT (6 weeks, 6, 12, 18 and 24 months). To determine the overall effect on acute and late toxicity, the Weighted Overall Toxicity Burden (WOTB) was calculated, defined as the sum of all toxicities weighted by toxicity grading. In addition, the WOTB Area Under the Curve (WOTB-AUC) was calculated representing the WOTB from the start of treatment until 24 months after completion of treatment.

Results

The two groups were well balanced regarding gender, age, race, T-stage, N-stage, AJCC-stage, and EBV-status. However, there was a significant difference regarding the chemotherapy regimens used between the two groups. In the photon cohort, 33% of patients were treated with conventional RT, 7% with concurrent chemoradiation, 2% with induction chemotherapy + concurrent chemoradiation and 57% with concurrent chemoradiation + adjuvant chemotherapy, while this was 25%, 37%, 36% and 2% in the proton cohort, respectively.

The mean dose to all relevant organs at risk (i.e., oral cavity, pharyngeal constrictor muscles, parotid, and submandibular glands) were significantly lower with IMPT compared to photons. This was particularly true for the mean dose to the oral cavity which decreased from 27.2 Gy with IMRT/ VMAT to 10.7 Gy with IMPT ($p<0.001$).

From January 2018, a plan comparison was made in all NPC patients referred for radiotherapy to our centre between IMPT and VMAT. In total, 97 out of 99 patients qualified for protons based on the estimated risk difference on dysphagia and xerostomia resulting from the dose reductions obtained with IMPT.

IMPT resulted in significant reductions of various acute and late toxicities (Figure 1), including xerostomia, loss of taste, dysphagia, tube feeding dependence, sore mouth, and mucosal reactions. Only acute dermatitis was significantly worse at the end of IMPT, but completely recovered at 5 weeks after treatment in all patients.

The WOTB was significantly lower after IMPT (Figure 2) at all time points. In the IMPT group, the WOTB-AUC as measure for overall toxicity was 68% lower. The WOTB-AUC reduction was 60% in the acute phase (week 1 to 7), 69% in the recovery phase (from end of treatment to 6 months after RT) and 70% in the late phase (from 6 to 24 months after RT).

Figure 1: Acute and late toxicity prior to (T0), weekly during (W1-W7) and after (W12 and every 6 months) treatment. Red color indicxates more toxicity.

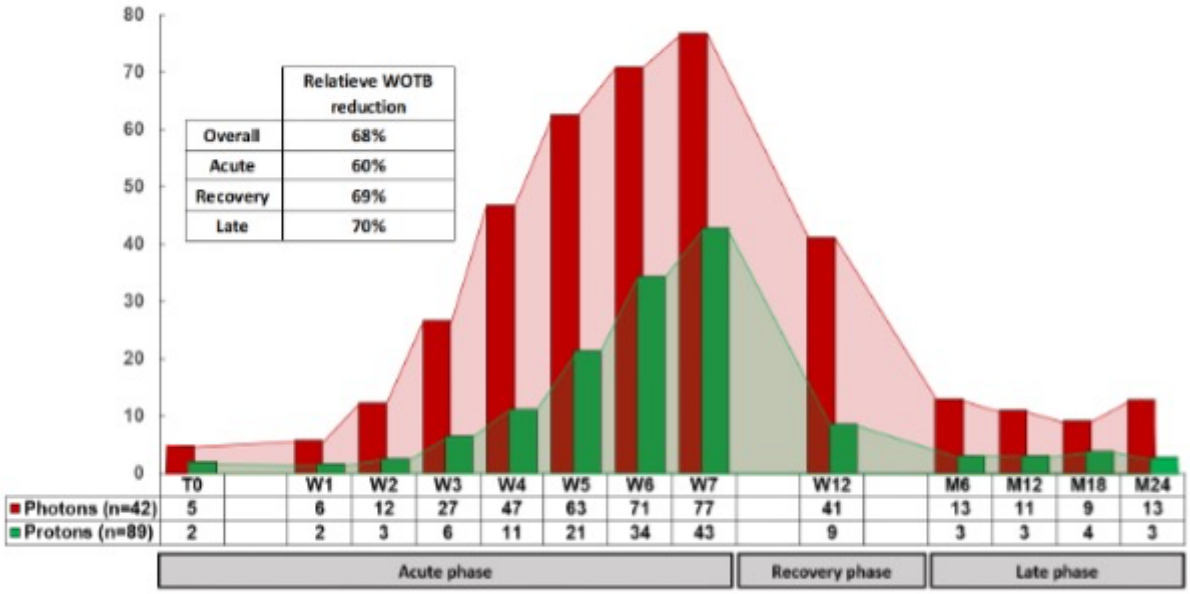


Figure 2: Weighted Overall Total Toxicity Burden (WOTB) from start of RT to 24 months after treatment (P<0.001)

Conclusion

In this prospective cohort study, patients treated with IMPT had statistically significant and clinically relevant reductions of various acute and late toxicities as compared to modern photon techniques like IMRT and VMAT as a historical control group.

151

Compartmentalization in postoperative radiotherapy for oral cavity cancer

Olgun Elicin[1], Manuel Waser[2], Simon A. Mueller[3], Daniel M. Aebersold[1], Elena Riggenbach[1], Roland Giger[2]

[1]Inselspital, Bern University Hospital, University of Bern, Radiation Oncology, Bern, Switzerland. [2]Inselspital, Bern University Hospital, University of Bern, Otorhinolaryngology, Head and Neck Surgery, Bern, Switzerland. [3]University Hospital Zurich, Otorhinolaryngology, Head and Neck Surgery, Zurich, Switzerland

Topic

Innovative treatments

Keywords

oral cancer, compartmentalization, radiotherapy

Purpose/Objective

The volume treated with postoperative radiotherapy in patients with oral cavity squamous cell carcinoma is a mediator of toxicity affecting quality of life. Current guidelines only allow for very limited modification of postoperative radiotherapy target volumes. Our strategy of compartmentalization in

patients with oral cavity squamous cell carcinoma considers the tumor bed and each hemi-neck as separate compartments for postoperative radiotherapy. The intent of the compartmentalization strategy is to apply the required dose only to the compartment at risk. The indication is based on the presence of major (extracapsular extension, close or positive margins) and minor (perineural invasion, vascular invasion, lymphatic invasion, pT≥3, pN≥2b and involvement of level IV or V lymph nodes) pathologic risk factors in the corresponding compartments. This retrospective study analyzed the oncologic outcome of patients treated after the establishment of compartmentalization strategy.

Material/Methods

This retrospective cohort study identified 187 oral cavity squamous cell carcinoma patients treated surgically with curative intent from 2014 to 2019 with a follow-up of at least 2 years. Patients with distant metastases, synchronous malignancy or previous head and neck cancer were excluded. One hundred and three patients qualified for postoperative radiation therapy. Postoperative radiation therapy was administered only to the at-risk compartments and according to a refined compartmentalization concept. Oncological outcome of this compartmentalization concept cohort was compared to a historical cohort of 98 patients treated before the compartmentalization concept was implemented.

Results

Median follow-up time was 4.5 years (range, 0.3 - 7.4) in the compartmentalization concept cohort and 4.8 years (range, 0.2 - 8.9) in the historical cohort. In the compartmentalization cohort, a total of 72/103 patients (70%) had a pathological risk profile that allowed for further compartmentalization and hence benefitted from a reduced treatment volume or omission of postoperative radiation therapy altogether (Table 1).

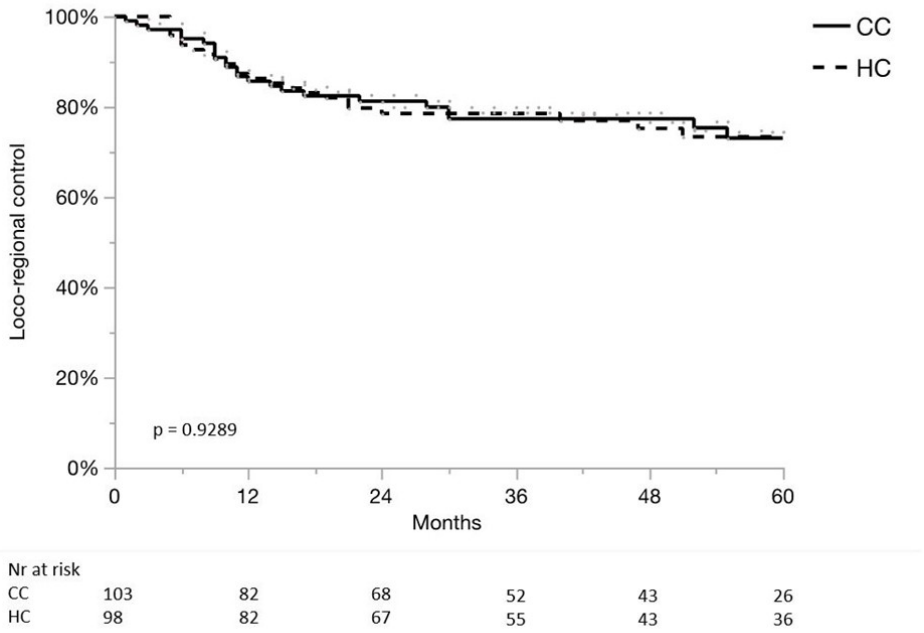
Table 1: **Compartmentalization strategy used in the CC (compartmentalization concept) cohort**

# of CC	Spared compartment*	# of spared compartment(s)	Percent (n)
1	Tumor bed	1	4.9% (5)
2	One hemineck	1	26.2% (27)
3	Both heminecks	2	11.7% (12)
4	Tumor bed and one hemineck	2	24.3% (25)
5	All three compartments	3	2.9% (3)
0	No compartmentalization used	0	30.1% (31)

*: PORT was omitted in a total of 25 (24.3%) patients through the compartmentalization strategy

Loco-regional control at 3 and 5 years was 77% and 73% in the compartmentalization cohort vs. 79% and 73% in the historical cohort (p=0.93) (Figure 1, CC: compartmentalization cohort, HC: historical cohort), progression-free survival was 72% and 64% vs. 75% and 68% (p=0.58), respectively. Similarly, difference in outcomes of local control, isolated regional control, distant metastasis-free survival and overall survival between the two cohorts were not statistically significant.

Figure 1:



Conclusion

Our de-intensified postoperative irradiation concept limiting the treatment volume to the at-risk compartment or avoiding adjuvant radiotherapy altogether for low-risk patients with oral cavity squamous cell carcinoma does not seem to compromise disease control when compared to the historical cohort and the literature without the compartmentalization concept.

References

Kelly JR, Husain ZA, Burtness B. Treatment de-intensification strategies for head and neck cancer. Eur. J. Cancer 2016;68:125-133.

152

Optimizing Head and Neck Cancer Radiotherapy using '5+5 mm' DAHANCA Radiotherapy Guidelines

Ruta Zukauskaite[1], Morten H Kristensen[2], Jesper G Eriksen[2], Jørgen Johansen[1], Eva Samsøe[3], Lars Johnsen[4], Camilla K Lønkvist[5], Cai Grau[6], Christian R Hansen[4,7,8]

[1]Odense University Hospital, Oncology, Odense, Denmark. [2]Aarhus University Hospital, Oncology, Aarhus, Denmark. [3]Zealand University Hospital, Oncology, Næstved, Denmark. [4]Odense University Hospital, Laboratory of Radiation Physics, Odense, Denmark. [5]Herlev Hospital, Oncology, Herlev, Denmark. [6]Aarhus University Hospital, Danish Centre for Particle Therapy,, Aarhus, Denmark. [7]Aarhus University Hospital, Danish Centre for Particle Therapy, Aarhus, Denmark. [8]University of Southern Denmark, Department of Clinical Research, Odense, Denmark

Topic

Quality of life and outcomes

Keywords

radiotherapy guidelines, CTV, local control

Purpose/Objective

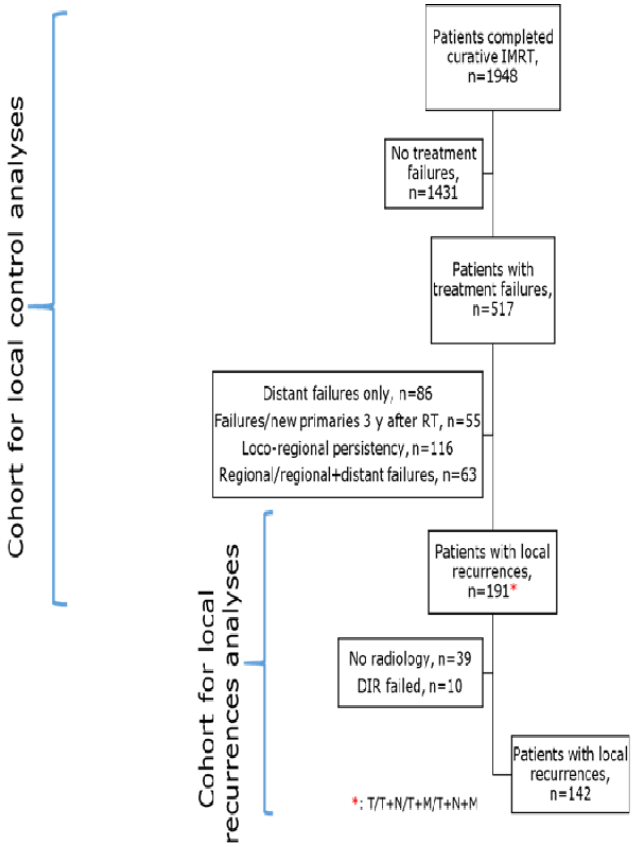
Primary radiotherapy treatment is preferred for squamous cell carcinomas in the head and neck region (HNSCC) owing to the preservation of anatomical structures and function. The delineation of treatment volumes, particularly the expansion from the gross tumour volume (GTV) to the high-dose clinical target volume (CTV1), is critical in radiotherapy planning. Historically, the choice of margin size for GTV-CTV1 has varied between different treatment centres in Denmark from zero to over 10 millimetres or could encompass the whole organ (volume) where the tumour is located. Therefore, the first DAHANCA IMRT guidelines could be referred to as volumetric-based. In 2013, national consensus guidelines were introduced by the Danish Head and Neck Cancer Group (DAHANCA), recommending an isotropic margin of five millimetres corrected only for air or natural anatomical barriers resulting in a more uniform geometrical margin.

With over a decade of experience in applying geometrically-based GTV-CTV1 guidelines, the primary aim of this study was to assess whether the implementation of the guidelines in 2013 led to improved consistency in CTV1 volumes across different treatment centres. Additionally, we analysed whether changes in GTV-CTV1 margins moving from volumetric to geometric guidelines impacted 3-year local tumour control and local recurrence pattern in patients treated three years before and three years after implementation of the geometrical guidelines.

Material/Methods

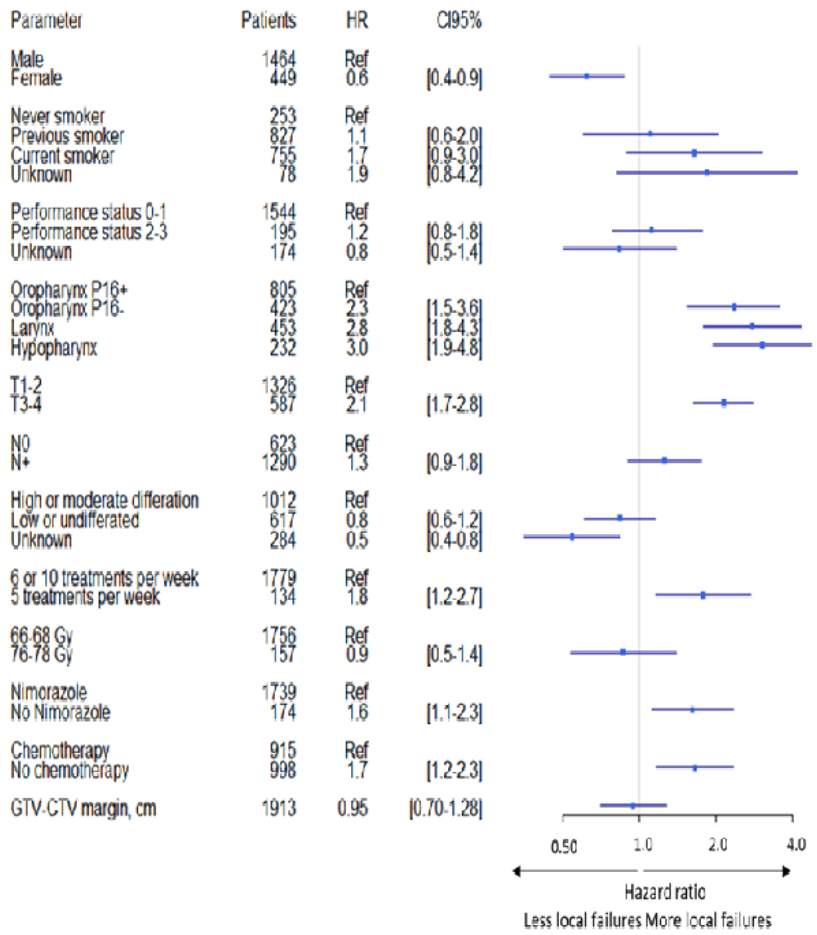
The cohort consisted of 1,948 patients diagnosed with oro-/hypopharyngeal and laryngeal squamous cell carcinomas across three national treatment centres. The patients underwent definitive intensity-modulated radiotherapy (IMRT) in 2010-2012 when volumetric guidelines were used, and in 2013-2015, when geometric guidelines were adopted. The GTV-CTV1 margins were quantitatively assessed by calculating the median surface distance from the primary GTV to CTV1. Three-year local control (LC) rates were determined, and local recurrence patterns were examined (Figure 1) using a centre of mass

(COM) analysis. Hazard ratios and corresponding 90% CIs were calculated using the Cox proportional hazard model to identify factors that influenced local tumour control.



Results

The transition from volumetric to geometric guidelines substantially reduced median GTV-CTV1 margins, declining from a median of 9.0 mm (IQR 0.0-9.7) to 4.7 mm (IQR 4.0-5.5). Importantly, adopting geometric guidelines led to increased consistency in CTV1 volumes between treatment centres. Median CTV1 changed from 76 to 61 cm3 for Centre1, from 28 to 53 cm3 for Centre2, and from 42 to 62 cm3 for Centre3 for the periods 2010-2012 and 2013-2015, respectively. The three-year LC rates exhibited a notable trend towards improvement, increasing from 0.84 to 0.87, although statistical significance was not reached (p=0.06). Cox regression analysis indicated that factors such as sex (female), tumour site (HPV p16+ oropharyngeal), T stage (T1-2), treatment schedule (6 or 10 fractions per week), and the administration of nimorazole and chemotherapy were associated with superior three-year LC. At the same time, GTV-CTV1 margin size did not appear to influence local control significantly (Figure 2).



Out of 146 radiology-verified local recurrences (LR), 102 (70%) were inside the CTV1. 45 (63%) and 57 (76%) LRs were inside CTV1 in 2010-2012 and 2013-2015, respectively. The LRs were covered by the 95% isodose in 75% in 2010-2012 and 91% in 2013-2015.

Conclusion

The implementation of geometrically-based GTV-CTV1 margins resulted in reduced variation in treatment volumes across 3 different centres. Although our analysis did not demonstrate a direct impact of GTV-CTV1 margin size on local tumour control, a promising trend towards improved local control was observed in the newest cohort. Most recurrences occurred within CTV1 and were encompassed by the prescribed dose. A relevant next step could involve randomised trials comparing standard radiotherapy protocols with reduced margins and escalated doses to CTV1, further exploring the potential benefits of geometrically-based treatment strategies.

162

Outcomes following ablative therapy of pulmonary oligometastases in patients with HPV-positive head and neck cancer

Sophia Ly[1], Shao Hui Huang[1], Scott Bratman[1], B.C. John Cho[1], Ali Hosni[1], Ezra Hanh[1], John Kim[1], Andrew McPartlin[1], Jolie Ringash[1], Brian O'Sullivan[1], C. Jillian Tsai[1], John Waldron[1], David Goldstein[2], Enrique Sanz Garcia[3], Anna Spreafico[3], Jie Su[4], Li Tong[1], Ilan Weinreb[5], Bayardo Perez-Ordonez[5], Andrew Hope[1]

[1]Princess Margaret Hospital, Department of Radiation Oncology, Toronto, Canada. [2]Princess Margaret Hospital, Department Otolaryngology-Head & Neck Surgery, Toronto, Canada. [3]Princess Margaret Hospital, Division of Medical Oncology, Toronto, Canada. [4]Princess Margaret Hospital, Department of Biostatistics, Toronto, Canada. [5]University Health Network, Department of Pathology, Toronto, Canada

Topic

HPV or EBV related cancers

Keywords

HPV, Head and neck cancers, Lung metastasis

Purpose/Objective

Local ablation of oligometastases has been shown to improve patient survival (1). Oligometastases are more frequent in viral-related head and neck squamous cell carcinomas (HNSCC) compared to non-viral HNSCC, with lung as the most common site (2). We reviewed patients with HPV-positive (+) HNSCCs who developed lung metastases, and report outcomes for all patients, focusing on those receiving definitive intent local ablation.

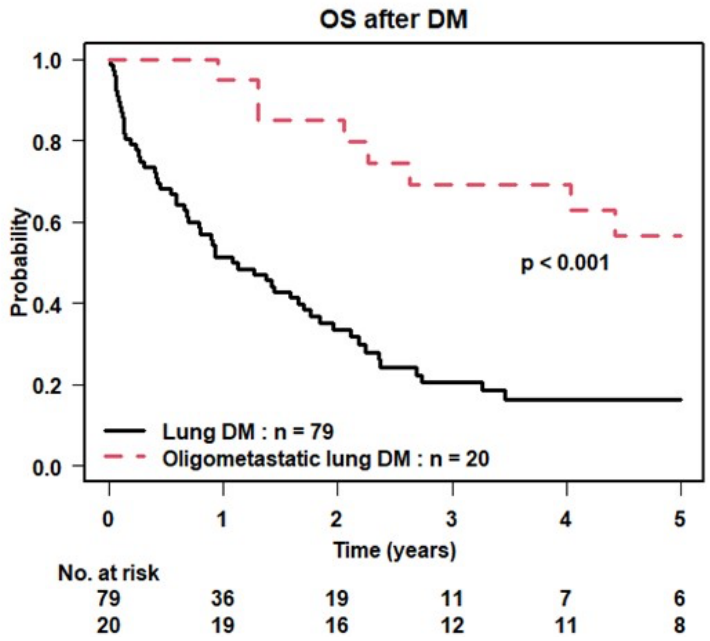
Material/Methods

We reviewed all HPV(+) HNSCCs patients who developed distant metastases (DM) to lung ± other organs after definitive radiotherapy or chemoradiotherapy at our institution from January 2003 to December 2021. DM in lung were further classified as oligometastases (≤5 lesions) vs polymetastases. Among those patients classified as oligometastases, we pragmatically sub-staged according to the American Joint Commission on Cancer 8th edition for primary non-small cell lung cancer (NSCLC) (3) (oligometastasis mimicking the behavior of NSCLC) to assess differences in outcome after local ablative therapy. Oligometastases in lung were confirmed by p16(+) staining to rule out lung primary when possible. Definitive intent local ablation (LA) was defined as either surgical resection or definitive-intent [EQD2 ≥40 Gy; alpha/beta=10 Gy] (chemo)radiation. Overall survival (OS) and progression free survival (PFS) after lung metastases were estimated by Kaplan Meier curves, with log rank test for outcome comparison.

Results

Of 1908 consecutive patients treated during the study period, 170 (9%) developed DM to lung and other sites. Lung was the only DM site in 79 patients (4%), of whom, 20 (1%) had oligometastases and underwent LA: 15 underwent surgery (1 lobectomy, 2 segmentectomies, 12 wedge resections), 1 surgery + radiation, 3 radiation alone and 1 chemoradiation. Median follow-up was 2.0 years (range 0-13.5). For OM patients receiving LA, OS at 3 and 5 years after detection of metastasis was 69% and 57%; PFS was 40% at 3 years and 34% at 5 years. When patients who developed isolated lung metastases were staged as per the TNM 8th edition for lung cancer, most patients were N0 (n=16) and early stage. Some patients with N+ disease (n=4) or very advanced T category disease (T4, n=1) were treated with definitive intent as well. OS of oligometastatic lung DM treated with local ablative treatment according to lung cancer N stage showed 75% at 3 years and 75% at 5 years for N+ disease, and 67% at 3 years and 50% at 5 years for N0 disease ($p = 0.587$). PFS of oligometastatic lung DM treated with ablative treatment according to lung cancer N stage was not statistically different with 25% at 3 years and 25% at 5 years for N+ disease, and 44% at 3 years and 36% at 5 years for N0 disease ($p = 0.678$).

For comparison, across all 170 patients with DM to lung and other sites, OS at 3 and 5 years after detection was 22% and 16%. For the 150 patients who did not receive LA, these rates were 15% and 10% respectively. For the 79 with lung-only DM who did not receive LA, these rates were 21% and 16% respectively. These were statistically different compared to OS at 3 and 5 years for OM patients receiving LA ($p < 0.001$).



Conclusion

Patients with oligometastatic HPV(+) HNSCC to lung treated with local ablation with definitive intent have significantly longer OS compared to those with polymetastatic disease who had palliative treatment or best supportive care treatment. Isolated lung lesions, large lung lesions, and lung lesions with nodal involvement treated with definitive intent all showed substantially longer OS compared with patients who did not receive ablative therapy. Isolated pulmonary DM in patients with HPV(+) HNSCC should be considered for local ablation with definitive intent.

References

1. Palma, D.A.; Olson, R.; Harrow, S.; Gaede, S.; Louie, A.V.; Haasbeek, C.; Mulroy, L.; Lock, M.; Rodrigues, P.G.B.; Yaremko, B.P.; et al. Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): A randomised, phase 2, open-label trial. Lancet 2019, 393, 2051–2058.

2. Huang, S.H.; Perez-Ordonez, B.; Weinreb, I.; Hope, A.; Massey, C.; Waldron, J.N.; Kim, J.; Bayley, A.J.; Cummings, B.; Cho, B.J.; et al. Natural course of distant metastases following radiotherapy or chemoradiotherapy in HPV-related oropharyngeal cancer. Oral Oncol. 2012, 49, 79–85.

3. Amin MB. American Joint Committee on Cancer and American Cancer Society AJCC cancer staging manual. 8th Ed. Chicago IL: American Joint Committee on Cancer, Springer; 2017.

167

Detection of Oligo-metastases in oropharyngeal carcinoma following (Chemo)Radiation Therapy

Revadhi C Chelvarajah[1], Ye Liu[1], Jie Su[2], Ali Hosni Abdalaty[1], Scott Bratman[1], B.C John Cho[1], Ezra Hahn[1], Andrew Hope[1], John Kim[1], Brian O'Sullivan[1], Jolie Ringash[1], C. Jillian Tsai[1], John Waldron[1], Anna Spreafico[3], Enrique Sanz Garcia[3], David Goldstein[4], Christopher Yao[4], Li Tong[1], Shao Hui Huang[1], Andrew McPartlin[1]

[1]Princess Margaret Cancer Centre, Radiation Oncology, Toronto, Canada. [2]Princess Margaret Cancer Centre, Biostatistics, Toronto, Canada. [3]Princess Margaret Cancer Centre, Division of Medical Oncology, Toronto, Canada. [4]Mount Sinai Hospital, Head and Neck Surgical Oncology, Toronto, Canada

Topic

HPV or EBV related cancers

Keywords

oligometastatic, screening, HPV +ve oropharyngeal

Purpose/Objective

HPV status is predictive for loco-regional control and overall survival (OS) following (chemo)radiation therapy (cRT) for oropharyngeal squamous cell carcinoma (OPSCC)[1], but rates of subsequent distant metastases (DM) are similar for HPV positive and negative disease[2]. Emerging data suggests a benefit from ablative therapy for low volume metachronous metastases, with long-term disease control reported[3]. Diagnosis of oligo-metastatic (oligo-DM) vs poly-metastatic (poly-DM) disease may therefore facilitate curative salvage treatment and improve patient outcomes. This study investigates factors associated with identification of oligo-DM vs poly-DM and subsequent disease outcomes to inform follow up practice for OPSCC following initial complete response to cRT.

Material/Methods

All OPSCC patients treated with curative cRT between 2010 and 2020 who subsequently developed DM were identified from our prospectively maintained Anthology of Outcomes system. Imaging 10-16 weeks post treatment for response assessment was routinely performed, with subsequent imaging at clinician discretion. Patients who had evidence of DM at first response assessment (within 16 weeks of RT) were excluded. Tumor HPV status was ascertained by p16 immunohistochemistry staining, supplemented by Polymerase Chain Reaction (PCR) for high-risk HPV DNA in case of equivocal p16 staining. Clinical characteristics and disease outcomes were compared by volume of metastases: oligo-DM (defined as ≤ 5 metastatic lesions, max 5cm diameter) vs poly-DM, tumor HPV status. OS was estimated with Kaplan-Meier method from time of diagnosis of DM. Multivariable analysis (MVA) identified prognostic factors for OS.

Results

Among 1627 consecutive patients treated, 124 (7.6%) subsequently developed DM and were eligible for analysis (91 HPV-positive and 33 HPV-negative). Median follow-up from diagnosis of DM was 31.5 (range 5.5 – 193.9) months. The most common site of DM was pulmonary only (48%) and 61 (49%) patients were asymptomatic at time of DM diagnosis. Dissemination was oligo-DM in 47 (38%) and poly-DM in 77 (62%) patients. Identification of oligo-DM was significantly more likely in patients who were

asymptomatic vs symptomatic at the time of DM detection (62% vs 42%, p=0.049), and those with scan interval of < 6 months from last imaging to scan diagnosing DM (p = 0.05). HPV positive (vs HPV negative) disease was not significantly associated with incidence of oligo-DM (40%vs 33%, p=0.67) but was associated with longer interval to diagnosis of DM (median interval from cRT completion: 16.8 [range 4.3-93.8] months vs 8.6 [4.6-122.1] months, p=0.002).

OS at 5 years after DM detection was significantly better for patients diagnosed with oligo-DM vs poly-DM (26% vs 3%, p<0.001). Ablative salvage therapy (surgery or ≥ 50 Gy cRT to all disease) was delivered to 40% of patients with Oligo-DM vs 0% with poly-DM (p<0.001) (Table 1). On MVA oligo-DM receiving ablative salvage treatment (hazard ratio [HR] 0.26, 95% confidence interval [CI] 0.12-0.57, p<0.001) and HPV-positive disease (HR 0.51, 95% CI 0.33-0.79, p=0.003) were favorable prognostic factors for OS. There was a trend towards worse OS in patients with symptomatic DM at diagnosis (HR 1.44, 95% CI 0.96-2.17, p=0.08).

Table 1: Clinical factors based on DM volume distribution

	Total (n=124)	Oligo-DM (n=47)	Poly-DM (n = 77)	P value
Symptomatic				0.05
Asymptomatic	61	29 (62)	32 (42)	
Symptomatic	63	18 (38)	45 (58)	
Imaging intervals				0.05
<= 6 months	30	17 (57)	13 (43)	
6-12 months	37	12 (32)	25 (68)	
>12 months	57	18 (32)	39 (78)	
Curative intent salvage treatment				<0.001
No/NA	105	28 (60)	77 (100)	
Yes	19	19 (40)	0 (0)	

Conclusion

Detection of Oligo-DM (vs poly-DM) is more likely in asymptomatic patients and those who have undergone screening imaging at ≤ 6-month interval. For both HPV positive and negative OPSCC the most common site of DM failure following initial response to cRT is the lung, with HPV-positive DM tending to manifest later. Better OS was observed in patients with oligo-DM receiving ablative therapy, and for HPV positive disease. Based on these results prospective studies of regular surveillance imaging in asymptomatic patients during follow up may be considered.

References

1. Gillison ML, Koch WM, Capone RB, et al. Evidence for a causal association between human papillomavirus and a subset of head and neck cancers. J Natl Cancer Inst 2000;92(9):709–20.

2. O'Sullivan B, Huang SH, Siu LL, et al. Deintensification candidate subgroups in human papillomavirus-related oropharyngeal cancer according to minimal risk of distant metastasis. J Clin Oncol. 2013 Feb 10;31(5):543-50

3. Huang SH, Perez-Ordonez B, Weinreb I, et al. Natural course of distant metastases following radiotherapy or chemoradiotherapy in HPV-related oropharyngeal cancer. J Oral Oncology 2013;49:79-85

169

Outcomes of Stereotactic Body Radiation Therapy for Re-Irradiation of Squamous Carcinomas of the Head and Neck

Michelle I Echevarria[1], George Q Yang[1], Christine H Chung[2], Kedar Kirtane[2], Caitlin McMullen[2], Krupal Patel[2], Tapan Padhya[2], Jimmy J Caudell[1]

[1]Moffitt Cancer Center, Radiation Oncology, Tampa, USA. [2]Moffitt Cancer Center, Head and Neck, Tampa, USA

Topic

Innovative treatments

Keywords

SBRT, re-irradiation, recurrent

Purpose/Objective

Stereotactic Radiation Therapy (SBRT) has been implemented for re-iradiation of recurrent or second primary cancers of the head and neck to improve the therapeutic ratio in this difficult scenario. We reviewed our experience at a single institution.

Material/Methods

After IRB approval, a database of patients receiving re-irradiation was queried. Patients were excluded if receiving conventionally fractionated radiotherapy (RT), non-squamous histology, were enrolled on non-published clinical trials, or metastatic disease. All patients were seen in a multi-disciplinary clinic and/or reviewed in multi-disciplinary tumor board. All patients were ineligible for or refused surgical intervention. Patients were simulated with thermoplastic masks and 2 mm cuts on CT scan with and without contrast. Additional imaging including PET and/or MRI were fused. Gross tumor volume (GTV) was delineated and expanded 2-3 mm for the planning target volume. Elective nodes were not targeted. Minimum dose to PTV was 90% of prescription, with 110 - 130% prescription allowed within GTV/PTV. SBRT was delivered every other day for 5 fractions, with daily cone beam CT imaging, and 6 degree of freedom couch correction. Locoregional control (LRC), progression free survival (PFS), and overall survival (OS) were calculated from the end of RT and estimated via Kaplan-Meier method and comparisons made via log-rank test. Multi-variate cox regression model of OS was performed. Acute (during within three months from completion of treatment) and late (three or more months from completion of treatment) grade 3-5 CTCAE toxicities were collected.

Results

A total of 76 patients were available for analysis, with a median follow up of 31.5 months for patients alive at last contact, and 12 months for the entire cohort. Median age was 66 (range 36 – 92) with a median RT interval of 29.5 months (range 5 -315). Median dose of initial RT was 70 Gy (range 44 – 79.2 Gy). The majority of patients were former smokers (n=45, 59.2%), followed by never smokers (n=20, 26.3%), and current smokers (n=11, 14.5%). There were 56 men (73.7%) and 20 women (26.3%). Performance status was zero (n=22, 28.9%) and 1-2 (n=54, 71.1%), with 50 patients being recurrent (65.8%) and 26 having a second primary (34.2%). All patients were treated with 5 fractions to a median dose of 40 Gy (range 25 – 40 Gy). Systemic therapy was utilized in 29 patients (38.2%), primarily concurrently (n=27). Concurrent systemic therapy was cisplatin (n=20, 26.3%), cetuximab (n=4, 5.3%), or immunotherapy (n=3, 3.9%). Median gross tumor volume (GTV) was 11.42 cc (range 0.93 – 58.31 cc). Acute grade 3-4 toxicity was seen in 5 patients (6.6%), consisting of feeding tube in 2, aspiration pneumonia in 1, tracheostomy in 1, and stroke in 1. Actuarial rates for the entire cohort at 1 and 2-years for LRC were 43.5% and 33.3%, for PFS, 40.6% and 31.1%, and OS 49.6% and 33.1%. On univariate analysis median GTV, treatment site (nasopharynx/base of skull/neck/skin vs other), and recurrence were prognostic for OS. On multivariate analysis, GTV (HR 1.037, 95% CI 1.018 – 1.056, $p < 0.001$) and recurrent disease (HR 0.344, 95% CI 0.194 – 0.609, $p < 0.001$). For the subset of patients (n=26) with a GTV ≤ 11.4 cc and recurrent disease, 2-year OS was 80.1% with a median OS of 37 months. Of 73 patients followed for more than 3 months post treatment, 15 (20.5%) developed a late grade 3-4 toxicity, including feeding tubes in 7, aspiration pneumonia in 3, soft tissue necrosis in 3, or a cranial neve deficit in 3.

Conclusion

SBRT for re-irradiation for patients with smaller, recurrent squamous cell carcinomas of the head and neck had the best performance. While severe acute toxicities are low, additional studies are needed to improve survival and decrease the risk of late toxicity.

177

ACTivity as medicine In Oncology for Head and Neck (ACTIOHN): Feasibility of recruitment and retention. Trial registration number ISRCTN82505455

Jo Patterson[1], M Gemma Cherry[2], Debra Fisher[2], Andy Levy[3], Simon N Rogers[4], Rachel Brooker[5], Val Bryant[6], Steven Lane[1], Michael Nugent[7], Ruth Price[8], Andrew Schache[1], Bridget Young[2], Adrian Midgley[9]

[1]University of Liverpool, Liverpool Head and Neck Centre, Liverpool, United Kingdom. [2]University of Liverpool, Institute for Population Health, Liverpool, United Kingdom. [3]Edge Hill University, 2 Health Research Institute, Liverpool, United Kingdom. [4]4 Arrowe Park Hospital, Wirral University Teaching Hospital NHS Foundation Trust,, Maxillo-Facial, Liverpool, United Kingdom. [5]Clatterbridge Cancer Centre, Oncology, Liverpool, United Kingdom. [6]PPI Representative, CHANGE, Sunderland, United Kingdom. [7]South Tyneside and Sunderland NHS Foundation Trust, Head and Neck, Sunderland, United Kingdom. [8]Liverpool University Hospitals NHS Foundation Trust, Physiotherapy, Liverpool, United Kingdom. [9]Edge Hill University, 2 Health Research Institute, Ormskirk, United Kingdom

Topic

Supportive care, rehabilitation

Keywords

physical exercise, feasibility, behavioural change

Purpose/Objective

Physical exercise is a safe, cost-efficient, and effective intervention for cancer survivors. Regular exercise can reduce symptoms such as cancer-related fatigue, depression, prevent and reduce co-morbidities, attenuate toxicity related to cancer treatment, and reduce cancer-specific and all-cause mortality [1-4]. Exercise is generally recommended for all cancer survivors and should be started as early as possible [5]. However, there is limited evidence in head and neck cancer (HNC) [6], which has multiple challenges; patients typically present with substantial weight loss, inactivity and low cardiorespiratory fitness; treatments are gruelling with substantial short and long-term symptom burden; many live in areas of high deprivation, residing some distance from their treating centre and have low levels of health literacy; integrating interventions to this complex care pathway is challenging [7-13] .

Objective: To investigate the feasibility of introducing a remotely delivered, personalised, collaborative, and flexible exercise programme into the HNC care pathway.

Material/Methods

This prospective single arm feasibility and acceptability study aimed to recruit seventy HNC patients from two UK Centres, over 12 months. A conservative retention rate of 60% was predicted, to provide a minimum of 42 patients on study completion. The intervention was a personalised 8-week exercise programme delivered remotely by cancer exercise specialists, trained in behaviour change techniques. Patients were invited to participate any time between diagnosis and 8 weeks post-treatment, according to their preference. Intervention content was based on patient needs, preferences, and goals, guided by physical activity cancer guidelines. Primary outcomes included recruitment and retention. A qualitative sub-study included patient and healthcare professionals semi-structured interviews to evaluate intervention experiences and processes.

Results

One hundred and eighteen patients were eligible for the study, 107 patients were approached, and 76 consented (71%). Recruitment uptake was different for each site 54% vs 82%. Reasons for non-participation were; too much to think about, additional paperwork, uninterested in exercise.

Participants M:F ratio 3:1; mean age 60.5 years (range 34-80). The majority had oropharyngeal (54%) or oral cancer (33%), 56% had T1/2 tumours. Fifteen patients (19%) had over the recommended alcohol intake (14 units/week), 8 (10.5%) were current smokers. Treatment included surgery alone (28.8%) surgery and adjuvant (chemo)radiotherapy (50.0%) or primary (chemo)radiotherapy (21.2%). The majority of patients consented to ACTIOHN pre-treatment (45%). Data collection finishes in February 2024. To date, 32 patients have completed ACTIOHN, 27 are on treatment and 17 have withdrawn. Key themes from on-going patient interviews (N=17) are; therapeutic alliances; understanding what the intervention involved; personalisation; treatment impact; programme impact; paperwork, and from eight healthcare professionals; describing the programme; personalisation; nutrition; treatment impact; buy-in.

Conclusion

This high uptake indicates that the ACTIOHN intervention was acceptable to HNC patients. Overall patients and HCPs were positive about the intervention. However, there were substantial system challenges, and despite many consenting to participate pre-treatment, a proportion of surgical patients were unable to start ACTIOHN until post-treatment. Patients appreciated a strong therapeutic bond and tailoring of the intervention to their needs and preferences. ACTIOHN requires further investigation to test effectiveness and fit with the pathway.

References

1. Gerritsen, JKW, Vincent AJPE. Exercise improves QOL in patients with cancer: a systematic review and meta-analysis of RCTs. Br J Sports Med. 2016;50:796-803.

2. Pederson BK, Saltin B. Exercise as medicine - evidence for prescribing exercise as therapy in 26 different chronic diseases. Scand J Med Sci Sports. 2015;25 Suppl:1-72

3. Kleckner IR, Dunne RF, et al. Exercise for toxicity management in cancer – a narrative review. Oncol Hematol Rev. 2018;14:28-37.

4. McTiernan A, Friedenreich CM, et al. Physical activity in cancer prevention and survival: a systematic review. Med Sci Sports Exerc. 2019;51:1252-61.

5. Schwartz A, de Heer HD, et al. Initiating exercise interventions to promote wellness in cancer patients and survivors. Oncology. 2017;31(10):711-717.

6. Parke SC, Oza S, et al. Identifying gaps in research on rehabilitation for patients with HNC: a scoping review. Arch of Phys Med and Rehab. 2019;100:2381-2388. 6.

7. Capozzi LC, Nishimura KC, et al. The impact of physical activity on health-related fitness and QOL for patients with HNC: a systematic review. Br J Sports Med. 2016;50:325-338.

8. Midgley AW, Levy AR, et al. Should HNC survivors be considered a distinct special population within the context of exercise prescription? Br J Oral Maxillofac Surg. 2020;58(7):738-743.

9. Midgley AW, Levy AR, et al. Should HNC survivors be considered a distinct special population within the context of exercise prescription? Br J Oral Maxillofac Surg. 2020;58(7):738-743.

10. Midgley AW, Lowe D, et al. Exercise program design considerations for HNC survivors. Eur Arch Otorhinolaryngol. 2018;275(1):169-179.

11. Taib, B.G., Oakley, J., et al. (2018). Socioeconomic deprivation and the burden of HNC – Regional variations of incidence and mortality in Merseyside and Cheshire, NW England. Clin Otolaryng. Doi.10.1111/coa.13067.

12. Legh-Jones, H., Moore, S. (2012). Network social capital, social participation, and physical inactivity in an urban adult population. Social Science and Med. 74: 1362-1367.

13. Rogers SN, Travers A, et al. Importance of activity and recreation for the QOL of patients treated for cancer of the head and neck. Br J Oral Maxillofac Surg. 2019;57(2):125-134

183

Development of photon and proton RT plan quality in the clinical H&N trial DAHANCA 35

Camilla P Nielsen[1,2], Kenneth Jensen[3], Simon L Krogh[1], Carsten Brink[1,2], Ebbe L Lorenzen[1,2], Bob Smulders[3,4], Anne I.S. Holm[5], Eva Samsøe[3,6], Martin S Nielsen[7], Patrik Sibolt[8], Peter S Skyt[3], Ulrik V Elstrøm[3], Jørgen Johansen[9], Ruta Zukauskaite[2,9], Jesper G Eriksen[5,10], Mohammad Farhadi[6], Maria Andersen[7], Christian Maare[8], Jens Overgaard[10], Cai Grau[3], Jeppe Friborg[3,4], Christian R Hansen[1,2,3]

[1]Odense University Hospital, Laboratory of Radiation Physics, Odense, Denmark. [2]University of Southern Denmark, Institute of Clinical Research, Odense, Denmark. [3]Aarhus University Hospital, Danish Centre of Particle Therapy, Aarhus, Denmark. [4]Rigshospitalet, University Hospital of Copenhagen, Department of Oncology, Copenhagen, Denmark. [5]Aarhus University Hospital, Department of Oncology, Aarhus, Denmark. [6]Zealand University Hospital, Naestved, Department of Oncology, Næstved, Denmark. [7]Aalborg University Hospital, Department of Oncology, Aalborg, Denmark. [8]University Hospital Herlev, Department of Oncology, Herlev, Denmark. [9]Odense University Hospital, Department of Oncology, Odense, Denmark. [10]Aarhus University Hospital, Department of Experimental Clinical Oncology, Aarhus, Denmark

Topic

Innovative treatments

Keywords

proton therapy, plan quality, treatment planning

Purpose/Objective

The aim in radiotherapy treatment planning is to have sufficient target coverage and as low a dose to the Organs at Risk (OARs) as possible, adhering to the relevant guidelines. A high and consistent radiotherapy plan quality is vital when treatment plans are used as the foundation for patient selection in clinical trials. Proton therapy, being a substantially newer treatment modality than conventional

photon therapy, is at risk of having a steeper learning curve in treatment planning. This inequality is important to investigate in a clinical study comparing the two, as this could influence the trial results.

This study aims to evaluate the development of radiotherapy treatment plan quality for head and neck cancer patients receiving photon and proton therapy over time in the context of the DAHANCA 35 trial.

Material/Methods

From May 2019 to June 2023,189 patients were included in the ongoing DAHANCA 35 trial, with 63 patients in the pilot phase and 126 in the subsequent randomisation phase. In the pilot phase, all included patients were offered proton treatment, and in the randomisation phase, patients were randomised 1:2 (photon:proton). Patients were first seen at a local treatment centre, where a photon and comparative proton plan were prepared. If patients were offered proton treatment, a new clinical proton plan was made at the proton treatment centre and subsequently used for treatment. This study analysed 189 photon plans, 189 comparative proton plans, and 140 clinical proton plans.

The treatment plans were prepared conforming to the DAHANCA guidelines [1] to ensure the clinical relevance of all treatment plans

The plan quality was assessed separately for photon plans, comparative proton plans, and clinical proton plans in three time intervals.

The mean dose was investigated individually for 13 OARs relevant for head and neck cancer: oesophagus, glottic larynx, supraglottic larynx, mandible, extended oral cavity, left and right parotid glands, upper-, middle-, and lower pharyngeal constrictor muscles, left and right submandibular glands, and thyroid gland.

Furthermore, treatment plan quality was analysed using a new metric called Normalised Toxicity Index (NTI), calculated as a normalised average of the mean dose to the OARs compared to the threshold mean dose recommended by the DAHANCA guidelines.

An NTI > 1 indicated that the OARs, on average, received a dose higher than the recommended thresholds, and an NTI < 1 indicated that the OARs received a dose below the thresholds. Hence, a lower NTI indicated better plan quality concerning OAR doses.

The Kruskal-Wallis test was used to investigate a potential difference in the intervals for mean dose and NTI for each treatment type. The significance level was Bonferroni adjusted to account for multiple testing.

Results

The three time intervals were defined with 63 patients in the pilot phase constituting one interval (Pilot phase), the subsequent 64 patients from the randomisation phase in the next interval (Randomisation 1), and the remaining 62 patients from the randomisation phase in the third interval (Randomisation 2). The periods were 22 months for the Pilot phase, 19 months for Randomisation 1, and 14 months for Randomisation 2.

Across the 13 OARs, the mean dose to individual OARs did not show a general time-dependent change, except for the right parotid gland in the clinical proton plans. Figure 1 shows a box plot with samples overlaid for the mean dose to the extended oral cavity as an example of the OARs.

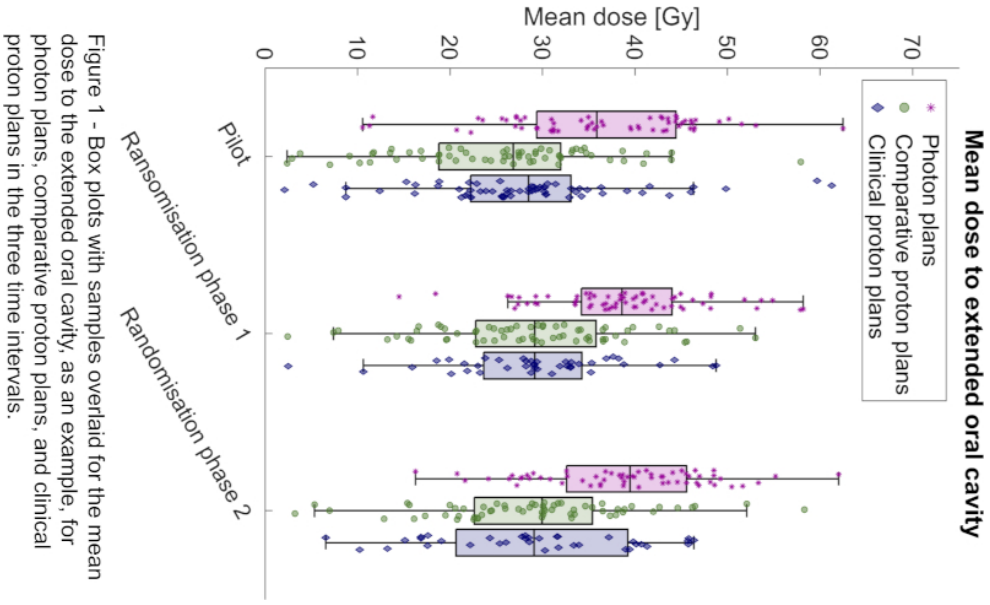


Figure 1 - Box plots with samples overlaid for the mean dose to the extended oral cavity, as an example, for photon plans, comparative proton plans, and clinical proton plans in the three time intervals.

The NTI was not significantly different for the photon plans, comparative proton plans, and clinical proton plans in the three consecutive intervals, as shown in Figure 2. The median NTI for the clinical proton plans was 0.88 (interquartile range [0.70,1.00]) for the Pilot phase, 0.83 [0.75,0.89] for Randomization 1, and 0.79 [0.67,0.98] for Randomization 2. The plan quality of the clinical proton plans appears stable from this new NTI metric.

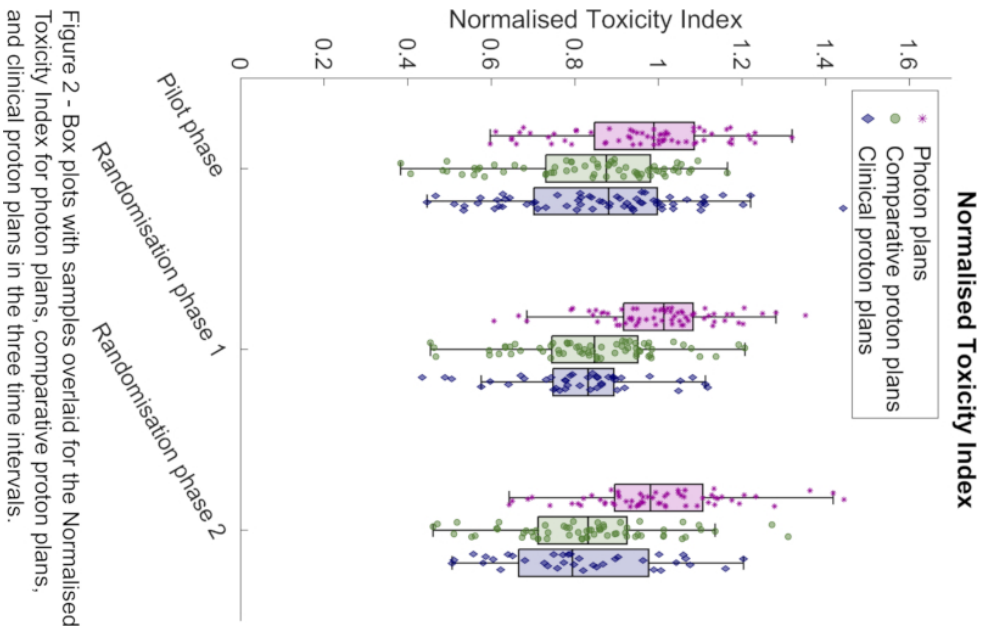


Figure 2 - Box plots with samples overlaid for the Normalised Toxicity Index for photon plans, comparative proton plans, and clinical proton plans in the three time intervals.

Conclusion

The analyses conducted in this study did not show a general time-dependent change in plan quality in any of the three types of plans. This could be caused by the nationally developed proton treatment planning template.

A stable treatment plan quality can help ensure a consistent selection for clinical trials, thus providing transparency for analysis of the outcome of the trials. The plan quality will continuously be followed to ensure consistency.

References

1. Jensen K, Friborg J, Hansen CR, et al. The Danish Head and Neck Cancer Group (DAHANCA) 2020 radiotherapy guidelines. Radiother Oncol. 2020 Oct;151:149-151.

185

Long-Term Results of Induction Chemotherapy Followed by 50 Gy Radiation Therapy Alone for Low-Risk HPV-Positive Oropharynx Cancer

Aditya Juloori[1], Ari Rosenberg[2], Daniel Huang[1], Nishant Agrawal[3], Alex Pearson[2], Zhen Gooi[3], Elizabeth Blair[4], Jared Hara[5], Muzamil Arshad[1], Zaid Iftekaruddin[5], Rohan Katipally[5], Daniel Haraf[5], Everett Vokes[6]

[1]The University of Chicago, Radiation Oncology, Chicago, USA. [2]The University of Chicago, Medical Oncology, Chicago, USA. [3]The University of Chicago, Otolaryngology, Chicago, USA. [4]The University of Chicago, Otolaryngology, chicago, USA. [5]The University of Chicago, Radiation Oncology, chicago, USA. [6]The University of Chicago, Medical Oncology, chicago, USA

Topic

HPV or EBV related cancers

Keywords

immunotherapy, HPV positive, volume reduction

Purpose/Objective

The standard of care for non-operative management of human papillomavirus-related oropharynx cancer (HPV-OPC) consists of concurrent cisplatin chemotherapy with radiotherapy (RT) to a total dose of 70 Gy. While the oncologic outcomes of this treatment approach have been excellent, there are considerable acute and late toxicities. Here, we report the 5-year survival and toxicity outcomes of 2 prospective HPV-OPC response-adapted de-escalation trials, in which low-risk (LR) patients were treated with volume- and dose-reduced RT to 50 Gy to involved sites, without elective nodal RT or concurrent chemotherapy.

Material/Methods

Patients with LR HPV-OPC and ≥50% response to induction by RECIST 1.1 treated per 2 prospective phase II trials as well as on a prospective cohort registry were included for analysis. Patients were considered LR if the following criteria were met: T1-T3, N0-N2b (AJCC 7th edition), and ≤20 pack-year smoking history. Patients were treated with induction chemo- or chemoimmunotherapy followed by RT alone to 50 Gy to involved sites. In the early trial iteration, patients underwent a planned neck dissection following RT to confirm pathologic clearance of lymph nodes. Clinicodemographic characteristics were summarized using descriptive statistics. Overall survival (OS), progression-free survival (PFS), and local control (LC) were estimated using the Kaplan-Meier method.

Results

From January 2015 through March 2020, 73 patients met LR criteria, of which, 54 (74%) had ≥50% response by RECIST and were de-escalated to RT alone. The median follow-up was 58 (range 10-92) months. The median age was 58 (range 38-84) years, and 92.6% were male. 57.4% of patients never smoked, and 42.6% smoked no more than 20 pack-years. The primary site was tonsil for 53.7% and base of tongue for 46.3%. 24.1% were T1, 53.7% were T2, and 22.2% were T3. 1.9% were N0, 5.6% were N1, 11.1% were N2a, and 81.5% were N2b. The 5-year OS, PFS, and LC were 96.3% (95% CI 91.3%-100%), 96.2% (95% CI 91.2%-100%), and 98.1% (95% CI 94.6%-100%), respectively. 2 (3.7%) patients required a G-tube during RT and none at 1 year following completion of RT. Of the 30 patients with a planned neck dissection, 2 (6.7%) had residual pathologic nodal disease.

Conclusion

With a median follow-up of 5 years, this analysis demonstrates excellent long-term local control, survival, and toxicity rates among patients with low-risk HPV+ oropharynx cancer treated with induction systemic therapy followed by radiotherapy to 50 Gy without concurrent chemotherapy, including a large proportion of patients with N2b disease. Chemo-selection provides a means of identifying a favorable cohort of HPV+ oropharynx cancer patients who can safely receive RT dose de-escalation. Further work is needed to identify this population by other means, including radiographic and genomic factors.

188

Influence of hypoxia on the radiotherapy response in HPV+ and HPV- head and neck cancer

Marilyn Wegge[1], Rüveyda Dok[1], Ludwig J. Dubois[2], Sandra Nuyts[1]

[1]KU Leuven, Laboratory of Experimental Radiotherapy, Leuven, Belgium. [2]The M-lab, Dept. of Precision Medicine, Maastricht, Netherlands

Topic

Biology and molecular targeting

Keywords

Hypoxia, radiotherapy, head and neck cancer

Purpose/Objective

Radiotherapy (RT) plays a key role in the treatment of HPV+ and HPV- head and neck cancer (HNSCC). Low tissue oxygen levels, also called hypoxia, has a negative influence on the RT response resulting in a poor prognosis. Moreover, cancer cells adapt to these hypoxic circumstances by various molecular alterations leading to tumor progression, genetic instability, treatment resistance, and tumor recurrence. Unfortunately, hypoxia is a common feature in HNSCC and, despite the development of various targeting strategies, can still not be overcome. Better understanding of the hypoxia-induced molecular alterations in cancer cells is needed to develop successful hypoxia targeting agents, thereby improving the RT response and prognosis of patients with HNSCC.

Material/Methods

The role of hypoxia in tumor regrowth was assessed using hypoxia fate mapped 3D HNSCC spheroid models by spheroid growth curves. The hypoxia fate mapped models were generated by introduction of a hypoxia fate mapping system [1] in three HPV+ and three HPV- HNSCC cell lines. This system allowed tracking of hypoxic cells by an oxygen-dependent fluorescent permanent switch from red (DsRed) in normoxic to green (GFP) fluorescence in hypoxic conditions. Fate mapped spheroids were dissociated into single cells and sorted into non- (DsRed+) and (post-)hypoxic (GFP+) populations. Of both populations, the radiosensitivity and DNA damage repair capacity were assessed.

Results

Hypoxia fate mapped HNSCC spheroids showed an increase in GFP levels in hypoxic conditions. Moreover, in 3D spheroids the GFP positive fraction increased with increasing area of the spheroids. This correlated with pimonidazole (hypoxyprobe) stainings, thereby validating the hypoxia fate mapping system. In response to RT, fate mapped spheroids showed an average 1.9-fold increase of the (post-)hypoxic population in the regrowth phase, indicating that these cells play a role in tumor regrowth. Assessment of the radiosensitivity of the (post-)hypoxic cells showed an average 1.5-fold increase in clonogenic survival compared to the non-hypoxic ($p<0.0001$). This increased survival was not mediated by DNA double strand break induction and/or repair, since yH2AX foci did not differ between both populations. Further molecular assessments of the (post-)hypoxic cells revealed an average 1.9-fold lower percentage of micronucleated cells 48h after RT compared to non-hypoxic cells ($p<0.0001$) and a 2-fold higher radiosensitization by ATR/Chk inhibition, suggesting that the more aggressive behavior of these cells might be linked to a mitotic survival advantage. These results were found in both HPV+ and HPV- HNSCC, however, the HPV+ HNSCC kept their intrinsic higher radiosensitivity.

Conclusion

Our results show an important role for radioresistant (post-)hypoxic cells in regrowth after RT, independent of HPV status. We found that the aggressive behavior of these cells might be linked to hypoxia induced molecular alterations resulting in the ability to overcome mitotic cell death. These results will help in understanding the failure of hypoxic radiosensitizers. Moreover, it will pave the way for alternative treatment strategies with a focus on targeting hypoxia driven biological alterations, resulting in a better outcome for patients with HNSCC.

References

1. Godet, I.; Shin, Y. J.; Ju, J. A.; Ye, I. C.; Wang, G.; Gilkes, D. M. Fate-Mapping Post-Hypoxic Tumor Cells Reveals a ROS-Resistant Phenotype That Promotes Metastasis. Nat. Commun. 2019, 10, 1–18, doi:10.1038/s41467-019-12412-1.

207

ctDNA-based WES enhances actionable alterations detection in locally advanced head and neck cancer

Gema Bruixola[1], Jorge Martín-Arana[1], Francisco Gimeno-Valiente[1], Victor Seguí[1], Jose Francisco Catalá-Senent[2], Juan Antonio Carbonell-Asins[3], Elena Duréndez[1], Nuria Grimalt[1], Delfina Dualde[4], Clara Alfaro[5], Olga Pons[6], Vicente Escorihuela-García[7], María Eugenia Iglesias[8], Andrés Cervantes[1,9], Noelia Tarazona[4,9]

[1]Hospital Clínico Universitario. INCLIVA Biomedical Research Institute., Medical Oncology, Valencia, Spain. [2]INCLIVA Biomedical Research Institute., Bioinformatics Unit, Valencia, Spain. [3]INCLIVA Biomedical Research Institute., Biostatistics Unit, Valencia, Spain. [4]Hospital Clínico Universitario. INCLIVA Biomedical Research Insitute. University of Valencia., Radiology, Valencia, Spain. [5]Hospital Clínico Universitario. INCLIVA Biomedical Research Insitute. University of Valencia., Pathology, Valencia, Spain. [6]Hospital Clínico Universitario, Radiation Oncology, Valencia, Spain. [7]Hospital Clínico Universitario, Otorhinolaringology, Valencia, Spain. [8]Hospital Clínico Universitario, Maxillofacial Surgery, Valencia, Spain. [9]CIBERONC Instituto de Salud Carlos III, Medical Oncology, Madrid, Spain

Topic

Biology and molecular targeting

Keywords

whole-exome sequencing, ctDNA, locally advanced

Purpose/Objective

Unresectable locally advanced head and neck cancer (LAHNSCC) presents high heterogeneity[1], which has yet to be elucidated at the molecular level. Consequently, it hampers the guidance of standard chemoradiotherapy (ChRT) and the implementation of precision medicine.

Our study aims at assessing intratumor heterogeneity (ITH) and tumor evolution by examining the mutation profiles from WES in paired tissue and plasma both at baseline and relapse.

Material/Methods

Primary tumor (PT) biopsies from 61 unresectable LAHNSCC patients at baseline, along with parallel biopsies at relapse and paired plasma samples (baseline and relapse) from the INCLIVA Biobank's Head and Neck Cancer Collection were obtained. Patients provided informed consent, and the study received ethical approval from our Institutional review board.

WES of the collected samples was performed on a HiSeq 3000 (Illumina) using the KAPA HyperExome (Roche) panel. UMI barcodes were added to correct background noise.

Samples were selected based on a minimum average coverage (50x for WBC, 100x for FFPE and 250x for plasma samples). Only patients with White Blood Cells (WBCs) and plasma samples were included. Single-Nucleotide Variants (SNV), Copy Number Variants (CNVs) and small insertions and deletions (Indel) were called with an in-house bioinformatics pipeline. Minimum Variant allele frequencies (VAF) were set to 0.1% and 10% for plasma and tissue samples, respectively.

Oncogenic somatic variants and related treatments were identified and annotated with OncoKB and Ensembl v107. Functional enrichment was performed using the cluster Profiler 4.6.2 R package and databases org.Hs.eg.db 3.16.0 and MSigDB 2023.1.

Results

A total of 37 unresectable LAHNSCC cases meeting quality criteria were included in our analysis (Figure 1). Clinicopathologic characteristics and treatment details are given in Table 1.

Figure 1. Study design and sample collection.

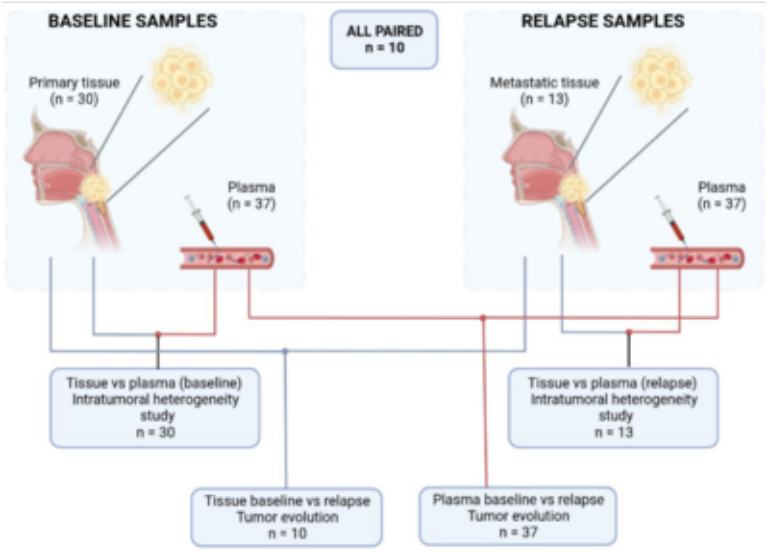
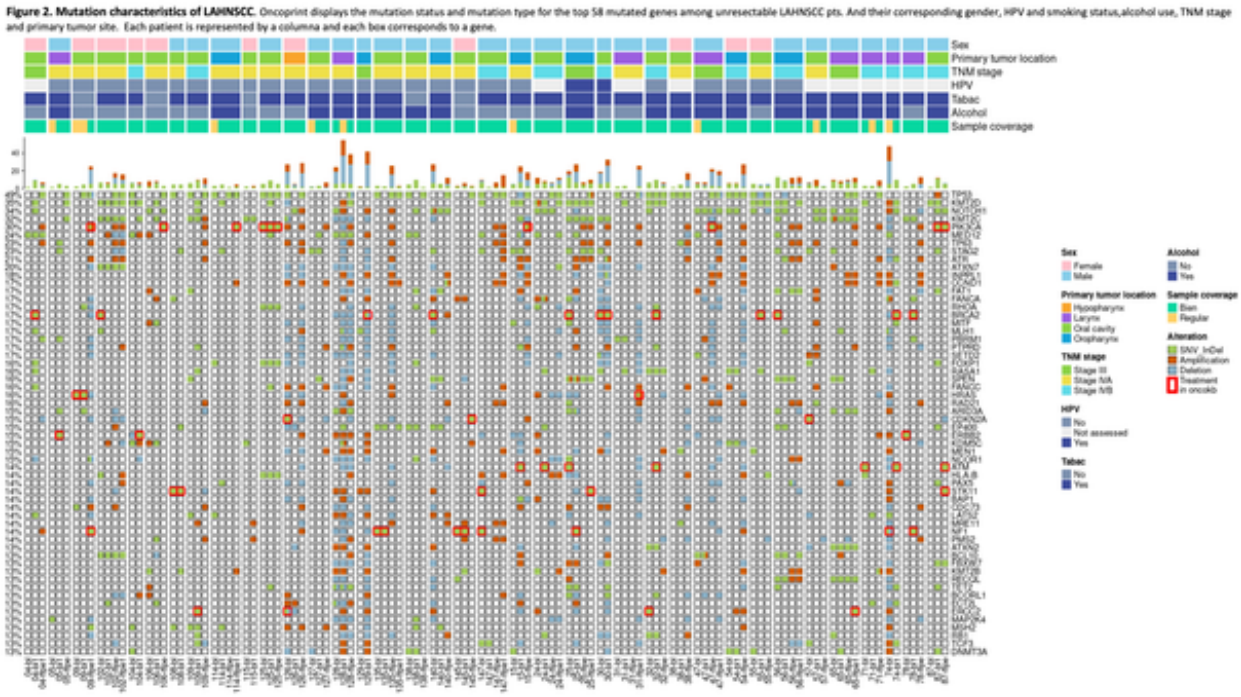


Table 1: Patient, tumor and treatment characteristics		
Characteristics		N= 37 (%)
Age (years)	Median, (range)	66,0 (44,6-83,1)
Sex	Male Female	26 (70,3) 11 (29,7)
ECOG PS	1	37 (100)
Tobacco history	>=10 pack/years	32 (86,5)
Primary tumor site	Larynx Oropharynx Hypopharynx Oral cavity	8 (21,6) 7 (18,9) 1 (2,7) 21 (56,8)
Tumor stage	III IVA IVB	5 (13,5) 20 (54,1) 12 (32,4)
HPV status	Negative Positive Not determined	25 (67,6) 2 (5,4) 10 (27)
Chemotherapy	Cisplatin Cetuximab	17 (45,9) 20 (40,1)
Treatment response	Complete response Partial response Disease progression Not evaluated	6 (16,2) 17 (45,9) 13 (35,1) 1 (2,7
Type of relapse	Locoregional	20 (54)

Table 1: Patient, tumor and treatment characteristics		
	Distant metastases only	5 (13,5)
	Locoregional + distant metastasis	12 (32,4)

In Figure 2, we've employed an oncoprint to depict the WES results, showing the genomic status of the 58 most frequently mutated genes (CNVs and In/Del) in paired samples.



To discern the baseline genomic heterogeneity, we compared the WES results between a single biopsy of the PT and the paired baseline ctDNA from 30 patients. Among all the SNVs and In/Del mutations, an average of 88.2% of events displayed discrepancies between PT and ctDNA. Significantly, up to 67% of oncogenic mutations were exclusively identified in ctDNA. To assess ITH at relapse, we analyzed WES results from paired relapsed tissue biopsies and ctDNA (n=13). Our observations revealed a median concordance of 12.50%, with up to 58% of oncogenic mutations exclusively detected in plasma.

To elucidate tumor evolution, we compared WES results of PT vs. relapsed tissue biopsies (n=10) and WES results of baseline ctDNA vs. ctDNA at relapse (n=37). When focusing on tissue analysis, a median concordance of 40% was observed, with up to 38% of oncogenic mutations exclusively identified in the relapsed tissue biopsy. In contrast, focusing on plasma results, discordance was higher, with only a 10.34% median concordance and up to 50% of oncogenic mutations found only in plasma at relapse.

In our WES analysis of WBC, we identified pathogenic germline variants in 43.2% (16/37) of cases, highlighting mutations in BRCA2, CHEK2 and KIT as potentially actionable. No enrichment of APOBEC signatures or apoptosis pathways were detected. However, further analysis of defective DNA mismatch repair signatures and treatment-related signatures is currently underway.

Conclusion

Our findings confirm the significant ITH in LAHNSCC, characterized by limited concordance between tissue and plasma mutational profiles. WES of ctDNA proves more effective at capturing this ITH, uncovering mutations absent in tissue profiles. Additionally, ctDNA-based WES enhances mutation

detection during LAHNSCC relapse, offering valuable insights into resistance mechanisms to ChRT and enabling the potential use of targeted therapies to address these challenges.

References

1. Mroz EA, Patel KB, Rocco JW. Intratumor heterogeneity could inform the use and type of postoperative adjuvant therapy in patients with head and neck squamous cell carcinoma. Cancer. 2020 Jan 1;126(9):1895-1904. doi: 10.1002/cncr.32742. Epub 2020 Feb 21. PMID: 32083741; PMCID: PMC7160035.

210

Using quantitative diffusion-weighted MRI to predict treatment outcome and Human Papillomavirus status in patients with oropharyngeal squamous cell carcinoma

Heleen Bollen[1], Sarah Deschuymer[2], Annouschka Laenen[3], Frederik De Keyzer[4], Rüveyda Dok[5], Vincent Vandecaveye[4], Robert Hermans[4], Sandra Nuyts[1]

[1]University Hospitals Leuven, Radiotherapy-Oncology, Leuven, Belgium. [2]University Hospitals Ghent, Radiotherapy-Oncology, Ghent, Belgium. [3]Catholic University Leuven, Biostatistics, Leuven, Belgium. [4]University Hospitals Leuven, Radiology, Leuven, Belgium. [5]Catholic University Leuven, Laboratory of experimental radiotherapy, Leuven, Belgium

Topic

Imaging, radiomics and artificial intelligence

Keywords

Diffusion-weighted MRI, HPV status, outcome

Purpose/Objective

There is an increasing interest in the identification of prognostic and predictive patient characteristics in head and neck squamous cell carcinoma. Human papillomavirus (HPV)-positive status is a well-known characteristic that has been linked to a favorable outcome after treatment with (chemo)RT for oropharyngeal squamous cell carcinoma (OPC). The apparent diffusion coefficient (ADC), a quantitative variable derived from diffusion-weighted (DW) MRI, seems to be a less investigated, but promising parameter for pre-treatment identification of (non-)responders to radiotherapy (RT). This study aimed to 1) confirm the predictive value of ADC in response to RT on a large prospective dataset and 2) investigate the differences in quantitative diffusion-weighted (DW) MRI parameters according to HPV status in OPC.

Material/Methods

We prospectively analyzed all patients undergoing either RT or chemoRT for histologically proven OPC between 2005 and 2018. OPC were considered HPV+ if more than 70% diffuse nuclear and cytoplasmic p16 immunohistochemistry staining was present. MRI with echo-planar DW sequences at 6 b-values (0-1000 s/mm²) were acquired before (chemo)RT treatment and during the fourth week of (chemo)RT. For each scan, an experienced head and neck radiologist manually delineated the entire primary tumor volume on the apparent diffusion coefficient (ADC) map, and several first-order histogram parameters (ADC mean, ADC median, ADC 10th percentile, ADC 90th percentile, ADC minimum and ADC maximum) were extracted. Delta (Δ) ADC values, the percentage of ADC changes between baseline and during RT at week 4, were calculated using the formula ΔADC = [(ADCduring – ADCpre)/ADCpre]*100. All ADC parameters were compared between HPV+ and HPV- OPC using the Mann-Whitney-U test, while oncological outcomes were compared using the log rank test. The predictive value of tumor ADC and ΔADC for local control (LC), loco-regional control (LRC), distant metastases-free survival (DMFS) and overall survival (OS) was examined using Cox regression models, applying logarithmic transformation upon continuous predictors. The significance threshold was set at a p-value of <0.05.

Results

One hundred seventy-eight patients with OPC were included. HPV status was known for 158 patients, of which 61 (39%) were considered HPV positive. Median follow-up time was 5.1 years. The estimated 5-year LRC was 75.2 % (89.3 % for HPV+ vs. 63.7% for HPV-, p<0.01). The 5-year OS was 54.9% (75.2% for HPV+ vs. 46.2% for HPV-, p<0.01). Kaplan-Meier curves are presented in Figure 1. The pretreatment ADC values were significantly higher in patients who developed a locoregional recurrence after RT, with a hazard ratio (HR) of 1.85 for the ADC mean (p=0.04). High tumor ADC values during RT were significantly associated with favorable LC (HR 0.4, p<0.01), LRC (HR 0.4, p<0.01), OS (HR 0.4, p<0.01) and DMFS (HR 0.5, p<0.01). Lower ΔADC was predictive for poorer LC (HR 0.8, p<0.01), LRC (HR 0.8, p<0.01), DMFS (HR 0.9, p<0.01) and OS (HR 0.9, p<0.01). These observations were valid for the entire population and for the HPV negative subgroup only.

Boxplots of the mean ADC values pretreatment, during treatment and ΔADC mean according to HPV status are presented in Figure 2. Between HPV+ and HPV- OPC, there was a significant difference in pretreatment first-order ADC 10th percentile (mean value of 82.4 *10^-5 mm2/s for HPV+ vs. 90.3 for HPV-, p=0.03) and a trend towards a lower pretreatment mean ADC in the HPV+ group (mean value of 111.4 *10^-5 mm2/s for HPV+ and 125.2*10^-5 mm2/s for HPV-, p=0.07). During the 4th week of RT, the ADC mean, median, minimum, 10th percentile and 90th percentile ADC values were all significantly higher in HPV+ OPC compared to HPV- OPC. The ΔADC mean value was significantly higher in the HPV+ OPC group (mean value of 95.0% for HPV+ vs. 55.3% for HPV-, p<0.01).

Figure 1: LRC (a) and OS (b) according to HPV status. Of 178 patients included, HPV status was known for 158 patients.

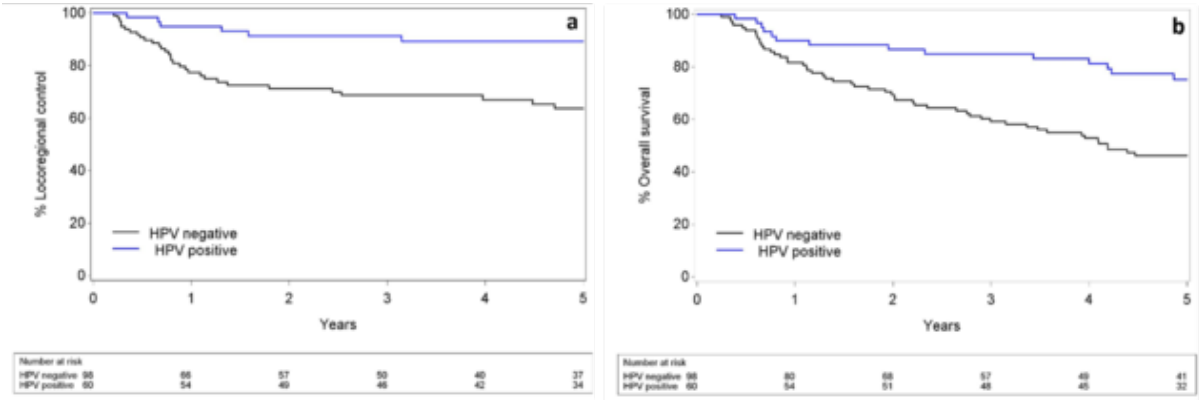
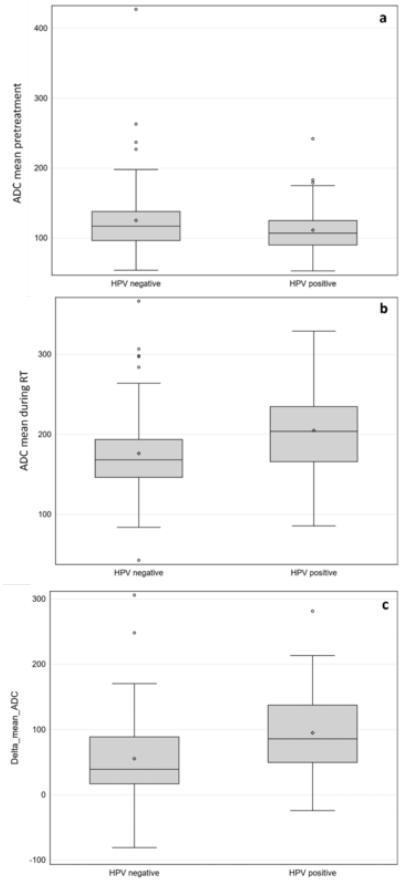


Figure 2: Boxplot of pretreatment ADC mean values (x10-5 mm²/s) (a), ADC mean values during RT (x10-5 mm²/s) (b) and ΔADC mean (%) (c) according to HPV status



Conclusion

Low pre-treatment ADC and high rise of ADC during (chemo)RT were established as significant indicators for favorable LRC in patients with OPC. These findings could allow treatment regimens to be modified according to the patient's individual risk for recurrence. ΔADC and ADC during RT showed significant differences between HPV+ and HPV- patients. However, since these findings were not confirmed on pretreatment ADC values, DW-MRI parameters currently cannot be reliably used to distinguish between the two clinical entities before start of the treatment.

215

Development of a Macrophage-based Prognostic Scoring System and Evaluation of Bufalin as a Macrophage Phenotype Modulator in Head and Neck Cancer using 2D and 3D Models

Nour Mhaidly, Géraldine Descamps, Sven Saussez, Fabrice Journé

University of Mons, Human Anatomy and Experimental Oncology, mons, Belgium

Topic

Immuno-oncology

Keywords

head and neck cancer, macrophages,bufalin

Purpose/Objective

Tumor-associated macrophages are key components of the tumor microenvironment (TME) and have been shown to play important roles in the progression of head and neck cancer. As a result, novel treatment approaches are focused on reprogramming M2 macrophages to adopt the M1 phenotype.

Material/Methods

A 3D coculture model was established to analyze the influence of cancer cells on monocyte recruitment and their polarization. Macrophages phenotypes were determined by immunofluorescence, western blot and RT-QPCR. Interleukines were analyzed by using CBA array.

Results

First, a scoring system based on the high or low density of M1 CD80+ and M2 CD163+ macrophages and on the tumor-infiltrated phenotype was developed in a clinical series of 54 head and neck squamous cell carcinoma patients. Interestingly, this macroscore was found to be more powerful than TNM criteria and p16 status and also significantly associated with poor prognosis for these patients. In vitro, the 3D model demonstrated that cancer cells are responsible for monocyte recruitment and M2 polarization, resulting in an immunosuppressive microenvironment with an increased production of IL8 and IL10 cytokines.Finally, we focused on a new compound found in toad venom. Bufalin is an endogenous cardiotonic steroid with reported anti-cancer and immunomodulatory properties. Our data indicated that bufalin reprogram M2 macrophages towards the M1 phenotype underlining its potential as an antitumor immune modulator.

Conclusion

Overall, this research highlights the power of the macroscore as a new valuable prognostic biomarker and sheds light on the immunosuppressive tumor microenvironment. Moreover, it indicates that modulating macrophages in the tumor microenvironment using bufalin could be a promising immunotherapeutic strategy for the treatment of cancer.

255

Predicting patient-level extranodal extension using pre-treatment computed tomography imaging

Sejin Kim[1,2], Andrew J Hope[1,3], Shao Hui Huang[1,3,4], Eugene Yu[1,5,6], Scott Bratman[1,3], Brian O'Sullivan[1,4,3], John R De Almeida[1,4], Christopher MKL Yao[1,4], Chris McIntosh[1,2,7], Benjamin Haibe-Kains[1,2,7]

[1]University Health Network, Princess Margaret Cancer Centre, Toronto, Canada. [2]University of Toronto, Medical Biophysics, Toronto, Canada. [3]University of Toronto, Department of Radiation Oncology, Toronto, Canada. [4]University of Toronto, Department of Otolaryngology-Head&Neck Surgery, Toronto, Canada. [5]University of Toronto, Department of Medical Imaging, Toronto, Canada. [6]University Health Network, Department of Otolaryngology-Head&Neck Surgery, Toronto, Canada. [7]University of Toronto, Computer Science, Toronto, Canada

Topic

Imaging, radiomics and artificial intelligence

Keywords

extranodal extension, deep learning, prognosis

Purpose/Objective

Extranodal extension (ENE) is strongly associated with worse outcomes in patients with head and neck squamous cell carcinoma (HNSCC) and is included in staging systems for HNSCC[2,3]. While histopathological determination remains the gold standard, pathologic confirmation is not always available for every patient or may not be available at the time when evidence of ENE may alter the treatment plan. This study aims to develop an automated method of pre-treatment radiographic imaging ENE (iENE) detection without human intervention to increase the chances of clinical adoption and improve risk stratification of patients with ENE.

In a previous study by Kann et al, a deep learning model was used to predict the presence of iENE in pre-treatment computed tomography (CT) scans of lymph nodes (LNs) cropped along their borders[1]. The model trained on 2673 LNs from 270 patients achieved a notable AUC score of 0.91 on the held-out test set, and 0.84 when tested on multi-institutional data. This performance gap may be attributed to the strong correlation between ENE status and LN diameter, as revealed by their regression analysis of clinical variables. Additionally, deploying their model in clinical settings necessitates substantial human involvement, as it requires contouring single or multiple suspicious LNs for inference.

To address these issues, we introduce a deep learning model designed to predict patient-level ENE without LN segmentations. Not relying on manual segmentation or cropping along the LNs borders improves potential adoption and serves as a regularization technique to reduce feature correlation with LN volume.

Material/Methods

We utilized a retrospective dataset comprising 922 oropharyngeal cancer patients and their radiotherapy (RT) treatment planning CT scans, each annotated by a radiologist for the presence of iENE. Our model analyzes 256x256x128 voxels centered around the larynx, encompassing LNs across all neck levels. Due to the input's considerable size, conventional 3D convolutional neural networks proved inefficient due to GPU memory limitations. To circumvent this, we leveraged ACS convolutions (ACSConv), which adapt 2D convolutions for 3D volumetric images, allowing us to capitalize on ImageNet pre-trained weights for more robust feature learning and quicker convergence.

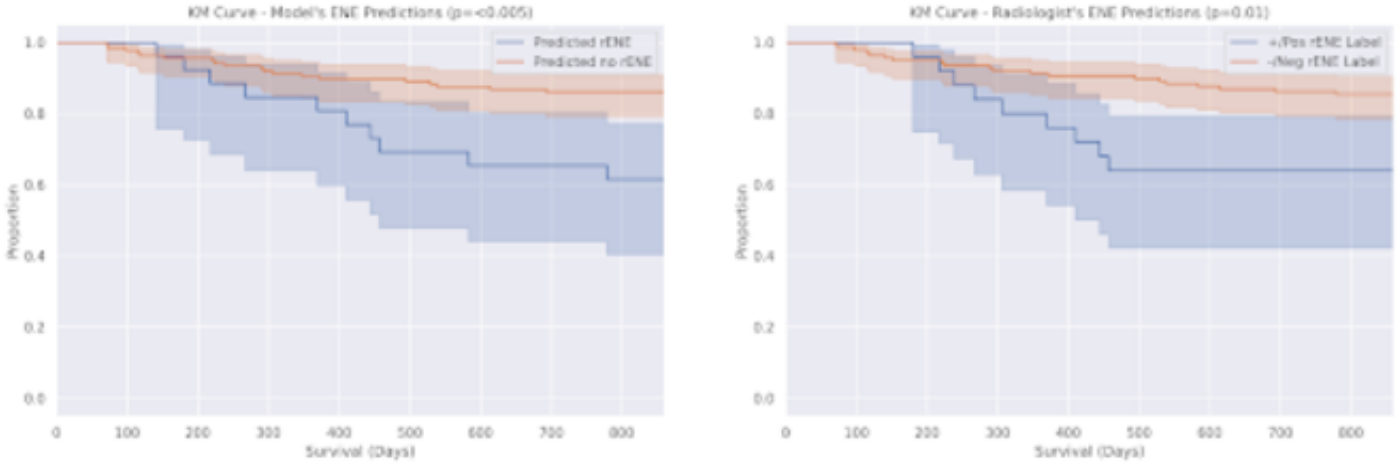
Our dataset was divided into 759 cases for training and 163 for held-out testing, with the date of diagnosis as the separation point, simulating a pseudo-prospective in-silico trial. The model was trained across four cross-validation folds on the training set, and the results from these four models were ensembled during inference.

Results

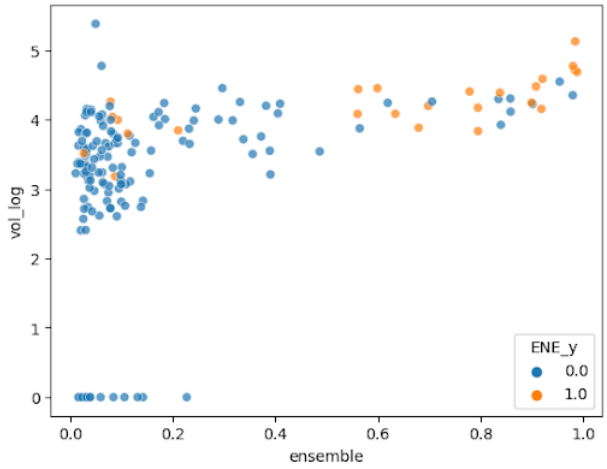
Our ACSConv models, without pre-training, achieved an area under the receiver operating characteristic curve (AUROC) of 0.80-0.83 and an area under the precision-recall curve (AUPRC) of 0.47-0.61 on the held-out test set, whereas our ImageNet pre-trained ACSConv model improved with an AUROC of 0.87-0.91 and an AUPRC of 0.52-0.69. This highlights the benefit of using ImageNet pre-trained weights, which encapsulate robust features learned from millions of standard images.

However, it's crucial to recognize that these performance metrics solely gauge the model's alignment with iENE, not histopathology. To demonstrate the model's risk stratification capabilities, we examined overall survival using Kaplan-Meier curves. The radiologist's iENE determination did not yield a

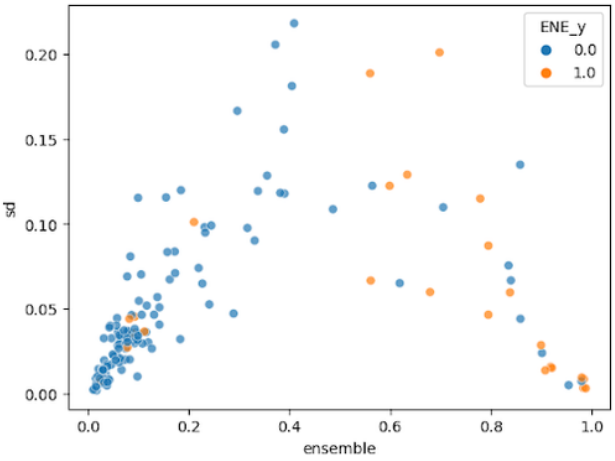
statistically significant difference (p=0.01), whereas the model's predictions resulted in significant differences (p<0.005). The increased prognostic power may be attributed to inherent limitations of radiological determination compared to histopathology. Alternatively, the model may be less sensitive and highlight severe cases, increasing its prognostic power. External validation on unseen cohorts will further elucidate the model's prognostic capabilities and limitations.



Additionally, we assessed the model's predictions against the volume of the largest LN gross tumor volume (GTVn) and found a moderate Spearman's correlation coefficient of 0.531. This suggests that while the model does consider GTVn volume, it certainly incorporates information beyond LN borders, potentially shedding light on issues with GTVn determination.



To account for potential variability in larynx segmentation models, we explored the impact of test-time augmentations on model inference. This simulated variations in larynx segmentation and its effect on iENE model performance. Notably, we observed no significant differences in prediction standard deviations between patients with or without iENE. An interesting trend emerged, showing that prediction standard deviations increased as the model's confidence decreased (closer to 0.5). This underscores the necessity for a deeper investigation into deep learning model behaviors to enhance safety and increase the likelihood of clinical adoption.



Conclusion

Our study presents a novel deep learning model for the automated detection of pre-treatment iENE. With improved performance and prognostic capabilities, this model holds potential for enhancing risk stratification in HNSCC patients and merits further validation on external datasets and in clinical practice.

References

1. Kann, Benjamin H., Sanjay Aneja, Gokoulakrichenane V. Loganadane, Jacqueline R. Kelly, Stephen M. Smith, Roy H. Decker, James B. Yu et al. "Pretreatment identification of head and neck cancer nodal metastasis and extranodal extension using deep learning neural networks." Scientific reports 8, no. 1 (2018): 14036.

2. Huang, Shao Hui, Rebecca Chernock, Brian O'Sullivan, and Carole Fakhry. "Assessment criteria and clinical implications of extranodal extension in head and neck cancer." American Society of Clinical Oncology Educational Book 41 (2021): 265-278.

3. Olsen, Kerry D., Michela Caruso, Robert L. Foote, Robert J. Stanley, Jean E. Lewis, Steven J. Buskirk, Deborah A. Frassica, Lawrence W. DeSanto, W. Michael O'fallon, and Verna R. Hoverman. "Primary head and neck cancer: histopathologic predictors of recurrence after neck dissection in patients with lymph node involvement." Archives of Otolaryngology–Head & Neck Surgery 120, no. 12 (1994): 1370-1374.

POSTERS

18

Evaluation of late sequelae in locally advanced head and neck cancer patients after NACT and IMRT

Raja Chhabra

Sanjay gandhi post graduate institute of medical sciences, Radiotherapy, Lucknow, India

Topic

Innovative treatments

Keywords

Dysphagia optimised RT

Purpose/Objective

To study the effect of NACT and CTRT on late sequelae i.exerostomia, dysphagia, aspiration and hearing loss and to correlate with the dose received by parotid glands, pharyngeal constrictormuscles and cochlea.

Material/Methods

127 patients of LAHNC treated with the above-mentioned strategy, between January 2013 to December 2019, were studied retrospectively. These were biopsy proven Stage ¾ tumors of the oropharynx, larynx, hypopharynx and unresectableoral tongue. Following initial work up, these patients were treated by NACT- 1-2 cycles of cisplatin-based doublet chemotherapy was the preferred regime at that time. SIB-IMRT was planned for a dose of 66Gy/30#/6 weeks to the high risk PTV; low risk PTV-54Gy/30#. Concurrently weekly cisplatin was planned at a dose of 35mg/m2 (max - 50mg) under adequate hydration and anti-emetic cover.

Dose to the parotid glands, pharyngeal constrictor muscles and cochlea was correlated with the late toxicity encountered during follow up.

Results

Median age of these patients was 49 years; males predominated, tobacco addiction was documented in 82% cases, average KPS was 80 and median baseline weight was 56 kg. Oropharyngeal malignancies were the commonest (32%), 80% were T3/T4 disease, 95% had lymph node positive disease and96% of the cases belonged to stage III/IV disease. Cisplatin capecitabine was the commonest combination used as NACT (in ¾ cases), 96% patients received ≥ 1 cycles of NACT; 47% patients received ≥ 5 concurrent CDDP and median RT dose - 64Gy, the CTRT compliance was 60% and overall treatment time of RT was 46 days. Acute toxicity such as neutropenia following NACT was seen in 18% cases and mucositis during CTRT was encountered in 85% of the patients, percentage weight loss during treatment was 6.2%. Deaths during treatmentor ≤ 30 days of treatment was seen in 20 cases - 4 died duringtreatment and 16 ≤ 30 days. Late toxicity was reported by 67patients - xerostomia - 56%; hearing loss - 44% and dysphagia in 40% cases. Significant xerostomia was seen in patients receiving >27Gy mean dose to the contralateral parotid gland and significant dysphagia/aspiration was seen in patients who received dose>52Gy to the inferior constrictor muscle. Prognostic factors influencing the survival outcomes - laryngeal primaries and patients receiving RT dose >64Gy had superior survival.

Conclusion

NACT followed by CTRT appears a doable option, however should be used after proper patient selection and with adequate caution. Cisplatin and capecitabine is an active and tolerable combination. Concurrent CTRT (SIB-IMRT) had anacceptable compliance and significant toxicity. Oropharyngeal tumors had significant aspiration and related deaths.

23

Head and neck cancer rates in India: An analysis of recent trends

Delfin Lovelina Francis[1], Saravanan Sampoornam Pape Reddy[2]

[1]Saveetha Dental College and Hospital, SIMATS, Public Health Dentistry, Chennai, India. [2]RR Army Hospital, Periodontology, NewDelhi, India

Topic

Epidemiology and prevention

Keywords

Developing Countries, Head and Neck Cancers

Purpose/Objective

India is classified as a lower-middle-income group country by the World Bank. Head and neck cancers are among the 10 most common cancers globallyand are the most common cancers in developing countries, especially in Southeast Asia. In India, it accounts for one fourth of male cancers and one tenth of female cancers. This is mainly attributed to tobacco, areca nut, alcohol, etc. Oral cancers are most common amongst all head and neck squamous cell cancers (HNSCC). HNSCC in the developing world differ from those in the Western world in terms of age, site of disease, etiology, and molecular biology. Poverty, illiteracy, advanced stage at presentation, lack of access to health care, and poor treatment infrastructure pose a major challenge in management of these cancers. The Cancer Atlas project by the Indian Council for Medical Research (ICMR) has shown the incidences of various cancers in different parts of India. Ninety percent of the oral cancer patients in rural areas belong to the lower or lower-middle socio-economic class, and 3.6% are below the poverty line.

Material/Methods

The tumor registry data was taken from South Indian cancer registry (Chennai-1986-98) and from a rural (Kancheepuram - 1988-98) registry, which has data for a long period since 1982 and 1987 respectively to identify the change in trends of head and neck cancers. Chennai, a South Indian urban cancer registry caters to an area of 170sq.km and a population of 4.2 millions. The rural registry data was available only from Barshi. It is the first rural registry in India that covers a total population of around 0.4 million in 346 villages spread over 3713 sq.km. in Solapur district of Maharashtra. The National Cancer Registry Programme of the Indian Council of Medical Research(ICMR) monitors these cancer registry data. The data from these two registries were usedtoanalyze change in trends within the country.

Results

Incidence rate is higher in more developed countries than less developed countries. Male preponderance is forthcoming. The South Indian cancer registry recorded a total of 6857 head and neck cancers during the time period 1986 to 1998, out of which 4777 were males (23% of all male cancers), and 2080 werefemales (9% of female cancers). In the rural registry, a total of 325 head and neck cancerswere registered during the time period 1988 to 1998, out of which 272 were males (28%of all male cancers) and 53 were females (5% of all female cancers).The overall male: female ratio of head and neck cancers in urban population is 2:1and inrural population is 5:1.

Conclusion

A trend is emerging showing that the type of oral cancers that patients present with are changing, with a definite increase in the number of patients presenting with tongue cancer. We are also seeing that a considerable number of these patients are presenting without the known associated risk factors. However, what might be causing these cancers is still to be proven, with HPV and dietary factors being at the forefront of alternative etiological factors.

24

Landscape of esophageal cancer in Kenya: Experience from Garissa Regional Cancer Center

Omar Abdihamid[1], Abdulsadiq Ibrahim[1], Houda Abdourahman[2], Thinwa Kareu[1], Abdullahi Hadi[3], Abeid Omar[4], Miriam Mutebi[5]

[1]Garissa Regional Cancer Center, Oncology, Garissa, Kenya. [2]Hopital De Balbala Cheiko, Oncology, Djibouti, Djibouti. [3]University of Pretoria, Department of Gastroenterology, Pretoria, South Africa. [4]Kenyatta University Teaching Research and Referral Hospital, Oncology, Nairobi, Kenya. [5]Aga Khan University, Department of Surgery, Nairobi, Kenya

Topic

Epidemiology and prevention

Keywords

Esophageal cancer, Garissa cancer center, Kenya

Purpose/Objective

In Kenya, cancer is the second leading cause of non-communicable disease deaths, and the trend of cancer deaths is projected to increase as per the 2018 GLOBOCAN report showing 47,887 new cases annually with a mortality of 32,987. Common cancers in men in Kenya are esophageal cancers (EC), prostate, colon, and rectum cancers. In contrast, breast, cervical, and EC are the leading cancers in women. However, EC is the most diagnosed cancer in both males and females and the leading cancer-related mortality in Kenya.

Published studies regarding the epidemiological factors that may or may not drive the high incidence of EC in Kenya include poor diet and nutritional insufficiencies with high intake of red meat, use of alcohol and tobacco, environmental carcinogenic exposure, intake of hot beverages, and genetic susceptibility citing a remarkable positive close family history of esophageal cancers.

Despite the availability of radiation and chemotherapy services at the Garissa Regional Cancer Center (GRCC), there is limited data about the clinicopathologic features and treatment outcomes of EC in this region. Therefore, this is the first study to look at the epidemiological patterns of EC in the northern Kenya region.

Material/Methods

This was a retrospective study involving patients' file review of confirmed EC cases diagnosed or treated at the GRCC, a regional referral cancer center between 2019 and 2023. Data collected on each patient's chart included age, sex, risk factors, family history, histological type, stage at diagnosis, treatment type, and survival outcomes. For patients who were no longer in contact with the staff through clinic visits, the patients or their next of kin were contacted through phone calls for patients' survival status. Data were collected and stored using the STATA software.

Results

124 esophageal cases were identified, 64 (48%) were males and 60 (52%) were females with a mean age of 57.56 years. In terms of risk factors, hot beverage consumption was the highest (47 cases, 57%), followed by history of peptic ulcer disease (27 cases, 33.5%), smoking (8.9%), gastroesophageal reflux disease (2 cases, 1.6%), unknown (8.7%), and 37% of the patients were lost to follow up with no identifiable risk factors.

Stage of diagnosis at presentation was stage 1 (1 case, 0.8%), stage 2 (22 cases, 17.8%), stage 3 (25 cases, 20.2%), stage 4 (50 cases, 40.3%), not staged (26 cases, 21%). The majority had squamous cell carcinoma (105 cases, 84.7%), followed by adenocarcinoma (5 cases, 4%), anaplastic (5 cases, 4%), SCC+ adenocarcinoma (1 case, 0.8%), unknown histology (4 cases, 3.2%).

In terms of diagnostic modality, 92 cases (74.2%) had triple modality assessment (Endoscopy, histology, and staging scans), 4 cases (3.2%) had only imaging scans, and 24 cases (20%) had endoscopy+ histology only.

20 cases (16.1%) had a family history of cancer (irrespective of sub-type). Most of the patients were of ethnic Kenyan-Somali background (108 cases, Somali, 87.1%), and other tribes (7 cases, 0.6%). 96 cases (77.4%) were from Garissa County, 12 cases (9.8%) were from Wajir county, 12 cases (12.8%) from Tana River County, and 4 cases (3.2%) from other counties. Most patients paid cash for their treatment (92 cases,77%) while only (27 cases, 23%) paid through the National Hospital Insurance Fund (NHIF).

Conclusion

This study is the first esophageal study in northern Kenya and confirmed the clinicopathological features of one of the most common cancers in Kenya and more so among Kenyan-Somalis. The study also validates the predominance of histological subtypes of esophageal squamous cell carcinoma with the late presentation, short survival, and significant loss of follow-up.

Our data demonstrates the need for the county government of Garissa in collaboration with the National Cancer Control Program to prioritize EC on the national health agenda, including promoting preventative strategies, cost-effective early screening, early detection, and timely treatment and designing interventions to improve treatment adherence such as using appointment reminders via mobile phones, setting up an up-to-date cancer registry, and enhancing referral pathways. We recommend future esophageal cancer studies employing a large prospective design with a large sample size to determine the impact of the new GRCC on the outcomes of Esophageal cancer patients and the local community.

33

Impact of surgery to radiotherapy interval on oncological outcomes in tongue squamous cell carcinoma

Sepehr Fekrazad[1], Shayan Shojaei[2], Asma Mousavi[2], Mohammad Shirkhoda[3], Ali Kazemian[4,5], Reza Ghalehtaki[4,5]

[1]Cancer Research Institute, Radiation Oncology Research Center, Tehran, Iran, Islamic Republic of. [2]Tehran University of Medical Sciences, Faculty of Medicine, Tehran, Iran, Islamic Republic of. [3]Cancer Research Institute, Department of General Surgery, Subdivision of Surgical Oncology, Tehran, Iran, Islamic Republic of. [4]Cancer Research Institute, Tehran University of Medical Sciences, Radiation Oncology Research Center, Tehran, Iran, Islamic Republic of. [5]Cancer Institute, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Department of Radiation Oncology, Tehran, Iran, Islamic Republic of

Topic

RTT

Keywords

TSCC, Radiotherapy, Loco-regional Recurrence,

Purpose/Objective

Tongue squamous cell carcinoma (TSCC) is one of the most prevalent types of head and neck malignancies, and its treatment typically involves surgery combined with radiotherapy and chemotherapy. Despite advancements in treatment, TSCC recurrence remains a significant concern, affecting approximately 20% of treated patients. This study aims to assess the impact of the time interval between radiotherapy and surgery on oncological outcomes in TSCC patients.

Material/Methods

A total of 215 patient records (98 females and 117 males) with biopsy-proven TSCC receiving various treatments were extracted. The Inclusion criteria were patients who received external beam radiotherapy, had no detectable metastasis, underwent oncological surgery, and received a minimum radiation dose of 60 Gy. Ultimately, 108 patients met these criteria and were included in the analysis. The surgical procedure involved glossectomy, and the prescribed radiotherapy dose exceeded 60 Gy. Patients were stratified based on tumor stage (early-stage and locally advanced stage) and the timing of radiotherapy initiation after surgery (less than 47 days and more than 47 days). The study analyzed loco-regional control, loco-regional recurrence, disease-free survival, and overall survival as endpoints. These endpoints were compared between different subgroups based on tumor stage and surgery to radiotherapy interval.

Results

A retrospective analysis was conducted on the medical records of 108 patients who underwent surgical treatment followed by radiotherapy between 2011 and 2022. In early-stage patients, radiotherapy within 47 days after surgery demonstrated superior disease-free survival (DFS) outcomes. However, in

locally advanced-stage patients, the opposite trend was observed, with a longer interval between surgery and radiotherapy associated with improved DFS outcomes. These patterns were similarly reflected in overall survival (OS) outcomes. Notably, the difference in loco-regional recurrence (LLR) outcomes was more pronounced among advanced-stage patients.

Conclusion

In conclusion, this study highlights that advanced-stage TSCC patients tend to experience earlier recurrence, potentially necessitating additional surgical interventions or precluding the administration of radiotherapy, as investigated in our study. These findings shed light on the significance of the time interval between surgery and radiotherapy in TSCC management.

34

Impact of antibiotic use in the primary treatment of nasopharyngeal carcinoma

Jason Chan[1], Zigui Chen[2], Jamie Chen[1]

[1]CUHK, Otorhinolaryngology, Head and Neck Surgery, Shatin, Hong Kong. [2]CUHK, Department of Microbiology, Shatin, Hong Kong

Topic

HPV or EBV related cancers

Keywords

Naopharynx, antibiotics, microbiome

Purpose/Objective

Patients with nasopharyngeal carcinoma (NPC) benefit from antibiotics when there are infective complications during and around chemoradiotherapy, but there is some indication that antibiotics used peri treatment may affect patients' outcomes. Here we sought to elucidate the exact impacts of antibiotics on NPC patients' outcomes around primary treatment.

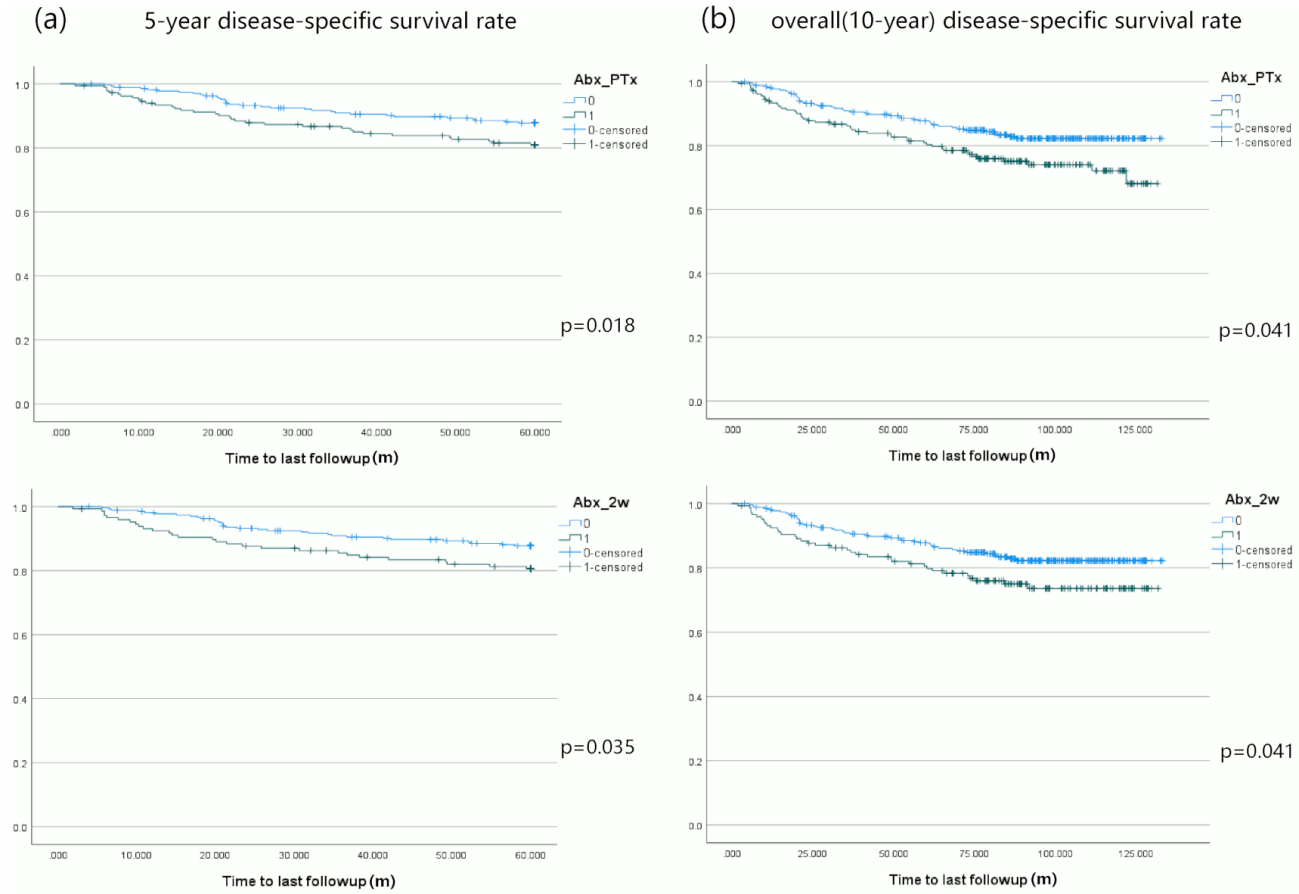
Material/Methods

This was a retrospective cohort study in a tertiary academic center in Hong Kong SAR. NPC patients treated for primary disease between 2010 and 2014 were evaluated for the impact of antibiotics prescribed around primary treatments on recurrence-free survival (RFS), disease-specific survival (DSS), and overall survival (OS), which was analyzed by multivariate Kaplan–Meier and Cox Proportional Hazard Regression analysis. The data were analyzed and performed with SPSS, V27.0 and GraphPad, V8.0

Results

A total of 455 patients with primary NPC were included in the study. The cohort consisted of predominantly males (75.6%). Patients who had advanced tumor stage (p=0.019), received NC (p=0.008) or CCRT (p=0.002), were more likely to be prescribed antibiotics. On univariate analysis smoking (p=0.02), advanced stage of disease (p=0.007), lymph node metastasis (p= 0.004), NC administration

(P<0.001) and antibiotic use was associated with a poorer year DSS in NPC patients. Antibiotic use around primary NPC treatment (5-year: HR 1.644 95%CI [1.015, 2.665], 10-year: 1.640 [1.085, 2.480]), within 2 weeks (5-year: 1.685 [1.015, 2.799], 10-year: 1.600 [1.030, 2.486]) or 1 week (5-year: 1.811 [1.073, 3.055]), were associated with significantly worse DSS in NPC patients, Figure 1 shows the Kaplan Meir curves. The negative elements included using specific antibiotics (5-year: 2.53 [1.331, 4.807], 10-year: 2.215 [1.236, 3.969]) and oral administration as well (5-year: 1.731 [1.069, 2.805], 10-year: 1.647 [1.087, 2.497]). Multivariate analysis showed a trend towards worse DSS at 5 years with antibiotic use at 1 week around therapy (P=0.054).



Conclusion

In NPC, antibiotics use around primary treatment, regardless of stage, had a poorer prognosis, especially disease-specific survival. In clinical practice, events leading to the prescription of antibiotics or the administration of antibiotics should be carefully considered in NPC patients treated for primary NPC.

References

1. Chen YP, Chan ATC, Le QT, Blanchard P, Sun Y, Ma J. Nasopharyngeal carcinoma. Lancet. 2019;394(10192):64-80.

2. Chang ET, Ye W, Zeng YX, Adami HO. The Evolving Epidemiology of Nasopharyngeal Carcinoma. Cancer Epidemiol Biomarkers Prev. 2021;30(6):1035-47.

3. Barnes L, Eveson J, Reichart P, Sidransky D. World Health Organization classification of tumours: pathology and genetics of head and neck tumours. 2005.

4. Bossi P, Chan AT, Licitra L, Trama A, Orlandi E, Hui EP, et al. Nasopharyngeal carcinoma: ESMO-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up(†). Ann Oncol. 2021;32(4):452-65.

5. Tang LL, Chen YP, Chen CB, Chen MY, Chen NY, Chen XZ, et al. The Chinese Society of Clinical Oncology (CSCO) clinical guidelines for the diagnosis and treatment of nasopharyngeal carcinoma. Cancer Commun (Lond). 2021;41(11):1195-227.

6. Chen YP, Ismaila N, Chua MLK, Colevas AD, Haddad R, Huang SH, et al. Chemotherapy in Combination With Radiotherapy for Definitive-Intent Treatment of Stage II-IVA Nasopharyngeal Carcinoma: CSCO and ASCO Guideline. J Clin Oncol. 2021;39(7):840-59.

7. Xia C, Jiang C, Li W, Wei J, Hong H, Li J, et al. A Phase II Randomized Clinical Trial and Mechanistic Studies Using Improved Probiotics to Prevent Oral Mucositis Induced by Concurrent Radiotherapy and Chemotherapy in Nasopharyngeal Carcinoma. Front Immunol. 2021;12:618150.

8. Hou J, Zheng H, Li P, Liu H, Zhou H, Yang X. Distinct shifts in the oral microbiota are associated with the progression and aggravation of mucositis during radiotherapy. Radiother Oncol. 2018;129(1):44-51.

9. Jiang C, Wang H, Xia C, Dong Q, Chen E, Qiu Y, et al. A randomized, double-blind, placebo-controlled trial of probiotics to reduce the severity of oral mucositis induced by chemoradiotherapy for patients with nasopharyngeal carcinoma. Cancer. 2019;125(7):1081-90.

10. Nenclares P, Bhide SA, Sandoval-Insausti H, Pialat P, Gunn L, Melcher A, et al. Impact of antibiotic use during curative treatment of locally advanced head and neck cancers with chemotherapy and radiotherapy. Eur J Cancer. 2020;131:9-15.

11. Köstler WJ, Hejna M, Wenzel C, Zielinski CC. Oral mucositis complicating chemotherapy and/or radiotherapy: options for prevention and treatment. CA Cancer J Clin. 2001;51(5):290-315.

12. Taplitz RA, Kennedy EB, Bow EJ, Crews J, Gleason C, Hawley DK, et al. Antimicrobial Prophylaxis for Adult Patients With Cancer-Related Immunosuppression: ASCO and IDSA Clinical Practice Guideline Update. J Clin Oncol. 2018;36(30):3043-54.

13. Sun Y, Li WF, Chen NY, Zhang N, Hu GQ, Xie FY, et al. Induction chemotherapy plus concurrent chemoradiotherapy versus concurrent chemoradiotherapy alone in locoregionally advanced nasopharyngeal carcinoma: a phase 3, multicentre, randomised controlled trial. Lancet Oncol. 2016;17(11):1509-20.

14. Yin J, Xie J, Lin J, Weng C, Lu S, Xu P, et al. Evaluation of the efficacy of the anti-ulcer oral mucosal protective agent RADoralex® in the prevention and treatment of radiation-induced oral mucosal reactions induced during treatment of nasopharyngeal carcinoma. Cancer Biol Ther. 2022;23(1):27-33.

15. Maxwell MB, Maher KE. Chemotherapy-induced myelosuppression. Semin Oncol Nurs. 1992;8(2):113-23.

16. Saloustros E, Tryfonidis K, Georgoulias V. Prophylactic and therapeutic strategies in chemotherapy-induced neutropenia. Expert Opin Pharmacother. 2011;12(6):851-63.

17. Zhou S, Huang H, Chen Q, Tan KS, Zhu Z, Peng Y, et al. Long-term defects of nasal epithelium barrier functions in patients with nasopharyngeal carcinoma post chemo-radiotherapy. Radiother Oncol. 2020;148:116-25.

18. Bonomi M, Batt K. Supportive Management of Mucositis and Metabolic Derangements in Head and Neck Cancer Patients. Cancers (Basel). 2015;7(3):1743-57.

19. Anderson CM, Lee CM, Saunders DP, Curtis A, Dunlap N, Nangia C, et al. Phase IIb, Randomized, Double-Blind Trial of GC4419 Versus Placebo to Reduce Severe Oral Mucositis Due to Concurrent Radiotherapy and Cisplatin For Head and Neck Cancer. J Clin Oncol. 2019;37(34):3256-65.

20. Berger K, Schopohl D, Bollig A, Strobach D, Rieger C, Rublee D, et al. Burden of Oral Mucositis: A Systematic Review and Implications for Future Research. Oncol Res Treat. 2018;41(6):399-405.

21. Roy S, Trinchieri G. Microbiota: a key orchestrator of cancer therapy. Nat Rev Cancer. 2017;17(5):271-85.

22. Zhu XX, Yang XJ, Chao YL, Zheng HM, Sheng HF, Liu HY, et al. The Potential Effect of Oral Microbiota in the Prediction of Mucositis During Radiotherapy for Nasopharyngeal Carcinoma. EBioMedicine. 2017;18:23-31.

23. Reyes-Gibby CC, Wang J, Zhang L, Peterson CB, Do KA, Jenq RR, et al. Oral microbiome and onset of oral mucositis in patients with squamous cell carcinoma of the head and neck. Cancer. 2020;126(23):5124-36.

24. Vesty A, Gear K, Biswas K, Mackenzie BW, Taylor MW, Douglas RG. Oral microbial influences on oral mucositis during radiotherapy treatment of head and neck cancer. Support Care Cancer. 2020;28(6):2683-91.

25. Gunn GB, Mendoza TR, Garden AS, Wang XS, Shi Q, Morrison WH, et al. Minocycline for symptom reduction during radiation therapy for head and neck cancer: a randomized clinical trial. Support Care Cancer. 2020;28(1):261-9.

26. Duan H, Yu L, Tian F, Zhai Q, Fan L, Chen W. Antibiotic-induced gut dysbiosis and barrier disruption and the potential protective strategies. Crit Rev Food Sci Nutr. 2022;62(6):1427-52.

27. Thaiss CA, Zmora N, Levy M, Elinav E. The microbiome and innate immunity. Nature. 2016;535(7610):65-74.

28. Vonarbourg C, Mortha A, Bui VL, Hernandez PP, Kiss EA, Hoyler T, et al. Regulated expression of nuclear receptor RORγt confers distinct functional fates to NK cell receptor-expressing RORγt(+) innate lymphocytes. Immunity. 2010;33(5):736-51.

29. Atarashi K, Tanoue T, Oshima K, Suda W, Nagano Y, Nishikawa H, et al. Treg induction by a rationally selected mixture of Clostridia strains from the human microbiota. Nature. 2013;500(7461):232-6.

30. Zhou CB, Zhou YL, Fang JY. Gut Microbiota in Cancer Immune Response and Immunotherapy. Trends Cancer. 2021;7(7):647-60.

31. Fessler J, Matson V, Gajewski TF. Exploring the emerging role of the microbiome in cancer immunotherapy. J Immunother Cancer. 2019;7(1):108.

32. Gorjifard S, Goldszmid RS. Microbiota-myeloid cell crosstalk beyond the gut. J Leukoc Biol. 2016;100(5):865-79.

33. Uribe-Herranz M, Rafail S, Beghi S, Gil-de-Gómez L, Verginadis I, Bittinger K, et al. Gut microbiota modulate dendritic cell antigen presentation and radiotherapy-induced antitumor immune response. J Clin Invest. 2020;130(1):466-79.

34. Yang K, Hou Y, Zhang Y, Liang H, Sharma A, Zheng W, et al. Suppression of local type I interferon by gut microbiota-derived butyrate impairs antitumor effects of ionizing radiation. J Exp Med. 2021;218(3).

35. Daillère R, Vétizou M, Waldschmitt N, Yamazaki T, Isnard C, Poirier-Colame V, et al. Enterococcus hirae and Barnesiella intestinihominis Facilitate Cyclophosphamide-Induced Therapeutic Immunomodulatory Effects. Immunity. 2016;45(4):931-43.

36. Ghoreschi K, Laurence A, Yang XP, Tato CM, McGeachy MJ, Konkel JE, et al. Generation of pathogenic T(H)17 cells in the absence of TGF-β signalling. Nature. 2010;467(7318):967-71.

37. Viaud S, Saccheri F, Mignot G, Yamazaki T, Daillère R, Hannani D, et al. The intestinal microbiota modulates the anticancer immune effects of cyclophosphamide. Science. 2013;342(6161):971-6.

38. Gehrke T, Hackenberg S, Polat B, Wohlleben G, Hagen R, Kleinsasser N, et al. Combination of salinomycin and radiation effectively eliminates head and neck squamous cell carcinoma cells in vitro. Oncol Rep. 2018;39(4):1991-8.

39. Aydemir L, Iplik ES, Ertugrul B, Kasarci G, Atas MN, Ulusan M, et al. Levofloxacin might be safe to use for OSCC patients. Med Oncol. 2021;38(8):87.

40. Dong J, Li Y, Xiao H, Zhang S, Wang B, Wang H, et al. Oral microbiota affects the efficacy and prognosis of radiotherapy for colorectal cancer in mouse models. Cell Rep. 2021;37(4):109886.

41. Tian X, Mei T, Yu M, Li Y, Ao R, Gong Y. The impact of antibiotic selection and interval time among advanced non-small cell lung cancer patients receiving prior antibacterial treatment and first-line chemotherapy. Cancer Med. 2022;11(24):4849-64.

42. Chambers LM, Kuznicki M, Yao M, Chichura A, Gruner M, Reizes O, et al. Impact of antibiotic treatment during platinum chemotherapy on survival and recurrence in women with advanced epithelial ovarian cancer. Gynecol Oncol. 2020;159(3):699-705.

43. Pinato DJ, Howlett S, Ottaviani D, Urus H, Patel A, Mineo T, et al. Association of Prior Antibiotic Treatment With Survival and Response to Immune Checkpoint Inhibitor Therapy in Patients With Cancer. JAMA Oncol. 2019;5(12):1774-8.

44. Cortellini A, Di Maio M, Nigro O, Leonetti A, Cortinovis DL, Aerts JG, et al. Differential influence of antibiotic therapy and other medications on oncological outcomes of patients with non-small cell lung cancer treated with first-line pembrolizumab versus cytotoxic chemotherapy. J Immunother Cancer. 2021;9(4).

37

Oral microbiome's impact on mucositis and locoregional tumor control in HNSCC patients undergoing radiotherapy

Alexander Rühle[1,2], Elsa Beatrix Monroy Ordonez[1], Máté Krausz[3], Andreas R Thomsen[1], Daniel Schnell[1], Tanja Sprave[1], Henning Schäfer[1], Anca-Ligia Grosu[1], Bodo Grimbacher[3], Michele Proietti[3], Michael Henke[1], Nils H Nicolay[1,2]

[1]University of Freiburg-Medical Center, Department of Radiation Oncology, Freiburg, Germany. [2]University Medical Center Leipzig, Department of Radiation Oncology, Leipzig, Germany. [3]University of Freiburg-Medical Center, Institute for Immunodeficiency, Center for Chronic Immunodeficiency, Freiburg, Germany

Topic

Immuno-oncology

Keywords

Microbiome, radiotherapy, mucositis

Purpose/Objective

Recent studies have shown a potential function of the gut microbiome in the immunological modulation of anti-cancer treatments. However, the role of the oral microbiome in head-and-neck squamous cell carcinoma (HNSCC) patients undergoing radiotherapy in terms of radiation-induced toxicities as well as tumor response is largely unknown. Here, we examined a potential influence of the oral microbiome composition on acute radiation-induced mucositis and locoregional tumor control (LRC).

Material/Methods

Saliva samples of two independent prospective trials (SALIVA and ZiSStrans trial [DRKS00012947]), in which HNSCC patients undergoing (chemo)radiation were enrolled, were analyzed in terms of their oral microbiome composition. In both trials, unstimulated saliva was collected before the first radiotherapy application and stored at -80°C. Baseline oral microbiome was examined using V3-4 16S rRNA sequencing, and bioinformatic analyses were carried out in R (v4.3.1). Kaplan-Meier analyses were carried out regarding LRC.

Results

A total of 106 HNSCC patients (53 in the SALIVA trial, 53 in the ZiSStrans trial), who were treated with definitive (chemo)radiation, had stored saliva samples available and could be analyzed. Median age was 60 years (SALIVA) and 61 years (ZiSStrans), most common tumor localization was the oropharynx (n=25 in both trials), and majority of patients had a positive smoking history (n=29 [SALIVA], n=27 [ZiSStrans]). Fourty-four (83%) and 30 (57%) patients in the SALIVA and ZiSStrans trial developed acute grade 3-4 mucositis during treatment, respectively. Grade 3-4 mucositis occurred after a median radiation dose of 34 Gy (SALIVA) and 31.5 Gy (ZiSStrans). 2-year LRC rate was 69% and 72% in the SALIVA and ZiSStrans trial, respectively. No differences in alpha diversity were found in terms of patient age, sex, T stage, N stage, tumor localization and smoking status in both trials ($p>0.05$), neither did the beta diversity analysis reveal relevant differences between these groups. Furthermore, neither alpha nor beta diversity was associated with development of grade 3-4 mucositis in the two trials ($p>0.05$). In the ZiSStrans trial, Shannon index was significantly higher in patients with no locoregional recurrence after 2 years ($p=.03$), which was not validated in the SALIVA trial ($p=0.35$). Lower Lachnoanaerobaculum abundance ($p=0.02$ [SALIVA], $p=0.03$ [ZiSStrans], ALDEx2, Wilcoxon-test) were associated with increased 2-year locoregional recurrence rates in both the SALIVA and ZissTrans trial. 2-year LRC was 96% (SALIVA) and 85% (ZiSStrans) in patients with Lachnoanaerobaculum abundance above the median value versus

35% (SALIVA) and 58% (ZiSStrans) in patients with Lachnoanaerobaculum abundance below the median ($p<0.05$, log-rank).

Conclusion

While we could not find an association between the baseline oral microbiome and development of acute grade 3-4 mucositis, we identified higher Lachnoanaerobaculum abundance associated with increased LRC after radiotherapy in both independent prospective trials. In terms of oral mucositis, further in-depth analyses of the oral microbiome composition in both prospective trials are ongoing to examine potential associations between distinct bacterial genera and the onset of grade 3-4 mucositis. Prospective longitudinal analyses of the alterations in patients' oral microbiome composition are necessary in order to improve the understanding of the complex interactions between the microbiome and the immune system in patients with HNSCC undergoing radiotherapy.

40

Factors Affecting the Longevity of Voice Prosthesis after Total Laryngectomy

José Miguel Costa[1], Joan Lop[2], Paula Mackers[3], Rosa Delia Ramírez[1], Maite Sistachs[3], Isabel Vilaseca[1], Francesc Xavier Avilés[1], Eduardo Lehrer[1], Anna Sumarroca[3]

[1]Hospital Clínic, ENT, Barcelona, Spain. [2]Hospital del Mar, Pathology, Barcelona, Spain. [3]Hospital del Mar, ENT, Barcelona, Spain

Topic

Supportive care, rehabilitation

Keywords

Voice rehabilitation, larynx cancer

Purpose/Objective

The most disabling sequela of total laryngectomy is loss of voice. Tracheoesophageal puncture with insertion of a voice prosthesis provides speech rehabilitation and recovery for these patients, although it is not free of complications or inconveniences such as frequent prosthesis replacement. The aim of our study is to identify whether there are factors that influence a greater frequency of voice prosthesis replacement in laryngectomised patients.

Material/Methods

We retrospectively reviewed data from a total of 45 laryngectomised patients in two hospitals with Provox Vega voice prostheses. The dependent variable chosen was the annual change of prosthesis and the independent variables were: treatment with radiotherapy or chemotherapy previous to surgery, date of surgery, radiotherapy +/- chemotherapy after surgery, type of surgery: simple total laryngectomy (STL), total laryngectomy with pharyngectomy (FTL), total laryngectomy with extension to first tracheal rings (TLT) - mostly due to previous tracheostomy -, the type of prosthesis placement (primary or secondary).

Results

The mean number of prosthesis replacements per year per patient was 3.9 replacements/year (range 1-14), with a median of 4 replacements/year, and a mean lifetime of three months. The only variable that was significantly related to less prosthesis change was TLT (2.7 changes/year), compared to STL (4.3 changes/year) and FTL (4.9 changes/year) ($p<0.05$). The other variables were not significantly related to more or less prosthesis changes.

Conclusion

The voice prosthesis is useful and in our study its useful life is about 3 months in laryngectomised patients regardless of the previous or subsequent treatment received, the date of surgery or the type of fitting. However, the type of surgery may influence the duration of the prosthesis, with TLT showing the best results.

References

Lewin JS, Baumgart LM, Barrow MP, et al. Device Life of the Tracheoesophageal Voice Prosthesis Revisited. JAMA Otolaryngol Head Neck Surg. 2017 Jan 1;143(1):65-71. doi: 10.1001/jamaoto.2016.2771.

J R Shultz, J Harrison. Defining and predicting tracheoesophageal puncture success. Arch Otolaryngol Head Neck Surg. 1992 Aug;118(8):811-6. doi: 10.1001/archotol.1992.01880080033009.

A. Krishnamurthy, S. Khwajamohiuddin. Analysis of Factors Affecting the Longevity of Voice Prosthesis Following Total Laryngectomy with a Review of Literature. Indian J Surg Oncol. 2018 Mar; 9(1): 39–45. doi: 10.1007/s13193-017-0700-z

A. Serra, P. Di Mauro, D. Spartaro et al. Post-laryngectomy voice rehabilitation with voice prosthesis: 15 years experience of the ENT Clinic of University of Catania. Retrospective data analysis and literature review. Acta Otorhinolaryngol Ital. 2015 Dec; 35(6): 412–419.doi: 10.14639/0392-100X-680

43

Clinical-dosimetric relationship between lacrimal gland dose and ocular toxicity after intensity-modulated radiotherapy for nasopharyngeal carcinoma

Lina Kchaou[1], Semia Zarraa[1,2], Yousfi Amani[1,2], Emna Boudhina[1], Kouti Emir[1], Alia Mousli[1,2], Chiraz Nasr[1,2]

[1]Salah Azaiez Institute, Radiation Oncology, Tunis, Tunisia. [2]University of Tunis El Manar, Faculty of Medecine, Tunis, Tunisia

Topic

Quality of life and outcomes

Keywords

Nasopharynx, Lacrimal gland, Dry eye Syndrom

Purpose/Objective

To evaluate the relationship between lacrimal gland dose and ocular toxicity among those patients.

Material/Methods

Between September 2020 and May 2022, we selected 20 patients treated for NPC by IMRT technique to a curative dose of 70Gy at Salah Azaeiz Institute. The lacrimal gland was contoured on the axial slice as Organ at risk (OAR). The following dosimetric parameters were evaluated: mean dose and maximum dose. A Tear Break-up Time (TBUT) test was conducted to assess dry eye syndrome.

Results

The median follow-up time was 9 months (5 - 22 months). Based on the dose-volume histogram analysis, averages of mean and maximum doses to the ipsilateral lacrimal gland were 11.4 Gy (range, 3.7-29.9 Gy) and 30.3 Gy, (range, 14.4-46.9 Gy) respectively. The median time of the TBUT test was 7 seconds. The incidence of late Grade 3+ toxicities was 15%. We reported a severe dry eye syndrome in two patients and the mean dose to their lacrimal gland were superior to 25 Gy.

Conclusion

High-grade ocular toxicity is a potential complication that detrimentally affect the quality of life in patients treated by IMRT for NPC. The incidence of these complications has been shown to increase with higher doses to the lacrimal gland. To reduce the toxicity and prevent dry eye syndrome lacrimal gland should be contoured as OAR and dose constraints should be given.

46

Lobectomy vs total thyroidectomy for papillary thyroid carcinoma with lymph node metastasis

Xiabin Lan, Shijia Zhang, Kehui Zhou

Zhejiang Cancer Hospital, Department of Thyroid Surgery, Hangzhou, China

Topic

Salivary gland, skull base, skin and thyroid cancers

Keywords

total thyroidectomy, lobectomy, lymph node

Purpose/Objective

Although the guidelines recommend total thyroidectomy (TT) and subsequent radioactive iodine ablation as the management options for patients with papillary thyroid carcinoma (PTC) and lymph node metastasis, the direct evidence for this management is lacking [1]. Currently, there are few studies comparing unilateral lobectomy (uLT) and TT for patients with unilateral PTC and ipsilateral cervical lymph node metastasis (IC-LNM) [2, 3]. The present study was carried out to compare the prognosis of patients with unilateral PTC and IC-LNM treated with uLT vs TT so as to find out which surgery was optimal for these patients without other clinical risk features.

Material/Methods

Thyroid cancer patients at Zhejiang Cancer Hospital between February 2012 and January 2022 were retrospectively reviewed. Patients with unilateral PTC and IC-LNM who underwent uLT or TT for the primary tumor and simultaneous ipsilateral cervical lymph node dissection were included in this study. Patients with any of the following features were excluded: bilateral lobe tumors; tumor size ≥ 4 cm; extensive extrathyroidal invasion; with contralateral cervical lymph node metastasis; distant metastasis; non-primary surgery. Additionally, a propensity score matching (PSM) was performed on patients treated with u-LT or TT. Recurrence-free survival (RFS), overall survival (OS), hospitalization costs, postoperative complications, and other clinical characteristics were compared between the two groups.

Results

Ultimately, 682 patients with unilateral PTC and IC-LNM were available in the study. Among the 682 patients, 443 (65.0%) patients were treated with uLT and 239 (35.0%) patients were treated with TT. After PSM with potential prognostic factors (such as gender, age, primary tumor size, multifocality, extrathyroidal invasion, and T stage), a total of 225 pairs of patients were eligible for analysis. After a median of 35 months (range: 16 - 4160 days) follow-up, 22 (10.1%) and 12 (5.4%) patients experienced recurrences in the uLT group and TT group, respectively. The recurrence risk in the TT group was not statistically different from that in the uLT group (adjusted hazard ratio = 0.540; 95% CI, 0.265-1.097; p = 0.088). No significant differences in RFS and OS were observed between uLT and TT groups **(Figure 1)**. However, TT group was significantly related with higher risk of transient and permanent hypoparathyroidism (p< 0.01), higher L-T4 doses (p< 0.001), longer hospital stays (p< 0.01), and higher hospitalization costs (p< 0.001) than uLT group.

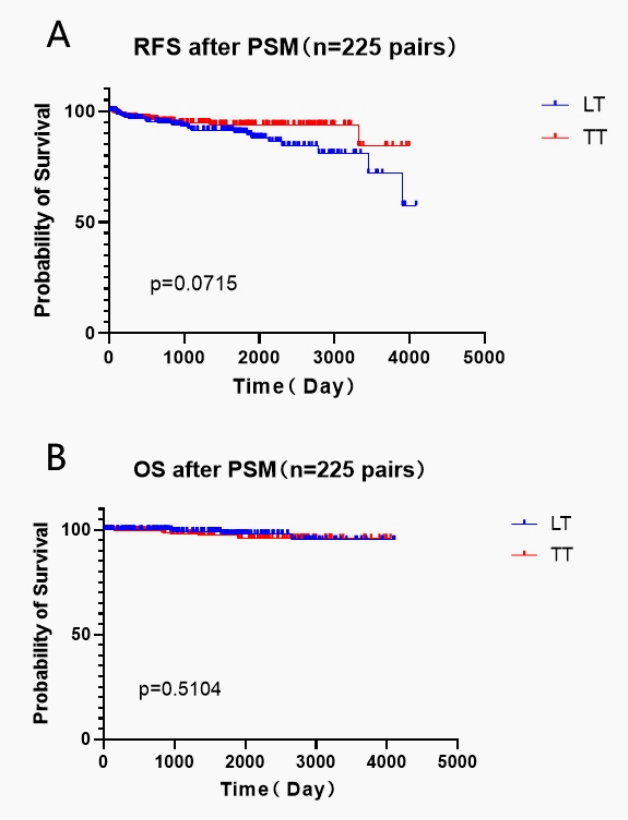


Figure 1. Recurrence-free survival (RFS, **A**) and overall survival (OS, **B**) of lobectomy (LT) and total thyroidectomy (TT) groups after propensity score matching (PSM)

Conclusion

This study suggested that there was no difference in recurrence and survival between patients with unilateral PTC and IC-LNM treated with uLT and TT for the primary tumor. However, uLT group had a lower risk of postoperative complications and a lower hospitalization cost than TT group. Therefore, uLT could be recommended for selected patients of unilateral PTC and IC-LNM without other risk features.

References

1. Haugen B R, Alexander E K, Bible K C, et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid,2016,26(1):1-133.

2. Song J, Qiu W, Yan T, et al. Comparison of Lobectomy and Total Thyroidectomy in Unilateral Papillary Thyroid Microcarcinoma Patients with Ipsilateral Lateral Lymph Node Metastasis Without Gross Extrathyroidal Extension. World J Surg,2020,44(8):2677-2684.

3. Wang Z, Xiang J, Gui Z, et al. Unilateral Tnm T1 And T2 Papillary Thyroid Carcinoma With Lateral Cervical Lymph Node Metastasis: Total Thyroidectomy or Lobectomy?. Endocr Pract,2020,26(10):1085-1092.

50

Treatment induced lymphedema in oral cancer patients: A wolf in sheep's clothing.

Siddhartha Basuroy[1], Tashnin Rahman[1], Mouchumee Bhattacharyya[2], Rakesh Mahapatra[3], Mridul Ali[4], Ashok Kumar Das[1], Raj Jyoti Das[1], Kishore Das[1], Anupam Das[1], Kaberi Kakati[1]

[1]Dr Bhubaneswar Borooah Cancer Institute, Head and Neck Oncology, Guwahati, India. [2]Dr Bhubaneswar Borooah Cancer Institute, Radiation Oncology, Guwahati, India. [3]Dr Bhubaneswar Borooah Cancer Institute, Occupational Therapy, Guwahati, India. [4]Dr Bhubaneswar Borooah Cancer Institute, Speech and Swallowing, Guwahati, India

Topic

Quality of life and outcomes

Keywords

Lymphedema, Oral Cancers, Dysphagia

Purpose/Objective

1. To study the incidence and the course of development and regression of head and neck lymphedema(HNL) in patients undergoing curative treatment for oral cancer.

2.To study the effect of HNL on airway, speech and swallowing functions immediately and after 6 months of treatment

Material/Methods

A prospective observational study was conducted in the Department of Head and Neck Oncology, and the Department of Radiotherapy in Dr. B.Borooah Cancer Institute, Guwahati, over a period of 1 year. Ethical committee approval was obtained prior to commencing the study. All patients undergoing treatment for oral cancer with the curative intent, by means of Surgery +/- Adjuvant therapy, with or without Neoadjuvant Chemotherapy were included in the study. Any recurrent cases, or patients developing recurrent or residual disease were excluded from the study. Patients with pre op overt hypothyroidism, chronic kidney disease, chronic liver disease, severe burns or scars in head and neck region were excluded from the study; as these would affect lymphedema scores. Also, patients with pre operative dysphonia or dysphagia due to any cause other than oral cancer were excluded from the study to avoid any bias in dysphonia/dysphagia scores during follow up.

Details of staging, pre-treatment disease volume, surgery and its extent, adjuvant therapy, radiation fields, techniques and dose, chemotherapy dose and schedule were recorded. MD Anderson Head and Neck Lymphedema Rating Scale for external lymphedema and Modified Patterson scale for internal HNL were used to analyze the lymphedema scores.[1-2] External lymphedema was evaluated clinically, whereas internal lymphedema was evaluated by analyzing the videographic recordings of flexible laryngoscopy. Voice Handicap Index and MD Anderson Dysphagia Inventory for dysphagia evaluation, were used to evaluate dysphonia and dysphagia.[3-4] Evaluation of these parameters were done at each follow up visit, as per the institution's follow up protocol. Range of motion in neck and mobility oral/pharyngeal structures were evaluated at each follow up. Repeat imaging was done was as per institutional protocol/ as and when indicated.

Patients were classified into 2 groups:

1. Patients undergoing surgery, with no adjuvant therapy
2. Patients undergoing surgery, with adjuvant therapy(RT+/-CT)

The effect of NACT on HNL was evaluated separately.

Results

A total of 98 patients were included in the study, of which 17 patients were excluded from the analysis due to residual/recurrent disease/ death/ lost to follow up.

Out of 81 patients, 28 underwent surgery alone, with no adjuvant therapy. At the initial presentation, 76% patients had combined external and internal lymphedema. The extent of lymphedema was determined by the pattern of growth (infiltrative vs proliferative), and extent of resection. Extent of glossectomy (type I vs Type II or beyond, p=0.037), segmental mandibular resection(p=0.039) significantly affected internal lymphedema scores. Extent of neck dissection, choice of reconstruction, maxillectomy and tumor volume did not affect lymphedema scores at the end of 6 months. External edema in most patients subsided by the end of 2nd follow up, at around 3 months after surgery. Internal edema, however persisted in 59% of the patients at the end of 3 months, and 14% patients at the end of 6 months. Highest internal lymphedema scores were recorded for base of tongue in the initial (3.21) follow up and at the end of 6 months (0.94). Dysphagia and dysphonia scores correlated with internal lymphedema scores.

Out of 81 patients, 53 patients were included in the surgery with adjuvant therapy group. A total of 44 patients received radiation alone, and 9 patients received chemoradiation. 86% patients had combined external and internal lymphedema at first presentation. Addition of chemotherapy did not show any statistically significant difference in the lymphedema scores. The field of radiation, pathological nodal status (pN0 vs pN+, p=0.034) and extent of glossectomy statistically affected the lymphedema scores at

the end of 6 months. External lymphedema scores dropped by the end of 4-6 months in 84% patients, whereas internal lymphedema persisted in 63% patients. There was no statistically significant difference between base of tongue and other subsites of laryngopharynx with regard to internal lymphedema. The dysphagia and dysphonia scores were worse in this group, however, they correlated with internal lymphedema scores. The proportion of patients requiring manual lymphatic decompression therapy was higher in surgery with adjuvant therapy group vs surgery only group (p= 0.00026).

Conclusion

HNL is a commonly encountered, yet often neglected effect of curative treatment in early and locally advanced oral cavity. The behaviour of HNL in early and advanced oral cavity cancers following treatment may differ. Internal lymphedema may contribute to dysphagia and dysphonia in these patients.

References

1. Smith BG, Hutcheson KA, Little LG, Skoracki RJ, Rosenthal DI, Lai SY, Lewin JS. Lymphedema outcomes in patients with head and neck cancer. Otolaryngol Head Neck Surg. 2015 Feb;152(2):284-291. doi: 10.1177/0194599814558402.

2. Starmer HM, Drinnan M, Bhabra M, Watson LJ, Patterson J. Development and reliability of the revised Patterson Edema Scale. Clin Otolaryngol. 2021 Jul;46(4):752-757. doi: 10.1111/coa.13727.

3. Barbara H. Jacobson, Alex Johnson, Cynthia Grywalski, Alice Silbergleit, Gary Jaconsen, Michael S. Benninger. The Voice Handicap Index (VHI): Development and Validation. American Journal of Speech-Language Pathology, Vol 6(3), 66-70, 1997

4. Chen AY, Frankowski R, Bishop-Leone J, et al. The Development and Validation of a Dysphagia-Specific Quality-of-Life Questionnaire for Patients With Head and Neck Cancer: The M. D. Anderson Dysphagia Inventory. Arch Otolaryngol Head Neck Surg. 2001;127(7):870-876.

51

Dosimetric evaluation of dysphagia in early stage larynx cancer treated with definitive radiotherapy

Yunus Babayigit[1], Oguzhan Bascik[1], Sumerya Duru Birgi[1], İrem Kar[1,2], Cengiz Kurtman[1], Serap Akyurek[1]

[1]Ankara University School of Medicine, Department of Radiation Oncology, Ankara, Turkey. [2]Ankara University School of Medicine, Department of Biostatistics, Ankara, Turkey

Topic

Innovative treatments

Keywords

early stage larynx cancer, radiotherapy, dysphagia

Purpose/Objective

Current studies have identified the relationship between organs at risk (OAR) doses and swallowing functions in patients with head and neck cancer treated with radiotherapy (RT). Our aim is to evaluate the relationship between OAR doses and acute dysphagia in early stage larynx cancer patients received definitive RT and to examine the effect of the RT technique on OAR doses.

Material/Methods

Early-stage patients (Tcis-2N0M0) diagnosed between July 2014 and September 2022 were evaluated retrospectively. OAR (tongue base-TB, upper pharyngeal wall-UPW, middle pharyngeal wall-MPW, lower pharyngeal wall-LPW, whole pharyngeal wall-WPW, proximal esophagus-PE) were delineated subsequently and the dose-volume parameters were generated on previous treatment plans. Acute toxicities observed in the first 6 months were determined according to CTCAE v5. The relationship between OAR doses and grade(G) 2-3 dysphagia was investigated. For significant parameters ($p<0.05$), the cut-off values were determined by ROC analysis.

Results

Of the 43 patients, the median age was 69 years (range: 49-84) and 41 (95%) patients were male. The characteristic features of the patients were summarized in Table-1. The median follow-up was 30 (range: 1-101) months. The median local relapse-free survival was 30 (1-101) months and the 3-year local control rate was 94.3%. G1 dysphagia was observed in 21 (49%) of the patients and G2-3 dysphagia was observed in 19 (44%) patients. The dose volume parameters of OAR were summarized in Table-2. In terms of the relationship between Dmean(Gy), Dmax(Gy), V50(cc), V55(cc), V60(cc), V65(cc) values for the OARs of the patients and dysphagia; For WPW, V50(p=.03), V55(p=.03), V60(p=.02); For MPW, V50(p=.04), V55(p=.03), V60 (p=.05), V65(p=.03); For TB, V65(p=.03) were significantly associated with G2-3 dysphagia. In terms of G2-3 toxicity, for WPW; MPW and TB respectively: WPW V50> 13.3cc, V55> 12.9cc, V60 >12.5cc; MPW V50> 3cc, V55> 3cc, V60> 2.7cc, V65>0.6cc and TB V65>0.05cc were determined as cut off values. Intensity-modulated radiotherapy (IMRT) technique and volumetric arc therapy (VMAT) technique were used in 25 (58%) and 17 (40%) patients, respectively. When the planning technique and the average dose-volume parameters in OARs were compared, WPW-Dmean, V50,V55, V60, V65; UPW- Dmean, V55, V60; LPW-Dmean, V65 and PE-Dmax had significantly decreased in VMAT plans. However, there was no clinically significant difference between the two techniques in terms of dysphagia (p = .41). Local recurrence was observed in 4 (9%) patients during follow-up. Both regional and distant metastases were detected in only 1 patient. At the last follow-up 7 patients (16%) died due to non-cancerous reasons, 36 patients (84%) were disease free with complete response.

Table-1: Characteristic features of patients

Features		Number (%)
Performance	ECOG1	33(77%)
	ECOG2	10(23%)
Cigarette	Current	11(26%)
	Ex-smoker	25(58%)
	Never	6(14%)

Pathology SCC Other	 42(98%) 1(2%)
T Stage Carcinoma in situ T1 T2	 13(30%) 27(63%) 3(7%)
Radiotherapy Technique 3D IMRT VMAT	CRT 1(2%) 25(58%) 17(40%)
RT Dose 63Gy/28fx 64.4Gy/28fx 65.3Gy/29fx Other	 29(67%) 6(14%) 5(12%) 3(7%)
Dysphagia Grade 1 Grade2 Grade3	 21(49%) 16(37%) 3(7%)

Table-2:The dose volume parameters of OAR

	Dmean(Gy)	Dmax(Gy)	Volume(cc)	V50(cc)	V55(cc)	V60(cc)	V65(cc)
WPW	29±6	67±1	36±7	15±4	14±4	14±4	7±6
UPW	6±7	39±24	21±5	1±1	1±1	1±1	0±1
MPW	57±15	65±10	4±1	4±1	3±2	3±2,	1±2
LPW	65±2	67±1	10±2	10±2	10±2	10±2	5±4
PE	13±7	62±10	11±2	1±1	1±1	1±1	0±1
TB	7±6	61±15	38±7	2±3	2±3	1±2	1±1

Conclusion

In this study, a significant relationship was observed between acute G2-3 dysphagia and WPW, MPW, TB dose volume values in early stage laryngeal cancer receiving definitive RT. Although there was a

decrease in OAR values with the VMAT plans, no clinical significance was determined between RT techniques.

52

Functional outcome after Locally Advanced Tongue cancer resections by Pull-through approach: Study from a tertiary cancer care center.

Arpit Bandi[1], Shivam Pandya[2], Priyank Rathod[1], Shashank Pandya[1], Tanmayee Jatania[3], Anish Chowdhury[2], Nikunj Makwana[4]

[1]GCRI, Surgical Oncology, Ahmedabad, India. [2]Gcri, Surgical Oncology, Ahmedabad, India. [3]GCRI, surgical Oncology, Ahmedabad, India. [4]Gcri, surgical Oncology, Ahmedabad, India

Topic

Quality of life and outcomes

Keywords

tongue cancer, pull-through, reconstruction

Purpose/Objective

Oral SCC (OSCC) is the eighth most prevalent cancer in the world. [1] Head and neck cancer account for more than 650,000 cases and 330,000 deaths annually worldwide. India is the world capital accounting for one-third of the global burden.[2] About 60–80% of the patients in India suffering from oral cancer are detected in the advanced stages with tongue malignancies invariably involving floor of mouth (FOM) either by primarily or forming the base of resection.[3,4]

Advanced oral cavity lesions, particularly that of tongue and FOM are associated with morbidities like speech, swallowing and breathing difficulty.[5] Hence, a balance between adequate oncological margins and optimal functional outcome is a challenge.

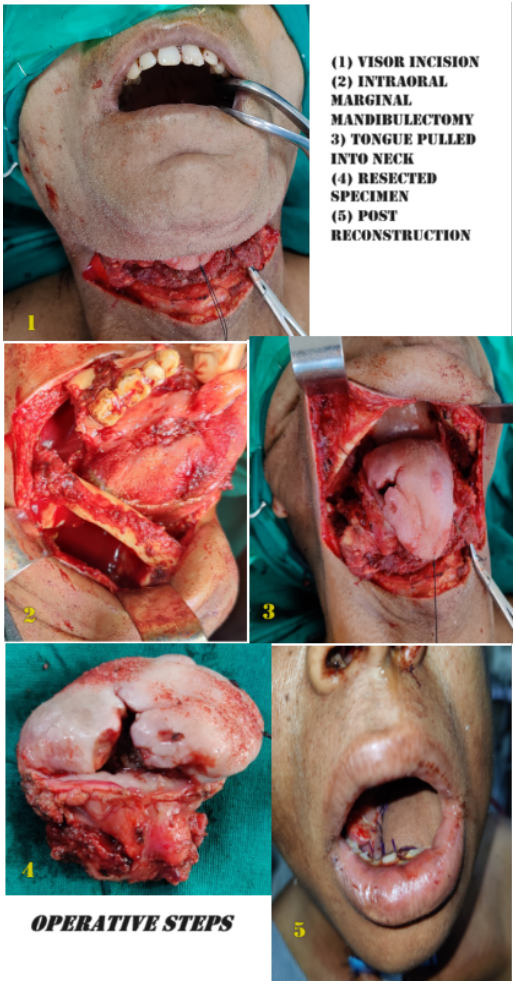
Mandibular lip-split and the pull-through are the two commonly used surgical techniques.[6-8] High recurrence rates of 30% with lip-split approach has led us to opt for a more secure radical approach.[9] Para-hyoid region zone is the most common site of early recurrence which is neither included in the dissection specimen nor accessible by trans-oral approach.[10] Therefore, the pull-through technique was devised for en-bloc resection of tongue cancers with cervical lymphatics. We aim to assess the oncological and functional of this Pull-through technique in locally advanced Tongue and FOM cancers.

Material/Methods

A retrospective observational study was done for patients operated in the institute from Jan 2021 - Jan 2023. 75 patients with locally advanced carcinoma tongue or FOM undergoing resection by pull through approach were included in the study.

Surgical Technique (Image1: attachment)

In this technique, the Visor approach was used and Subplatysmal skin flaps raised. Bilateral level IA/IB dissection was performed, and the suprahyoid muscles divided from their bony attachment to enter the oral cavity. Subsequently, the gingivo-labial sulcus was incised on either side carefully considering for the margins and the tongue was dropped into the neck, thereby providing access to all parts of the tongue and oropharynx. Mandibulectomy, if required, was done beforehand intraorally delivering the segment with the specimen in toto. Resection and reconstruction was then performed under direct vision. Reconstruction was done either with pedicled or free flap insertion. Reattachment of the digastric muscles or remnant genioglossus, and geniohyoid muscles on both sides with the flap was done to reconstruct the floor.



Post-operative Follow-Up

Patients were followed up postoperatively and received adjuvant treatment as per NCCN guidelines and were provided with rehabilitatory support. Six months after the treatment, Speech, swallowing, and breathing was assessed using HNC FIT (Functional Integrity) scales.[11,12]

Results

Patient Characteristics

A total of 75 patients were included in the study with 55 (73.33%) males and 20 (26.66%) females with a mean age of 47 years (range 30–76 years).

Procedural parameters

Out of a total of 75 patients, 3(4%) underwent total glossectomy, 11(14.66%) near total and 18(24%) anterior oblique glossectomy. 18 of the 75 patients underwent mandibular resections (6 - segmental and 12- marginal).

Histopathology

19 patients had T2 lesions, 26 T3 lesions and 30 T4 primaries. 31 patients (41.3%) had node negative disease while 44 (58.6%) were node positive with 16 having positive contralateral neck nodes. 24 of 75 patients (32%) had lympho-vascular invasion while 37 (48%) had perineural invasion.

Functional outcome

As an institutional protocol, all patients undergoing major tongue resections were tracheostomised. The median duration of tracheostomy removal was 15th postop day (1st Follow-up) and 57(76%) patients were tracheostomy free by the completion of adjuvant treatment. However, 6(8%) patients had permanent tracheostomies.

Ryle's tube feeding was started postoperatively escalating to oral feeds by POD5. Swallowing and speech rehabilitation was provided and on 6 monthly follow up, 17 of 75 (22.5%) patients tolerated solid food (HNCFIT food intake grade 3), 19 (25.3%) soft and 21 (28%) liquid diet, a total of 40 (53.3%) patients in grade 2.

9 (12%) patients required Ryle's tube due to inadequate oral intake (grade 1), while 8 (10.6%) were entirely dependent on tube feeds (grade 0).

Out of 75 patients, 4 (5.3%) had no phonation (HNCFIT grade0), 8(10.5%) unclear speech (Grade1), 14(18.66%) had comprehensible speech with telephoning possible (grade 2), 44 (58.6%) had understandable speech with voice change(grade3), 5(6.66%) had normal voice (grade 4).

Patient Characteristics		
Age		
<40 years	22	29.3%
40-60 years	38	50.6%
>60 years	15	20.1%
Sex		
Male	55	73.33%
Female	20	26.66%
Location		
Right half (Predominantly)	40	53.33%
Left half (predominantly)	26	34.66%
Total	9	12%
Surgical Details		
Treatment (glossectomy)		
Total	3	4%
Near total	11	14.66%
Anterior oblique	18	24%
WLE	53	70.66%
Mandibular Resection	18	24%
Marginal Mandibulectomy	12	
Segmental Mandibulectomy	6	
Reconstruction		
NL flap	9	12%
Infrahyoid/Submental flap	4	5.3%
PMMC flap	45	60%
FRAFF	5	6.66%
ALT flap	12	16%
Histopathology		
T2	19	25.3%
T3	26	34.6%
T4	30	40%
N1 or Higher	44	58.6%
>N2c	16	21.3%
Margins		
Involved	0	
< 5mm	8	10.6%
>5mm	67	89.4%
LVI +	24	32%
PNI +	37	48%
Functional Outcome		
Tracheostomy Decannulation		
Up to Postop day 15	24	32%
Up to completion of Adjuvant	33	44%
Post adjuvant completion	12	16%
Permanent TStomy	6	8%
Feeding (6 monthly follow-up)		
Toleration Solid diet	17	22.6%
Semisolids	19	25.3%
Liquids orally	21	28%
Oral Liquids + RT supplement	9	12%
Ryles Tube only	8	10.6%
Speech (6 monthly follow-up)		
No phonation	4	5.3%
Unclear speech	8	10.6%
Comprehensible speech	14	18.6%
Communicating with voice change	44	58.6%
Normal Speech	5	6.66%

Conclusion

The pull-through approach had the advantages of good accessibility and functional outcome and ensures resection with adequate margins. Effective surgical treatment can contribute to the improved quality and length of survival of these patients.

References

1. Bray, F.; Ferlay, J.; Soerjomataram, I.; Siegel, R.L.; Torre, L.A.; Jemal, A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J. Clin. 2018, 68, 394.

2. Laprise C., Shahul H.P., Madathil S.A., Thekkepurakkal A.S., Castonguay G., Varghese I., Shiraz S., Allison P., Schlecht N.F., Rousseau M.C., Franco E.L., Nicolau B. Periodontal diseases and risk of oral cancer in Southern India: results from the HeNCe Life study. Int. J. Canc. 2016;139:1512–1519. doi: 10.1002/ijc.30201.

3. Borse V, Konwar AN, Buragohain P. Oral cancer diagnosis and perspectives in India. Sens Int. 2020;1:100046. doi: 10.1016/j.sintl.2020.100046. Epub 2020 Sep 24. PMID: 34766046; PMCID: PMC7515567.

4. Sharma S., Satyanarayana L., Asthana S., Shivalingesh K.K., Goutham B.S., Ramachandra S. Oral cancer statistics in India on the basis of first report of 29 population-based cancer registries. J. Oral Maxillofac. Pathol. 2018;22:18–26. doi: 10.4103/jomfp.JOMFP_113_17

5. Devine JC, Rogers SN, McNally D, Brown JS, Vaughan ED (2001) A comparison of aesthetic, functional and patient subjective outcomes following lip-split mandibulotomy and mandibular lingual releasing access procedures. Int J Oral Maxillofac Surg 30(3):199–200

6. Baek, C.H.; Lee, S.W.; Jeong, H.S. New modification of the mandibulotomy approach without lip splitting.Head Neck 2006, 28, 580–586.

7. Butler FS, Harrigan WF. Radical surgery for intraoral cancer with preservation of the mandible: the en bloc pull-through procedure. Am J Surg 1957: 94: 857–864.

8. Cheng SJ, Ko HH, Lee JJ, Kok SH. Comparison of long-term outcomes between pull-through resection and mandibular lip-split surgery for T4a tongue/floor of mouth cancers. Head Neck 2018: 40: 144–153.

9. Tsai MS, Lai CH, Lee CP, et al. Mortality in tongue cancer patients treated by curative surgery: a retrospective cohort study from CGRD. Peer J. 2016;4:e2794.

10. Başerer N. New Pull Through Resection Technique in Tongue and Floor-of Mouth Cancers. J Dent Oral Biol. 2017; 2(10): 1069.

11. Dejaco D, Riedl D, Gasser S, Schartinger VH, Innerhofer V, Gottfried T, Steinbichler TB, Riechelmann F, Moschen R, Galvan O, Stigler R, Gassner R, Rumpold G, Lettenbichler-Haug A, Riechelmann H. A Tool for Rapid Assessment of Functional Outcomes in Patients with Head and Neck Cancer. Cancers (Basel). 2021 Nov 3;13(21):5529. doi: 10.3390/cancers13215529. PMID: 34771691; PMCID: PMC8582907.

12. Riechelmann H, Dejaco D, Steinbichler TB, Lettenbichler-Haug A, Anegg M, Ganswindt U, Gamerith G, Riedl D. Functional Outcomes in Head and Neck Cancer Patients. Cancers (Basel). 2022 Apr 25;14(9):2135. doi: 10.3390/cancers14092135. PMID: 35565265; PMCID: PMC9099625.

53

Reirradiation with Stereotactic Ablative Radiotherapy in Recurrent Nasopharyngeal Carcinoma

Melek Tugce Yilmaz[1], Ecem Yigit[1], Alper Kahvecioglu[1], Fazli Yagiz Yedekci[1], Sezin Yuce Sari[1], Mustafa Cengiz[1], Gokhan Ozyigit[1], Ibrahim Gullu[2], Sercan Aksoy[2], Gozde Yazici[1]

[1]Hacettepe University, Radiation Oncology, Ankara, Turkey. [2]Hacettepe University, Medical Oncology, Ankara, Turkey

Topic

Multidisciplinary management

Keywords

Nasopharyngeal carcinoma, reirradiation, SABR

Purpose/Objective

Local recurrence (LR) rates in nasopharyngeal carcinoma (NPC) following definitive radiation (RT) ± chemotherapy (CT) range from 7–15%. A prospective trial comparing endoscopic surgery and re-irradiation in recurrent cases found that surgery improved survival in a carefully chosen group of patients with low-volume mucosal recurrence. However, the fact that the recurrent disease is mostly multifocal and infiltrative in nature makes a limited group of patients suitable for surgery. In this study, we aimed to report our stereotactic ablative radiotherapy (SABR) outcomes in cases diagnosed with recurrent NPC.

Material/Methods

The data of 83 patients who underwent SABR in our department between 2007 and 2022 with the diagnosis of local-regional recurrent NPC, which was unresectable or had surgical margin positivity after resection were evaluated retrospectively. The Kaplan-Meier method was used for survival analyses (IBM SPSS v.23).

Results

Patient, tumor, and treatment characteristics are presented in Table 1. The median age was 53 (range, 19-78). The median follow-up was 24 months (range, 3–151 months). The median interval between patients' first and second RT's was 39 months (range, 4–238 months). The initial response evaluation following reirradiation found a complete response in 38%, a partial response in 40%, stable disease in 8%, and progression in 1%. In follow-up, LR developed in 20 patients (24%) and distant metastasis (DM) developed in 14 patients (17%). The most common sites of DM were the lung, bone, and liver. SABR provided 76% local control (LC). The 1- and 2-year overall survival (OS), local recurrence-free survival (LRFS), and distant metastasis-free survival (DMFS) rates were 67% and 53%, 65% and 46%, and 62% and 49%, respectively. In univariate analysis, LRFS (60% vs. 34%, p=0.002) and DMFS (63% vs. 31%, p=0.007) rates were higher in patients with recurrent tumor volume ≤36 cc compared to patients with tumor volume >36 cc. Age (≤53 vs. >53 years), gender (male vs. female), interval between RTs (≤2 vs. >2 years), surgery before SBRT (yes vs. no), SBRT dose (≤30 vs. >30 Gy) and device (robotic- vs. linear accelerator-based), and site of recurrence (primary vs. neck recurrence) could not be identified for prognostic significance for OS, LRFS, and DMFS parameters. A notable proportion of patients experienced late toxicity, with 20% exhibiting grade 3 or 4 toxicity and 12% experiencing grade 5 toxicity. Fourteen patients (17%) experienced massive hemorrhage as a result of carotid blow-out syndrome (CBOS); two patients (2%) suffered from cerebrovascular disease as a result of carotid artery stenosis; five patients (6%) experienced brain parenchymal necrosis; three patients (3.5%) had permanent gastrostomies; and three patients (3.5%) had hearing loss. There was no observed disparity in toxicity levels between doses administered consecutively or every other day.

Table 1. Patient, tumor, and treatment characteristics.

Characteristic	Number of Patients (n=83, %)
Gender Male Female	 56 (67.5) 27 (32.5)
Interval between RT's (median) <2 year ≥2 year	39 months (4-238 months) 29 (35) 54 (65)
RT dose, median (range) / fractions, median (range)	70 Gy (60-74 Gy) / 33 fractions (30-33)
Recurrence location Primary	 73 (88)

Neck Primary and neck	4 (5) 6 (7)
SABR dose / fractions (median)	30 Gy (24-50 Gy) / 5 (1-6)
SABR technique CyberKnife© Novalis® Linac (VMAT)	 72 (87) 8 (9) 3 (4)
Fractionation Consecutive days Every other day	 63 (76) 20 (24)
GTV volume, median (range)	36 cc (1-204 cc)
Treatment outcomes Complete response Partial response Stabile disease Progression Unknown	 31 (38) 33 (40) 6 (8) 1 (1) 11 (13)

Conclusion

Using SABR as a reirradiation method for people with recurrent NPC has shown to be very effective at achieving LC while keeping treatment-related side effects at a level that can be tolerated. There is a positive correlation between a smaller recurring tumor volume and higher levels of local recurrence-free survival (LRFS) and distant metastasis-free survival (DMFS).

54

Reirradiation With Stereotactic Ablative Radiotherapy In Recurrent Head And Neck Cancers

Ecem Yigit, Melek Tugce Yilmaz, Alper Kahvecioglu, Fazli Yagiz Yedekci, Sezin Yuce Sari, Mustafa Cengiz, Gokhan Ozyigit, Ibrahim Gullu, Sercan Aksoy, Gozde Yazici

Hacettepe University, Radiation Oncology, Ankara, Turkey

Topic

Multidisciplinary management

Keywords

head and neck cancer, reirradiation, SABR

Purpose/Objective

Reirradiation has been identified as a viable treatment modality for patients with recurrent head and neck cancer (rHNC). Retrospective series demonstrate the superiority of intensity-modulated radiation therapy (IMRT) over stereotactic ablative radiotherapy (SABR) for patients in the Multi-Institution Reirradiation Collaborative (MIRI) class 2 risk group (treatment interval > 2 years without resection or treatment interval ≤ 2 years without organ dysfunction). he objective of this study was to investigate the efficacy and toxicity of SABR in patients classified as "RPA Class 2" rHNC.

Material/Methods

The data of 85 cases diagnosed with rHNC who underwent reirradiation with the SABR technique between 2007 and 2022 in our department were evaluated retrospectively. We did not incorporate cases of primary nasopharynx cancer due to its comparatively more favorable prognosis in relation to other types of head and neck cancers. The Kaplan-Meier method was used for survival analyzes (IBM SPSS v23).

Results

Patient, tumor and treatment characteristics are presented in Table 1. The median age was 59 (range, 19-87). The median follow-up period was 12 months (range,1-178 months). The first assessment following SABR revealed that 30% of the patients achieved a full response, 35% achieved a partial response, 11% had stable disease, and 4% experienced disease progression. During follow-up, local recurrence (LR) developed in 31 patients (36%) and distant metastasis (DM) developed in 24 patients (28%). The local control (LC) rate with SBRT was 64%. The most common sites of DM are the lung, bone, and liver. In 31 patients who developed LR after SABR, the median time to LR development was 8 months (range, 2-55 months). Subsequently, a third course of radiation therapy (RT) was administered to 16 of them (52%). The 1- and 2-year overall survival (OS), local recurrence-free survival (LRFS) and distant metastasis-free survival (DMFS) rates were 50% and 30%, 39% and 21%, 46% and 27%, respectively. In univariate analysis, age (≤59 vs. >59 years), gender (male vs. female), interval between treatments (≤2 vs. >2 years), organ dysfunction before SABR (present vs. absent) or surgery (present vs. absent), SABR dose (≤30 vs. >30 Gy), technique (robotic vs. linear accelerator-based), recurrent tumor volume (≤43 vs. >43 cc), and recurrence location (primary vs. neck) parameters did not have prognostic effect on OS, LRFS and DMFS. The rate of grade 3 or 4 late toxicity was 11%, and the rate of grade 5 toxicity was 9%. Eight patients (9%) developed massive hemorrhage secondary to carotid blow out syndrome (CBOS), 6 patients (7%) developed brain parenchymal necrosis, 2 patients (2.5%) required permanent gastrostomy, and 1 patient (1.5%) developed optic neuropathy and vision loss. The administration of SABR in consecutive or alternate day fractions shown comparable effects on toxicity.

Table 1. Patient, tumor, and treatment characteristics

Characteristic	Number of Patients (n=85, %)
Gender	
Male	54 (64)
Female	31 (36)
Tumor location	
Paranasal Sinus	20 (24)
Larynx & hipopharynx	25 (30)
Oral cavity	15 (18)
Salivary Gland Tumor	15 (18)
Oropharynx	6 (6,5)
Other	4 (3,5)
Interval between RT's (median)	26 months (4-301 months)
<2 year	39 (46)
≥2 year	46 (54)
RT dose, median (range) / fractions, median (range)	66 Gy (30-72 Gy) / 30 (5-33)
Recurrence location	
Primary	67 (79)
Neck	11 (14)

Primary and neck	3 (3)
SABR dose / fractions (median)	30 Gy (15-50 Gy)/ 5 (1-6)
SABR technique CyberKnife© Novalis® Linac (VMAT)	 61 (72) 12 (14) 12 (14)
Fractionation Consecutive days Every other day	 21 (25) 64 (75)
GTV volume, median (range)	43 cc (1.7-214 cc)
Treatment outcomes Complete response Partial response Stabile disease Progression Unknown	 26 (30) 30 (35) 11 (13) 4 (3.5) 14 (16.5)

Conclusion

The utilization of the SABR as a method of reirradiation in rHNC patients has demonstrated favorable outcomes in terms of achieving effective LC while maintaining acceptable levels of treatment-related toxicity. We provide a study that demonstrates highly favorable survival outcomes with SABR for patients classified as RPA class 2 rHNC. There is a need for prospective randomized studies to be conducted in order to ascertain the ideal approach for reirradiation, specifically comparing SABR and IMRT. These studies would also help identify the patient population that would benefit the most from such reirradiation techniques.

80

How applicable are the results of the DARS trial to current practice? A comparison of average dose to the pharyngeal constrictor muscles.

Adam Muse[1], Jonathan Chambers[1], Rachel Dearden[2], Jenifer Young[3], Naomi Cole[1]

[1]Torbay and South Devon NHS Foundation Trust, Oncology, Torquay, United Kingdom. [2]Torbay and South Devon NHS Foundation Trust, Physics, Torquay, United Kingdom. [3]Torbay and South Devon NHS Foundation Trust, Radiotherapy, Torquay, United Kingdom

Topic

Quality of life and outcomes

Keywords

Dysphagia

Purpose/Objective

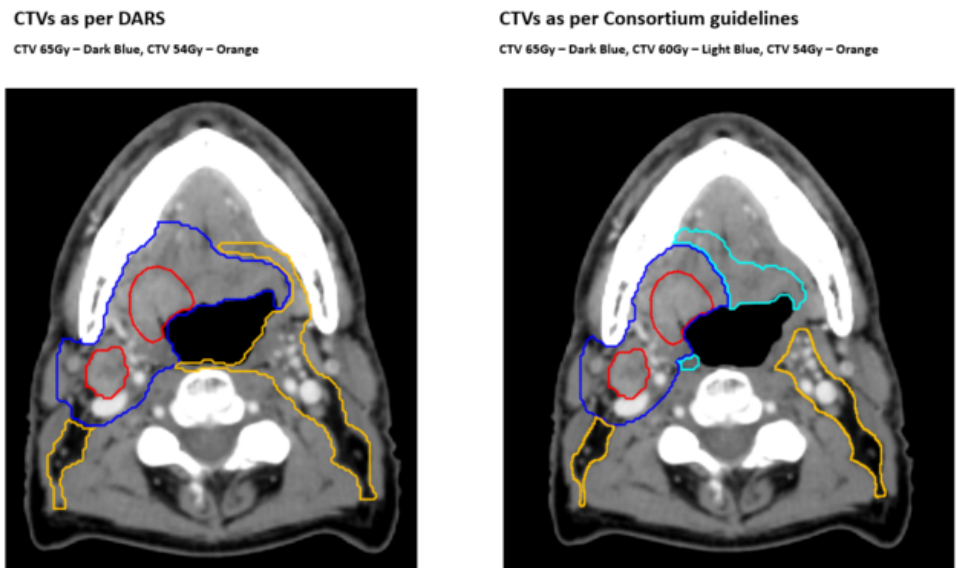
The DARS trial is a phase 3, multicentre, randomised controlled trial published by Nutting et al in 2023 (1). Within the trial, patients with oropharyngeal or hypopharyngeal cancer were randomised to

dysphagia optimised intensity-modulated radiotherapy (DO-IMRT) or standard IMRT. The trial demonstrated that patients in the DO-IMRT group had significantly higher MD Anderson Dysphagia Inventory (MDADI) composite scores at 12 months than patients in the standard IMRT group.

The DARS protocol for the delineation of the primary tumour clinical target volumes (CTVp) included an anatomical approach. A 10 mm margin was added to the Gross tumour volume (GTV) to construct a high-dose clinical target volume, which was to receive 65Gy in 30 fractions. The remaining primary tumour subsite was then delineated to form a low dose CTV to receive 54Gy in 30 fractions (2).

In 2017 the consensus guidelines on delineation of the primary tumour CTV were published by Gregoire et al (3). These guidelines recommend two CTVs for the primary tumour. A 5mm margin is added to the GTV to construct the high-dose CTV, and an additional 5mm rim of tissue is added to form the lower dose CTV. Our centre has adopted these guidelines, and their use is recommended in RCR consensus statements. (4)

Given the differences in the delineation of the high and low dose CTVs between consensus guidelines and the approach used in the DARS trial, one could question how applicable the results of the DARS trial are to wider practice as doses to OARs are likely to be different.



We aimed to assess the validity of the DARS trial findings by comparing average mean dose to the pharyngeal constrictor muscles when CTVs were delineated according to the consensus guidelines (3) and compare these to the standard IMRT and DO-IMRT groups within the DARS trial (2).

Material/Methods

Patients treated at our institution between March 2020 and March 2023 were screened for eligibility, mirroring the criteria used in the DARS trial. Patients had to have been treated for oropharyngeal or hypopharyngeal cancer, with radical radiotherapy and bilateral neck treatment. Patients with a primary tumour involving the posterior pharyngeal wall or the post cricoid oesophagus were excluded. Patients had their primary contoured with a 5+5 expansion, as per the consensus guidelines (3) and received 3 dose levels. The high dose CTV received 65Gy in 30 fractions, as per DARS, but the lower dose CTV around the primary received 60Gy in 30 fractions. The nodal high dose CTV was between 5 and 10mm around the nodal GTV and received 65Gy in 30 fractions. The elective lymph node CTV received 54Gy in 30 fractions. PTV margins were 3-5mm. The IMRT treatment was planned using Pinnacle, using 2 full VMAT arcs.

The pharyngeal constrictor muscles were delineated on the CT planning scans, either by a radiation oncologist, or by the LIMBUS AI outlining software and edited appropriately. As per the DARS protocol, the superior and middle pharyngeal constrictor muscles (SMPCM) were defined as a single structure with the inferior pharyngeal constrictor muscle (IPCM) defined separately. No dose constraints had been applied to the constrictors when planning, and PTV coverage had not been compromised for them. The mean dose to each structure, not overlapping with CTV65Gy or CTV60Gy, (Plan_SMPCM and Plan_IPCM) was calculated.

Results

22 eligible patients were identified. 3 (14%) were female and 19 (86%) were male with a median age of 59. 21 patients (95%) had P16 positive oropharyngeal SCC and 1 patient (5%) had hypopharyngeal SCC.

In our cohort, the median of the mean dose to the Plan_SMPCM was 55.3Gy (IQR 53.6-57.1). The median of the mean dose to the Plan_IPCM was 45.6Gy (IQR 42.6-48.0). (See table for comparison)

	DARS, standard IMRT	Torbay IMRT	DARS, DO-IMRT
Plan_SMPCM Median	57.2 Gy	55.3 Gy	49.7 Gy
Plan_SMPCM IQR	56.3 – 58.3 Gy	53.6 – 57.1 Gy	49.4 – 49.9 Gy
Plan_IPCM Median	49.8 Gy	45.6 Gy	28.4 Gy
Plan_IPCM IQR	47.1-52.4 Gy	42.6 – 48.0 Gy	21.3 – 37.4 Gy

Conclusion

The average dose to the pharyngeal constructor muscles in our cohort was lower than in the standard arm of DARS, likely reflecting the difference in high and low dose CTV volumes. The average dose, particularly to the IPCM, was significantly higher in our patient group, than in the DARS cohort planned with DO-IMRT. These data support the observation in the DARS trial that DO_IMRT is associated with significantly lower radiation doses to the pharyngeal constrictor muscles, even when accounting for differences in target volume delineation. 83% of patients in the DARs trial had HPV positive OPC, and we conclude DO_IMRT should be considered a standard of care in these good prognosis patients.

References

1. Nutting C, Finneran L, Roe J, Sydenham MA, Beasley M, Bhide S, Boon C, Cook A, De Winton E, Emson M, Foran B, Frogley R, Petkar I, Pettit L, Rooney K, Roques T, Srinivasan D, Tyler J, Hall E; DARS Trialist Group. Dysphagia-optimised intensity-modulated radiotherapy versus standard intensity-modulated radiotherapy in patients with head and neck cancer (DARS): a phase 3, multicentre, randomised, controlled trial. Lancet Oncol. 2023 Aug;24(8):868-880.

2. Petkar I, Rooney K, Roe JW, et al. DARS: a phase III randomised multicentre study of dysphagia-optimised intensity-modulated radiotherapy (DO-IMRT) versus standard intensity-modulated radiotherapy (S-IMRT) in head and neck cancer. BMC Cancer 2016; 16: 770.

3. Gregoire V, Evans M, Le Q et al. Delineation of the primary tumour Clinical Target Volumes (CTV-P) in laryngeal, hypopharyngeal, oropharyngeal and oral cavity squamous cell carcinoma: AIRO, CACA, DAHANCA, EORTC, GEORCC, GORTEC, HKNPCSG, HNCIG, IAG-KHT, LPRHHT, NCIC CTG, NCRI, NRG Oncology, PHNS, SBRT, SOMERA, SRO, SSHNO, TROG consensus guidelines.

4. Radiotherapy and Oncology 2017.10.016. Head and neck cancer: RCR consensus statements. Royal College of Radiologists, 2022.

85

ex-vivo 7T MRI to determine resection margins for tongue cancer resection specimens

Carlijn J. Guichelaar[1], Klijs J. de Koning[2], Annette van de Toorn[3], Gerben E. Breimer[4], Jan Willem Dankbaar[5], Bart de Keizer[5], Rob Noorlag[2], Remco de Bree[2], Marielle E. P. Philippens[1]

[1]University Medical Center Utrecht, Radiotherapy, Utrecht, Netherlands. [2]University Medical Center Utrecht, Head and Neck Surgical Oncology, Utrecht, Netherlands. [3]University Medical Center Utrecht and Utrecht University, Biomedical MR Imaging and Spectroscopy Group, Utrecht, Netherlands. [4]University Medical Center Utrecht, Pathology, Utrecht, Netherlands. [5]University Medical Center Utrecht, Radiology and Nuclear Medicine, Utrecht, Netherlands

Topic

Imaging, radiomics and artificial intelligence

Keywords

image-guided surgery, resection margin, ex-vivo MR

Purpose/Objective

The preferred treatment for oral squamous cell carcinoma is complete surgical tumour resection to achieve local-regional control. [1] Complete surgical removal requires an adequate resection margin of at least 5 mm of healthy tissue around the tumour. Unfortunately, international literature reports 30% to 85% inadequate resection margins (i.e., positive and close margins). [2] This study aims to investigate whether adequate tongue cancer resection margins can accurately be determined using *ex-vivo* high-field magnetic resonance imaging (MRI). This proposed technique could help improve the localisation of inadequate margins during surgery.

Material/Methods

Nine fresh resection specimens of tongue cancer patients were scanned with a small-bore 7 Tesla (7T) MRI scanner (Biospec 70/20, Bruker, Ettlingen, Germany) interfaced with a Philips console. For each resection specimen, four MRI scans were obtained: a 3D T2-weighted (T2W) Turbo Spin Echo (TSE) scan with an isotropic voxel size of 0.3 mm^3 and three orthogonal multi-slice T2W TSE scans with an in-plane resolution of 0.125 mm^2 and a slice thickness of 1 mm. After completion of the MR protocol, the resection specimens were processed according to routine clinical histopathological workup. The tumour was delineated by a histopathologist (HP) on the hematoxylin and eosin (HE) stained histopathological slices and by two independent radiologists (R1 and R2) on the coronal multi-slice MR scan.

For each patient, a 3D representation of the resection specimen was created using the following three steps: 1) For each HE-slice, the MR-slice with the highest resemblance was found by visual inspection **(Fig. 1A, 1B)**. 2) These corresponding slices were registered using point-based registration based on visual corresponding anatomical points (e.g., specimen contour, tumour-protrusions, mucosa) **(Fig. 1C)**. 3) The registered HE-slices were digitally stacked to create a 3D-specimen of all HE-slices **(Fig. 1D)**. This method to create the 3D-specimen was previously discussed and used in the work by Caldas-Magalhaes et al. [3] The delineated tumour created by the radiologists (tR1 and tR2) and histopathologist (tHP) were interpolated and mapped to the other MRI-scans (i.e., sagittal, axial, and 3D TSE scan) **(Fig. 1D)**.

The accuracy of the inadequate margin detection by R1 and R2 was determined using two different methods. First, the minimal resection margins in all five directions (anterior, posterior, craniomedial, caudolateral and central) were measured based on tR1 and tR2 and compared to the measurements reported by the HP. Second, the 95th percentile Hausdorff distance (HD_{95}) of the overestimation (O-HD_{95}) and underestimation (U-HD_{95}) of tR1 and tR2 was calculated with respect to the ground truth (tHP) in all five directions. The relationship between the measured resection margins based on tR1, tR2 and tHP was evaluated using Pearson's correlation coefficient (PCC). Only the craniomedial, caudolateral, and central resection margins were included in the PCC analysis.

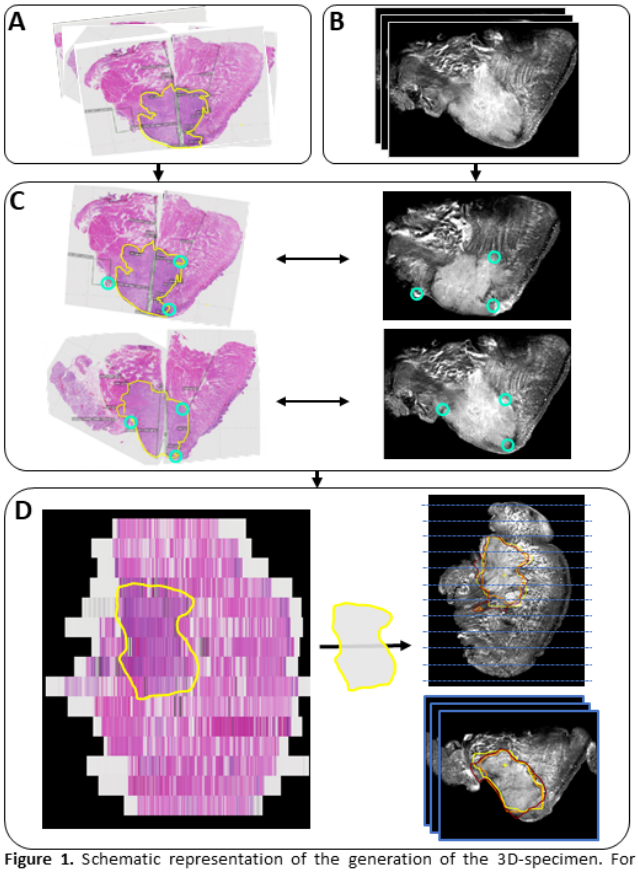


Figure 1. Schematic representation of the generation of the 3D-specimen. For every HE-slice (A), the coronal multi-slice MRI-slice (B) with the most resemblance is selected. The corresponding slices are registered using point-based registration (C). The registered HE-slices are digitally stacked to create the 3D-specimen (D-left), and tHP, shown in yellow, is mapped to the MRI-scans (D-right). tR1 and tR2 are visualised in D-right with the orange and red delineation, respectively.

Results

According to the histological report, one of the nine resection specimens was adequately resected. Based on the in-plane measurements, R1 and R2 were able to accurately determine which tumours were (in)adequately removed in 7/9 and 8/9 cases. Two of these cases were inadequate but considered adequate by the radiologists, and the other case was determined inadequate by R1 but adequate according to the HP. All these three incorrect cases had a T-stage of 1.

Based on the tumour segmentation, the sensitivity and specificity of the detection of inadequate margins with respect to the final histopathological report were 77% and 50% for R1 and 65% and 57% for R2, respectively. The median U-HD_{95} and O-HD_{95} for R1 were 0.9 mm (range: 0.0-1.7 mm) and 2.5 mm (range: 0.6-11.8 mm). For R2, the median U-HD_{95} and O-HD_{95} were 0.5 mm (range: 0.3-5.3 mm) and 2.5 mm (range: 1.2-6.6 mm).

The PCC of the measured margins between the HP and two radiologists was 0.67 and 0.71 for R1 and R2, respectively. Between both radiologists, the PCC of the measured margins was 0.75. **Figure 2** shows an example of a 3D-specimen and the corresponding MRI-slices.

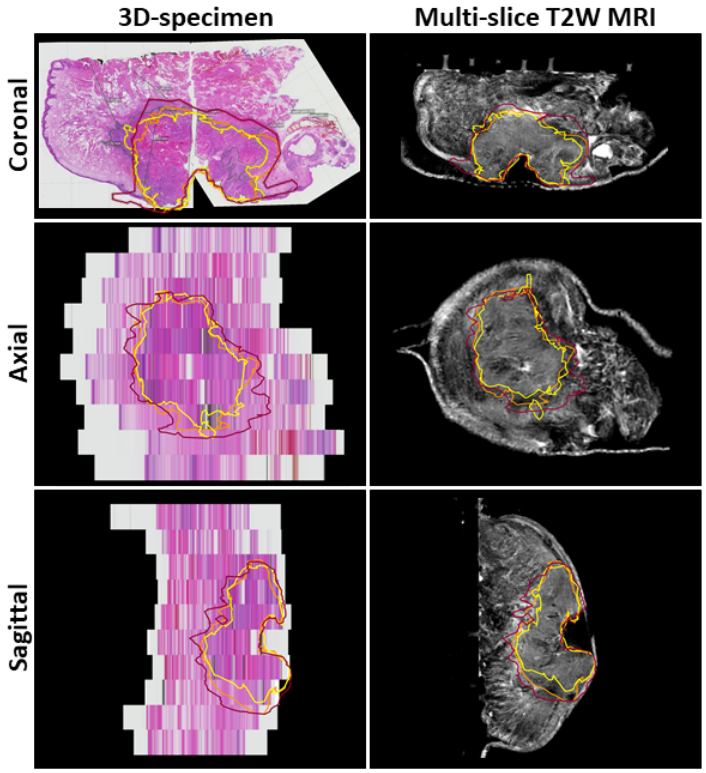


Figure 2. Example of the coronal, axial, and sagittal views of a digitally stacked 3D-specimen (left column) and the corresponding multi-slice T2W TSE images (right column). The tumour segmentations delineated by HP, R1 and R2 are shown in yellow, orange and red, respectively.

Conclusion

Ex-vivo 7T MRI enables accurate margin predictions for tongue cancer resection specimens. The radiologists' assessment of in- and adequate resections based on *ex-vivo* 7T MRI generally aligns with the histopathology reports. The sensitivity of both radiologists for adequate margin detection is reasonable. However, the specificity is low, which might be caused by the radiologists' overestimation of the tumour on *ex-vivo* 7T MRI. This study offers a proof of principle for future studies to validate and further improve the detection of inadequate margins for oral cavity resection specimens using *ex-vivo* 7T MRI. This technique could provide guidance for surgeons to localise inadequate margins and enable them to perform accurate re-resections during surgery.

References

1. Chinn SB, Myers JN. Oral Cavity Carcinoma: Current Management, Controversies, and Future Directions. J Clin Oncol. 2015 Oct 10;33(29):3269-76.

2. Smits RWH, Koljenovic S, Hardillo JA, Ten Hove I, Meeuwis CA, Sewnaik A, et al. Resection margins in oral cancer surgery: room for improvement. Head Neck 2016;38:E2197–203.

3. Caldas-Magalhaes J, Kasperts N, Kooij N, van den Berg CA, Terhaard CH, Raaijmakers CP, Philippens ME. Validation of imaging with pathology in laryngeal cancer: accuracy of the registration methodology. Int J Radiat Oncol Biol Phys. 2012 Feb 1;82(2):e289-98.

90

Impact of vitamin D supplementation on head and neck cancer patients receiving radiotherapy

Enas A. Elkhouly, Achraf A Abdelghany, Amira H Hegazy, Lama K Wahb, Reham A Abdelaziz

Menoufia University, Clinical Oncology department, Shebin Alkom, Egypt

Topic

Innovative treatments

Keywords

oral mucositis, radiotherapy, vitamin D

Purpose/Objective

The aim is to evaluate impact of vitamin D supplementation on oral mucositis in patients with head and neck cancer patients receiving radiotherapy with or without chemotherapy and to assess its effect on response to treatment.

Material/Methods

This is a prospective randomized clinical study conducted on sixty eight patients diagnosed as head and neck cancer that would receive either radiotherapy alone or concurrent chemo-radiotherapy at clinical oncology and nuclear medicine department, Menoufia university .Intervention group vitamin D prescribed .Control group :without vitamin D. All the patients were examined clinically weekly after the start of radiotherapy for WHO mucositis score. Response to treatment was assessed according to revised RECIST guideline (version 1.1) after 2-3 months end of treatment.

Results

Vitamin D supplementation reduced oral mucositis in head and neck cancer patients receiving radiotherapy with or without chemotherapy with significant p-value < 0.001 at week one ,two ,three, four, five , six and p-value was 0.042 at seventh week . Skin toxicity, taste changes and dysphagia were significantly better in intervention arm than control arm with significant P-value at week one, two, three, four, five, six and seven (0.011, 0.16, 0.001, <0.001.0.001*5*, 0.001 and 0.121 respectively) .Response to treatment was better in intervention arm with significant p - value <0.001.

Conclusion

This study demonstrates that vitamin D administration had beneficial effect on reducing oral mucositis and other complications like skin toxicity, taste changes and dysphagia during radiotherapy with or without chemotherapy in head and neck cancer patients. It also improved response to treatment.

91

The prognostic value of tumour p16 status in non-oropharyngeal head and neck squamous cell carcinoma.

Lessandra YS Chee[1], Shao Hui Huang[1,2], Jie Su[3], Ilan Weinreb[4], Bayardo Perez-Ordonez[4], Scott Bratman[1], John Cho[1], Ezra Hahn[1], Andrew Hope[1], Ali Hosni[1], John Kim[1], Andrew McPartlin[1], Brian O'Sullivan[1,2], Jolie Ringash[1,2], C.Jillian Tsai[1], John de Almeida[2], Christopher MKL Yao[2], Enrique Sanz Garcia[5], Li Tong[1], John Waldron[1,2]

[1]Princess Margaret Cancer Centre, Department of Radiation Oncology, Toronto, Canada. [2]Princess Margaret Cancer Centre, Department of Otolaryngology - Head & Neck Surgery, Toronto, Canada. [3]Princess Margaret Cancer Centre, Department of Biostatistics, Toronto, Canada. [4]Princess Margaret Cancer Centre, Department of Pathology, Toronto, Canada. [5]Princess Margaret Cancer Centre, Department of Medical Oncology, Toronto, Canada

Topic

HPV or EBV related cancers

Keywords

HPV, Human papillomavirus, survival

Purpose/Objective

Compared to oropharyngeal squamous cell carcinoma (SCC), the association between p16 status and outcome in non-oropharyngeal head and neck squamous cell carcinoma (HNSCC) is less clear. We conducted this single-institutional study to evaluate the prognostic value of p16 status in this population.

Material/Methods

A retrospective review was conducted for all newly diagnosed non-metastatic HNSCC arising from larynx, hypopharynx, sinonasal mucosa, and oral cavity tested for p16 and treated with curative intent between Jan 2009 and December 2021 in our institution. p16 immunohistochemistry (IHC) staining was routinely performed in laryngeal and hypopharyngeal cancer during 2014 and 2017 for EORTC1219 trial eligibility, and for selected non-oropharyngeal HNSCC if the patients were non-smokers/non-drinkers, or if tumours were non-keratinizing or of basaloid morphology. All p16 IHC was performed and interpreted at our institution by experienced head and neck pathologists. p16 positivity was defined by diffuse cytoplasmic and nuclear staining in >70% tumour cells. A proportion of tumours was also tested for HPV DNA by polymerase chain reaction (PCR). Overall survival (OS), disease-free survival (DFS), locoregional control (LRC) and distant control (DC) were compared between p16-positive and p16-negative cohorts. Multivariable analysis was performed to evaluate the prognostic value of tumour p16 status on OS.

Results

Of 3176 consecutive non-oropharyngeal HNSCC, p16 was tested in 466 (15%) patients, of whom 91 (20%) were p16-positive (26 larynx, 20 hypopharynx, 35 sinonasal tract, and 10 oral cavity) and 375 (80%) were p16-negative (162 larynx, 67 hypopharynx, 31 sinonasal tract, and 115 oral cavity). PCR for HPV DNA was performed in 39 p16-positive and 28 p16-negative cases and revealed 100% concordance

between p16 IHC and HPV DNA. The most common HPV genotypes were single infection HPV-16 (69.2%), single infection HPV-18 (10.3%), co-infection HPV 16 & 18 (2.6%), co-infection HPV 16 & 51 (2.6%) and other HPV genotypes (15.4%). The median age of patients tested was 62.5 years (range 54.5-70.5). Patients with p16-positive tumour had lower smoking pack-years compared to patients with p16-negative tumour (median 12.5 vs 30, p<0.001). There was no difference in TNM-8 T-category (p=0.09) and N-category (p=0.20) distribution between the two cohorts. Sinonasal primary site had the highest p16-positive rate (35/66, 53%), followed by hypopharynx (20/87, 23%), larynx (26/188, 14%), and oral cavity (10/125, 8%). Median follow up was 4.6 years (range 0.2-13.2). p16-positive non-oropharyngeal HNSCC had higher 5-year OS (80% vs 58%, p<0.001), DFS (73% vs 48%, p<0.001), LRC (89% vs 75%, p=0.003), and DC (91% vs 80%, p=0.007) vs p16-negative. Multivariable analysis, adjusting for primary disease site, age, smoking history, TNM-8 T-categories, N-categories, and use of systemic therapy, confirmed the prognostic importance of p16-positivity on OS (adjusted hazard ratio 0.46, 95% confidence interval 0.28 to 0.75, p=0.002). Sub-site analysis revealed p16-positive laryngeal and hypopharyngeal SCCs had higher 5-year OS (larynx: 89% vs 63%, p=0.015; hypopharynx: 77% vs 35%, p=0.003); and DFS (larynx: 85% vs 52%, p=0.004; hypopharynx: 67% vs 24%, p<0.001) vs p-16 negative counterparts. A non-significant trend toward better 5-year OS (82% vs 42%, p=0.051) and DFS (75% vs 42%, p=0.054) were observed in p16-positive sinonasal SCCs. However, no difference in OS (57% vs 66%, p=0.852) and DFS (50% vs 56%, p=0.906) was observed in p16-positive versus p16-negative oral cavity SCC (Table 1).

Table 1. Outcomes by p16 Status in Non-Oropharyngeal Squamous Cell Carcinoma

5-year Outcomes		Case No	OS	DFS	LRC	DC
Total	HPV+	91	80%	73.0%	89%	91.0%
n=466	HPV(-)	375	58%	48.0%	75%	80.0%
	p value		<0.001	<0.001	0.003	0.007
Larynx	HPV+	26	89%	85.0%	100%	92%
n=188	HPV(-)	162	63%	52.0%	79%	82%
	p value		0.015	0.004	0.015	0.195
Hypoph	HPV+	20	77%	67.0%	83%	78%
n=87	HPV(-)	67	35%	24.0%	68%	66%
	p value		0.003	<0.001	0.117	0.12
Sinonasal	HPV+	35	82%	75.0%	84%	97%
n=66	HPV(-)	31	42%	42.0%	63%	88%
	p value		0.051	0.054	0.053	0.227
OSCC	HPV+	10	57%	50.0%	90%	100.0%
n=125	HPV(-)	115	66%	56.0%	76%	85.0%
	p value		0.852	0.906	0.302	0.193

Conclusion

In this selected cohort of non-oropharyngeal HNSCC, p16-positive status carries a survival advantage (HR 0.46) which is similar to the 0.49 HR of HPV-positive status reported in RTOG 0129 (Ang et al. 2010)

for oropharyngeal carcinoma. This 5-year OS difference is mainly seen in laryngeal (26% absolute OS difference) and hypopharyngeal (42% absolute OS difference) SCC, possibly in sinonasal SCCs, but not in oral cavity SCC. The association of p16 and HPV, as well as its prognostic value should be confirmed in large systematically tested datasets.

References

Ang KK, Harris J, Wheeler R, Weber R, Rosenthal DI, Nguyen-Tân PF, Westra WH, Chung CH, Jordan RC, Lu C, Kim H, Axelrod R, Silverman CC, Redmond KP, Gillison ML. Human papillomavirus and survival of patients with oropharyngeal cancer. N Engl J Med. 2010 Jul 1;363(1):24-35. doi: 10.1056/NEJMoa0912217.

94

Influence of chemotherapy regimens prior to nivolumab on the survival of recurrent/metastatic SCCHN.

Cristina Martí Blanco[1], Lola Delamo Palomares[1], Clara Lucía Gonzálvez[1], Sergio Peralta Muñoz[1], Vanessa Morente Laguna[2], Laia Adalid Llansa[3], David Gómez Gómez[4], Mauricio Murcia Mejía[4], Monica Arguis Pinel[4], Carla Merma Linares[5], Josep Gumà Padró[1]

[1]Hospital Universitari Sant Joan de Reus, Medical Oncology, Reus, Spain. [2]Hospital Universitari Sant Joan de Reus, Pathology, Reus, Spain. [3]Hospital Verge de la Cinta, Pathology, Tortosa, Spain. [4]Hospital Universitari Sant Joan de Reus, Radiation Oncology, Reus, Spain. [5]Hospital Universitari Joan XXIII, Otolaryngology and Head -Neck Surgery, Tarragona, Spain

Topic

Immuno-oncology

Keywords

sequencing, taxanes, overall survival

Purpose/Objective

Since the incorporation of immunotherapy in the treatment of recurrent/metastatic SCCHN, the best sequencing with existing chemotherapy regimens has been investigated. In the KESTREL trial, patients treated at progression with immunotherapy had a 10-month increase in OS. The same is observed in the TTCC-2019-02 study, real world evidence taxol/cetuximab of TTCC group, in which the increase in survival was 13 months in patients treated with immunotherapy at progression. But, in the TPEX trial, patients treated in the experimental arm with immunotherapy at progression showed a 7-month overall survival superior to those treated with chemotherapy at progression, while those treated with EXTREME and at progression with immunotherapy the increase in OS was only of 2 months.

Patients with recurrent/metastatic tumors usually undergo multiple treatments. This study aims to determine the relationship between overall survival (OS), survival since treatment with nivolumab (Snivo) and progression-free survival (PFS) depending on the chemotherapy drug received in previous lines (taxanes and/or cetuximab).

Material/Methods

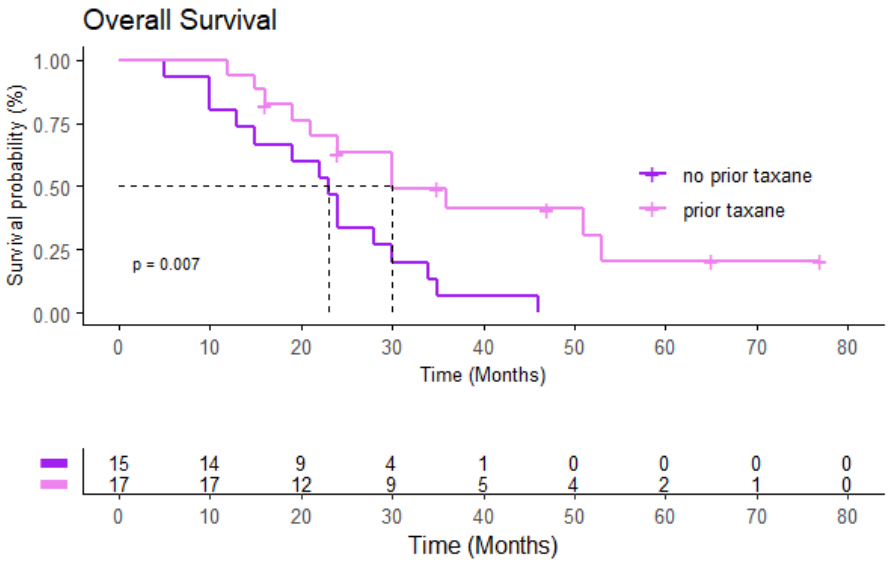
This is a retrospective, observational study that collects patient characteristics, tumor and previous treatments of all patients treated with nivolumab in care at the Sant Joan de Reus University Hospital from January 2018 to April 2023. Information has been collected from the digitized medical history.

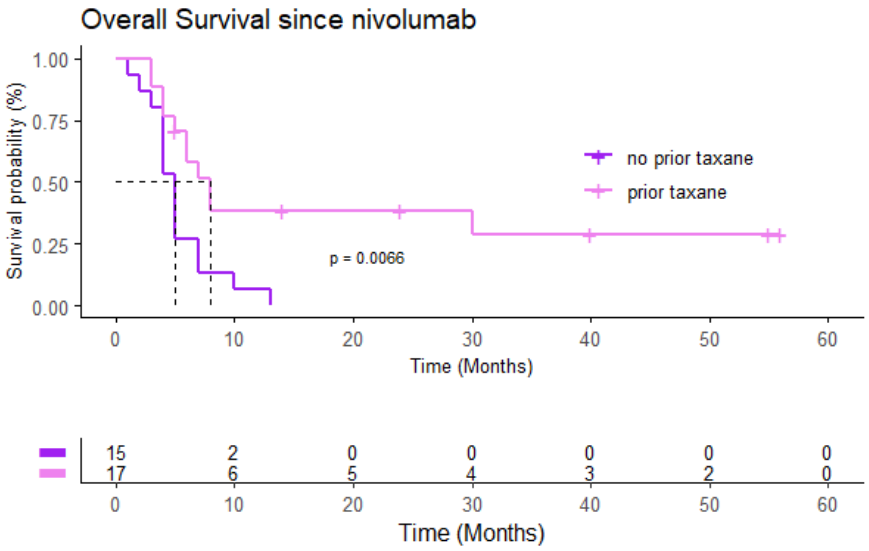
The relationship between previous treatments and survival (overall and progression-free) has been determined using the Kaplan Meier method and the log-rank test to compare the survival rate between groups. A p-value <0.05 has been considered statistically significant. To determine the possible variables influencing survival, the univariate and multivariate Cox proportional hazard model was used. The response rate to nivolumab and according to previous treatments has been calculated.

Results

32 patients have been included, 90% men with an average age of 51 years and the majority with significant toxic habits. 46.9% are located in the oral cavity, 15.6% stage IVC at diagnosis and 25% p16 positive. CPS could only be determined in 6 cases. 37.5% present local progression and 40.6% local and distant progression. 53.1% of patients have undergone regimens with taxanes and 59.4% with cetuximab. 10 patients have been treated with nivolumab in the first line of recurrent/metastatic disease.

The median OS is 24 months (95% CI 22-35), mSnivo is 5.5 months (95% CI 5-8) and mPFS is 4 months (95% CI 3-5). There are no differences depending on whether nivolumab is administered in the first line or successive (p 0.17) but if previously treated with taxanes the OS is superior compared to those who are not (30 vs 23 months, p=0.007, HR 0.33). The same is observed in Snivo (8 vs 5 m, p=0.006, HR 0.34). There are no differences in PFS with nivolumab if it has been previously treated with taxanes (p=0.15). There is also no difference in OS, Snivo and PFS if previously treated with cetuximab (p=0.98, p=0.097 and p=0.15 respectively) but there is a trend towards higher Snivo in patients not previously treated with cetuximab.





Disease control rate of 34.4% has been observed, with 4 complete responses (12.5%) and ORR 21.9%. There are no statistically significant differences according to previous treatment, but all CRs are in the previous taxane arm and there is a trend towards greater CR, ORR and DCR in those not previously treated with cetuximab.

In the univariate Cox hazard model, only prior treatment with taxanes has been identified as an independent survival factor, so a multivariate analysis has not been carried out.

Conclusion

Treatment with taxanes prior to nivolumab has been identified as an independent survival factor, presenting an improvement in both OS and survival since nivolumab with a reduction in the risk of death of more than 65%. The results are consistent with those observed in the CheckMate 141, TPEx studies or real world evidence taxol/cetuximab study of TTCC group. Since this is an observational study that suggests a sequencing scheme, these data would have to be validated in future clinical trials.

References

Psyrri A. Fayette J, Harrington K. Durvalumab with or without tremelimumab versus the EXTREME regimen as first-line treatment for recurrent or metastatic squamous cell carcinoma of the head and neck: KESTREL, a randomized, open-label, phase III study. Ann Oncol. 2023 Mar;34(3):262-274

Cirauqui Cirauqui B, Martinez Trufero J, Plana Serrahima M, et al. Real Wolrd Evidence of First-line Cetuximab (CX) plus Paclitaxel (PX) in Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck (SCCHN) - TTCC-2019-02. Annals of Oncology (2022) 33 (suppl_7): S295-S322.

Guigay J, Aupérin A, Fayette J, et al. Cetuximab, docetaxel, and cisplatin versus platinum, fluorouracil, and cetuximab as first-line treatment in patients with recurrent or metastatic head and neck squamous-cell carcinoma (GORTEC 2014-01 TPExtreme): a multicentre, open-label, randomised, phase 2 trial. Lancet Oncol 2021;22:463-475.

Ferris R. Blumenschein G, Fayette J, et al. Nivolumab for Recurrent Squamous-Cell Carcinoma of the Head and Neck. N Engl J Med 2016;375:1856-1867

95

Head and neck cancers with synchronous primary cancers in Ireland

Liam O'Connell, Niall O'Dwyer, Orla McArdle

Saint Lukes Radiation Oncology Network, Radiation Oncology, Dublin, Ireland

Topic

Radiobiology

Keywords

Synchronous, primaries, radiotherapy

Purpose/Objective

Head and neck cancer (HNC) patients presenting with synchronous primary cancers face significant treatment challenges and pose complex treatment decisions for clinicians. Rates of synchronous primary cancers have been reported between 1.3% to 5.8%.1 One study in the UK of 3436 patients with head and neck squamous cell carcinoma (SCC) identified a second primary rate of 9.1% of which the most common sites were head and neck (50%) and lung (34%).2 We designed a case series to assess rates of HNC with synchronous primary cancers and the outcomes of their treatment.

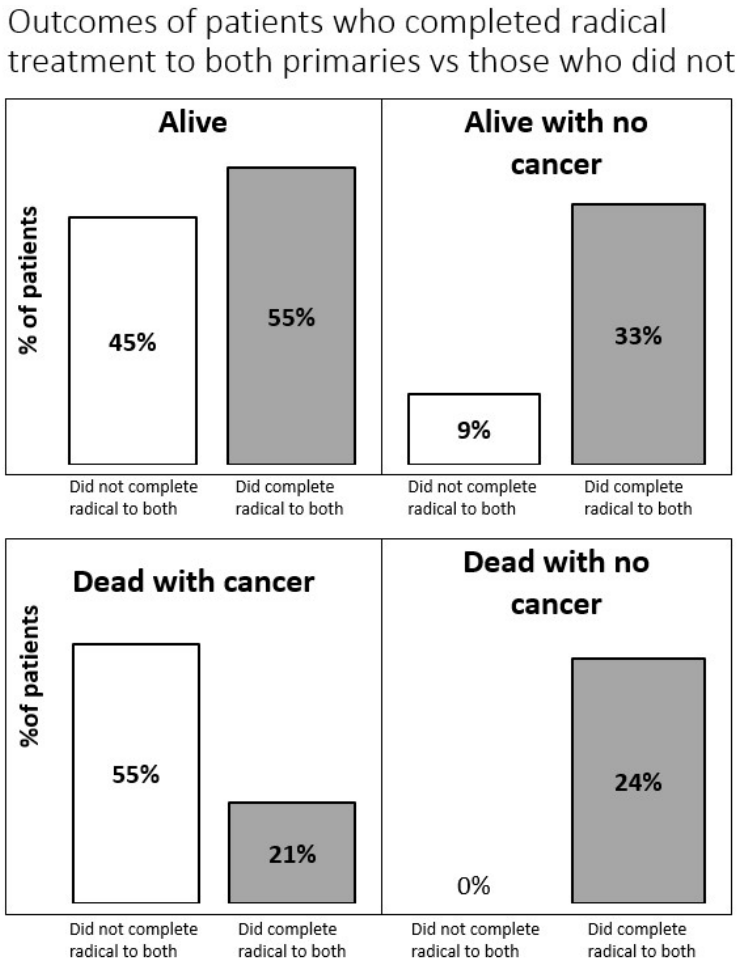
Material/Methods

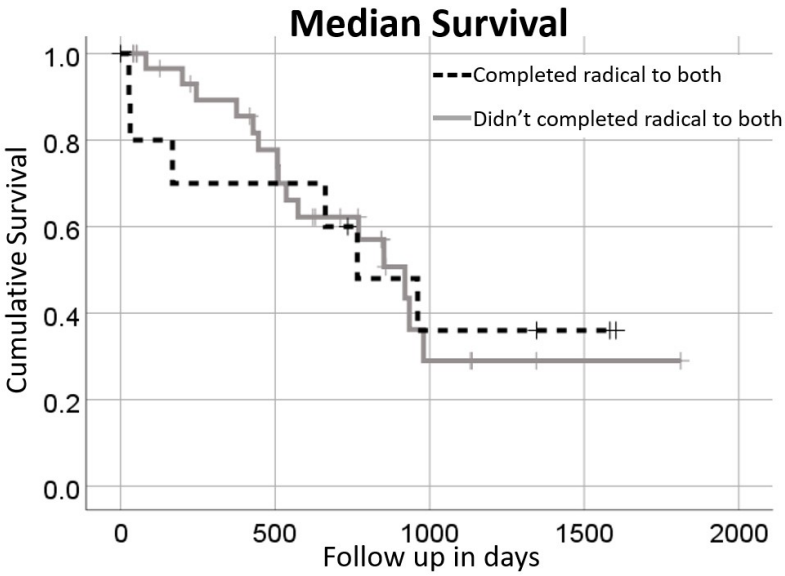
We identified HNC patients with synchronous primary cancers in the St Luke's Radiation Oncology Network from July 2017 to July 2022. Clinical data was obtained through review of patients electronic medical records. The inclusion criteria we used were as defined by two separate studies; Warren and Gates 1932; both neoplasms must be malignant, both must be anatomically separate, second primary must not be a possible metastasis from the first primary and Charles G. Moerte 1961; both cancers diagnosed within 6 months.

Results

We screened 2057 HNC patients who underwent radiotherapy. Forty-four (2%) patients met the inclusion criteria. The mean age was seventy-two. Seventy-five percent of the patients were male and 25% were female. The median follow up was 13.3 months. The most common HNC sites were laryngeal with 36% of patients, skin and oral cavity with 18% of patients each and oropharynx with 14% of patients. For TNM staging of the HNC, none were T1, 20% were T2, 23% were T3, 28% were T4 and 11% were unknown. For N staging, 52% were N0, 4% were N1, 32% were N2 and 11% were N3. The most common second primary cancer sites were lung with 32% of patients, skin with 9% of patients followed by breast, colon, thyroid and oesophageal all with 7% of patients each. HNC was diagnosed first in 57% of patients, the second primary cancer was diagnosed first in 14% of patients and the cancers were diagnosed simultaneously in 30% of patients. Six patients had squamous cell carcinoma HNC and lung cancer, the lung cancers were deemed separate primaries via multidisciplinary team consensus. The patients' treatments were as follows; 45% had surgery for their HNC, 52% had surgery for their second primary cancer, 20% had chemotherapy for their HNC, 30% had chemotherapy for their second primary cancer, all patients had radiotherapy to their HNC and 48% of patients had radiotherapy to both cancers. Of patients who had simultaneous radiotherapy one patient had to stop early due to lung cancer progression and one patient stopped oral cavity cancer radiotherapy early due to mucositis. Three (7%) patients had palliative treatment for their second primary cancer. One patient died due to

treatment, five days after pneumonectomy due to trachea-oesophageal fistula and subsequent aspiration. There were no other deaths attributed to treatment but the causes of death were unknown for two patients. Seventy-five percent of patients managed to complete radical treatment to both cancers. The median survival of patients who completed radical treatment to both cancers 2.5 years versus 2.1 years among patients who did not. Outcomes at the end of follow up for patients who completed radical treatment to both cancers versus those who did not are as follows; alive (55% versus 45%), alive with no cancer (33% versus 9%), dead with cancer (21% versus 55%) and dead with no cancer (24% versus 0%).





Conclusion

Head and neck cancer with a synchronous primary cancer is a rare condition comprising 2% of those treated in the St Luke's network. Three times more men had synchronous primary cancers than women. Larynx was the most common HNC site and lung was the most common second primary cancer site. The majority of patients who underwent simultaneous radiotherapy to both cancers finished treatment. The median survival of patients who completed radical therapy to both cancers was 2.5 years versus 2.1 years for those who did not complete radical therapy to both. There was a higher percentage of patients alive and without cancer at the end of follow up among patients who completed radical treatment to both primary cancers than those who did not. Further research is required to determine the best management for this complex patient cohort.

References

1. Pan SY, Huang CP, Chen WC. Synchronous/Metachronous Multiple Primary Malignancies: Review of Associated Risk Factors. Diagnostics (Basel). 2022

2. Jones AS, Morar P, Phillips DE, Field JK, Husband D, Helliwell TR. Second primary tumors in patients with head and neck squamous cell carcinoma. 1995

96

Selected inoperable oral cavity cancers may be salvaged using definitive radiotherapy (RT) and chemo-radiotherapy (CRT): A single center experience.

Shashank Shenoy, Ankita Mallick, Sudipta Pati, Sanjoy Chatterjee, Indranil Mallick

Tata Medical Center, Radiation Oncology, Kolkata, India

Topic

Quality of life and outcomes

Keywords

radical chemoradiation, unresectable, oral cavity

Purpose/Objective

Upfront surgical resection is considered as standard curative treatment in oral cancers with radiotherapy (RT) being used as adjuvant in locally advanced cases. The prognosis of surgically unresectable patients is considered poor and palliative options are offered. Institutional series on treatment of oral cancers with definitive radiation therapy or chemo-radiation (CRT) often include a mix of surgically unresectable and medically inoperable patients. The primary objective of this study was to report the outcomes of definitive non surgical therapy in locally advanced unresectable oral cavity squamous cell carcinoma (LA-OCC).

Material/Methods

We retrospectively examined patients with Stage III/IV previously untreated, non-metastatic, surgically unresectable LA-OCC treated definitively from 2011 to 2021.Following multidisciplinary discussions

such patients were offered RT or CRT with or without neoadjuvant chemotherapy (NACT). NACT was offered only when the multidisciplinary team (MDT) felt that the disease burden was heavy and the patient's performance score (PS) was optimal, to tolerate definitive RT post NACT. A dose of 66Gy/30Fr/6 weeks with concurrent weekly cisplatin 40mg/m2 or 55Gy/20Fr/4 weeks with RT alone was prescribed. Overall and progression free survival (OS, PFS) and treatment toxicities were analyzed.

Results

Sixty-nine patients met the inclusion criteria, median age 54 years (range 27-86) of whom 59 (85%) were males. Oral tongue was the most common (38%), followed by buccal mucosa (32%), hard palate (13%), and others (17.3%). T4a, T4b, N2-3 disease was present in 28 (40.6%), 26 (37.7%) and 39 (56.5%) patients respectively. The commonest causes for unresectability were high ITF/ base of skull involvement (47.8%) and extension into oropharynx (42%). There were four distinct treatment cohorts: Cohort A: NACT + CRT (n = 26, 37.6%); B: NACT + RT (when not fit for CRT post NACT; N = 6,8.6%), C: CRT (N=15,21%) and D: only RT (N=22, 31.8%). The median follow up was 10 months. Median OS and PFS of the whole group was 16 months with a 95% CI (8.8 -23.2 months) and 10 months 95% CI (7.7-12.3 months). The projected loco-regional control at 1 year, 2 years and 3 years were 63.8%, 60.4% and 45.3% respectively The median OS of cohort A was 16 months (7.5-24.4), cohort B was 8 months (3.5-12.5) , cohort C was Not Reached and cohort D was 21 months respectively. There were no differences in outcomes based on bone involvement or NACT. Seventeen patients (25%) needed admissions for toxicities and nasogastric tube insertion was required in 32 patients (47%). There were nine (13%) early deaths within three months of completion of RT/CRT, majority (66.5%) attributable to disease progression.

Conclusion

Carefully selected patients LA-OCC cancers respond well to definitive intent RT/CRT with acceptable toxicities. NACT may be used in selected patients, however in patients who remain unfit for CRT post NACT, outcomes are poor.

97

Real-world data on oral cancer with positive cervical nodes and extra-capsular extension: Insights and outcomes.

Rohit Avinash Vadgaonkar[1], Chandrasekhar Dravid[2], Sasi Krishna Kavutarapu[3], Nageswara Rao Noothanapati[3], Varsha Ramesh Bandal[1], Sneha Nachu[1], Sonali Nayak[4], Anupurva Dutta[4], Pankaj Chauhan[5], Raviteja Miriryala[1], Umesh Mahantshetty[1]

[1]Homi Bhabha Cancer Hospital and Research Centre, radiation oncology, Visakhapatnam, India. [2]Tata Memorial Hospital, Head and Neck oncology, Mumbai, India. [3]Homi Bhabha Cancer Hospital and Research Centre, Head and Neck oncology, Visakhapatnam, India. [4]Homi Bhabha Cancer Hospital and Research Centre, Pathology, Visakhapatnam, India. [5]Homi Bhabha Cancer Hospital and Research Centre, Dental and Prosthetics Surgery, Visakhapatnam, India

Topic

Multidisciplinary management

Keywords

Multi-discplinary approach, Survival rate

Purpose/Objective

To evaluate the treatment parameters, recurrence patterns, survival outcomes, and associated prognostic factors in patients with oral squamous cell carcinoma (OSCC) having pathologically positive cervical nodes with extra-capsular extension (ECE) following a multi-modal treatment.

Material/Methods

This is a retrospective audit from a single institute involving 137 consecutive patients of OSCC who underwent curative surgery and on histopathology had positive cervical lymph nodes with ECE. The study encompassed the period from January 1, 2017, to December 31, 2022. Univariate analyses and multivariate analysis were carried out using the Kaplan-Meier method with log-rank testing and Cox regression with the forward conditional method respectively.

Results

Out of 137 patients, 108 (78.8%) were male, and the median age at diagnosis was 49 years (IQR: 40-59 years). The most frequently affected sites of OSCC at presentation were the buccal mucosa/ gingiva-buccal sulcus/ retro molar trigone in 72 (52.6%), followed by the tongue in 59 (43.1%) and hard palate in 6 (4.4%). Neo-adjuvant chemotherapy was prescribed for 13 (9.5%) patients. All underwent radical surgery, which included composite resection in 66 (48.1%), glossectomy in 54 (39.4%) and wide excision in 17 (12.4%). Reconstruction procedures were performed in 122 (89.1%) cases, with 98 involving pedicle myocutaneous mucosal flap (PMMC) and 24 involving free flaps. All patients underwent modified radical neck dissection (MRND) comprising unilateral (UMRND) in 66 (48.2%), and bilateral (BMRND) in 71 (51.8%). Adjuvant treatment included radiotherapy (RT) alone in 18 (13.1%) and radiotherapy with concurrent chemotherapy (CRT) in 100 (73%).

Pathological primary tumor stages were distributed as follows: T1 in 6 (4.4%), T2 in 17 (12.4%), T3 in 45 (32.8%), and T4 in 69 (50.4%). Among them, 31 (22.6%) exhibited close margins (≤ 5 mm), and one had a microscopically positive margin at primary. The median lymph node yield was 59 (IQR: 40-81), with a median of 4 positive nodes (IQR: 4-6). Most commonly, positive lymph nodes were found in ipsilateral cervical level IB in 106 (77.4%), followed by level II in 101 (73.7%). Cervical nodes with evidence of positive ECE were predominantly located in level IB (n=85, 62%), followed by level II (n=62, 45.3%). Positive nodes were also observed in levels IV and V in 17 (12.4%), and more than 5 positive cervical nodes were present in 54 (39.4%).

At a median follow-up duration of 40 months, the outcomes were as follows: 74 (54%) remained disease-free, 57 (41.6%) experienced disease recurrence, and 6 (4.4%) were lost to follow-up. The pattern of recurrence was further characterized as follows: isolated local failure (LF) in 15 (10.9%), isolated regional failure (RF) in 9 (6.6%), combined loco-regional failure (LRF) in 10 (7.3%), isolated distant failure in 11 (8%), local and distant failure in 5 (3.6%), and regional and distant failure in 7 (5.1%). Among the LFs, the predominant recurrences were observed within post-operative flaps in 21 (70%), at the skull base, and the infratemporal fossa (ITF) in 6 (20%). Regional failure (RF) occurred in 26 patients, and the pattern of regional failure was stratified based on the extent of neck dissection and the presence of ECE in initially pathologically positive cervical nodes, as detailed in Table 01. RF involving only one level is seen in 12 (46.2%). Contralateral RF in unaddressed neck regions was observed in one-third of patients [4/13 (30.8%)] with URMND. Three of these cases (75%) showed recurrence at the same ECE level, while one case (25%) showed recurrence at a different level. A total distant failure was

observed in 23 (16.8%), with the most common sites being the lung in 14, bone in 13, non-regional lymph nodes in 6, and other sites in 10.

The 2-year survival estimates for disease-free survival (DFS), loco-regional control (LRC), and overall survival (OS) are presented in Table 02. Multivariate analysis indicated that worse 2-year DFS and OS were significantly associated with the non-cohesive pattern of invasion (p= 0.001), positive nodes at levels IV and V (p= 0.017), presence of > 5 positive nodes (p-value = 0.016), and not receipt of adjuvant concurrent chemotherapy (p = 0.001).

Conclusion

One of the most extensive collections of real-world data on patients with oral squamous cell carcinoma who have positive cervical nodes with extracapsular extension reveals consistently unfavorable outcomes and highlights the effectiveness of adjuvant multimodal treatments. The recurrence pattern not only involves loco-regional relapses but also frequently includes distant metastases. Alongside, our findings suggest that all cervical nodal regions are at risk for failure and warrant aggressive loco-regional and systemic treatments.

100

Challenges encountered in radiotherapy of parotid gland cancers : a tunisian single center experience

Haifa Haj Abdallah, sabrine tbessi, fadoua bouguerra, hayfa chahdoura, nadia bouzid, samia kanoun, sameh tebra

farhat hached hospital, radiotherapy, Sousse, Tunisia

Topic

Salivary gland, skull base, skin and thyroid cancers

Keywords

parotid gland cancers, postoperative radiotherapy

Purpose/Objective

Malignant salivary gland tumors are a relatively rare entity, affecting mostly the parotid gland. They represent 4% of head and neck cancers. They are characterized by the high frequency of local recurrences. Given their great diversity, these tumours lead to multiple therapeutic issues. The aim of our study is to describe the epidemioclinical features and therapeutic results of parotid cancers treated in our center.

Material/Methods

We report through a retrospective study, 20 cases of parotid gland cancer treated by postoperative radiotherapy (PORT) in our department between 2000 and 2021 .

Results

The median age was 45 years [35-56]. The sex ratio was 8/12. The main symptom was retro-auricular swelling in 85% of cases. All patients had an MRI of the anatomical region during the pre-therapeutic

assessment. Most patients had a locally advanced tumour classified respectively: stage III (50%) IVa (35%) and IVb (15%) . Treatment consisted of a total parotidectomy associated with ipsilateral lymph node dissection in all patients. The histological subtypes were mucoepidermoid carcinoma , salivary duct carcinoma and adenoid cystic carcinoma (ACC) in respectively 55% ,25% and 20%. The median size was 3 cm [2-5cm]. Histological lymph node invasion (LNI) was present in 70% of cases. surgical margins were positive (R1) in 35% of cases. Lymphovascular emboli (LVEs) were present in 45% of cases .

Radiotherapy was delivered for all patients , using conformational 3D and conventional 2D PORT respectively in 60% and 40% of cases. The median dose of RT was 54 Gy [50-66] . The target volumes were the parotid compartment taking into account the pathways of dissemination and anatomical barriers , and the ipsilateral cervical lymph nodes mostly including level Ib , II , III and IV .

After a median follow-up of 48 months (12-252) , 6 patients were in a complete remission (30%) , 9 patients had a locoregional recurrences (45%) treated with surgery . Five patients had presented a metastatic relapse (25%) after a median period of 12 months, of which 3 patients died .

by analyzing the prognostic factors , a correlation was noted between the poor prognosis of the treated parotid tumor and the ACC histological type ($p<0.03$) , the LNI ($p< .005$) , the LVEs ($p<0.04$) and the positive surgical margins ($p<0.0002$).

Conclusion

The main treatment for malignant parotid gland tumors remains surgery. However adjuvant treatment when indicated, is based on PORT. By reviewing scarce data from the literature, Their prognosis depends on several factors such as surgical margins , LNI , LVEs and histological subtype ,as it has been demonstrated by our unicenter study.

102

Onco-biota as prognostic factors in Head and Neck Squamous Cell Carcinoma

Legre Berta[1], Carla Merma[2], Maria Ines Molejon[3], Ximena Terra[1], Isabel Vilaseca[1], Francesc Xavier Aviles-Jurado[1,3]

[1]Hospital Clinic, Otorrinolaringology, Barcelona, Spain. [2]Hospital Joan XXIII, Otorrinolaringology, Tarragona, Spain. [3]Institut d'Investigació Sanitària Pere Virgili (IISPV), Otorrinolaringology, Tarragona, Spain

Topic

Innovative treatments

Keywords

HNSCC, biomarker, microbiota

Purpose/Objective

Head and Neck Squamous Cell Carcinoma (HNSCC) is diagnosed in more than half a million patients worldwide each year, and nearly one hundred thousand in the European Union, being the third tumor

in developed countries and the sixth malignant tumor with the highest incidence worldwide. Sixty percent of patients with HNSCC present an advanced stage of the disease when diagnosed. In HNSCC the explanation regarding the stagnant incidence and the mechanisms of tumorigenesis is still insufficient. Apart from tobacco, alcohol and infection by human papilloma, it is likely that other undefined factors are playing important roles in HNSCC tumor development and progression. Recent studies have suggested that local or distant cancer-associated microbiota can influence the cancer cells to exhibit cancer-specific inflammatory, immune and metabolic responses, which modulate cancer initiation, progression and response to treatment. In this study, we aim to understand whether microbiota contributes to HNSCC development or whether the abundance of bacterial organisms modulate the response in HNSCC therapy.

Material/Methods

For this purpose, we identified the differences in the onco-biome compared to healthy tissue, analyze the saliva and gut microbiota changes before and after cancer therapy and their association with the outcome and analyze the relationship between the microbial communities found with therapy response.

Results

Our results demonstrate that alpha diversity of the oral microbiome was significantly higher than healthy mucosa matrix using several indices ($P < 0.01$; p-value: 6.0167e-08*; [Mann-Whitney]. we also found that alpha diversity was higher in the responder group (R) (n=60) compared to non-responder patients (NR) (n=13) using several indices only in oral and fecal matrix. Microbial density changes analysis showed enrichment of genus Prevotella_7 (Bacteriodetes phylum) in NR in Oral, and tumor matrix ($P < 0.01$). These analysis also showed enrichment of genus Fusobacterium in R patients. Noticeably, an inverse relationship in the abundance of Fusobacterium and Streptococcus species was observed in the oral matrix Pre- vs PostTreatment.

Conclusion

The findings showed here indicated that microbial diversity and taxonomic composition of the microbiome may be useful biomarkers for HNSCC as well as provide a solid framework for future microbiome research.Our results in the present study can increase our knowledge about the impact of microbial communities on HNSCC development and response to treatment. The individual profiles of therapy response markers in relation to microbiota profiles would make possible to optimize the therapeutic approach.

103

A five-year experience of intensity modulated radiotherapy in nasopharyngeal carcinomas in Tunisia

Omar Nouri[1], Wafa Mnejja[1], Mariem Frikha[1], Wicem Siala[1], Afef Khanfir[2], Leila Farhat[1], Nejla Fourati[1], Jamel Daoud[1]

[1]Habib Bourguiba Hospital, Radiotherapy, Sfax, Tunisia. [2]Habib Bourguiba Hospital, Medical Oncology, Sfax, Tunisia

Topic

HPV or EBV related cancers

Keywords

Therapeutic results, Nasopharyngeal cancer, IMRT

Purpose/Objective

Intensity modulated radiation (IMRT) technique, associated with induction chemotherapy (IC) and/or concomitant chemotherapy (CC) is actually the recommended treatment modality for nasopharyngeal carcinomas (NPC). The aim of this study was to evaluate the therapeutic results and the patterns of relapse with this treatment protocol.

Material/Methods

A retrospective monocentric study of 145 patients with NPC treated between June 2016 and July 2021. All patients received IMRT with integrated simultaneous boost (SIB) of 33 daily fractions at a dose of 69.96 Gy for high-risk volume, 60 Gy for intermediate risk volume and 54 Gy for low-risk volume. High risk volume dose was 66.5 Gy in children.

Survival analysis was performed according to Kaplan-Meier method and Log-rank test was used to compare factors that may influence survivals.

Results

Median age was 48 years (11-80) with a sex ratio of 2.9. One hundred-twenty tumors (82.7%) were classified as stages III-IV according to the 2017 UICC TNM classification. Ten patients (6.9%) were metastatic at diagnosis. One hundred-thirty-five patients (93.1%) received IC, 104 of which (77%) were TPF-based (taxanes, cisplatin and 5 fluoro-uracil). One hundred-thirty-eight patients (95.2%) received CC, mostly cisplatin in 134 cases (97%).

After a median follow up of 56 months [28-86], 46 patients (31.7%) had a relapse: 12 (8.2%) experienced local and/or regional relapse after a median of 18 months [6-43], 29 (20%) experienced distant relapse after a median of 9 months [2-24] and 5 patients (3.4%) had both. Thirty-five patients (24.1%) died including 5 (3.4%) from a cause other than their cancer. Three-year overall survival (OS), cancer specific survival, disease free survival, metastasis free survival and loco-regional free survival were respectively 78.1%, 81.3%, 67.8%, 74.5% and 88.1%.

Anatomo-clinic factors predicting OS were an age > 50 years (88.7 vs 70.5%; p=0.004), diabetes history (81.2 vs 66.7%; p=0.027), UICC N classification (100 vs 95 vs 77.5 vs 68.8% respectively for N0, N1, N2 and N3; p=0.008), the practice of a lymph node biopsy (84.2 vs 57%; p=0.05), and UICC TNM stages III-IV (93.8 vs 73.6% respectively for stage I-II vs III-IV; p=0.044). Therapeutic factors predicting OS were number of CC courses (less than 4 courses: 65.8 vs 86%; p=0.03, less than 5 courses: 71.5 vs 89%; p=0.041), a weight loss > 10% during treatment (84.1 vs 60.9%; p=0.021) and a total cumulative cisplatin dose, including IC and CC, < 380 mg/m² (64.4 vs 87.6%; p=0.003). Radiotherapy delay and total duration did not significantly affect OS.

No grade 3-4 late side effects were noted in the evaluable 127 patients (87.6%). The most common toxicity was dry mouth that was grade 2 in 47 cases (37%) and grade 1 in 55 cases (43.3%).

Conclusion

IMRT for nasopharyngeal carcinoma granted a high loco-regional control rate for patients during the last five years. However, distant relapses remain frequent and conditionate the prognosis. We identified many anatomo-clinic and therapeutic prognosis factors. Therefore, high risk patients require a more aggressive therapeutic approach such as radiotherapy dose escalation or adding adjuvant chemotherapy.

104

Dosimetrically Treatment plan evaluation of Head and Neck cancer patients with IMRT techniques.

Rida Malik

Pakistan Institute of Engineering and Applied Sciences PIEAS Islamabad Pakistan, DPAM, Islamabad, Pakistan

Topic

RTT

Keywords

IMRT techniques, H&N , PSQA, Plan Quality Index

Purpose/Objective

IMRT delivery techniques (Sliding Window & Multiple Static Segments) for head & neck cancer cases were evaluated in this study. Planning target volume (PTV) coverage, Conformity Index, Homogeneity Index, doses to organ at risks (OARs) and PQI are considered as evaluation parameters. Detail about the parameters used for comparison is given in section 2.9 of materials and methods. While comparing techniques, it was made sure that target coverage and doses to OARs stayed within the constraints given by International Commission on Radiation Units and Measurements guidelines (ICRU).

Material/Methods

Dosimetric comparison of Dynamic intensity modulated radiotherapy and Static Intensity modulated radiotherapy using seven and nine fields was done in this study. Twenty patients i.e. 15 patients of NPC and 5 patients of larynx were randomly selected. All treatment plans were created by SIB (Simultaneous Integrated Boost) technique with a prescribed dose of 66.9 Gy within 33 fractions. After CT simulation, delineation of planning target volume (PTV) and organs at risk (OARs) was done by oncologist. Brainstem, spinal cord, and parotid glands were contoured as OARs. Four different plans (7FSW, 7FSS, 9FSW, and 9FSS) were created for each patient using Eclipse treatment planning system.

Results

The quality of IMRT plans has been significantly affected by the number of different techniques used in this study. In NPC patients, the 9F-IMRT techniques (SW and SS) produced an appropriate homogeneous dose of PTVs and resulted in pronounced sparing of nearby OARs from 7F-IMRT (SW and SS). This study shows that the results relating to PTV coverage are identical between SW and SS IMRT but in case of

beam angles, 9-fields showed better PTVs coverage than 7-fields. PTV has a major contribution to the conformity index, homogeneity index, PQI, and D95%.

Conclusion

PTV coverage and low doses to OARs were obtained better in Static segment than sliding window. In case of 7 and 9 beam angles, nine fields showed good results than seven fields.

105

Pembrolizumab plus platinum and taxanes as first-line and as neoadjuvant/induction therapies in PF-unfit patients with PDL1-positive squamous cell carcinoma of the head and neck

Santiago Cabezas-Camarero[1,2], Miguel Sotelo-Lezama[3,4,5], Óscar De-la-Sen[6], Alejandro Encinas-Bascones[6], Farzin Falahat[6], Almudena Alonso-Ovies[6], Elisa Varela-Reyes[6], Miguel Alonso-Juarranz[6], Manuel de Pedro-Marina[6], Jesús Gimeno-Hernández[7], Maria Cruz Iglesias-Moreno[7], Elena Cerezo-Druet[8], Fernando Puebla[8], Pedro Pérez-Segura[1,2]

[1]Hospital Clinico Universitario San Carlos, Medical Oncology, Madrid, Spain. [2]IDISSC, IDISSC, Madrid, Spain. [3]Hospital María Auxiliadora, Medical Oncology, Lima, Peru. [4]Clinica San Felipe, Medical Oncology, Lima, Peru. [5]Aliada Cancer Center, Medical Oncology, Lima, Peru. [6]Hospital Clinico Universitario San Carlos, Craniomaxillofacial Surgery, Madrid, Spain. [7]Hospital Clinico Universitario San Carlos, ENT Head and Neck Surgery, Madrid, Spain. [8]Hospital Clinico Universitario San Carlos, Radiation Oncology, Madrid, Spain

Topic

Immuno-oncology

Keywords

pembrolizumab, taxane, carboplatin

Purpose/Objective

Pembrolizumab (P) is approved in the first-line (1L) setting in patients with squamous cell carcinoma of the head and neck (SCCHN) with a CPS ≥ 1 and has shown promising activity in the locally-advanced (LA) setting. However, there are no alternatives for patients who are platinum-5FU (PF)-unfit and in need of a rapid tumor response. Taxanes are active agents in SCCHN that could effectively substitute 5FU as shown in Keynote-B10, Frail-Immune and DEPEND trials [1-3]. We evaluated the combination of pembrolizumab plus platinum and taxanes (PCT) +/- prophylactic (p) G-CSF in PF-unfit patients at our institution.

Material/Methods

Retrospective study of patients diagnosed with SCCHN and treated with PCT at Hospital Clínico Universitario San Carlos, Madrid (Spain). A descriptive study, as well as objective response rate (ORR), progression-free survival (PFS), overall survival (OS) and safety in the 1L and in the LA setting, were analyzed.

Results

Within the period August 2019 – October 2023, 18 patients (1L: n=6; LA: n=12) were identified. **Among 1L:** Male/Female: 2/4; age: 65y (56-86). Subsite: oral cavity (OC): n=5, larynx (n=1). Median CPS: 40 (5-80). No. combo PCT cycles: 6 (2-9). No. maintenance P cycles: 4 (1-8). ORR: 67% (2 CR, 2 PR, 2 SD). After a median follow-up (F-U) of 9 months (m) (1-25), median PFS and OS were 8 m (4.7 - 11.3) and NR (NR-NR), respectively. pG-CSF in 4/6 pts. G3/4 toxicity: G3 neutropenia: 4/6, G3 thrombopenia: 1/6. There were no toxic deaths. **Among LA:** Male/Female: 8/4; age: 72y (47-96). P + wkCBDCA-paclitaxel: n=10/12; P + 3wkCBDCA-paclitaxel: n=1/12, P + 3wkCDDP-docetaxel: n=1/12. Subsite: oropharynx: n=3, OC: n=5, CUP: n=1, Sinonasal: n=3. Median CPS: 30 (3-100). No. combo PCT cycles: 3 (2-4). No. maintenance P cycles: 0 (0-4). ORR after PCT (n=10): 90% (4 CR, 5 PR, 1 PD). Post-PCT Tx: Surgery: n=3; CRTx: n=5; Maint P: n=6. After a median follow-up (F-U) of 4 m (0-34), median PFS and OS were 6 m (NR - NR) and NR (NR-NR), respectively. pG-CSF in 6/12 pts. G3/4 toxicity: G3 neutropenia: 6/12, G3 thrombopenia: 4/12, G3 pneumonia: 1/12, G3 IR-colitis: 1/12, G4 IR-transaminitis: 1/12. There were no toxic deaths.

Updated results for the LA population (as of March 2024) will be presented at the meeting.

Conclusion

PCT and particularly weekly PCT +/- pG-CSF is a highly effective and safe chemoimmunotherapy option for PF-unfit patients in need of a rapid response and a positive CPS, both in the 1L and LA settings. Trials with weekly PCT should be conducted in comorbid and/or elderly patients with LA and R/M SCCHN not candidates for high-dose CT and in need of rapid response.

References

1. Dzienis MR, Cundom JE, Fuentes CS, et al. 651O-Pembrolizumab (pembro) + carboplatin (carbo) + paclitaxel (pacli) as first-line (1L) therapy in recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC): Phase VI KEYNOTE-B10 study. Ann Oncol. 2022;33((Suppl 7)):S295–S322. doi: 10.1016/j.annonc.2022.07.775.

2. Fayette J, Cropet C, Gautier J, et al. Results of the multicenter phase II FRAIL-IMMUNE trial evaluating the efficacy and safety of durvalumab combined with weekly paclitaxel carboplatin in first-line in patients (pts) with recurrent/metastatic squamous cell carcinoma of the head and neck (R/M SCCHN) not eligible for cisplatin-based therapies. Journal of Clinical Oncology 41, no. 16_suppl (June 01, 2023) 6003-6003. doi: 10.1200/JCO.2023.41.16_suppl.6003.

3. Ronsenberg A, Juloori A, Agrawal N, et al. Neoadjuvant nivolumab, paclitaxel, and carboplatin followed by response-stratified chemoradiation in locoregionally advanced HPV negative head and neck squamous cell carcinoma (HNSCC): The DEPEND trial. ournal of Clinical Oncology 41, no. 16_suppl (June 01, 2023) 6007-6007. doi: 10.1200/JCO.2023.41.16_suppl.6007.

107

Prognostic and Survival analysis of patients with locally advanced nasopharyngeal carcinoma with optic pathways involvement.

khalil mahjoubi[1], Ons Bettaieb[2,3], sarra sghaier[1,4], semia zarraa[1], ali essadok[1], amani yousfi[1], alia mousli[1], khedija ben zid[1], chiraz nasr[1]

[1]institut Salah Azaiez, radiotherapy, tunis, Tunisia. [2]institut salah azaiez, radiotherapy, Tunis, Tunisia. [3]Farhat Hached Hospital, radiotherapy, Sousse, Tunisia. [4]Farhat Hached Hospital, radiotherapy, SOUSSE, Tunisia

Topic

HPV or EBV related cancers

Keywords

radiotherapy, nasophayngeal, pronostic

Purpose/Objective

To evaluate the prognostic and Survival of patients with locally advanced nasopharyngeal carcinoma with opticpathways involvement, treated by intensity-modulated radiotherapy (IMRT) and concomitant Cisplatin, with or without induction chemotherapy.

Material/Methods

We retrospectively reviewed data for 40 consecutive patients treated by IMRT in the radiotherapy departement of Salah azeiez hospital in Tunisia, between 2014 and 2018.

Results

The mean patient age at diagnosis was 42,65 years (19-81) and the sex ratio was 1,85. All patients had undifferentiated carcinoma of the nasopharynx (UCNT) and were staged T4 according to the seventh edition of the American Joint Committee on Cancer (AJCC) staging system. Patients presented a variety of ocular symptoms, along with other signs such as; diplopia (28,2%), proptosis (10,3%), exophtalmie (5,1%) and oculomotor nerve pulsy (5,1%).Symptomatic orbital invasion by tumor occurred in 19 of the 40 patients (48,7%). Ocular signs, but no orbital invasion, was present in 13 patients (32,5%). The CT scan showed orbital involvement in 21 cases (52,5%), sphenoidal involvement in 32 cases (80%), ethmoidal involvement in 22 cases (55%) and skull base invasion in 38 cases (95%). Neoadjuvant chemotherapy was adminisered to 22 patients (55%). All patients underwent concomitant cisplatin based chemoradiotherapy.

The median follow-up was 48,5 months (24 to 83 months), 20 patients (50%) died and 20 (50%) were still alive. A total of 18 (45%) patients experienced failures (30%) and distant metastases (25%). Locoregional failures were seen in 12 (30%) patients. 10 patients (25%) experienced local failure and 2 (5%) patients experienced a nodal failure. Three patients (7,5%) presented unilateral blindness which might be resulted from radiation-induced optic neuropathy. At last follow-up, 19 out of 40 patients (47,5%) were alive without any disease

The mean overall survival (OS) was 40,22 months (HR=4,161, 95%CI 32,070-48,382). The 5-year rate of OS was 47,4%. The mean disease free survival (DFS) was 37,740 months (HR=4,754, 95%CI 28,421-47,058). The 5-year rate of DFS was 49 %.

The univariate analysis revealed that orbital involvement did significantly affect overall survival (P=0,000). Orbital involvement was also identified as an independent prognostic factor for OS (hazard ratio 0,159; 95 % CI 0.043–0.588; P = 0.006). However, Tumor volume higher than 100 cm3 (hazard ratio=0,130 ; 95 % CI 0,022 – 0,771; P = 0,025) and dose at CTVp1 lower than 66 Gy (hazard ratio=0,137 ; 95 % CI 0,028–0,665; P = 0,014) were identified as an independent prognostic factors for DFS.

Conclusion

T4 non metastatic locally advanced NPC with optic pathways involvement is uncommon and it confers a particular bad prognosis. Indeed, the IMRT modality provides adequate local-regional control for T4 NPC. However, even with the most sophisticated treatment techniques, the clinical outcome remains low for this subgroup.

References

1. Wided BAH, Hamouda B, Hamadi H, Mansour BA. Nasopharyngeal Carcinoma Incidence in North Tunisia: Negative Trends in Adults but not Adolescents, 1994-2006. Asian Pacific Journal of Cancer Prevention. 14 avr 2015;16(7):2653-7.

2. Frikha M, Bouaziz M, Daoud J, Ghorbel A, Elloumi M, Boudaya M, et al. [Evaluation of tumoral and lymph node response to neoadjuvant chemotherapy in undifferentiated nasopharyngeal carcinoma]. Bull Cancer. mars 1997;84(3):273-6.

3. Wong WM, Young SM, Amrith S. Ophthalmic involvement in nasopharyngeal carcinoma. Orbit. 4 mars 2017;36(2):84-90.

4. Hsu W-M, Wang A-G. Nasopharyngeal carcinoma with orbital invasion. Eye. août 2004;18(8):833-8.

5. Cao C, Jiang F, Jin Q, Jin T, Huang S, Hu Q, et al. Locoregional extension and patterns of failure for nasopharyngeal carcinoma with intracranial extension. Oral Oncology. avr 2018;79:27-32.

109

Real world data on Low-Dose Nivolumab with Triple Metronomic Chemotherapy: Retrospective analysis of 50 consecutive patients from LMICs

Palak Bhatt[1], Rushabh Kothari[1], Itesh Khatwani[2], Gaurang Modi[2], Mehul Patel[3], Shashikant Limbachiya[3], Manthan Merja[3], Yogesh Kheni[3], Rushit Dave[1], Ronak Vyas[1], Manish Sadhwani[1], Nishant Vidyasagar[3], Jagruti Koladiya[3], Rushabh Raval[3], Viral Soni[1], Ishita Thaker[2], Geeta Khatwani[2], Rati Doshi[2]

[1]Narayana Multispeciality Hospital, Medical Oncology, Ahmedabad, India. [2]Oncowin Cancer Center, Medical Oncology, Ahmedabad, India. [3]Starlit Cancer Center, Surgical Oncology, Ahmedabad, India

Topic

Immuno-oncology

Keywords

Real world evidence, low dose immunotherapy

Purpose/Objective

In HNSCC, survival with chemotherapy is dismal in a palliative setting. In LMICs, access to cetuximab and IO is less than 3%.[1] Therefore, treatment options are limited to chemotherapy. There is evidence suggesting that low-dose nivolumab, in combination with triple metronomic chemotherapy (TMC), improves OS.[2] Yet, real-world data on the use of low-dose nivolumab remains scarce. This retrospective

study aims to evaluate response rates associated with the combination of TMC and low-dose nivolumab in HNSCC patients.

Material/Methods

A retrospective analysis was conducted on 50 consecutive HNSCC patients with PS 0-1 who underwent combined TMC (Tab. Erlotinib 150mg once a day, Tab. Methotrexate 9mg/m² once a week, Cap. Celecoxib 200mg twice a day) and low-dose nivolumab(20 mg every 21 days) therapy from August 2022 to June 2023 with palliative intent(recurrent/metastatic/inoperable).Platinum sensitivity was defined as >6 months of gap from platinum exposure or platinum naive.

Descriptive statistics were performed for demographic details. Response assessments, including complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD), were conducted according to RECIST 1.1 criteria at 3 months. Response rate (RR) and clinical benefit rate (CBR) was calculated as per intention to treat.

Results

A total of 50 patients were included in this study, with 44 (88%) being male and 6 (12%) female. The median age was 49 years (35-78 years). ECOG PS-0 was observed in 3 (6%) patients, while 47 (94%) had ECOG PS-1. The primary site of malignancy was buccal mucosa in 33 (66%) patients, tongue in 12 (24%) patients, hard palate in 1 (2%) patient, and other primary sites in 4 (8%) patients. A history of surgery was present in 27 (54%) patients, and 26 (52%) had a history of radiation. 18 (36%) had no previous chemotherapy exposure. 31 (62%) had platinum exposure, and 21 (42%) had exposure to taxane. 30 (60%) were platinum-sensitive and 20 (40%) were platinum-resistant. In the whole cohort, 3 patients (1 in platinum sensitive and 2 in platinum resistant cohort) lost to follow up and 1 patient died (platinum resistant cohort).

In the whole cohort, the response rate (RR) was 64% (n=32), and the clinical benefit ratio (CBR) was 80% (n=40). RR and CBR in the platinum-sensitive cohort were 76.67% (n=23) and 90% (n=27) respectively. RR and CBR in the platinum-resistant cohort were 45% (n=9) and 65% (n=13) respectively.

Whole Cohort	Total Patients	CR	PR	SD	PD
	50 (3 LUF, 1 Death)	2 (4%)	30 (60%)	8 (16%)	6 (12%)
Platinum Sensitive	30 (1 LUF)	1 (3.33%)	22 (73.33%)	4 (13.33%)	2 (6.67%)
Platinum Resistant	20 (2 LUF, 1 Death)	1 (5%)	8 (40%)	4 (20%)	4 (20%)

Conclusion

The novel combination of low dose nivolumab and TMC has clinically meaningful response rates in real world setting. It is useful options in resource constraint setting.

References

1. Patil V et al. Ecancer 16 1464

2. Patil V et al. J Clin Oncol 2023;41(2):222-232

110

Oncological outcomes and pattern of care in sinonasal malignancy treated with a multimodality approach.

Anjali V Ramdulari, Aswin Ravi, Anindya Dutta, Swarnaditya Roy, Ahitagni Biswas, Suman Bhasker

All India Institute of Medical Sciences, Department of Radiation Oncology, New Delhi, India

Topic

Multidisciplinary management

Keywords

sinonasal malignancy, paranasal malignancy,

Purpose/Objective

The study aimed to assess the patterns of care and treatment outcomes in patients with sinonasal malignancy (SNM), treated at our institute from January 2018- March 2023.

Material/Methods

Patients with biopsy proven SNM were included in this retrospective analysis. Progression free survival (PFS) was defined as the time interval from the date of diagnosis to the date of disease progression (locally, regionally, or distant). Overall survival (OS) was defined from the date of diagnosis to the last follow-up or death. Univariate Cox regression analysis was done to evaluate the relationship between treatment factors and survival outcomes. Time to event data was evaluated using Kaplan. -Meier method.

Results

A total of 93 patients with diagnosed SNM between 2018-2023 were included in the study. The median age at diagnosis was 42.4 years (IQR= 23.3- 55.8). 81.7% of the patients were male. Maxillary sinus was the most common site involved (57.1%) followed by nasal cavity (38.9%) and ethmoid sinus (12%). The most common histological types were carcinoma (50.5%) followed by sarcoma (19.4%), esthesioneuroblastoma (7.5%), and lymphoma (7.5%). Among carcinoma, squamous cell carcinoma (61.6%) was the most common subtype followed by adenoid cystic carcinoma. The mean tumor size was 5.6 centimetres (range 1.6- 12.2). 20.4% of patients had regional lymph nodal involvement and 5.4% of patients had metastatic disease at presentation. Intent of treatment was curative in 76.3% of patients. Primary surgical treatment was done in 45.2% patients, of which 45% of patients received adjuvant radiotherapy and 37.5% of patients received adjuvant chemoradiation. Radical chemoradiotherapy was administered in 28.8% of patients. All patients received conformal IMRT/VMAT radiotherapy to a dose of 60Gy -66Gy in 30-33 fractions. Median follow-up was 27.9 months (IQR: 8.8-46.9). In the curative treatment group, the median OS was 35.6 months (IQR: 16.2- 54.3) and the median PFS was 29.5 months (IQR: 12.8- 51.7). In univariate analysis, patients who did not complete the planned treatment were associated with decreased OS (p-value= 0.03; HR= 5.57; 95%CI= 1.21- 25.57), advanced-stage disease was associated with inferior PFS (p- value= 0.026; HR= 9.81; 95%CI=1.29- 74.44). In multivariate analysis, the advanced stage was associated with worse PFS (p-value= 0.03; HR= 10.18; 95%CI=1.32- 78.4). The disease progressed locally in 20.5%, regionally in 5.4%, and distant metastasis in 9.7% of patients' post-radical treatment. Lung was the most common site of metastasis. Out of 23.7% of patients who received palliative treatment, 40.9% of patients received both palliative radiotherapy

and chemotherapy, 31.8% received palliative radiotherapy alone and 0.4% received palliative chemotherapy alone. The median OS was 13.5 months (IQR: 6.4- 19.7) and the median PFS was 5.3 months (IQR: 1.6- 12.8) in the palliative group.

Conclusion

Sinonasal tumors are a complex and diverse group of cancers. The advanced stage of presentation, histologic diversity, and anatomical proximity to critical neurovascular structures make the treatment of SNM challenging. The median OS was 35.6 months and the median PFS was 29.5 months, with inferior PFS in advanced-stage disease. Early diagnosis and multi-disciplinary approach are imperative in the management of SNM.

111

"A Retrospective study comparing sequential boost versus integrated boost using volumetric Arc Radiotherapy along with concurrent chemotherapy for Locally Advanced Head and Neck Cancer".

THAMIZHOLI SELVARAJU, DHIRU TALUKDAR, SHABNAM BISWAS

Assam cancer care Foundation, Radiation oncology, Barpeta, India

Topic

Innovative treatments

Keywords

LAHNC, VMAT, SIB

Purpose/Objective

Radiotherapy for LAHNC has changed considerably over the past two decades with the advent of conformal Radiotherapy techniques. Whereas these techniques differ in treatment related outcomes including survival and toxicity remains unanswered. Our objective of this study is to compare sequential versus Simultaneous Integrated boost using VMAT for LAHNC.

Material/Methods

A single institutional Retrospective data on Histologically proven squamous cell LAHNC treatment with Definitive chemoradiation 66-70Gy. Treatment was delivered via sequential boost or SIB using VMAT. Sequential Arm was delivered in 3 Phases, Phase I- 46-50Gy, Phase II- 10-14Gy, and Phase III- 10Gy, whereas SIB Arm 66Gy (High risk), 60Gy (Intermediate risk), and 54Gy (Low risk). Both arms received concurrent chemotherapy with weekly Inj.Cisplatin 40mg/m2. Toxicity was graded weekly during treatment and 3 monthly follow-ups. RFS, DFS and OS were estimated.

Results

At 2years, the estimated OS was 70% in sequential arm and 62% in SIB Arm. There was no difference in Local, regional, or distant RFS. There was No difference in weight loss and gastrostomy tube placement. But treatment Gaps were more appreciated in SIB Arm in comparison to sequential Arm. Rates of Acute

toxicity Grade III/IV Dermatitis and Dysphagia were higher in SIB Arm in comparison to sequential Arm. Late Toxicity like Post RT Neck Oedema and Neck fibrosis seen more commonly seen in SIB Arm comparing to sequential Arm, whereas Xerostomia remains same in both arms.

Conclusion

There were no difference in disease related outcomes between the two treatment delivery approaches. A higher rates of Acute toxicity like Grade III/IV Radiation dermatitis, dysphagia and late toxicity like Post RT Neck Oedema, Fibrosis was observed more in SIB arm compared to sequential Arm.

References

1. Vlacich et al. A comparative analysis between sequential boost and integrated boost intensity modulated radiation therapy with concurrent chemotherapy for locally advanced head and neck cancer., Radiation Oncology (2017) 12:13

2.Mohan R, Wu Q, Manning M,schmidt-ullrich R. Radiobiological considerations in the design of fractionation strategies for Intensity- modulated radiation therapy of head and neck cancer. Int J Radiat Oncol Biol Phys. 2000; 46:619-30

3.Orlandi E, Palazzi M, Pignoli P, Fallai C, Giostra A, Oilmi P. Radiobiological basis and clinical results of the simultaneous integrated boost (sib) in intensity modulated radiotherapy (imrt) for head and neck cancer: A review. Crit Rev Oncol Hematol. 2010; 73:111-25.

4.Doglan N, King S, Emami B, Mohideen N, Leybovich LB, Sethi A. Assessment of different imrt boost delivery methods on target coverage and normal-tissue sparing. Int J Radiat Oncol Biol Phys. 2003, 57:1480-91.

5.Marks LB. A standard dose of radiation for "Microscopic disease" is not appropriate. cancer 1990;66:2498-502.

112

Differentiated Thyroid Cancer with Synchronous second Primary Cancer : Retrospective study from a cancer institute in India

Anish Chowdhury, Jebin Aaron, Arpit Bandi, Priyank Rathod

Gujarat Cancer Research Institute, Surgical Oncology, Ahmedabad, India

Topic

Salivary gland, skull base, skin and thyroid cancers

Keywords

PTC, DTC, synchronous oral primary cancers

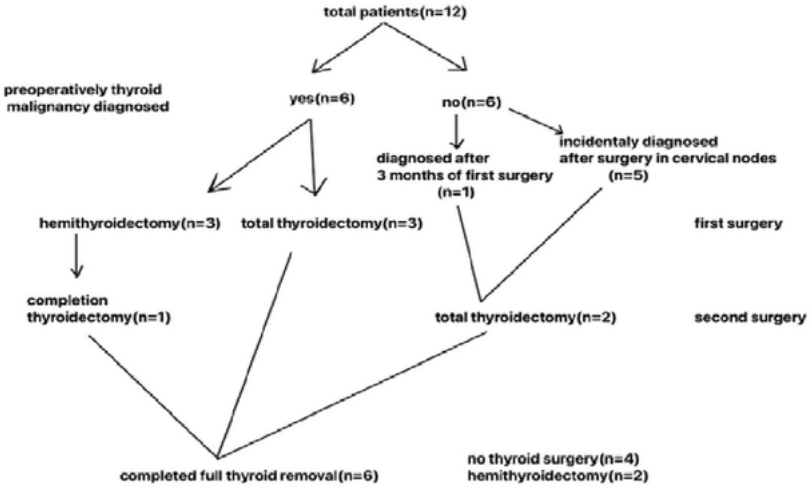
Purpose/Objective

Thyroid cancer is the most common endocrine malignancy, accounting for 1 % of all cancers [1]. The genetic syndromes associated with differentiated thyroid cancers(DTC) are Cowden syndrome, Familial Adenomatous Polyposis(FAP), Carney's complex, Pendred syndrome and Werner syndrome[2]. The incidence of synchronous second primary tumors(SSPC) associated with oropharyngeal malignancies was 1 to 10 %[3]. The incidence of other malignancies other than the above syndromes occurring synchronously with DTC is very rare. Only a few case reports and series are available. The incidence of synchronous second primary cancer(SSPC) with Differentiated Thyroid Cancers(DTC) is a very rare entity. Very few case reports and case series were published in the literature. The current study is aimed to enumerate the clinicopathological data of patients with DTC with SSPC.

Material/Methods

This is a single-center retrospective study. All the patients diagnosed with DTC and SSPC from January 2016 to July 2023 were included in the study. The demographic, clinicopathological data and survival data were collected from the institute's database. Patients were followed up telephonically and survival status was documented. Synchronous cancers are defined as more than one independent primary malignancy when the second(or third) cancer occurs within six months of diagnosis of the first malignancy[4].

Results



A total of 1395 patients were diagnosed with thyroid cancer during the study period. Twelve patients were found to have DTC with SSPC. All the patients had papillary thyroid cancer as primary DTC. Ten patients had head and neck squamous cell carcinoma, one had malignant phyllodes tumor, and another patient with endometrioid adenocarcinoma as the SSPC. Six patients diagnosed during preoperative evaluation, one patient diagnosed 3 months after the oral malignancy diagnosis and five patients were diagnosed to have PTC in cervical nodes after neck dissection. Complete thyroid removal was done in six patients and hemithyroidectomy in two patients. Among the patients who underwent total thyroidectomy, four patients had undergone radioactive iodine scan followed by radioactive iodine ablation for two patients. Three patients had died during follow-up, two patients was lost to follow-up and the rest of the seven patients were alive. Out of those alive one patient had a follow-up of less than six months and was excluded from the survival calculation. The median follow up was 25.55 months. The median overall survival was 40.97 months.

Conclusion

DTC constitute 95% of thyroid malignancies. Five to fifteen percent of DTC has familial disease. The genetic syndromes associated with DTC are FAP, PTEN syndromes(Cowden syndrome, Bannayan- Riley-Ruvalcaba syndrome, PTEN hamartoma tumor syndrome), Werner syndrome, Carney complex, DICER1 syndrome, Pendred syndrome, Ataxia telangiectasia, Li Fraumeni syndrome, and Peutz Jeghers syndrome[5]. But, synchronous occurrence of a second malignancy with DTC is a rare phenomenon.

In the present study, the most common SSPC was SCC of the head and neck region(83.3%). 5 patients had incidental detection of thyroid cancer in cervical lymph nodes which were dissected during neck dissection done for other causes. L J Fliegelman et al published a paper on four cases of incidentally detected thyroid malignancy in cervical nodes[6]. Ansari-Lari et al also published cases of incidentally diagnosed PTC on cervical lymph nodes[7].

In the present study, one patient had synchronous papillary thyroid carcinoma with a malignant phyllodes tumor of the breast. No such case was found reported in the literature during our literature search.

In the present study, we reported a case of synchronous endometrioid adenocarcinoma with PTC. Badan Marius-loan et al reported one case of PTC with endometrioid carcinoma[8]. Patients with Cowden syndrome can have thyroid carcinoma and endometrial carcinoma[9].

The overall survival of the study group was 40.97 months. Biopsy-proven SCC recurrence was seen in two patients out of four patients with clinically documented recurrence. In the literature review on case series and case reports, it was concluded that the prognosis of the patient depends on the staging of oral synchronous primary and the treatment of thyroid cancer must be decided based on oral malignancy staging and treatment.

In conclusion SSPC with DTC is a very rare phenomenon. SCC of the head and neck region is the most common synchronous second primary malignancy associated with DTC. As there are no published guidelines for this clinical scenario, a multi-disciplinary panel discussion is a must to decide regarding management considering the staging and weighing the treatment benefit for both malignancies.

References

1. Balajam NZ, Mousavian AH, Sheidaei A, Gohari K, Tavangar SM, Ghanbari-Motlagh A, et al. The 15-year national trends of endocrine cancers incidence among Iranian men and women; 2005–2020. Sci Rep. 2023 May 10;13(1):7632.

2. Richards ML. Familial syndromes associated with thyroid cancer in the era of personalized medicine. Thyroid Off J Am Thyroid Assoc. 2010 Jul;20(7):707–13.

3. Xu CC, Biron VL, Puttagunta L, Seikaly H. HPV Status and second primary tumours in Oropharyngeal Squamous Cell Carcinoma. J Otolaryngol - Head Neck Surg. 2013 May 29;42(1):36.

4. De Luca A, Frusone F, Vergine M, Cocchiara R, La Torre G, Ballesio L, et al. Breast Cancer and Multiple Primary Malignant Tumors: Case Report and Review of the Literature. Vivo Athens Greece. 2019;33(4):1313–24.

5. Kamani T, Charkhchi P, Zahedi A, Akbari MR. Genetic susceptibility to hereditary non-medullary thyroid cancer. Hered Cancer Clin Pract. 2022 Mar 7;20:9.

6. Fliegelman LJ, Genden EM, Brandwein M, Mechanick J, Urken ML. Significance and management of thyroid lesions in lymph nodes as an incidental finding during neck dissection. Head Neck. 2001 Oct;23(10):885–91.

7. Ansari-Lari MA, Westra WH. The prevalence and significance of clinically unsuspected neoplasms in cervical lymph nodes. Head Neck. 2003;25(10):841–7.

8. Marius-Ioan B, Doina P. Triple Metachronous Malignancies with Thyroid Involvement: A Brief Overview of Five Case Reports over 20 Years of Institutional Experience. Diagnostics. 2020 Mar 20;10(3):168.

9. Porto ACS, Roider E, Ruzicka T. Cowden Syndrome: report of a case and brief review of literature. An Bras Dermatol. 2013;88(6 Suppl 1):52–5.

114

Point Of Care Ultrasound (POCUS) in Tracheostomy in Head and Neck Cancer : A Prospective Study.

Siddhartha Basuroy[1], Kaberi Kakati[1], Sonai Datta Kakati[2], Anupam Das[1], Deeksha Sharma[1], Tashnin Rahman[1], Ashok Kumar Das[1], Raj Jyoti Das[1], Kishore Das[1]

[1]Dr Bhubaneswar Borooah Cancer Institute, Head and Neck Oncology, Guwahati, India. [2]Dr Bhubaneswar Borooah Cancer Institute, Anesthesiology and Critical Care, Guwahati, India

Topic

Innovative treatments

Keywords

Tracheostomy, head and neck cancers, ultrasound

Purpose/Objective

In a high volume, tertiary care oncology centre in India, tracheostomy is a relatively common emergency procedure that is done to relieve airway obstruction.[1] However, in presence of bulky neck nodes, deviated trachea, post radiation fibrosis, lymphedema and inability to position the patient adequately; it may lead to difficulty in palpating and localizing the trachea.[2] Furthermore, disease related factors like subglottic extension and extra laryngeal extension may distort the airway anatomy , and may complicate tracheostomy tube insertion.

Purpose:

1.To study the role of Point Of Care Ultrasound (POCUS) in head and neck cancer patients undergoing tracheostomy.

Objectives:

1. To study the role of POCUS in localising the trachea in head and neck cancer patients undergoing tracheostomy.

2. To study the role of POCUS in localising the level of tracheotomy in head and neck cancer patients undergoing tracheostomy.

Material/Methods

The study was conducted as a prospective cross sectional study for diagnostic accuracy in the Department of Head and Neck Oncology in Dr B Borooah Cancer Institute, Guwahati, India. It was conducted over 8 months from March 2023 to September 2023. All patients, above 18 years of age, undergoing tracheostomy due to upper airway obstruction or bleeding due to head and neck malignancy were included in the study. Patients undergoing elective tracheostomy as a part of a major surgical procedure, like free flap, large tongue defects; or for prolonged intubation were excluded from the study. In addition, hemodynamically unstable patients in severe respiratory distress/stridor due to head and neck malignancies were excluded as POCUS is still in an experimental phase for upper airway evaluation.

A focused ultrasound of the neck was performed by same two surgeons, who have received training for airway ultrasound; and was supervised by a critical care physician. The limits of examination included hyoid to suprasternal notch vertically. The POCUS focused on the following parameters:

1. Location of the trachea and midline
2. Estimating the thickness of any abnormal soft tissue overlying the trachea (from skin to anterior surface of trachea)
3. Estimating the level of tracheostomy or tracheal cut, by localising any subglottic disease with tracheal extension
4. Location of cricothyroid membrane
5. Identifying any tracheal luminal narrowing or compression
6. Identification of any abnormal vessels The time taken for the assessment, and complications following or during the tracheostomy was recorded and compared with intraoperative findings and CT findings using appropriate tests of statistical significance. Tracheostomies were further classified into primary and revision tracheostomies; and post irradiation status of the neck.

Results

Out of the 65 tracheostomies, landmarks were clearly identifiable in 34 studies. Difficult tracheostomy groups were identified as:

1. Anterior neck mass >4 cm with inability to palpate trachea underneath (4)
2. Post irradiated neck with fibrosis with inability to palpate the trachea/ inadequate neck extension (22)
3. Bulky nodal disease reaching midline, with or without tracheal deviation/luminal compromise (7)
4. Abnormal large vessels reaching midline (1)
5. Tracheal extension of disease with or without luminal compromise (2)

Overlapping features were also noted across these 5 groups.

In patients with identifiable landmarks, there was no statistically significant difference in the outcome of successful tube insertion with or without POCUS (p=0.94). Sensitivity of POCUS to localise the trachea in post irradiated neck was 100%. In patients with anterior neck mass, POCUS identified the point of least dissection to reach the tracheal wall in all 4 patients. Similarly, POCUS identified the position of trachea and site of tracheotomy in 6 out of 7 patients (85.71%) with bulky nodal disease.

Tracheotomy level could be guided by POCUS in two scenarios:

1. To identify the ring below the tracheal extension
2. To select candidates for high tracheostomy if any gross extralaryngeal extension was identified (possible candidate for total laryngectomy). A total of 12 cases were revision tracheostomies. POCUS aided tracheostomy identified the trachea in all cases even in presence of granulations and fibrosis. The sensitivity to correctly identify the level of tracheotomy was 91.67%

Conclusion

POCUS can be immensely useful in head and neck cancer patients presenting in a “cannot intubate, cannot oxygenate” situation, with distorted neck anatomy. This is a fairly commonly encountered situation in the Indian subcontinent. POCUS can aid in difficult anticipated tracheostomy in localizing the trachea and planning of the surgery.

References

1. Chen, K., Varon, J., & Wenker, O. C. (1998). Malignant Airway Obstruction: Recognition and Management. The Journal of Emergency Medicine, 16(1), 83–92. doi:10.1016/s0736-4679(97)00245-x.

2.Hathiram, Bachi & Rai, Reema & Watve, Parag & Khattar, Vicky. (2010). Tracheostomy in Head and Neck Cancers. Otorhinolaryngology Clinics An International Journal. 2. 53-60.10.5005/jp-journals-10003-1017.

115

Gross tumor volume as a predictor of treatment outcomes in pediatric and adolescent nasopharangeal cancers treated with chemoradiotherapy

Amit Bahl[1], Naresh K Panda[2], Jaimanti Bakshi[2], Oinam A Singh[1]

[1]PGIMER, Radiotherapy & Oncology, Chandigarh, India. [2]PGIMER, Otorhinolaryngology, Chandigarh, India

Topic

Multidisciplinary management

Keywords

carcinoma, nasopharynx, radiotherapy, pediatric

Purpose/Objective

Gross tumor volume (GTV) as a predictive factor for treatment outcomes has been explored in adult head & neck cancer pateints. However the same has not been established in paediatric & adolescent nasopharangeal cancers. The aim of this analysis was to explore impact of GTV on recurrances in patients less than 19 years of age

Material/Methods

Data from 30 patients with age less than 19 years treated between 2015 to 2018 was retrospectively evaluated. For radiotherapy planning a high risk Planning Treatment Volume PTV 70 was prescribed a

dose of 70Gy/33 fractions at 2.12 Gy per fraction.An intermediate risk PTV 59.4 was prescribed 59.4 Gy/33 fractions at 1.8Gy per fraction.Concurrent chemotherapy was administered with injection Cisplatin 100 mg/m2 D1 delivered three weekly.Neoadjuvant or adjuvant chemotherapy was given using Injection Paclitaxel 175mg/m2 D1 and Cisplatin 75mg/m2 D1 repeated every 3 weekly for 2-3 cycles. The outcomes evaluated included disease recurrences & disease free survival . A p value <0.05 was considered significant

Results

Patients evaluated in this analysis had age ranging from 10-19 years (mean 15.77±2.73 years, mean ± SD). Majority of patients had stage IV (70 %, n=21) disease and 9 patients (30%) presented with stage III disease.

At 3 years of follow up recurrences were seen in 46.7% (14) patients. The average time to recurrence from diagnosis was 12.14±7.38 months (mean ± SD) with a range of 6-33 months. Distant metastasis, both locoregional and distant recurrence and nodal recurrence alone were seen in 30%(9), 10% (3) and 6.7% (2) of patients. Two of the treated patients failed in the nasopharynx. Distant metastasis to bone was most common. Lung, liver and brain were other sites of distant metastatic disease. Recurrence were seen in 3 (10%) patients presenting with stage III and 11(36.7%) with stage IV disease.

On univariate analysis only the Gross tumor volume (GTV) volume and lymph node size emerged as a significant prognostic factor for recurrences. Patients with recurrences had a mean GTV volume of 121.25±51.83cc (mean±SD) compared to 73.41±49.50cc (p=0.02, fishers exact test) in those without recurrence (Figure 1). Of the 14 patients with recurrence 85.7% (n=12) had a lymph node size with axial diameter of more than 4 cm at presentation. A poor disease-free survival(DFS) of 33.20±9.79 months (median ± SE) compared to 40 ± 4.58 months (p=0.006, log rank) was seen with those having a lymph node greater than 4 cm in size. On multivariate analysis only the GTV volume was statistically significant (p<0.03) for recurrences.

SIB prescription was used in 14 (46.67%) patients. A median DFS of 77 months versus 35±10.56 months was seen with SIB compared to Non SIB (p=0.18, log rank). Recurrences were seen in 6 (20%) and 8 (26.7%) patients treated with SIB and Non SIB VMAT(p=0.73). Adaptive radiotherapy was required in 11(36.7%) patients. For recurrent disease two patients underwent neck dissection followed by chemotherapy. Palliative chemotherapy and 8 Gy single fraction palliative radiotherapy for bony metastasis were other treatment modalities used to manage recurrent disease.

At last follow up complete response, stable disease and progressive disease was seen in 16 (53.3%), 1(3.3%), 9(30%) patients. Four patients (13.3%) were dead at time of analysis. Among these one patient died due to intussusception unrelated to disease, another one due to preexisting aplastic anemia. Two patients had disease related mortality.

Radiotherapy was well tolerated with Grade 3 mucositis, dermatitis and dysphagia seen in 16.1%, 6.5% and 3.2% of patients. Grade 2 dysgeusia and xerostomia was seen in 67.7% and 48.4% patients. Grade 1trismus (9.7%) was the only significant late toxicity was observed in this analysis. Doublet chemotherapy using Injection Paclitaxel and Cisplatin was not associated with any febrile neutropenia episodes and was well tolerated by patients.A median disease-free survival of 40±4.5 months (median± SE) and an overall survival of 78 % was observed at 4 year follow up.

Conclusion

Gross tumor volume and maximum axial lymph node size more than 4 cm showed significant association with recurrences in pediatric and adolescent nasopharyngeal cancer patients treated with radiotherapy and chemotherapy. Distant metastasis was the predominant cause of treatment failure.

116

Efficacy of nivolumab versus pembrolizumab in rmHNSCC. A prospective national multicenter study.

Sebastian Søby[1], Anita Gothelf[2], Niels Gyldenkerne[3], Jens Bentzen[4], Maria Andersen[5], Trine Tramm[6], Jesper Grau Eriksen[1]

[1]Aarhus University Hospital, Dept. of Experimental Clinical Oncology, Aarhus, Denmark. [2]Copenhagen University Hospital, Dept. of Oncology, Copenhagen, Denmark. [3]Odense University Hospital, Dept. of Oncology, Odense, Denmark. [4]Herlev Hospital, Dept. of Oncology, Copenhagen, Denmark. [5]Aalborg University Hospital, Dept. of Oncology, Aalborg, Denmark. [6]Aarhus University Hospital, Dept. of Pathology, Aarhus, Denmark

Topic

Immuno-oncology

Keywords

PD-L1, rmHNSCC, national

Purpose/Objective

The PD-1 inhibitor, nivolumab, was introduced to Danish PD-L1 positive patients as second-line treatment for recurrent/metastatic head and neck squamous cell carcinoma (rmHNSCC) in 2017. In 2020 pembrolizumab was introduced as first-line treatment for PD-L1 positive disease. Aim of the present study was to determine the real-life efficacy of single drug treatment with pembrolizumab compared to nivolumab.

Material/Methods

Patients were eligible if they were treated between 2017 and end of 2022, had histologically confirmed PD-L1 positive rmHNSCC, and had received either pembrolizumab or nivolumab. Patient, tumor and treatment related data were collected prospectively from patient files at the five Danish head and neck cancer centers and from the DAHANCA database. iRECIST was used for treatment response evaluation, and PD-L1 expression was determined using tumor proportion score (TPS) for nivolumab and combined proportion score (CPS) for pembrolizumab according to international recommendations.

Only patients treated with single agent PD-1 inhibition were eligible for the present study.

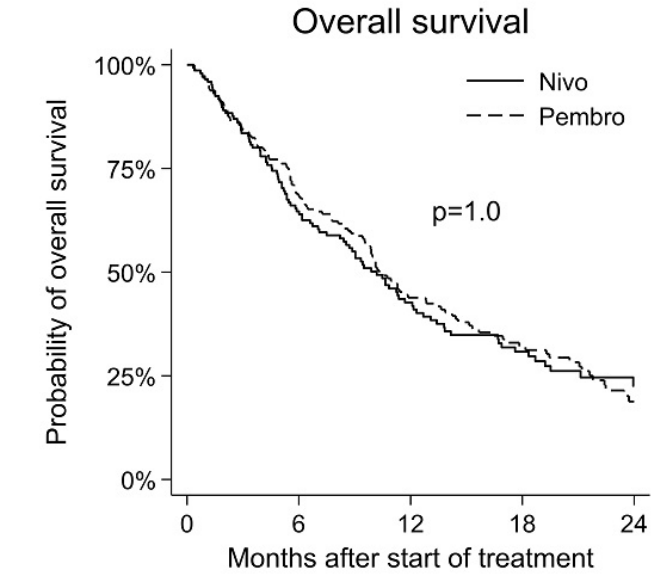
Descriptive statistics were used to describe patient, tumor and treatment. Endpoints were response rate (RR), overall survival (OS) and progression-free survival (PFS), calculated from start of treatment to date of event or censoring. Survival was estimated by the Kaplan-Meier method. Analyses were two-sided and $p<0.05$ were considered significant.

Results

In total 375 patients were identified out of which 229 (61%) received pembrolizumab and 146 (39%) nivolumab. At baseline, the median age was 68 years for pembrolizumab and 63 years for nivolumab ($p<0.001$). The two groups did not differ significantly in terms of gender with 74% being male and 26% female or in terms of type of recurrence, where metastatic disease was present in 74% of patients while

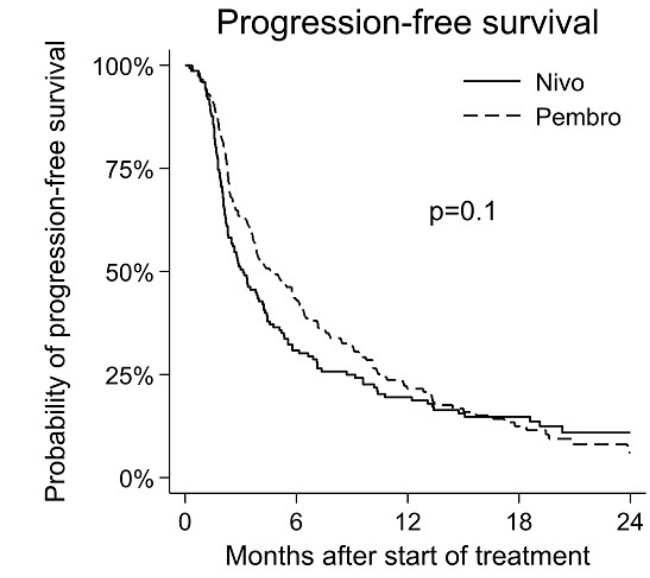
the remaining 26% had locally advanced cancers. The median number of treatment cycles administered was 5 (range: 1-54) for nivolumab and 5 (range: 1-31) for pembrolizumab.

In patients treated with pembrolizumab, 2% [95% CI: 1-6%] experienced complete remission and 19% [95% CI: 14-26%] had partial response. In the nivolumab group 7% [95% CI: 4-13%] achieved complete remission and 9% [95% CI: 5-15%] had partial response.
A median OS of 10 months [95% CI: 10-13 Mo.] and a median PFS of 5 months [95% CI: 4-6 Mo.] was observed for pembrolizumab. For nivolumab median OS was 10 months [95% CI: 9-12 Mo.] and median PFS 3 months [95% CI: 3-4 Mo.]. No significant difference in efficacy was observed between the two PD-1 inhibitors using OS or PFS as endpoints (figure 1+2).



Number at risk

Nivo 146	91	50	29	11
Pembro 229	129	65	36	14



Number at risk

Nivo 146	44	25	16	5
Pembro 229	80	30	13	3

WHO performance status (PS) showed an impact on treatment outcome. In the pembrolizumab group, patients with WHO PS=1 had a significant worse outcome (compared to WHO PS=0), HR=1.8 [95% CI: 1.1-3.0] (p=0.01), using OS as endpoint and HR=3.4 [95% CI: 2.0-5.9] (p<0.001) for patients with WHO PS≥2 (compared to WHO PS=0). Using PFS as endpoint, the WHO PS=1 group did worse compared to the WHO PS=0 group, HR=1.6 [95% CI: 1.1-2.4] (p=0.03) while HR=1.7 [95% CI: 1.1-2.7] (p=0.03) was observed for patients with WHO PS≤2 (compared to WHO PS=0).

In the nivolumab group, patients with WHO PS=1 had a significant worse outcome (compared to WHO PS=0), HR=2.9 [95% CI: 1.6-5.2] (p=0.001) using OS as endpoint and HR=10.1 [95% CI: 4.8-21.5] (p<0.001) for WHO PS≤2 (compared to WHO PS=0). For the endpoint PFS patients with WHO PS=1 had a HR=2.3 [95% CI: 1.4-3.7] (p=0.001) while HR=5.3 [95% CI: 2.7-10.4] (p<0.001) for WHO PS≤2 (both endpoints compared to WHO PS=0).

PD-L1 expression did not overall seem to bear any impact on treatment outcome. For patients with TPS ≥ 20% or CPS ≥ 20, HR=0.9 [95% CI: 0.6-1.2] (p=0.4) and HR=0.8 [0.6-1.1] (p=0.2) was obtained for the endpoints OS and PFS respectively. For patients treated with nivolumab using OS as endpoint HR=1.0 [95% CI: 1.0-1.0] (p=0.4) was seen, whereas PD-L1 expression ≥ 20% using PFS as endpoint showed a reduced risk of progression, HR=0.6 [95% CI: 0.4-0.8] (p=0.003).

Conclusion

Overall, this national phase IV multicenter study comparing pembrolizumab with nivolumab showed no significant difference in efficacy in terms of either OS or PFS despite one of the drugs being used as first line therapy and the other as second line therapy. The study suggest that PD-1 inhibitors can have a relevant place as either first- or second-line treatment, and that patient performance affects outcome of the treatment.

117

Classifying of patterns of locoregional failure using radiotherapy dose fields in head-and-neck cancer: Cambridge VoxTox Study

Ceilidh Welsh[1], Karl Harrison[2], Alfred J W Beard[3], Nick Early[4], Andrew Hoole[4], Amy Bates[5], Richard Benson[6], Sarah Jefferies[6], Raj Jena[6], Gillian C Barnett[6]

[1]University of Cambridge, Department of Oncology, Cambridge, United Kingdom. [2]University of Cambridge, Department of Physics, Cambridge, United Kingdom. [3]Cambridge University Hospitals, School of Clinical Medicine, Cambridge, United Kingdom. [4]Cambridge University Hospitals NHS Foundation Trust, Department of Medical Physics, Cambridge, United Kingdom. [5]Cambridge University Hospitals NHS Foundation Trust, Cambridge Clinical Trials Unit, Cambridge, United Kingdom. [6]Cambridge University Hospitals NHS Foundation Trust, Department of Oncology, Cambridge, United Kingdom

Topic

Imaging, radiomics and artificial intelligence

Keywords

registration, spatial mapping, recurrence

Purpose/Objective

Locoregional recurrence (LRR) represents a significant burden in cancer-related deaths, impacting 15-50% of patients treated for head-and-neck cancer (HNC) [1]. Accurately classifying the location of, and the dose delivered to, the failure site is a crucial step towards understanding the causes of LRR. The aim of this study is to classify and analyse patterns of loco-regional failure after radiotherapy treatment, for HNC patients, in the Cambridge VoxTox study. This classification methodology builds upon previous work done by Mohamed et al [2] by incorporating the radiotherapy dose-field, instead of CTV volumes, as the primary basis for investigating patterns of locoregional failure.

Material/Methods

Eighteen patients with evidence of local and/or locoregional failure following image-guided intensity-modulated radiotherapy (IMRT) for HNC were identified. Three patients were excluded from the analysis due to incomplete data. The relapse gross tumour volume (rGTV) and clinical target volumes (CTVs) were manually delineated on each patient's relapse diagnostic CT (rCT) by radiation oncologists. The thyroid cartilage (TC) was delineated by experienced HNC clinicians as a comparative organ at risk (OAR) on both the planning CT (pCT) and relapse diagnostic CT (rCT). The pCT was co-registered with the rCT using deformable image registration (DIR) to obtain the transform for spatial mapping between the two CT scans. The accuracy of the DIR for each patient was quantified using the target registration error (TRE) of the centroid of the thyroid cartilage (TC). The final cohort TRE was calculated as the absolute distance between centroid of TC on the pCT and centroid of TC mapped from the rCT to the pCT, averaged across all LRR patients included in the analysis. The clinically prescribed dose to the high-risk region (CTV1), intermediate-risk region (CTV2) and low-risk region (CTV3) was obtained from the patient's radiotherapy plan. A dosimetric structure set was then created by delineating structures that encapsulate regions receiving 95% of the dose clinically prescribed to these high-risk, intermediate-risk and low-risk CTVs. The rGTV was then spatially mapped onto the pCT and compared with each of the 95% dose structures using centroid and volume-based criteria. The failure was then classified into one of five categories, dependent on these criteria: A (central high dose), B (peripheral high dose), C (central elective dose), D (peripheral elective dose), and E (extraneous dose) [2]. Clinical patient variables were used to search for associations between treatment type and LRR classifications.

Results

In total, 15 recurrences were identified and classified using DIR methods. The cohort DIR TRE was evaluated as 4.5 mm. Of the 15 LRR, 9 were identified as Type A (central high dose), 1 as Type B (peripheral high dose), 1 as Type C (central elective dose), and 4 as Type E (extraneous dose). Among the 9 high-risk Type A failures, 8 received 65 Gy in 30 fractions with bilateral neck irradiation, and 1 received post-operative doses of 60 Gy in 30 with unilateral neck. The most common Type A primary site was oropharynx (67%). All Type E patients had primary surgery to the primary tumour volume; none underwent bilateral neck irradiation. Three Type E patients received post-operative doses (60 Gy in 30) to oral cavity or salivary gland, and one received a comorbidity-adjusted protocol of 50 Gy in 20. Oral cavity was the primary site for 75% of Type E patients. In previous work by Mohamed et al [2], no type E patients were classified, as patients who received adjuvant RT following definitive surgery were excluded from the analysis.

Conclusion

The majority of HNC LRRs in the VoxTox study originate within the high-dose volumes (Type A), with the majority receiving a maximal treatment dose of 65 Gy in 30 fractions. Type A, high-dose, classifications are suggestive of radiobiological resistance to treatment dose. Patients recurring in the extraneous dose regions (Type E), all received primary surgery with unilateral or no neck irradiation. The VoxTox study is a small dataset and presents a preliminary exploration of LRR classifications. However,

exploration in large datasets is crucial for investigating relationships between LRR failure patterns and clinical variables. As a result, work on a larger local validation dataset from Cambridge University Hospitals is ongoing.

References

[1] Rwigema JC, Heron DE, Ferris RL, Andrade RS, Gibson MK, Yang Y, et al. The impact of tumor volume and radiotherapy dose on outcome in previously irradiated recurrent squamous cell carcinoma of the head and neck treated with stereotactic body radiation therapy. Am J Clin Oncol. 2011;34(4):372–9. https://doi.org/10.1097/COC.0b013e3181e84dc0.

[2] Mohamed AS, Rosenthal DI, Awan MJ, Garden AS, Kocak-Uzel E, Belal AM, El-Gowily AG, Phan J, Beadle BM, Gunn GB, Fuller CD. Methodology for analysis and reporting patterns of failure in the Era of IMRT: head and neck cancer applications. Radiat Oncol. 2016 Jul 26;11(1):95. doi: 10.1186/s13014-016-0678-7. PMID: 27460585; PMCID: PMC4962405.

119

Survival Analysis of Localized Subglottic Squamous Cell Carcinoma: Therapeutic Options and Outcomes

Sakhr Alshwayyat[1], Tala Abdulsalam Alshwayyat[1], Mohammad Zubi[1], Mustafa Alshwayyat[1], Mohammad Al Kharabsheh[2]

[1]Jordan University of Science and Technology, School of Medicine, Irbid, Jordan. [2]Al- Balqa' Applied University, School of Medicine, Amman, Jordan

Topic

Quality of life and outcomes

Keywords

Squamous Cell Carcinoma,Prognosis,Survival Rate

Purpose/Objective

Primary subglottic Squamous Cell Carcinoma (SCC) is a rare malignancy that accounts for only 1–3% of all laryngeal carcinomas. The selection of therapeutic approaches depends on disease stage and clinical presentation. There are multiple therapeutic options for SCC, including chemotherapy (CTX) and adjuvant radiotherapy (ART). Owing to its rarity, there is no consensus on the best option for improving survival rates. We aimed to explore survival outcomes in terms of overall survival (OS) and cancer-specific survival (CSS) among patients diagnosed with localized SCC who underwent various treatment modalities.

Material/Methods

Data from 2000 to 2019 were obtained from the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) database. Patients who met any of the following criteria were excluded: diagnosis not confirmed by histology, not first tumor or other malignancies in the body, not localized stage or metastasis, and unknown data. Chi-square tests were used to compare clinicopathological

features, while survival rates and prognostic factors were identified using the Kaplan-Meier estimator, log-rank tests, and Cox proportional hazard regression.

Results

The study population comprised 476 patients. Among them 70 patients with “Surgery,” 101 patients with “CTX,” 89 patients with “Surgery + ART”, 22 with “Surgery + ART + CTX” and 194 “None.” Most patients (68.9%) were 60 years or older, with a median age of 62 years. The largest racial group was white (82.6%; n=328). A total of 79% of the patients had a tumor size greater than 2 cm, followed by 14.1% for 1-2 cm and 6.9% for less than 1 cm. The median tumor size was 2 cm. “Surgery + ART” had the most favorable survival outcome with a 5-year OS of 67.2%, followed by “Surgery” (54.5%), “Surgery + ART + CTX” (93%), “CTX” (51.2%) and then “None” with (46.4%). In terms of CSS, “Surgery + ART” had the most favorable survival outcome with a 5-year CSS of 55.5%, followed by “Surgery + ART + CTX” (55.4%), “CTX” (55.4%) and then “None” with (51.9%) and then “Surgery” (44.3%). Significant differences were found in OS but not CSS between the groups (P<0.0003 and P<0.56, respectively). Older age was a poor prognostic factor for the OS and CSS. White race was a good prognostic factor in OS only. Multivariable analysis confirmed that there is statistically significant difference between the effect of all therapeutic groups on OS, “Surgery + ART” (HR=0.46, 95%CI:0.3-0.7). However, there was no statistical difference in CSS (HR=0.8, 95%CI:0.57-1.4).

Conclusion

The results of this study showed that “Surgery + ART” had the most favorable effect on OS and CSS in SCC patients. Multicenter, prospective studies are required to validate and build upon these findings. However, our results provide a starting point for better understanding of these rare cancers.

120

Efficacy and Safety of Salvage Chemotherapy After Progression to Anti-PD(L)1 Agents in Patients with Recurrent/Metastatic Head and Neck Cancer

Santiago Cabezas-Camarero[1,2], Salomé Merino-Menéndez[3], María Nieves Cabrera-Martín[4], Miguel J. Sotelo[5,6,7], Pedro Pérez-Segura[1,2]

[1]Hospital Clínico Universitario San Carlos, Medical Oncology, Madrid, Spain. [2]IDISSC, IDISCC, Madrid, Spain. [3]Hospital Clínico Universitario San Carlos, Radiology, Madrid, Spain. [4]Hospital Clínico Universitario San Carlos, Nuclear Medicine, Madrid, Spain. [5]Hospital María Auxiliadora, Medical Oncology, Lima, Peru. [6]Clínica San Felipe, Medical Oncology, Lima, Peru. [7]Aliada Cancer Center, Medical Oncology, Lima, Peru

Topic

Immuno-oncology

Keywords

post-immunotherapy treatments, cetuximab

Purpose/Objective

Squamous cell carcinoma of the head and neck (SCCHN) has no defined standard of systemic treatment following rapid or symptomatic progression to PD1/PDL1 axis inhibitors. The exploratory analysis of PFS2 in the Keynote-048 study and several retrospective series suggest that immunotherapy (IO) results in better performance of subsequent treatments. Our objective was to analyze the efficacy and safety of salvage chemotherapy after progression to immunotherapy (SCAI) in patients with SCCHN in the recurrent/metastatic (R/M) setting.

Material/Methods

Retrospective study at Hospital Clinico Universitario San Carlos, including all patients with SCCHN treated with SCAI. Objective response rate (ORR), percentage change from baseline in target lesion size (PCBTL), progression-free survival (PFS), and overall survival (OS) since the start of SCAI, since 1st line and depending on the line of IO, were evaluated, as well as safety during SCAI.

Results

Between September 2017 and April 2023, 49 patients treated with SCAI were identified. M/F: 35/14. Age: 68 (48-97). Oral cavity/Oropharynx/Hypopharynx/Larynx/CUP: 8/28/4/6/3. Anti-PD1/Anti-PDL1: 36/13. IO 1st line/2nd line/3rd line: 31/15/3. SCAI (ERBITAX/CARBITAX/Cetuximab/wkCDDP-Cetuximab/EXTREME/TPEX/3wkCDDP-Docetaxel): 39/3/2/2/1/1/2. Total population efficacy (n=40): ORR=46% (CR=5, RP=14) and PCTLD= -34% (-100% to +44%). After 9 m of follow-up, the PFS and OS since the start of SCAI were 6 and 12 months, respectively, and after 21 m of follow-up since the start of 1st line, OS was 24 months. Efficacy of the population treated with ERBITAX (n=30): ORR=48%. After 9 m of follow-up, PFS=6 m and OS=12 m, with no differences in PFS (P=0.574) and OS (P=0.959) since SCAI, between patients treated with IO in 1st vs 2nd line. Toxicity (n=49): G1 (100%), G2 (32.7%), G3 (59.2%), G4 (6.1%).

Conclusion

SCAI achieves ORR and median OS superior to historical records from the pre-IO era, with a similar safety profile. Prospective studies should be carried out to clarify the role of SCAI in R/M SCCHN and help define the best therapeutic sequence in the IO era.

References

Harrington K, et al. Pembrolizumab With or Without Chemotherapy in Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma: Updated Results of the Phase III KEYNOTE-048 Study. J Clin Oncol 2022; 41:790-802.

123

Can machine-learning model predict overall survival in head and neck cancer patients?

Maria Angeles Gonzalez Ruiz, Amadeo Wals Zurita

Radiation Oncology Department, Virgen Macarena University Hospital, Seville, Spain

Topic

Imaging, radiomics and artificial intelligence

Keywords

machine-learning; head and neck cancer.

Purpose/Objective

To be able through a machine learning model, to predict overall survival in patients with head and neck cancer treated with curative intent in our centre between July 2018 and December 2022. Patients were treated with radiotherapy +/- chemotherapy with curative intent or surgery plus adjuvant radiotherapy.

Material/Methods

A machine learning model (Classification and Regression Trees (CRT)) and a deep learning model (Multilayer Perceptron (MLP)) were used to predict overall survival based on some clinical characteristics as well as dosimetric characteristics of our radiotherapy treatment.

404 patients with head and neck cancer (HANC) of different sublocations (extracted from a real-world database build with variables generated through the MOSAIQ (Elekta) corporate system of the Andalusian Health System) were used. Status alive or dead in October 2023 was known in all of them.

Those who received a dose equal to or greater than 50 Gy to CTV_BED or CTV_T were finally selected to transformation (n= 342 patients).

They were randomly into a training cohort (n=236) and a test cohort (n=106) according to a 7:3 ratio. The variables were selected after an exploratory Factor Analysis: Principal Component Analysis (PCA) and were analyzed and transformed (standardization and obtaining z values) to improve sample quality.

The receiver operating characteristic curve (ROC), Kaplan Meier curve and C-index were used to display the capability to prediction of the constructed models.

Results

Twenty clinical and dosimetric characteristics were evaluated and transformed for exploratory PCA analysis. Those with multicollinearity problems were excluded. Finally, they were selected: status, tumor sublocation, morphology, total prescribed dose, mean dose at PTV, PTV volume, fractions, total treatment time and theoretical total treatment time.

The MLP stratified survival model into high versus low risk with an area under the curve (AUC) for the training and test dataset of 0.72 and 0.74. C-index (Phi and V. de Cramer) was 0.65.

In CRT model the AUC was 0.75 and 0.77and C-index was 0.70.

With a median follow-up of 36 months, patients with high-risk because of the variables predicted by MLP have a poor overall survival than patients with low-risk (60% vs 80%; p = 0.075).

Conclusion

Machine and deep learning approaches could provide reliable outcome predictions in patients with HANC after RT. These prediction results could asses to clinical decision with intensification treatments in some patients but more information in this field is needed.

124

Impact of Therapeutic Options on Survival Rates in Localized Supraglottic Squamous Cell Carcinoma

Sakhr Alshwayyat, Tala Abdulsalam Alshwayyat, Maen Suliman Soudi, Zaina Monther AbuMelhim, Mustafa Alshwayyat

Jordan University of Science and Technology, School of Medicine, Irbid, Jordan

Topic

Quality of life and outcomes

Keywords

Squamous Cell Carcinoma,Survival Rate,Larynx Tumor

Purpose/Objective

Due to the rarity of supraglottic squamous cell carcinoma and its relatively poor outcomes, there is a consensus treatment strategy. Additionally, treatment trends over time have focused on organ-preservation therapy rather than on improving survival rates. Our goal was to determine whether there were any significant differences in overall survival (OS) and cancer-specific survival (CSS) among the therapeutic options for localized SCC using a large sample.

Material/Methods

Data between 2000 and 2019 were obtained from the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) database. Patients with a diagnosis not confirmed by histology, not the first tumor or other malignancies in the body, not localized stage or with metastasis, and unknown data were excluded. Chi-square tests were used to compare clinicopathological features, while the Kaplan-Meier estimator, log-rank tests, and Cox proportional hazard regression were used to identify survival rates and prognostic factors.

Results

6110 patients were included in the study. Among them, 855 patients underwent 'Surgery,' 1420 patients received 'CTX' (chemotherapy), 32 had 'Surgery + CTX,' 635 patients underwent 'Surgery + ART' (adjuvant radiation therapy), 224 had 'Surgery + ART + CTX,' and 2944 received 'None.' Most patients (61.2%) were

60 years or older, with a median age of 63 years. The largest racial group was white (84.3%; n=5150). A total of 76.7% of the patients had a tumor size of 1-2 cm, followed by 17.4% for tumors > 2 cm, and 6.0% for tumors measuring < 1 cm. The median tumor size was 1.8 cm. 'Surgery' had the most favorable survival outcome with a 5-year OS of 66.1%, followed by 'Surgery + ART + CTX' (62%), 'Surgery + ART' (58%), 'None' with (48.4%), 'CTX' (47.9%), and then 'Surgery + CTX' with (36.4%). In terms of CSS, 'Surgery + ART' had the most favorable survival outcome with a 5-year CSS of 92.8%, followed by 'Surgery + CTX' (90.6%), 'Surgery + ART + CTX' (89%), 'CTX' (88%), 'Surgery' (87.1%), and then 'None' with (85.9%). Significant differences were found in OS and CSS between the therapeutic groups (P<0.0001) for both OS and CSS. Older age, male sex, 1-2 cm tumor size, > 2 cm tumor size, and 'Surgery + CTX' were poor prognostic factors for OS. Older age and tumor size of > 2 cm were poor prognostic factors for CSS. However, 1-2 a tumor size was a good prognostic factor for CSS. Multivariable analysis confirmed a statistically significant difference between the effects of all therapeutic groups on OS and CSS. Table1

Treatment Group	OS Hazard Ratio	OS 95% CI	CSS Hazard Ratio	CSS 95% CI
Surgery	0.64	0.57 - 0.72	0.82	0.57 - 0.89
Surgery + ART	0.68	0.61 - 0.77	0.75	0.67 - 0.83
Surgery + ART + CTX	0.81	0.68 - 0.96	0.80	0.68 - 0.94

Conclusion

Our study showed significant variations in the survival outcomes among patients with supraglottic SCC. Therefore, this underscores the need for personalized treatment strategies for patients with supraglottic SCC and encourages further research to validate and expand upon these results for improved outcomes in this rare cancer.

125

The Impact of Joint Radiologist Input in Head and Neck Radiotherapy Peer Review on MDT's TNM Classification and Outcome

Thalia Afxentiou[1], Ashitha Ashraf[1], Shagun Juneja[1], Kanchana Rajaguru[2], Subhadip Ghoshray[3], Kevin Chiu[1]

[1]Mount Vernon Cancer Centre, Clinical oncology, London, United Kingdom. [2]East and North Hertfordshire Hospital, Radiology, Stevenage, United Kingdom. [3]Paul Strickland Scanner Centre, Radiology, London, United Kingdom

Topic

Multidisciplinary management

Keywords

Peer Review, Radiotherapy Quality Assurance, MDT

Purpose/Objective

Accurate TNM classification and staging in head and neck cancer is an important part in prognostication, and in determining the extent of radiotherapy target volume delineation [1]. As

standard of care locally, the TNM classification is performed in 2 regional supra-multidisciplinary team (MDT) meetings, prior to referral centrally for oncological treatment.

Peer review quality assurance of radiotherapy volumes is a widely accepted and recommended practice. As a tertiary cancer centre, there is routine radiologist input in the departmental peer review of head and neck radiotherapy volumes [2]. The aim of this study was to evaluate the recommended treatment changes, and potential differences between the final peer review's TNM classification and of the MDTs'.

Material/Methods

All head and neck intensity modulated radiotherapy (IMRT) cases discussed in the weekly peer review meeting between May and mid-October 2023 were prospectively evaluated. A standard data collection proforma based on UK Royal College of Radiologists (RCR) recommendations was used [3]. Any radiological/clinical progression of disease (PD) since the diagnostic radiology, final TNM staging, in addition to the RCR defined 'major' or 'minor' changes to the clinical target volumes (CTVs), were prospectively recorded.

Results

A total of 109 patients were included, of which there were 77 (71%) definitive (chemo)IMRT, 30 (28%) post-operative radiation (PORT) and 2 complex palliative IMRT (2%). Across all three cohorts, there were 34 (32%) HPV-mediated oropharynx, 21 (19%) Larynx, 18 (17%) Oral cavity, 10 (9%) Hypopharynx, 7 (6%) Nasopharynx, 6 5.5%) Cutaneous carcinoma, 4 (4%) Major salivary gland, 3 (3%) p16-negative Oropharynx, 3 (3%) Nasal cavity/Paranasal sinuses, and 3 (3%) unknown primary cases. There was a median of 2 consultant oncologists (range 1–4), and one radiologist (range 0 – 3) at each meeting.

In the definitive and palliative IMRT cohorts, excluding 7 patients who had received induction chemotherapy (6 Nasopharynx, 1 Nasal cavity), 16 out of 72 patients (22%) were found to have PD on their IMRT-CT simulation since their diagnostic radiology. With the final peer review TNM classification, a total of 15 (21%) patients were found to have been upstaged (Table 1). Of note, only 7 patients with PD (47%) were upstaged, while other 8 patients (11% of total) were upstaged from the original MDTs' classification despite lack of PD. The peer review upstaging led to 3 key changes in treatment plan, with 2 patients subsequently recommended for primary surgery instead, and 1 patient for additional concomitant chemotherapy. The median time from original diagnostic radiology to the MDT, and from diagnostics to IMRT-CT simulation, was 22 and 38 days respectively. For the PORT cohort, there were 3 (10%) discrepancies between the peer-review and the MDT recorded pathological (pTNM) classification: 2 patients were upstaged and 1 was down-staged.

Diagnosis	MDT TNM	MDT Stage	Peer review TNM	Peer Review Stage	Treatment change
HPV Mediated Oropharynx	T2N1M0	I	T4N1M0	III	
HPV Mediated Oropharynx	T2N1M0	I	T2N2M0	III	Contralateral neck irradiation
HPV Mediated Oropharynx	T2N0M0	I	T2N1M0	I	Concomitant chemotherapy, no upstage
HPV Mediated Oropharynx	T2N1M0	I	T4N1M0	III	
HPV Mediated Oropharynx	T2N1M0	I	T3N1M0	II	

Larynx	T1N0M0	I	T2N0M0	II	
Larynx	T1N0M0	I	T2N0M0	II	
HPV Mediated Oropharynx	T3N1M0	II	T3N2M0	III	More contralateral neck irradiation
HPV Mediated Oropharynx	T3N2M0	II	T4N2M0	III	
Hypopharynx	T2N1M0	II	T3N2bM0	IVa	
Nasopharynx	T2N0M0	II	T3N0M0	III	
Hypopharynx	T3N0M0	III	T4aN0M0	IVa	Primary surgery, with proven pT4a
Larynx	T3N1M0	III	T4aN2bM0	IVa	Primary surgery, with proven pT4a
Larynx	T1N1M0	III	T1N2cM0	IVa	More neck irradiation
Oral Cavity	T3N0M0	III	T3N2cM0	IVa	More neck irradiation
Oropharynx (p16-)	T3N1M0	III	T3N2bM0	IVa	More neck irradiation

Table 1: The extent of TNM upstage and changes

For the IMRT volume quality assurance, the peer review recommended changes to 66 out of the 109 (61%) patients; 47 out of 77 (61%) definitive IMRT, 18 out of 30 (60%) PORT, and 1 out of 2 (50%) palliative patients. In the definitive IMRT cohort, 36 (77%) patients underwent IMRT volume changes deemed to be 'major', while 11 patients (23%) as 'minor'. A total of 44 changes were made to the individual CTVs: 22 (50%) to the primary CTV (CTVp), and 22 (50%) to the nodal CTV (CTVn). For the PORT cohort, 9 (50%) patients underwent 'major' changes and 9 (50%) had 'minor' changes. There were 10 changes made to the individual PORT CTVp, and 9 to the CTVn.

Conclusion

Radiotherapy peer review with radiologist input is valuable in identifying gross error. Routine radiologist input may provide an additional layer of quality assurance to the MDT's TNM staging classification, and the subsequent recommended clinical management.

References

[1] Grégoire V, Evans M, Le Q T, Bourhis J, Budach V, Chen A, Eisbruch A, Feng M, Giralt J, Gupta T, Hamoir M, Helito J K, Hu C, Hunter K, Johansen J, Kaanders J, Laskar S G, Lee A, Maingon P, Mäkitie A, Micciche F, Nicolai P, O'Sullivan B, Poitevin A, Porceddu S, Składowski K, Tribius S, Waldron J, Wee J, Yao M, Yom S S, Zimmermann F and Grau C 2018 Delineation of the primary tumour Clinical Target Volumes (CTV-P) in laryngeal, hypopharyngeal, oropharyngeal and oral cavity squamous cell carcinoma: AIRO, CACA, DAHANCA, EORTC, GEORCC, GORTEC, HKNPCSG, HNCIG, IAG-KHT, LPRHHT, NCIC CTG, NCRI, NRG Oncolog Radiother. Oncol. 126 3–24

[2] Chiu K, Hoskin P, Gupta A, Butt R, Terparia S, Codd L, Tsang Y, Bhudia J, Killen H, Kane C, Ghoshray S, Lemon C and Megias D 2021 The quantitative impact of joint peer review with a specialist radiologist in head and neck cancer radiotherapy planning Br. J. Radiol. 20211219

[3] The Royal College of Radiologists 2017 Radiotherapy target volume definition and peer review RCR guidance Clin. Oncol. d 11

126

Prevalence of depression among patients with Head and Neck cancer

Cyrine Mokrani, Khadija Ben Zid, Najla Attia, Alia Mousli, Nesrine Kooli, Rim Abidi, Chiraz Nasr

Salah Azaiz Institute, Radiotherapy, Tunis, Tunisia

Topic

Quality of life and outcomes

Keywords

Depression, Quality of life, Head and Neck cancer

Purpose/Objective

Depression in oncology is considered to be a reactive response to cancer. However, its impact on patient's healthcare journey and quality of life is far from negligible (1). The prevalence of depression among head and neck cancer (HNC) patients is increasing over time but It's detection among them is underestimated (2). We aimed to investigate the prevalence and the factors associated with depression in HNC patients.

Material/Methods

A questionnaire survey of 30 patients with head and neck cancer undergoing treatment at the Salah Azaiz Institute in Tunisia, Using an Arabic version of < The Hospital Anxiety and Depression Scale (HADS) >. This scale detects anxiety and depression with a score of 19 or more.

Results

In our study, the majority of the population was aged over 50 (73%). Seven females were being treated among 27 males. Most patients had no family psychiatric history (74%). Only five patients had a personal psychiatric condition. The main treatment involved a combination of surgery, radiotherapy and chemotherapy (53%) followed by chemotherapy alone in 9 patients (30%). Being unmarried or living alone is associated with depression ($p<0.05$). Most patients were not admitted (54%). Depression was detected in 8 patients, 7 of whom were admitted ($p=0.06$). Patients who were hospitalized presented more depressive symptoms ($p=0.02$). No correlation was found between personal psychiatric history and depression. None of the patients had received a psychological consultation since the announcement of the diagnosis, and they were all unaware of psychologist's availability at the institute. The entire population reports family support. A high HADS score was associated with a less favorable clinical response to treatment in the entire population ($p<0.01$).

Conclusion

Screening for depression among head and neck cancer patients can be quick and easy. The aim is to target patients who are likely to benefit from psychological support.

References

(1) Prevalence of depression in cancer patients: a meta-analysis of diagnostic interviews and self-report instruments A. M. H. Krebber, L. M. Buffart, G. Kleijn, I. C. Riepma, R. de Bree, C. R. Leemans, A. Becker, J. Brug, A. van Straten, P. Cuijpers, I. M. Verdonck-de Leeuw

(2) Factors associated with depression over time in head and neck cancer patients: A systematic review Laura H.A. Korsten, Femke Jansen, Ben J.F. de Haan, Danielle Sent, Pim Cuijpers, C. René Leemans, Irma M. Verdonck-de Leeuw

127

THE INFLUENCE OF TREATMENT PACKAGE TIME IN THE OUTCOMES OF PATIENTS WITH HIGH-RISK ORAL CAVITY CARCINOMA RECEIVING ADJUVANT RADIATION AND CONCURRENT SYSTEMIC THERAPY: A SINGLE CENTER EXPERIENCE

Pedro Ferreira[1], Eduardo Netto[1], Susana Esteves[2], Sara Magno[3], Raul Colaço[1], Filomena Santos[1]

[1]Lisbon Institute of Oncology, Radiation Oncology, Lisbon, Portugal. [2]Lisbon Institute of Oncology, Clinical Research, Lisbon, Portugal. [3]Lisbon Institute of Oncology, Medical Oncology, Lisbon, Portugal

Topic

Multidisciplinary management

Keywords

Oral cavity, Treatment Package Time, Adjuvant

Purpose/Objective

To document and report the treatment package time (TPT) in high-risk oral cavity squamous cell carcinoma (OCSCC) receiving adjuvant treatment with concomitant chemoradiotherapy (CRT) as a quality performance indicator.

Material/Methods

We selected patients who underwent surgery followed by adjuvant CRT between 2017 and 2020 from the internal radiotherapy database. All patients were in the high-risk group characterized by extranodal extension (ENE) and/or positive surgical margin (PM). TPT comprised the number of days between surgery and the last radiotherapy session. Kaplan-Meier curves and multivariate analysis (MVA) were used to determine the impact of TPT on overall survival (OS) and disease-free survival (DFS).

Results

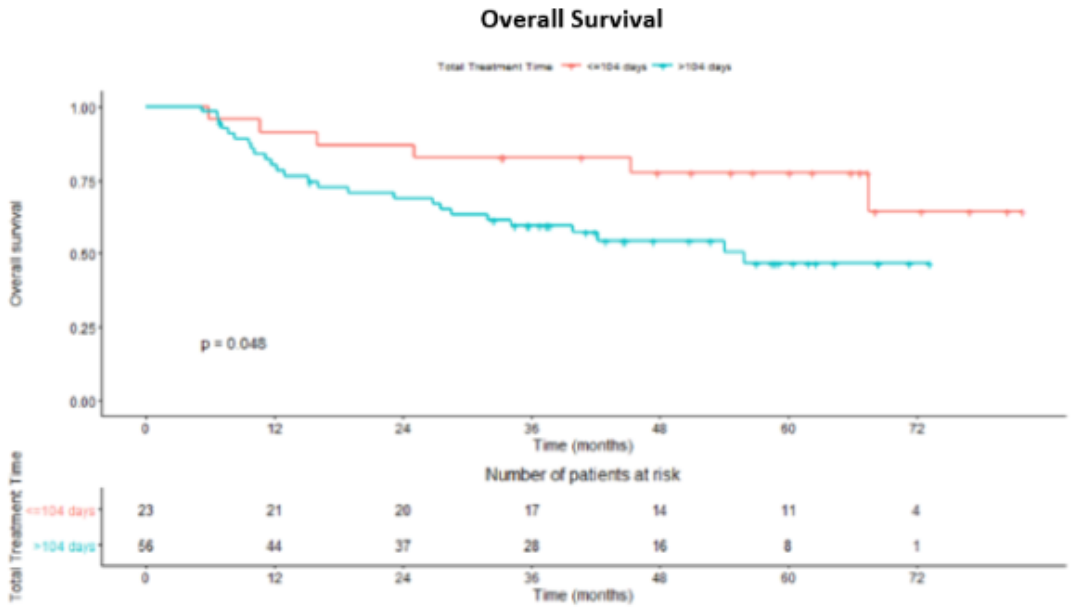
A total of 79 patients were included with a median age of 60 years (range: 39–70 years), a majority of male patients (84.8%, n=67) and heavy smokers (73.4%, n=58). The most frequent primary tumor locations were oral tongue (35.4%, n=28), gum/buccal mucosa (29.1%, n=23) and floor of the mouth (27.8%, n=22). ENE and PM were detected in 51.9% (n=41) and 84.8% (n=67) of cases, respectively. Median radiotherapy dose was 66Gy. Median cisplatin concomitant dose was 300mg/m^2. Median TPT was 109 days (85–159).

Characteristic	N = 79 N (%)
Median age in years (range)	60 (39-70)
Male	67 (84.8)
Heavy Smokers*	58 (73.4)
Heavy alcohol consumption**	46 (58.2)
PS ECOG 0-1	77 (97.5)
Hg <14.5g/dL in men and <13g/dL in women	35 (44.3)
Oral Cavity subsite	
Retromolar trigone	6 (7.6)
Oral tongue	28 (35.4)
Floor of mouth	22 (27.8)
Gum/Buccal mucosa	23 (29.1)
Performed staging PET-CT	3 (3.8)
Histological grade	
Grade 1-2	53 (67.1)
Grade 3	26 (32.9)
pT stage***	
1-2	19 (24.1)
3-4	60 (75.9)
pN stage***	
0-1	33 (41.8)
2	20 (25.3)
3	26 (32.9)
Disease stage***	
I-II	4 (5.1)
III	12 (15.2)
IVa	37 (46.8)
IVb	26 (32.9)
Median dissected LN (range)	42 (0-104)
Median positive LN (range)	2 (0-19)
Positive LN / dissected LN >7%	30 (38.0)
High-risk features	
Extra-Nodal Extension	41 (51.9)
Positive final surgical margin	67 (84.8)
Perineural invasion	36 (45.6)
Lympho-vascular invasion	35 (44.3)
Median time to start RT in days (range)	62 (41-115)
Median RT treatment duration in days(range)	45 (39-65)
Median TPT in days (range)	109 (85-159)
Median RT dose delivered in Gy (range)	66 (60-70)
Concomitant Cisplatin	69 (87.3)
Median cumulative dose of cisplatin in mg/m² (range)	300 (100-300)

*> 10 Median Smoking index (pack-years); **men: ≥5drinks/day, women ≥4drinks/day; ***(AJCC 8th)

Table 1 – Population characteristics of the study cohort

OS at 5-years in the TPT >104 days group was 77.4% (95%IC 61.8-97.1%) and in the TPT ≤104 days group was 46.7% (95%IC 33.5-65.0%). In a univariate analysis, the risk of death in the TPT >104 days was 2.4-times higher than in the TPT ≤104 days (IC95% 0,98-5,89; p=0,0547). In a MVA, OS was worse in the TPT >104-days group (n = 53) than in the TPT ≤104 days group (n =26) (HR 3.57; 95%CI 1.38-9.24; p-value=0.0088). T3/T4 disease (HR 3.67; 95%CI 1.37-9.83; p=0.0098) and a ratio of positive lymph nodes per nodes dissected (PLPND) >7% (HR 3.86; 95%CI 1.83-8.15; p=0.004) were associated with poorer OS. In a MVA stratified by T-stage (T1/T2 vs T3/T4), DFS was worse in the TPT >104-days group (HR 3.28; 95%CI 1.43-7.54; p-value=0.0051) and in the PLPND >7% (HR 2.62; 95%CI 1.34-5.12; p=0.0049). The main cause for a TPT >104 days was a delay in therapeutic decision, which occurred in 47.2% (n=25) of patients.



Conclusion

Our cohort of resected OCSSC followed by adjuvant concomitant chemoradiotherapy had a prolonged treatment package time (median 109 days). Advanced T-Stage, higher ratio of PLPND (>7%) and TPT were independently associated with decreased OS and DFS. Efforts must be done to optimize the multimodal cancer care pathway.

128

Impact of biological response-based adaptive radiotherapy on doses to swallowing OARS in modelled IMPT plans

Sarah Hargreaves[1,2], Owain Woodley[1], Jamil Lambert[3], Rhydian Maggs[1], Thomas Rackley[1], Mererid Evans[1,4]

[1]Velindre Cancer Center, Oncology, Cardiff, United Kingdom. [2]Bristol Cancer Institute, Oncology, Bristol, United Kingdom. [3]Rutherford Cancer Centre, Physics, Newport, United Kingdom. [4]Cardiff University, Division of Cancer and Genetics, School of Medicine, Cardiff, United Kingdom

Topic

HPV or EBV related cancers

Keywords

Adaptive radiotherapy, proton beam therapy

Purpose/Objective

The PEARL study is a phase 2 multi-centre trial for good prognosis HPV-associated oropharyngeal squamous cell carcinoma (OPSCC) patients, currently open in the UK. PEARL is investigating the dosimetric impact of re-planning a radical radiotherapy plan midway through a course of treatment,

based upon the biological response of the primary GTV on 18 FDG PET-CT. With the wider availability of proton beam therapy in the form of Intensity Modulated Proton Therapy (IMPT) as a potential option for radiotherapy in the management of OPSCC, in addition to substantial cost implications, improving methods to determine the patients who will benefit most from IMPT is required. The organ sparing benefits of IMPT are well documented. This modelling planning study investigated whether the benefits of proton therapy can be improved by applying biological response-based adaptation as per the PEARL study planning method.

Objectives:

1. Investigate the dosimetric impact of IMPT by comparing mean dose received by swallowing OARs (SWOARs) between non-adaptive VMAT and non-adapted IMPT plans
2. Investigate the dosimetric impact of adaptation by comparing dose received by SWOARs between non-adaptive IMPT and adapted IMPT plans
3. Investigate the relative dosimetric impact of adaptation by comparing dose received by SWOARs between adaptive VMAT and IMPT plans
4. Identify whether adaptation as per the PEARL Study protocol would influence the delta normal tissue complication probability (ΔNTCP) threshold for proton beam therapy funding in The Netherlands

Material/Methods

Anonymized patient datasets were used to model VMAT and IMPT plans using RayStation and optimised for SWOARs.

The following plans were generated:

1. 'NON-ADAPTIVE': Manually planned non-adapted VMAT
2. 'ADAPTIVE': Manually planned adapted VMAT
3. 'NON-ADAPTIVE_PROTON': Manually planned non-adapted IMPT
4. 'ADAPTIVE_PROTON': Manually planned adapted IMPT

NTCP calculations for dysphagia risk we performed using the validated dysphagia model described by Christianen et al (1). Individual calculations were performed on each case comparing adapted and non-adapted VMAT plans to non-adapted IMPT plans to explore whether they reached the threshold for proton beam treatment funding as per The Netherlands scheme. Mean dose to the superior pharyngeal constrictor muscle and the supraglottis was entered into the following calculation:

$1/\mathrm{NTCP} = (1+e)^{-s}$

where s = -6.09 + (mean dose to the superior pharyngeal constrictor muscle x 0.057) + (mean dose to the supraglottis x 0.037)

Results

All cases had a reduction in their total mean dose to SWOARs, adapted as per PEARL, and planned with IMPT. The magnitude of impact was ranked in the same order for all cases, with optimisation reducing the total mean dose the least, and adapted IMPT the most. Cases 1 and 2, and Cases 3 and 4, demonstrated similar total mean dose reductions despite having different degrees of biological GTV reduction on the iPET-CT. Adaptation had the greatest impact on Cases 2 and 3 for both VMAT and IMPT plans.

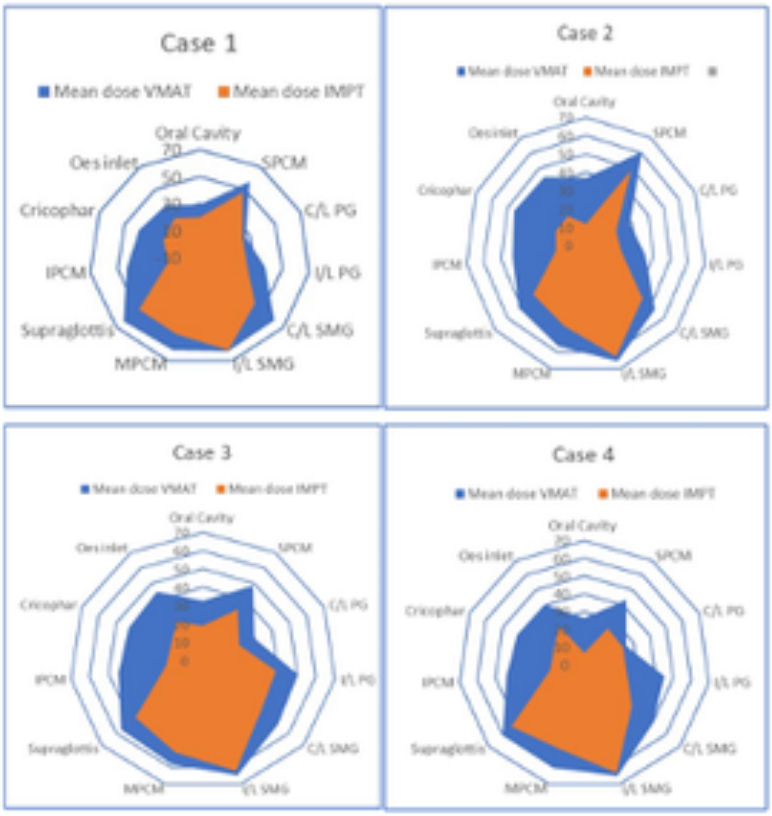


Fig. 1 Radar diagrams for Cases 1 – 4 in the style of Tambas et al (2) demonstrating the difference in mean dose to OARs in modelled non-adaptive VMAT and IMPT plans

The NTCP differences between non-adaptive VMAT plans and non-adaptive IMPT plans were >10% suggesting these cases would be candidates for IMPT funding as as per the National Indication Protocol Proton therapy (NIPP) - head and neck cancer criteria in The Netherlands.

Conclusion

Whilst primarily limited by the small number of cases, we have demonstrated that IMPT markedly reduces doses to SWOARs compared to VMAT planning in line with widely published studies. We have also demonstrated that adaptation based on the biological response to the tumour after 2 weeks of chemoradiotherapy can further improve the tissue sparing already achieved with IMPT. This is the first study to demonstrate that SWOAR sparing by IMPT can be improved with biological response guided adaptive radiotherapy.

Our results are in line with published data that IMPT can spare many head and neck SWOARs to a greater extent than VMAT in the treatment of oropharyngeal cancers. In the cases studied here, the impact of IMPT on the mean dose to SWOARs was greater than the impact of adaptation, when compared to standard VMAT planning. However, there may be additional dosimetric benefit when IMPT is adapted to tumour response during a course of radiotherapy treatment, particularly dose to more caudal SWOARs.

In this small cohort, adaptation on VMAT plans was unlikely to have affected a decision for IMPT treatment as per the Netherlands NTCP-based algorithm.

Further work with a larger cohort of patients, as well as real-time studies to collect prospective clinical data on xerostomia and dysphagia rates, is required to properly investigate the clinical advantages of adaptive IMPT.

References

1. Christianen ME, van der Schaaf A, van der Laan HP, Verdonck-de Leeuw IM, Doornaert P, Chouvalova O, Steenbakkers RJ, Leemans CR, Oosting SF, van der Laan BF, Roodenburg JL, Slotman BJ, Bijl HP, Langendijk JA. Swallowing sparing intensity modulated radiotherapy (SW-IMRT) in head and neck cancer: Clinical validation according to the model-based approach. Radiotherapy and Oncology. 2016 Feb; 118(2): 298 - 303

2. Tambas M, Steenbakkers RJHM, van der Laan HP, WOlters AM, Kierkels RGJ, Scandurra D, Korevaar EW, Oldehinkel E, van Zon-Meijer TWH, Both S, van den Hoek JGM, Langendijk JA. First experience with model-based selection of head and neck patients for proton therapy. Radiotherapy and Oncology 2020 Oct: 151; 206-213

129

Regional Experience of Cemiplimab, in Locally advanced and stage IV Head and Neck Cutaneous Squamous Cell Carcinomas

Anthi Zeniou[1], Jennifer Turner[2], Rahul Misra[1], Andriana Michaelidou[1], Kannon Nathan[2]

[1]Maidstone and Tunbridge Wells NHS Trust, Kent Oncology Centre, Maidstone, United Kingdom. [2]Kent and Canterbury NHS Trust, Kent Oncology Centre, Canterbury, United Kingdom

Topic

Management of elderly or frail patients

Keywords

Cemiplimab, Cutaneous Squamous Cell Carcinoma

Purpose/Objective

Cemiplimab has been approved for use in England for locally advanced, unresectable and metastatic cutaneous SCC (Squamous Cell Carcinoma). These cancers are usually morbid, have a detrimental impact on patient and carer quality of life and affect older adults, with limited treatment options. The aim of this study is to present a real world experience of the use, toxicity profile, and response rates of Cemiplimab.

Material/Methods

In this retrospective review, we present our regional experience of Cemiplimab (350 mg IV 3 weekly) in locally advanced and metastatic SCC, arising in the head and neck area. The electronic records of all patients who were exposed to at least one cycle of Cemiplimab were reviewed. Data was collected including comorbidities (ACE-27), performance status, and toxicity as well as response rates and overall survival.

Results

Our patient cohort includes 29 patients, treated between September 2019 and July 2023. Median Age was 76.5 years and 25 of the patients were male with 4 female patients. The median ACE-27 score was 2. All patients had a performance status of 0 or 1.

The majority of patients had locally advanced disease 86% (25/29). Of our patient cohort, 83% (24/29) patients had undergone primary surgery following diagnosis of head and neck cutaneous SCC, with 54% (13/24) patients receiving adjuvant radiotherapy following surgery with doses of either 55Gy in 20# over 4 weeks or 60-66Gy in 30-33# over 6 to 6.5 weeks. Of the patients who failed following surgery and/or adjuvant radiotherapy, the mode of failure was locoregional in 79% (19/24). Median Time to failure from primary diagnosis was 6 months.

Of the five patients who did not undergo surgery at diagnosis, 2 had locally advanced disease and 3 had metastatic disease. 3 of these 5 patients had palliative radiotherapy (20Gy/5#) after starting Cemiplimab and 1 of these patients received 20Gy/5# before starting Cemiplimab.

When patients commenced Cemiplimab, response was assessed either clinically, via CT, PET-CT and/ or MRI. The median number of cycles of Cemiplimab delivered was 7. The commonest side effects reported were fatigue (6 out of 29, 21%) and development of a new rash (5 out of 29, 17%). Only 3 of the 29 (10%) patients developed Grade 3 toxicity. All three patients discontinued treatment, one had developed hepatitis, the second patient developed pyoderma gangrenosum and it was unclear whether this was a direct toxicity from Cemiplimab, the 3rd patient developed colitis. All three required steroids and only 1 required hospitalisation. There were no toxicity associated deaths. Of the 3 patients who developed grade 3 toxicity, 2 have died of other causes and one is alive and disease free.

The median time to the first radiological response assessment was 9.9 weeks. The response rate to treatment at first response assessment was 69% (20/29) and overall response rate at the end of the study period was 52% (15/29). Of the 3 patients who had complete response at first assessment this was maintained through the study period, and of the 17 patients who had a partial response at first assessment, 6 patients went on to develop complete response. All 9 patients who achieved complete response were able to maintain this throughout the study period.

At the end of the study period median follow up was 7 months (0 to 37 months), with 12 patients still alive, 8 of whom have a complete response to treatment and 4 of whom have a partial response to treatment. Of the 29 patients in this study, 17 patients have died. 12 of disease progression and 5 of other causes. Median overall survival was 12 months.

We note that our study population was overwhelmingly male, however in terms of demographics and toxicity profile was reflective of the populations presented in clinical trials. The small sample size reflects the difficult clinical decision making involved in managing this heterogenous group of patients.

It is interesting that out of our patients who have achieved a complete response to treatment with Cemiplimab, none have progressed during the course of this study.

Conclusion

Cemiplimab offers a safe and effective treatment option to locally advanced unresectable or metastatic cutaneous SCCs of head and neck primary origin, which overwhelmingly affect older adults. Our review highlights the importance of careful case selection. An interesting question is whether patients who achieve complete response to treatment, require a full 2 years of Cemiplimab immunotherapy.

References

1. Migden, MR et al. PD-1 Blockade with Cemiplimab in Advanced Cutaneous Squamous-Cell Carcinoma. N Engl J Med 2018; 379:341-351. DOI: 10.1056/NEJMoa1805131

2. Migden, MR et al. Cemiplimab in locally advanced cutaneous squamous cell carcinoma: results from an open-label, phase 2, single-arm trial. Lancet Oncol. 2020 Feb;21(2):294-305. doi: 10.1016/S1470-2045(19)30728-4.

3. Baggi A, et al. Real world data of cemiplimab in locally advanced and metastatic cutaneous squamous cell carcinoma. Eur J Cancer. 2021 Nov:157:250-258. doi: 10.1016/j.ejca.2021.08.018.

130

head and neck rhabdomyosarcoma; clinicopathological features, trends, and role of adjuvant therapy.

Amr Aly

Faculty of medicines Suez Canal university, Pathology, Ismailia, Egypt

Topic

Quality of life and outcomes

Keywords

Rhabdomyosarcoma, adjuvant therapy, Trend analysis

Purpose/Objective

Rhabdomyosarcoma is an aggressive tumor that arises from the muscles and carries poor prognosis. Although it is the most common head and neck sarcoma, it is considered rare. This scarcity has led to a lack of information about its features. Therefore, we aim to assess its clinicopathological features and trends as well as define the role of adjuvant therapy.

Material/Methods

We identified 618 patients with head and neck rhabdomyosarcoma from the Surveillance, Epidemiological, and End Results (SEER) database diagnosed from 2000-2020. We analyzed Age-Adjusted Trends and incidence rates. Rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130) standard; Confidence intervals are 95% for rates (Tiwari mod) and trends. Percent change was calculated using 1 year for each end point; APC was calculated using weighted least squares method. Kaplan-Meier curve and Log rank test were done using SPSS 25 to perform survival analysis. Cox regression hazard model was also calculated to identify predictors for outcome.

Results

The incidence rate of Head and Neck Rhabdomyosarcoma was 4%. Age-adjusted trend analysis showed a percent change (PC) of 18.9 and an annual percent change (APC) of 0.06 (95% CI: -1.12 to 1.25). Age

group under 20 years showed the highest incidence rate of 5.5% however, it showed a decrease in its incidence rate compared in 2000 by 23% where it was 7.2%. Age groups 20-49 and 50+ showed slightly lower incidence rates of 4% but there has been a rise in their incidence of 54% and 91% respectively (2.6% and 2.1% in year 2000).

Males showed higher incidence rate; 5.6%, compared to females; 3.4% but both showed an increase in their incidence rates in year 2020 compared to year 2000; PC= 18% and 21% respectively. White race showed a 30% increase in its incidence rate from 2000 to 2020 to be 4.9% and Asian demonstrated only a 7% rise in its incidence to be 3.4%. For black, incidence rate decreased by 25% to be 4.2% in 2020 compared to 5.6% in 2000.

The 5-year relative survival was 46.1% ($P<0.05$). Surgery and radiotherapy showed to improve survival with hazard ratios (HR) of 0.73 and 0.74 respectively; $P<0.05$. Increasing age was associated with poorer outcomes; HR of 1.03; $P<0.05$. Sex, race, laterality and chemotherapy were not significant predictors for outcomes; $P>0.05$.

Conclusion

Head and neck rhabdomyosarcoma showed an incidence rate of 4%. Although it is considered a low incidence rate for a type of cancer, it is classified as a prevalent type compared to sarcomas which are considered rare tumors. There has been rising incident rates among all genders. For age group under 20, despite its declining incidence rates, it remains higher than other age groups. Other age groups are showing rising incidence rates. White and Asians are showing increasing rates while Black incidence rates are decreasing. Rhabdomyosarcoma are increasing in incidence rates among most of the population and so we recommend the implementation screening methods.

Head and neck rhabdomyosarcoma also showed poor survival outcomes. Patients who undergone surgery or had radiotherapy were 25% less likely to face poor outcomes so, we recommend them as treatment options of good prognostic value. Increasing age was associated with poorer prognosis. Sex, race, laterality and chemotherapy didn't affect prognosis. We can avoid the unfavorable side effects of chemotherapy as it wasn't found to impact outcome.

131

Proton arc therapy: advantages over conventional proton therapy and impact on range uncertainties

Sebastian Tattenberg[1,2,3], Peilin Liu[4], Anthony Mulhem[4,5], Xiaoda Cong[4], Christopher Thome[1,2], Xuanfeng Ding[6]

[1]Laurentian University, School of Natural Sciences, Sudbury, Canada. [2]Northern Ontario School of Medicine University, Medical Sciences Division, Sudbury, Canada. [3]TRIUMF, Life Sciences Division, Vancouver, Canada. [4]William Beaumont University Hospital, Department of Radiation Oncology, Royal Oak, USA. [5]Department of Human Biology, Michigan State University, East Lansing, USA. [6]William Beaumont University Hospital, Department of Radiation Oncology, Royal Oak, Canada

Topic

Innovative treatments

Keywords

proton therapy, arc therapy, range uncertainty

Purpose/Objective

Proton therapy for cancer reduces the integral radiation dose to the patient compared to conventional photon treatments.[1] The number of proton therapy centers globally has been growing rapidly as a result, but uncertainties in the *in vivo* proton range remain a considerable hurdle.[2,3] A variety of different approaches to reduce proton range uncertainties are therefore currently being pursued.[4,5,6,7,8,9,10] The associated benefits have been quantified previously but depend on clinical practices, including the number of gantry angles from which the tumor is irradiated.[11,12,13,14] For conventional proton therapy techniques like intensity-modulated proton therapy (IMPT), the target is irradiated from only a few directions, but proton arc therapy (PAT), for which the target is irradiated from hundreds of angles, may see clinical implementation by the time considerable range uncertainty reductions are achieved.[15,16,17,18,19] It is therefore crucial to determine the impact of PAT implementation on the importance of range uncertainty reductions.

Material/Methods

Five head-and-neck cancer patients were randomly selected from The Radiotherapy Optimization Test Set (TROTS).[20] For each patient, four different radiotherapy treatment plans were created in Version 6.0 of RayStation (RaySearch Laboratories, Stockholm, Sweden): an IMPT and a PAT treatment plan assuming current clinical range uncertainties of 3.5% ($IMPT_{3.5\%}$ and $PAT_{3.5\%}$), and an IMPT and a PAT treatment plan assuming that range uncertainties can be reduced to 1% ($IMPT_{1\%}$ and $PAT_{1\%}$). Treatment plans were evaluated with respect to target coverage and organ-at-risk (OAR) doses as well as normal tissue complication probabilities (NTCPs) resulting from organ irradiation during radiotherapy delivery. NTCPs were determined for both parotid glands (endpoint: parotid gland flow < 25% compared to pre-treatment after one year (grade 4 xerostomia)) and the larynx (endpoint: grade ≥ 2 larynx edema).[21,22,23] In accordance with clinical practice, radiotherapy treatment planning assumed a patient setup uncertainty of 3 mm, and dose calculations applied a constant relative biological effectiveness (RBE) value of 1.1 to account for differences between proton and photon irradiation.[12]

Results

For all four types of treatment plans and all delineated organs, OAR doses are shown in Table 1. Values are given in the nominal delivery scenario (in which neither patient setup nor proton range errors occur) as well as in the worst-case scenario (in which errors in patient setup and/or the proton range do occur during treatment delivery) and constitute average values over all five patients. On average, implementation of PAT ($IMPT_{3.5\%}$-$PAT_{3.5\%}$) reduced NTCPs in the nominal and worst-case scenario by 2.51 percentage points (pp) and 3.96 pp, respectively. In comparison, reducing range uncertainties from 3.5% to 1% during continued use of IMPT ($IMPT_{3.5\%}$-$IMPT_{1\%}$) reduced evaluated NTCPs by 0.64 pp and 1.27 pp, respectively. Average benefits of range uncertainty reductions subsequently to PAT implementation ($PAT_{3.5\%}$- $PAT_{1\%}$) were 0.81 pp in the nominal and 1.78 pp in the worst-case scenario.

Table 1 Organ-at-risk doses for all four types of treatment plans averaged over all five patients. Nom and WC refer to the nominal and the worst-case delivery scenario, respectively. All values are in units of Gy(RBE) and concern the mean dose within the organ in question, with the exception of the brainstem and the spinal cord, for which the maximum value within the organ is given. SMG refers to the submandibular glands while other abbreviations indicate swallowing muscles.

Organ	$IMPT_{1\%}$		$IMPT_{3.5\%}$		$PAT_{1\%}$		$PAT_{3.5\%}$	
	Nom	**WC**	**Nom**	**WC**	**Nom**	**WC**	**Nom**	**WC**
Brainstem	23.9	27.4	25.3	29.2	25.8	30.8	25.6	29.7
Larynx	27.1	30.4	27.3	30.7	23.3	26.1	24.1	27.3
MCI	18.8	21.6	19.2	22.4	14.5	17.2	15.8	19.6
MCM	54.9	57.6	55.2	58.1	49.2	52.9	49.7	53.9
MCP	9.2	11.7	9.6	12.4	7.0	9.1	7.7	10.3
Oesophagus	5.8	8.1	5.9	8.2	4.0	5.7	4.6	6.5
Oral cavity	24.0	27.3	25.0	28.8	22.0	24.7	23.4	26.8
Parotid (L)	16.3	20.2	17.0	21.2	14.8	18.1	15.6	19.7
Parotid (R)	18.7	23.6	19.4	24.5	16.2	20.3	17.4	22.0
SCM	51.0	55.4	51.9	56.0	47.3	51.1	48.4	52.9
SMG (L)	47.5	52.0	48.5	53.1	44.7	48.8	46.2	50.8
SMG (R)	57.7	59.9	57.9	60.1	56.3	58.3	56.7	59.4
Spinal cord	43.9	46.2	45.1	47.6	37.3	39.4	34.3	38.5

Conclusion

The average clinical benefit of implementing PAT was approximately three times higher than the benefit of a 3.5% to 1% range uncertainty reduction during continued use of IMPT. Reducing range uncertainties provided a similar clinical benefit for PAT and IMPT. Range uncertainty reductions are therefore expected to remain beneficial even when achieved subsequently to or in tandem with PAT implementation.

References

1. R. R. Wilson, “Radiological use of fast protons,” Radiology, vol. 47, no. 5, pp. 487–491, Nov 1946.

2. “Particle therapy facilities in clinical operation (last update: (August 2023),” https://www.ptcog.site/index.php/facilities-in-operation-public, accessed: 2023-08-25.

3. H. Paganetti, “Range uncertainties in proton therapy and the role of Monte Carlo simulations,” Phys Med Biol, vol. 57, no. 11, pp. R99–R117, Jun 2012.

4. E. Baer, A. Lalonde, G. Royle, H.-M. Lu, and H. Bouchard, “The potential of dual-energy CT to reduce proton beam range uncertainties,” Med Phys, vol. 44, no. 6, pp. 2332–2344, Jun 2017.

5. N. Peters, P. Wohlfahrt, C. Hofmann, C. Moehler, S. Menkel, M. Tschiche, M. Kraus, E. Troost, W. Enghardt, and C. Richter, “Reduction of clinical safety margins in proton therapy enabled by the clinical implementation of dual-energy CT for direct stopping-power prediction,” Radiother Oncol, vol. 166, pp. 71–78, Jan 2022.

6. K. Parodi, H. Paganetti, H. Shih, S. Michaud, J. Loeffler, T. Delaney, N. Liebsch, J. Munzenrider, A. Fischman, A. Knopf, and T. Bortfeld, “Pa- tient study of in vivo verification of beam delivery and range, using positron emission tomography and computed tomography imaging after proton ther- apy,” Int J Radiat Oncol Biol Phys, vol. 68, no. 3, pp. 920–934, Jul 2007.

7. C.-H. Min, C. Kim, M.-Y. Youn, and J.-W. Kim, “Prompt gamma mea- surements for locating the dose falloff region in the proton therapy,” Appl Phys Lett, vol. 89, no. 18, Nov 2006.

8. J. M. Verburg and J. Seco, “Proton range verification through prompt gamma-ray spectroscopy,” Phys Med Biol, vol. 59, no. 23, pp. 7089–7106, Dec 2014.

9. J. Tada, Y. Hayakawa, K. Hosono, and T. Inada, “Time resolved properties of acoustic pulses generated in water and in soft tissue by pulsed proton beam irradiation–a possibility of doses distribution monitoring in proton radiation therapy,” Med Phys, vol. 18, no. 6, pp. 1100–1104, Nov-Dec 1991.

10. J. Schauer, H.-P. Wieser, Y. Huang, H. Ruser, J. Lascaud, M. Würl, A. Chmyrov, M. Vidal, J. Herault, V. Ntziachristos, W. Assmann, K. Par- odi, , and G. Dollinger, “Proton beam range verification by means of ionoa- coustic measurements at clinically relevant doses using a correlation-based evaluation,” Front Oncol, vol. 12, no. 925542, Nov 2022.

11. S. van de Water, I. van Dam, D. Schaart, A. Al-Mamgani, B. Heijmen, and M. Hoogeman, “The price of robustness; impact of worst-case optimization on organ-at-risk dose and complication probability in intensity-modulated proton therapy for oropharyngeal cancer patients,” Radiother Oncol, vol. 120, no. 1, pp. 56–62, Jul 2016.

12. D. Wagenaar, R. Kierkels, A. van der Schaaf, A. Meijers, D. Scandurra, N. Sijtsema, E. Korevaar, R. Steenbakkers, A. Knopf, J. Landendijk, and S. Both, “Head and neck IMPT probabilistic dose accumulation: Feasibility of a 2 mm setup uncertainty setting,” Radiother Oncol, vol. 154, pp. 45–52, Jan 2021.

13. S. Tattenberg, T. Madden, B. Gorissen, T. Bortfeld, K. Parodi, and J. Ver- burg, “Proton range uncertainty reduction benefits for skull base tumors in terms of normal tissue complication probability (NTCP) and healthy tissue doses,” Med Phys, vol. 48, no. 9, pp. 5356–5366, Sep 2021.

14. S. Tattenberg, T. Madden, T. Bortfeld, K. Parodi, and J. Verburg, “Range uncertainty reductions in proton therapy may lead to the feasibility of novel beam arrangements which improve organ-at-risk sparing,” Med Phys, vol. 49, no. 7, pp. 4693–4704, Jul 2022.

15. A. Moreno, S. Frank, A. Garden, D. Rosenthal, C. Fuller, G. Gunn, J. Reddy, W. Morrison, T. Williamson, E. Holliday, J. Phan, and P. Blanchard, “Intensity Modulated Proton Therapy (IMPT) – The Future of IMRT for Head and Neck Cancer,” Oral Oncol, vol. 88, pp. 66-74, Jan 2020.

16. X. Ding, X. Li, J. Zhang, P. Kabolizadeh, C. Stevens, and D. Yan, “Spot-Scanning Proton Arc (SPArc) Therapy: The First Robust and Delivery-Efficient Spot-Scanning Proton Arc Therapy,” Int J Radiat Oncol Biol Phys, vol. 96, no. 5, pp. 1107–1116, Dec 2016.

17. B. de Jong, C. Battinelli, J. Free, D. Wagenaar, E. Engwall, G. Janssens, J. Langendijk, E. Korevaar, and S. Both, “Spot scanning proton arc therapy reduces toxicity in oropharyngeal cancer patients,” Med Phys, vol. 50, no. 3, pp. 1305–1317, Mar 2023.

18. B. A. de Jong, E. W. Korevaar, A. Maring, C. I. Werkman, D. Scandurra, G. Janssens, S. Both, and J. A. Langendijk, “Proton arc therapy increases the benefit of proton therapy for oropharyngeal cancer patients in the model based clinic,” Radiother Oncol, vol. 184, p. 109670, Jul 2023.

19. X. Li, G. Liu, G. Janssens, O. De Wilde, V. Bossier, X. Lerot, A. Pouppez, D. Yan, C. Stevens, P. Kabolizadeh, and X. Ding, “The first prototype of spot-scanning proton arc treatment delivery,” Radiother Oncol, vol. 137, p. 130-136, Aug 2019.

20. S. Breedveld and B. Heijmen, “Data for TROTS – The Radiotherapy Optimisa- tion Test Set,” Data Brief, vol. 12, pp. 143–149, Apr 2017.

21. C. Burman, G. Kutcher, B. Emami, and M. Goitein, “Fitting of normal tissue tolerance data to an analytic function,” Int J Radiat Oncol Biol Phys, vol. 21, no. 1, pp. 123–135, May 1991

22. T. Dijkema, C. Raaijmakers, R. Haken, J. Roesink, P. Braam, A. Houwel- ing, M. Moerland, A. Eisbruch, and C. Terhaard, “Parotid gland function after radiotherapy: the combined michigan and utrecht experience,” Int J Radiat Oncol Biol Phys, vol. 78, no. 2, pp. 449–453, Oct 2010.

23. T. Rancati, M. Schwarz, A. Allen, F. Feng, A. Popovtzer, B. Mittal, and A. Eisbruch, “Radiation dose-volume effects in the larynx and pharynx,” Int J Radiat Oncol Biol Phys, vol. 76, no. 3S, pp. S64–S69, Mar 2010.

135

Induction TPF chemotherapy and its outcomes in head and neck cancer, a single centre experience

Aravapalli S Naidu[1], Nabeela Janmohamed[1], Kannon Nathan[2], Anthi Zeniou[2], Rahul Misra[2], Andriana Michaelidou[2], Jennifer Y Turner[2]

[1]East Kent Hospitals University NHS Foundation Trust, Kent Oncology Centre, Canterbury, United Kingdom. [2]Maidstone and Tunbridge Wells NHS Trust, Kent Oncology Centre, Maidstone, United Kingdom

Topic

Quality of life and outcomes

Keywords

TPF, real world, neo-adjuvant

Purpose/Objective

Platinum, Docetaxel and Fluorouracil (5FU) (TPF) chemotherapy is a well-established regime used in locally advanced head and neck cancer patients to downstage disease prior to definitive treatment with chemo-radiotherapy. It has been shown to improved overall survival but can be associated with significant toxicity.1,2 We wished to examine our own experience in a large regional speciality oncology centre to review the survival and toxicity in our local patient cohort.

Material/Methods

A retrospective case review was conducted of all patients with head and neck cancers treated with platinum, Docetaxel and Fluorouracil (5FU) between January 2017 and December 2021. Data was collected on disease free survival (DFS), overall survival (OS), toxicity and further treatments.

Results

Eighty-four patients were identified; 82.1% (n=69) male and 17.8% (n=15) female, with a median age of 57.5 years. Most patients had primary disease in the oropharynx 85.7% (n=72) and of these 76.4% (n=55) were p16 positive. Using TNM8 staging, 33% were stage 4 (n=28) and 42% stage 3 (n=35). The median number of cycles of TPF given was 3.

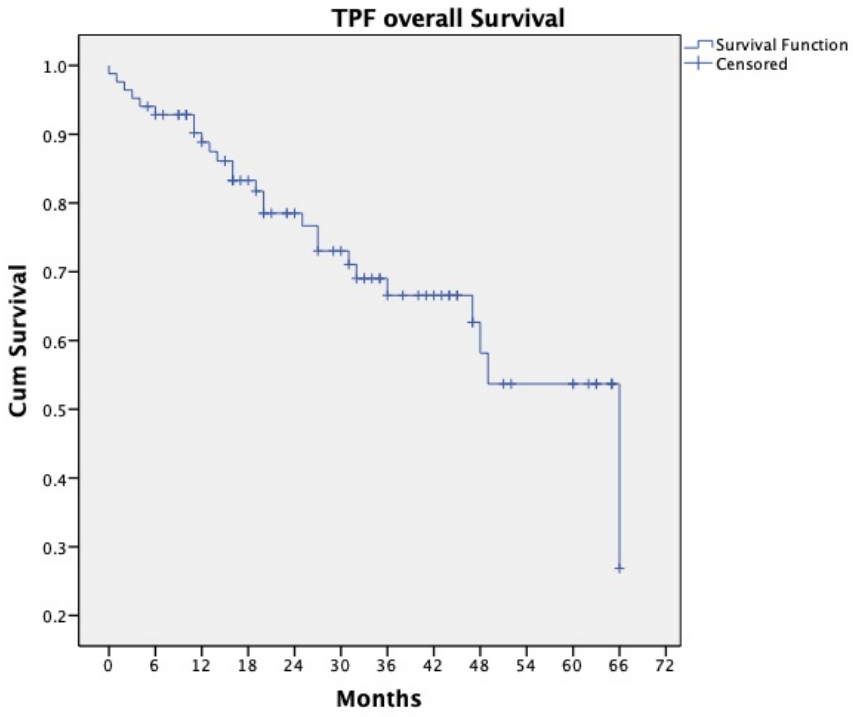
Seventy-nine patients (94%) experienced side effects with toxicity of any grade; however most toxicity was low grade and only 22% (n=19) of patents required dose reduction. The most common forms of toxicity were fatigue (74.7%), nausea (44.3%), and diarrhoea (38%). In this cohort, 27.4% (n=23) of patients needed inpatient admission. The most common reason for admission was neutropenia and sepsis. There were two TPF toxicity related deaths from sepsis in this cohort and one further patient died from non-chemotherapy or cancer related causes prior to proceeding to definitive radiotherapy.

Eight-one patients proceeded to definitive radiotherapy, 70Gy in 35# over 7 weeks. Fifty-six patients received concurrent cisplatin (n=28 weekly, n=28 3-weekly), 17 carboplatin (n=8 weekly, n=9 weekly dosing regimens respectively), three received radiotherapy without chemotherapy and five patients received a historical platinum/5 Fluorouracil regime, 2 cycles at weeks 1 and 4.

Out of 81 patients, 16 were scanned with PET-CT prior to radiotherapy; 11 of these patients showed complete metabolic response (CMR), four showed partial metabolic response (PMR) and one showed stable disease. End of treatment scans were completed in 79 patients; 79.7% (n=63) were in CMR, 10.1% (n=8) PMR, disease progression in 8.9%(n=7), and stable disease in 1.3% (n=1). Outcome was not available in two patients who were lost to follow up.

Median overall survival in the total cohort of patients is 66 months. Comparison by the concurrent chemotherapy regime received during radiotherapy showed no difference in overall or disease free survival. However it is worth noting, although the group receiving radiotherapy alone was small, the median overall survival was 19 months, (p=0.04).

Analysis of final outcomes showed that 67.8% (n=57) of patients are alive with no disease, 21.4% (n=18) died of head and neck cancer, 8.3% (n=7) died of other causes and 2.4% (n=2) died due to TPF toxicity. Overall median follow up was 26 months (range 1-68 months). The estimated overall survival at 3 years is 66.6% and at 5 years is 53.7%.



Conclusion

From this study we see that in a real-world scenario, TPF is an effective and achievable treatment choice in patients with locally advanced cancers of the head and neck. However careful selection of candidates for this regime must be considered in view of the associated mortality rate and to also allow for delivery of optimal definitive chemo-radiotherapy. In our cohort no TPF related deaths have been seen since 2018, which suggests an increased understanding amongst clinicians of suitability of patients for this regime and management of potential toxicities. The results obtained from our data are comparable to that of the results of the TAX324 study where estimates of overall survival were 63% at 3 years and 52% at 5 years.1,2 Therefore TPF is an important and valuable systemic regime in our arsenal of treatments for advanced head and neck cancer.

References

1) Posner, MR et al. Cisplatin and Fluorouracil Alone or with Docetaxel in Head and Neck Cancer. N Engl J Med 2007; 357:1705-15. DOI: 10.1056/NEJMoa07056

2) Lorch, JH et al. Long term results of TAX324, a randomized phase III trial of sequential therapy with TPF versus PF in locally advanced squamous cell cancer of the head and neck. Lancet Oncol 2011; 12 (2); 153-9. DOI 10.1016/S1470-2045(10)70279-5

138

Beyond Rigid Registration: The Role of Deformable Image Registration for Rescans and Replans in H&N Cancer Radiotherapy

Ciaran Malone[1], Samantha Ryan[2], Jill Nicholson[3], Fran Duane[3], Orla McArdle[3], Sinead Brennan[3], Elaine Tyner[1], Brendan McClean[1], Ruth Woods[2]

[1]SLRON, Physics, Dublin, Ireland. [2]SLRON, Radiation Therapy, Dublin, Ireland. [3]SLRON, Radiation Oncology, Dublin, Ireland

Topic

RTT

Keywords

Deformable registration, IGRT, Rigid Registration

Purpose/Objective

This study investigates whether spinal deviations exceeding 5mm from the planned position during Head & Neck cancer radiotherapy, detected using a rigid registration IGRT approach, warrant rescans or replans.

Material/Methods

Varian's Velocity™ software package was employed to perform Deformable Image Registration (DIR) on ten radical H&N cases which required re-scanning and re-planning when evaluated using a rigid

registration approach. The deformation field was used to generate Synthetic CT's (sCT) using Velocity to evaluate the dosimetric impact of the spinal deviations in Eclipse™.

Results

Our findings revealed that 6 out of the 10 plans (60%) exhibiting spinal deviations >5mm and evaluated using a rigid registration approach did not necessitate a replan or rescan, maintaining a dosimetric impact of <2% and adhering to institutional Dose Volume Constraint (DVC) tolerances. Conversely, only 4 of the 10 cases required a rescan and replan when deformation was utilised for evaluation.

Conclusion

Rigid registration cannot always account for the anatomical deviations in spinal positions noted during Head & Neck Radiothearpy. The substantial workflow implications of unnecessary rescans and replans accentuate the need for effective adaptive workflows like DIR in making informed decisions in Head & Neck radiotherapy.

139

Hypofractionated radiotherapy to the larynx is effective and well tolerated in T1 glottic larynx carcinoma

Love Goyal[1], Christopher Hughes[1], Kate Garcez[1], Lip Wai Lee[1], David Thomson[1,2], James Price[1,2]

[1]The Christie NHS Foundation Trust, Clinical Oncology, Manchester, United Kingdom. [2]The University of Manchester, Division of Cancer Sciences, Manchester, United Kingdom

Topic

Quality of life and outcomes

Keywords

hypofractionation, radiotherapy, larynx

Purpose/Objective

In the UK, hypofractionated radiotherapy (50 Gy in 16 fractions) to the larynx is an accepted standard for early cancer of the glottic larynx, but is only supported by Grade C evidence[1-2]. Alternative schedules (e.g., 63 Gy in 28 fractions) are supported by Grade B evidence, and may be advantageous from a late-toxicity perspective on account of a lower dose-per-fraction, but involve more visits to the department and may be less desirable from a patient experience perspective[3].

In this study, we assessed oncologic and toxicity outcomes for a contemporary cohort of patients treated over 16 fractions at a large UK tertiary cancer centre.

Material/Methods

A retrospective review of prospectively-collected data. Eligibility criteria: all patients who completed hypofractionated radiotherapy to the larynx for Tis /T1 N0 M0 squamous cell carcinoma of the glottis

at The Christie NHS Foundation Trust between 01/01/2016 and 31/08/2022. Relevant patient-, cancer- and treatment factors were collected.

A multivariable Cox proportional hazards (PH) model was fitted, with overall survival (OS) as the endpoint of interest. Multivariable logistic regression was used to explore variables associated with binary late toxicity outcomes. Competing risk regression, using the method of Fine and Gray, was used to assess local control (LC) as an alternative endpoint, with death as a competing event.

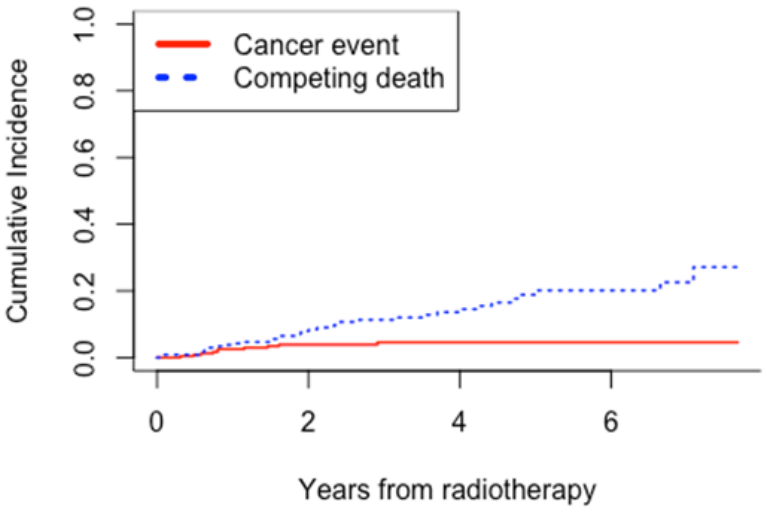
Results

236 patients met the eligibility criteria; patient characteristics are shown in the Table.

Characteristics	**N=236[1]**
Age (years)	70 (62, 77)
Sex	
Male	194 (82%)
Female	42 (18%)
ECOG performance status	
0	116 (49%)
1	81 (34%)
2	29 (12%)
3	10 (4.2%)
ACE-27 score	
0	89 (39%)
1	83 (37%)
2	36 (16%)
3	19 (8.4%)
Unknown	9
Weight (kg)	79 (69, 92)
Unknown	85
Smoking history	
Current smoker	71 (30%)
Ex-smoker	129 (55%)
Never / light former	33 (14%)
Unknown	3
Histological type	
SCC	189 (80%)
CIS	42 (18%)
Spindle	4 (1.7%)
Unknown	1
Tumour stage	
T1	193 (82%)
Tis	43 (18%)
Prescribed radiotherapy dose (Gy)	
50	196 (83%)
52.5	40 (17%)
[1]Median (IQR); n(%)	

There were 36 OS events at a median of 1.9 years from radiotherapy start (IQR 2.6 years). For surviving patients (n = 200), the median follow-up was 3.7 years (IQR 3.2 years).

10 patients developed locally recurrent disease at a median of 0.8 years from radiotherapy start. Of these, 9 had salvage surgery (laryngectomy); 1 of 9 developed a further (para-stomal) local recurrence and 8 remain cancer-free. Curves demonstrating the cumulative incidence of local recurrence, with death from non-cancer causes as a competing event, are shown in the Figure.



On multivariable Cox PH regression, the only covariates associated with OS were an ECOG PS of 3 (vs 0, HR 9.12; 95% CI 2.05 - 40.5; p=0.004) and moderate co-morbidity (ACE-27 2 vs 0, HR 2.86; 95% CI 1.02 - 8.04; p=0.046). On competing risk regression, increasing patient age was associated with a significantly reduced risk of local recurrence vs competing events (HR 0.96; 95% CI 0.93-0.99, p<0.01), as were both ECOG PS = 3 and ACE-27 = 2 (HR 0.02; 95% CI 0.01-0.04, p<0.01 and HR 0.01; 95% CI 0.00-0.02, p<0.01 respectively).

4 patients (1.7%) required NG feeding, at a median time of 19 days from radiotherapy start (IQR 5.75 days). On logistic regression, patients with an ECOG PS of 3 were more likely to require NG insertion (OR 1.26; 95% CI 1.14 - 1.39; p<0.001). 17 patients (7.2%) required emergency inpatient admission during or within six weeks of finishing radiotherapy. Patients with an ECOG PS of 3 were more likely to require admission (OR 1.36; 95% CI 1.10 - 1.68; p=0.004). 142 patients (60.2%) were prescribed strong opiate analgesia (i.e., oral morphine solution). Never / light former smokers were less likely to be prescribed opiates (OR 0.81; 95% CI 0.66 - 0.99; p=0.042). One patient (<1%) developed laryngeal cartilage necrosis and required a functional laryngectomy.

Conclusion

Hypofractionated radiotherapy to the larynx is effective (local tumour control of 96%) and well-tolerated for patients with Tis / T1 N0 M0 squamous cell carcinoma of the glottic larynx, and should remain a standard of care approach.

References

1. RCR. Radiotherapy Dose fractionation, Third Edition | the Royal College of Radiologists [Internet]. www.rcr.ac.uk. 2019. Available from: https://www.rcr.ac.uk/publication/radiotherapy-dose-fractionation-third-edition

2. Le QT, Fu KK, Kroll S, Ryu JK, Quivey JM, Meyler TS, et al. Influence of fraction size, total dose, and overall time on local control of T1–T2 glottic carcinoma. 1997 Aug 1;39(1):115–26.

3. Short S, Krawitz H, Macann A, West T, Morton R, McIvor N, et al. T1N0/T2N0 glottic carcinoma: A comparison of two fractionation schedules. Australasian Radiology. 2006 Apr;50(2):152–7.

140

Omitting postoperative contralateral radiotherapy in head and neck cancers. A single center report.

Maria González de Dueñas, Victoria Vera Barragán, Esther Agudo Rey, Maria Medina Cobacho, Patricia Ruiz Leal, Joaquin Cabrera Rodriguez, Carmen Corral Fernandez, Yesika Ríos Kavadoy, Juan Quiros Rivero, Francisca Ropero Carmona, Teresa Iglesias García, Julia Luisa Muñoz Garcia

Hospital Universitario de Badajoz, Radiation Oncology, Badajoz, Spain

Topic

Innovative treatments

Keywords

unilateral, post-operative, Head and Neck.

Purpose/Objective

Head and neck cancers (HNC) and their treatments with radiotherapy have been associated with acute and chronic toxicity mainly in relation with the volume of radiation.

Over the last years, the elective treatment of bilateral necks has been recommended by clinical practices guidelines. However, recently several retrospective and prospective studies have proposed the omission of the contralateral neck in radiation treatments, when lymphadenectomy is negative, to reduce the treatment volume and subsequently, to improve toxicity profiles in these patients without detrimental impact in overall survival.

We have sought the impact of omitting contralateral post-operative radiation therapy (PORT) by retrospective review of a cohort of patients in terms on Overall Survival (OS), Progression-Free Survival (PFS), Local Control (LC) and Contralateral Neck Recurrence (CLNR)

Material/Methods

Retrospective study of 31 patients diagnosed with squamous HNC treated with surgery complete bilateral neck dissection plus PORT in our centre between July 2019 and January 2023. PORT on the primary site was indicated in case of pT3-pT4 or in any case with <5mm surgical margin. Elective neck irradiation was administered in case of pN+ or pN0 if less tan 18 nodes were recovered,

The patients included presented a mean age of 63.5 years (44-81). Mean total length of treatment, measured from surgery until the end of radiotherapy was 3.48 months (2-5).

All the treatments were delivered with VMAT/IMRT on the postsurgical site of the primary tumour, and the ipsilateral elective neck.

The mean radiotherapy dose administered was 60.9 Gy (52-66), and the mean dose per fraction was 2.03 Gy (2-2.2). These doses were varied in relationship with status of the margins, ranged between 60-66Gy when the margins were affected. Minimum dose to pN+ neck was 60 Gy to involved node level, elective negative levels received 54Gy.

To analyse overall survival and time to progression free survival, Kaplan Meier curves was used. Log-rank test was used to analyse the difference in survival for categorical variables and the regression method for quantitative variables.

Results

The distribution of cancer location was: 23 cases in the oral cavity and 8 in the larynx. T staging: pT1 1 patient (3.2%), pT2 8 patients (25.8%), pT3 13 patients (41.9%), and pT4 9 patients (29%). N classification: pN0 19 patients (61.3%), pN1 8 patients (25.8%), pN2 3 patients (9.7%), and cN0 in 1 patient (3.2%). Global classification: stage I; 1 patient (3.2%), II; 7 patients (22.6%), III; 11 patients (35.5%), and IVA; 12 patients (38.7%).

Neck lymphadenectomy was radical in 4 patients (12.9%) and functional in 26 (83.9%). One patient did not undergo neck dissection during surgery for the primary but was included in the study. Mean number of lymph nodes recovered was 34.9 (8-90).

With a mean follow-up of 20 months (2-44) mean OS was 35.4 months (95%CI 29.9-40.9). The 2-year OS was 77.3%. The mean DFS was 34.3 months (95% CI 28.6-40.1), 2-year survival was 76%.

There was 4 local recurrences , 2-year actuarial LC was 87.1% with mean DFS 38.34 months (95%CI 33.29-43.4). There were 4 CLNR, with a median CLNR-free survival of 38.8 months (95%CI 34.1-43.6) 85.6% at 2 years.

The only factor associated with contralateral recurrence was N- Stage: N0-1 vs N2 2-year OS 95%-87.5% vs 33% respectively.

Median OS 42 vs13 months (p=0.02).

Conclusion

In conclusion, with a follow-up time of 20 months, we have observed that the omission of contralateral neck irradiation in patients with good prognosis factors as ipsilateral pN0-1 and bilateral neck lymphadenectomy is a safe current practice.

Despite being a study with a small number of events (n=4), our data suggest that omitting contralateral irradiation in pN2 patients is associated with a higher recurrence rate and worse survival. No other factors have been statistically significant with local recurrence rates neither OS.

References

1.Contreras JA, Spencer C, DeWees T, Haughey B, Henke LE, Chin R-I, et al. Eliminating postoperative radiation to the pathologically node-negative neck: Long-term results of a prospective phase II study. J Clin Oncol [Internet]. 2019;37(28):2548–55. Disponible en: http://dx.doi.org/10.1200/jco.19.00186

2.Koyfman SA, Ismaila N, Crook D, D'Cruz A, Rodriguez CP, Sher DJ, et al. Management of the neck in squamous cell carcinoma of the oral cavity and oropharynx: ASCO clinical practice guideline. J Clin Oncol [Internet]. 2019;37(20):1753–74. Disponible en: http://dx.doi.org/10.1200/jco.18.01921

142

Hypofractionated re-irradiation with Cyberknife for locoregionally recurrent head and neck cancer: a single-center study.

Viola Salvestrini, Chiara Mattioli, Carlotta Becherini, Isacco Desideri, Mauro Loi, Vanessa Di Cataldo, Lucia Angelini, Giulio Frosini, Giulio Francolini, Pierluigi Bonomo, Lorenzo Livi

Radiation Oncology Unit, Azienda Ospedaliero-Universitaria Careggi, University of Florence, Florence, Italy

Topic

Innovative treatments

Keywords

re-irradiation, recurrent disease, cyberknife

Purpose/Objective

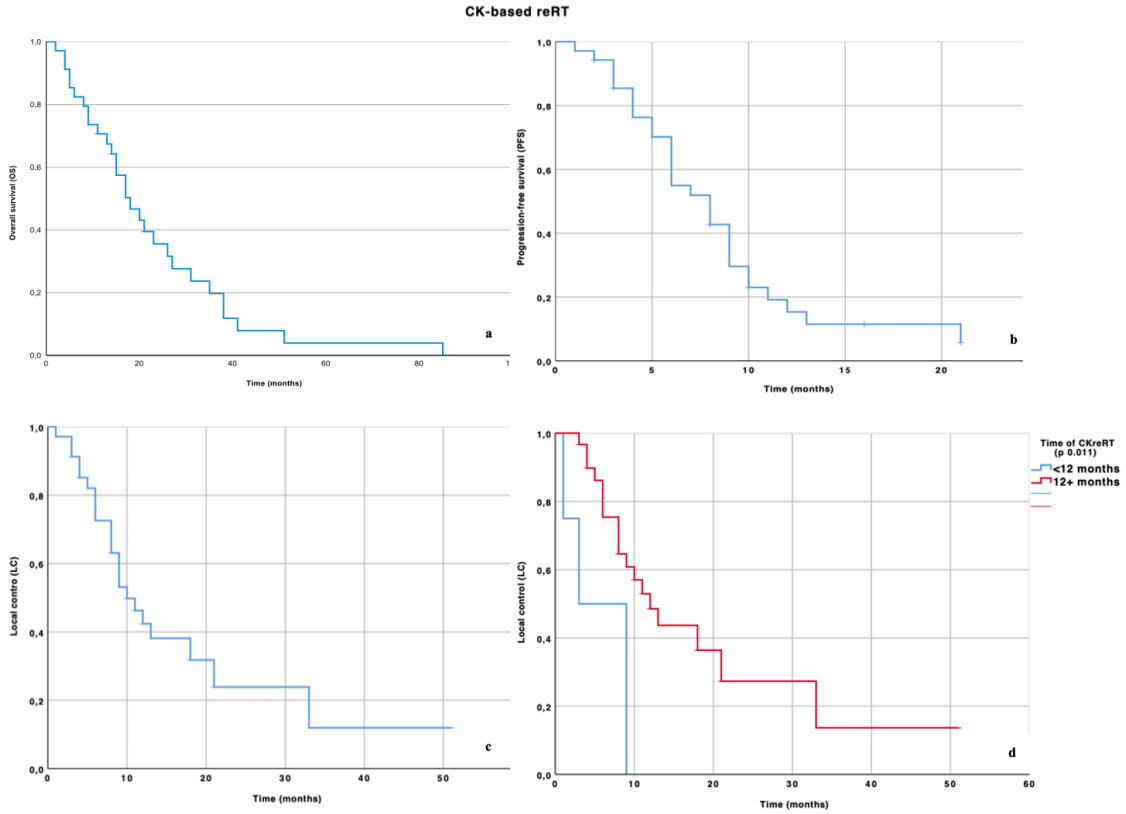
Loco-regional recurrence (LRR) is the predominant pattern of failure in locally-advanced head and neck cancer (HNC), both in squamous cell carcinoma (SCC) and non-squamous histotypes. Despite the proven role of radiotherapy (RT) as primary treatment strategy, there is sparse evidence on the use of reirradiation (ReRT) in recurrent HNC (rHNC). Various regimens of hypofractionation have been described in the literature, without a clear consensus. The aim of our single-centre study is to evaluate the clinical outcome of unresectable rHNC patients treated with Cyberknife-based (CK) hypofractionated reRT.

Material/Methods

We retrospectively analyzed data from consecutive patients with rHNC who received CK reRT at our institution. All eligible patients had a recurrent, non-metastatic, previously irradiated unresectable HNC. Each case was discussed at a multidisciplinary level before treatment. Local control (LC), progression-free survival (PFS) and overall survival (OS) were calculated using the Kaplan-Meier method and log rank test with time measured from the date of last day of reRT to date of local recurrence, progression of disease or death, respectively.

Results

Figure 1. Overall Survival (a), Progression-Free Survival (b) and Local Control (c) in respect with time to CK reRT < or ≥ 12 months (d).



First curatively intended course of RT was delivered from 1997 to 2020, concomitantly with chemotherapy or not. Thirty-five patients received Cyberknife (CK)-based hypofractionated reRT. The majority of patients (22, 63%) had a diagnosis of SCC and 13 patients (37%) had other histotypes than SCC. The median age of the cohort was 62 years at diagnosis. The CK reRT was performed from 2012 to 2022. The most commonly adopted schedules of reRT were 25Gy (57%) and 30Gy (43%) in 5 fractions on alternating days. After a median follow-up of 12 months (range 2-48), 6 out of 35 patients were alive. Causes of death were related to HNC in 12 patients and in 9 to other causes. The median LC and the 1-year LC rate were 10 months (95% CI 6,6-13,4 months) and 42%, respectively. The median PFS and OS and the 1-year PFS and OS rates were 8 months (95% CI 6.1-9,8 months), 18 months (95% CI 11,8-24,1 months) and 15% and 71% (Figure 1), respectively. At univariate analysis, a negative correlation between time to CK reRT < 12 months and LC (p 0.01) was reported. Moreover, a positive trend association between time from first to second irradiation ≥ 12 months and OS (p 0.09) was shown, in line with findings available from the literature. A significantly better OS was found in patients aged < 65 years (p 0.045).

Conclusion

From our analysis, hypofractionated ReRT can be viewed as a well-tolerated treatment option for rHNC with potential for prolonged local control in appropriately selected patients.

neoadjuvant chemotherapy followed by concurrent chemoradiotherapy for locoregionally advanced nasopharyngeal carcinoma: real world data from the national institute of oncology, Morocco

Rania El Gueddari[1,2], Abdou Sara[1,2], Imane Hassnaoui[1,2], Mona Taouchikht[1,2], Houda Fares[1,2], Edith Tatiana Ngbwa[1,2], Karima Nouni[1,2], Amine Lachgar[1,2], Hanane ElKacemi[1,2], Tayeb Kebdani[1,2], Khalid Hassouni[1,2]

[1]National Oncology Institute, Radiotherapy, Rabat, Morocco. [2]Faculty of medicine and pharmacy, Medicine, Rabat, Morocco

Topic

RTT

Keywords

Nasopharyngeal, Radiotherapy, Chemotherapy

Purpose/Objective

Treatment of nasopharyngeal cancer is based on radiotherapy associated to chemotherapy.

The standard for patients with locoregionally advanced carcinoma is induction chemotherapy associated to concurrent chemoradiotherapy.

The aim of our study is to determine the recurrence free survival and overall survival.

Material/Methods

Our study focused on non metastatic patients with locoregionally advanced nasopharyngeal carcinoma: T3-T4 with positive nodes.

Treated by induction chemotherapy and concurrent chemoradiotherapy between 2018 and 2021.

For the induction chemotherapy, patients received cisplatin associated to gemcitabine for three cycles.

In concurrent chemoradiotherapy, total dose was 69,96-70 Gray in 33-35 fractions 5 days a week using Volumetric Modulated Arc Therapy (VMAT) plus cisplatin weekly at a dose of 40 mg per square meter of body surface.

Treatment, side effects, loco-regional and distant control and overall survival were collected.

Results

A total of 153 patients were included in the study, patients with metastatic disease were excluded.

We had 61,4% of men vs 38,6% of women with a median age of 49 years old.

13,7% of patients had arterial hypertension or diabetes.

A total of 83,1% of the patients received three cycles of induction chemotherapy.

81,6% received the full dose of radiotherapy, the others interrupted the treatment for side effects.

52,3% of the patients received seven cycles of concurrent chemotherapy.

Side effects were reported in 41,8% of the patients with a higher incidence of neutropenia, anemia, nausea-vomiting, renal toxicity and mucositis.

Grade 3 or 4 toxic side effects were reported in 19,6% of the patients.

At a median follow-up of 44 months, the 2-year recurrence-free survival was 73,2%.

Overall survival at 2 years was 89.4%.

Conclusion

The results of our study are similar to literature's results; the induction chemotherapy followed by concurrent chemoradiotherapy in the locoregionally advanced nasopharyngeal carcinoma promotes distant control and increases overall survival.

Sides effects are unavoidable so they must be recognized and treated early to avoid grade 3 and 4.

144

EFFICACY AND SAFETY OF CHEMO-IMMUNOTHERAPY IN RECURRENT/METASTATIC HNSCC: A RETROSPECTIVE ANALYSIS

Viola Salvestrini, Giulio Frosini, Isacco Desideri, Carlotta Becherini, Lucia Angelini, Pierluigi Bonomo, Lorenzo Livi

Radiation Oncology Unit, Azienda Ospedaliero-Universitaria Careggi, University of Florence, Florence, Italy

Topic

Immuno-oncology

Keywords

Immunotherapy, recurrent and metastatic HNSCC

Purpose/Objective

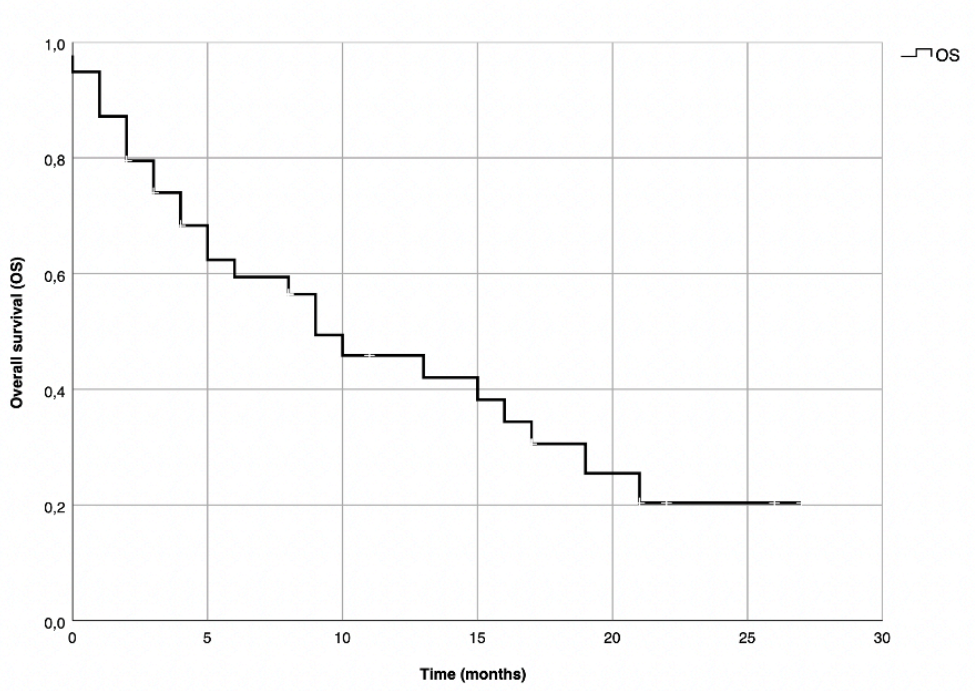
After KEYNOTE 048, PDL1 CPS score has become essential in treatment choice for patients with squamous cell carcinoma of the head and neck (HNSCC) not eligible for curative treatment. This report aims to analyze efficacy and safety outcomes in a cohort of patients treated in our center with first line systemic therapy (FLST) from 2021.

Material/Methods

We collected retrospectively data about stadiation and treatment from patients with recurrent/metastatic HNSCC treated in our center with FLST according to CPS. The primary endpoints were overall survival (OS) and progression-free survival (PFS) (considered from the start of FLST). Toxicity data were reported according to CTCAEv4.0.

Results

Figure 1. Overall survival (OS)



Thirty-nine patients who underwent FLST in our center between Jan 2021 and May 2023 were included in this retrospective study, with a median follow-up of 9 months [95%CI 1.2-16.8]. Median age was 63 years and PS ECOG mostly 0-1 (90%); CPS resulted negative in 8 (21%), >1 in 9 (23%) and >20 in 22 (56%) patients. 16 patients (41%) had distant metastases, the others locoregional disease not eligible for radical treatment. EXTREME schedule was chosen in the 8 CPS-negative patients; 20 of the CPS-positive cohort received Platinum+5FU+Pembrolizumab (PFP) and 11 Pembrolizumab alone. Considering all patients, median OS was 9 months [95%CI 3.1-14.8], 1-year OS 46%, 2-year OS 20%; median PFS was 5 months [95%CI 3.4-6.5] (Figure 1). One-year PFS 21%. Pembrolizumab group had a median OS of 9 months [95%CI 3.5-14.5] and 1-year OS of 38%; PFP group had median OS of 10 months [95%CI 0-23.9], 1-year OS 45% and 2-year OS 30%. At univariate analysis, younger age was associated with longer survival with a median OS of 17 months [95%CI 4.2-29.7] and 5 months [95%CI 1.7-8.3] for patients aged <70y and >70y respectively (p=0.01). Regarding toxicity, we reported 15 events > G3; the most frequent were mucositis (4) and neutropenia (4) in chemotherapy groups; only 3 occurred with Pembrolizumab alone.

Conclusion

In our cohort, patients with recurrent/metastatic HNSCC had efficacy and safety outcomes in line with published chemo-immunotherapy data (KN048). Younger age was significantly associated with longer survival.

145

Survival outcomes of elderly patients treated with a curatively-intended treatment for HPV-related oropharyngeal cancer: a multicenter cohort study

Pierluigi Bonomo[1], Viola Salvestrini[1], Andrea Romei[1], Chiara Doccioli[2], Liliana Belgioia[3], Marta Maddalo[4], Giuseppe Fanetti[5], Paola De Franco[6], Silvia Bertocci[7], Francesca De Felice[8], Stefano Ursino[9], Anna Merlotti[10], Daniela Alterio[11], Alessandro Nicola Iacovelli[12], Francesco Miccichè[13], Elisa D'Angelo[14], Carlotta Becherini[1], Isacco Desideri[1], Saverio Caini[15], Lorenzo Livi[1]

[1]Radiation Oncology Unit, Azienda Ospedaliero-Universitaria Careggi, University of Florence, Florence, Italy. [2]University of Florence, Department of Statistic, Computer Science and Applications "G.Parenti", Florence, Italy. [3]3IRCCS Ospedale Policlinico San Martino, Genoa, Health Science Department (DISSAL), Genoa, Italy. [4]ASST Spedali Civili of Brescia, University of Brescia,, Radiation Oncology, Department of Medical and Surgical Specialties, Radiological Science and Public Health, Brescia, Italy. [5]Centro di Riferimento Oncologico di Aviano (CRO) - IRCCS, Radiation Oncology, Aviano, Italy. [6]Ospedale Vito Fazzi, Radiation Oncology, Lecce, Italy. [7]Ospedale San Donato, Radiation Oncology, Arezzo, Italy. [8]University Hospital La Sapienza, Radiation Oncology, Rome, Italy. [9]University Hospital Santa Chiara, Radiation Oncology, Pisa, Italy. [10]Azienda Ospedaliera S. Croce e Carle, Radiation Oncology, Cuneo, Italy. [11]IEO European Institute of Oncology IRCCS, Radiation Oncology, Milan, Italy. [12]Fondazione IRCCS Istituto Nazionale dei Tumori, Radiotherapy Unit, Milan, Italy. [13]Fondazione Policlinico Universitario A. Gemelli IRCCS, Diagnostica per Immagini, Radiation Oncology and Hematology, Rome, Italy. [14]University Hospital of Modena, Radiation Oncology, Modena, Italy. [15]15Institute for Cancer Research, Prevention and Clinical Network (ISPRO), Cancer Risk Factors and Lifestyle Epidemiology Unit, Florence, Italy

Topic

Management of elderly or frail patients

Keywords

elderly, HPV-related oropharyngeal cancer

Purpose/Objective

The rising incidence of Human Papilloma Virus (HPV) related oropharyngeal squamous cell carcinoma (OPC) in the older population has been confirmed by recent epidemiologic reports. An increase of over 50% is expected in the population aged older than 65 years in the next decade. Some authors have focused their investigations on the "late" elderly subgroup defined as patients (pts) aged 75 years or older, still underrepresented in clinical trials. Indeed, there is a significant lack of data on their disease trajectory. The purpose of our experience was to evaluate the pattern of clinical practice in this specific subgroup of pts within the Italian Association of Radiotherapy and Clinical Oncology (AIRO).

Material/Methods

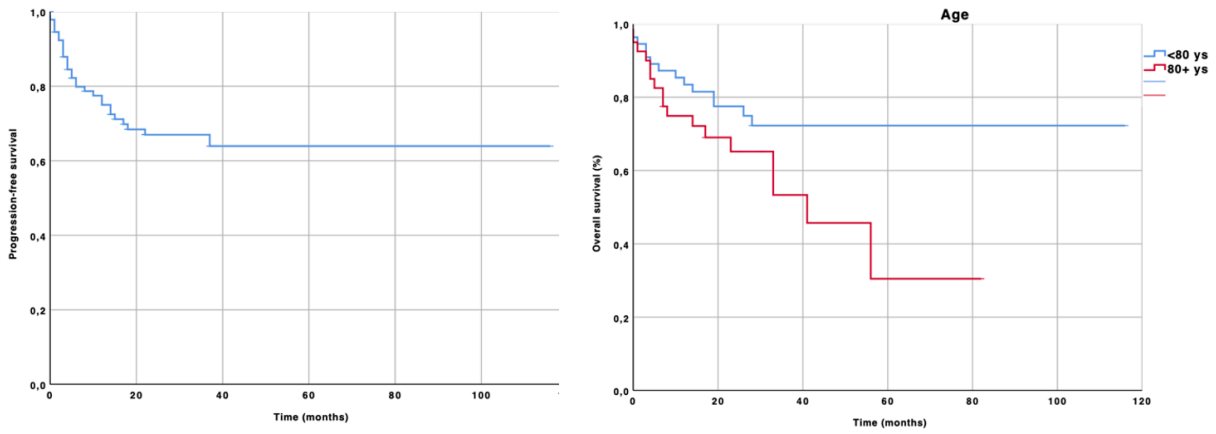
Table1 Clinical Features

Characteristic	No. of patients (%), n = 95
Median age, years (range)	78 years (75-88)
<80	55 (57,9%)
≥80	40 (42,1%)
ECOG	
0	44 (83.6%)
1	44 (16.4%)
2	7 (16.4%)
Primary tumor site	
Tonsil	59 (62,1%)
Base of Tongue	28 (29,5%)
Soft Palate	4 (4,2%)
Posterior Wall	2 (2,1%)
No primary identified (cT0)	1 (1,1%)

An observational retrospective study was conducted over a 6-year period (2015-2021). Consecutive patients older than 75 years at diagnosis with a histologically-confirmed HPV positive (p16 immunohistochemistry/HPV DNA-in situ hybridization) OPC eligible for a curatively-intended treatment were included. Overall survival (OS) was defined as the time from OPC diagnosis to last follow-up or death from any cause. Progression-free survival (PFS) was defined as the time from the last day of curative-intended treatment to disease progression or death from any cause. Median OS and PFS was estimated by the Kaplan-Meyer method. A log-rank test was employed to test different variables: smoking history, presence of caregiver, employed treatment modality and age (< or > 80 years) correlated with longer OS. Hazard ratios (HR) for the association between the variables of interest and the risk of death were obtained by univariate Cox regression analysis. A p-value <0.05 was considered statistically significant. Acute toxicity was evaluated according to CTCAE v. 5.0

Results

Figure 1. Progression-free survival (a) and Overall Survival for patients aged <80 or ≥80 years (b).



A cohort of 95 pts was included in our analysis. The median age was 78 years (table 1). ECOG PS 0-1 and locally advanced disease were reported for the vast majority of patients, 92.6% and 89.4% (in stage III/IV according to TNM 7thedition) respectively. As expected, exclusive radiotherapy (RT) was the most

common adopted strategy. After a median follow- up of 25 months (range: 0-116), 64 patients were alive (67.3%). The one and two-year PFS were 75% and 67%, the median PFS was not reached (Figure 1a). The one and two-year OS rates were 83% and 75%, respectively, whereas the median OS was not reached. Among the tested variables, belonging to the group of age >80 years was associated with a worse OS (p=0.0429; HR for death, 2.15, 95% CI 1.00-4.60, Figure 1b), whereas no impact on survival was associated to the smoking history (p=.011), treatment modality (p=0.32) and presence of caregiver (p=0.65). The toxicity profile was acceptable (>G3 toxicity of 29.4%), although 6 patients (6.3%) died due to potential treatment-related complications. Further analyses on radiation dose, target volumes and pattern of failure will be reported

Conclusion

To the best of our knowledge, our series represents one of the largest to date on “late” elderly population with non-metastatic HPV positive OPC treated with a curatively-intended, RT-based approach. Thanks to the appropriate selection of pts, an optimal survival outcome can be achieved with standard treatment options, in line with data reported for the younger population. Further prospective studies investigating larger series of older pts are warranted in order to confirm our conclusions.

147

Evolution of phase 1 clinical trials for head and neck cancer patients based on the experience of a dedicated phase I Unit.

Katerin Rojas[1,2,3], Alberto Hernando[1,4], Juan Assaf[1,2], Eduardo Garcia[5], María Vieito[1,4], Vladimir Galvao[1], Omar Saavedra[1], Guzman Alonso[1,4], Julia Lostes[1,4], Mafalda Oliveira[4,6], Oriol Mirallas[1], Arjun Oberoi[1,4], Giulia Pretelli[1], Belen Ortega[1,4], Raquel Granados[7,8], Jordi Giralt[7,8], Coro Bescos[9], Juan Lorente[10], Sahyly Siurana[11], Joseph Tabernero[1,4], Ana Oaknin[4,12], Enriqueta Felip[4,13], Elena Garralda[1,4], Irene Braña[1,2,4]

[1]Vall d’Hebron Institute of Oncology (VHIO)., Early Clinical Drug Development Group., Barcelona, Spain. [2]Vall d’Hebron Institute of Oncology (VHIO)., Head and Neck Group., Barcelona, Spain. [3]Vall d’Hebron Institute of Oncology (VHIO)., Medical Oncology Department., Barcelona, Spain. [4]Vall d’Hebron University Hospital., Medical Oncology Department., Barcelona, Spain. [5]Vall d’Hebron Institute of Oncology (VHIO)., Oncology Data Science (ODysSey) Group., Barcelona, Spain. [6]Vall d’Hebron Institute of Oncology (VHIO)., Breast Cancer Group., Barcelona, Spain. [7]Vall d’Hebron Institute of Oncology (VHIO)., Radiation Oncology Group., Barcelona, Spain. [8]Vall d’Hebron University Hospital., Radiation Oncology Department., Barcelona, Spain. [9]Vall d’Hebron University Hospital., Maxilofacial Surgery Department., Barcelona, Spain. [10]Vall d’Hebron University Hospital., Ear Nose Throat Department., Barcelona, Spain. [11]Vall d’Hebron University Hospital., Radiology Department (IDI)., Barcelona, Spain. [12]Vall d’Hebron Institute of Oncology (VHIO)., Gynecological Malignancies Group., Barcelona, Spain. [13]Vall d’Hebron Institute of Oncology (VHIO)., Thoracic Tumors Group., Barcelona, Spain

Topic

Innovative treatments

Keywords

Head and Neck cancer, Phase 1, Evolution

Purpose/Objective

Since the approval of anti-EGFR and anti-PD1 monoclonal antibodies in head and neck squamous cell carcinoma, there is an increased interest in developing novel therapeutics in head and neck malignancies. The purpose of this study is to analyze all phase I clinical trials conducted at the Vall d'Hebron Institute of Oncology for head and neck cancers since 2010. We aimed to evaluate the proportion of phase I studies with dedicated cohorts for head and neck cancers, assessing the types of agents in development and tumor types included, as well as analyzing the patient characteristics participating in these trials.

Material/Methods

We have reviewed all the phase 1 clinical trials conducted in the Early Drug Development Unit, from Vall d´Hebron Institute of Oncology from January 2010 to June 2023, and identify which of these studies have cohorts for head and neck cancers. We use descriptive statistics to describe the tumor types and drug types included in these cohorts. We have also collected data from all the patients with head and neck cancers, included in phase I clinical trials from January 2010 to December 2022 and describe tumor types and agents used to identify potential opportunities for development in head and neck tumors.

Results

Among the 634 phase I clinical trials activated from 2010 to 2023, 151 clinical trials had at least one cohort for patients with head and neck malignancies. Most of these studies include other solid tumors, and only 2 studies were tumor-specific. The majority of the 151 studies with dedicated head and neck cohorts were focused on head and neck squamous cell carcinoma (84%), while only 21% and 2.8% included salivary gland cancers or nasopharyngeal carcinomas (7.5% of studies include two or more histologies). Sixty-two studies evaluated agents in monotherapy, while 38% evaluated combinations. The anticancer agents evaluated included: targeted therapy 131 (87%), immunotherapy 61 (40%), chemotherapy 17 (11%), and hormone therapy 1 (0.7%). The proportion of studies evaluating immunotherapies was higher in the studies with dedicated head and neck cohorts, in comparison to the global pool of phase I studies conducted in the unit (32.5%). Although the absolute number of phase I studies with dedicated head and neck cohorts has progressively increased (29 studies in 2022), the proportion compared to the global pool of phase I studies remained stable since 2016 ranging from 25-30% of the total.

From January 2010 to December 2022 we have included 275 patients in phase I clinical trials: 63% had HNSCC, 28% had salivary gland cancers, 8% had nasopharyngeal carcinomas, and 1% had other tumor types. The new agents evaluated included: immunotherapies (52%), targeted agents (41%), novel chemotherapies or antibody-drug conjugates (6%), and other therapies such as nanoparticles (1%).

Conclusion

There is an increasing interest in developing novel drugs for head and neck cancers. In recent years, 25-30% of the phase clinical trials conducted in our institution have at least one cohort dedicated to head and neck malignancies, especially HNSCC. Despite these positive trends, clinical trial opportunities for rare/less frequent head and neck cancers remain limited.

148

Predictors and outcomes of Contralateral Lymph node involvement in node positive oral squamous cell carcinoma: A retrospective analysis of 180 patients.

Harsh Thakran[1], Sanjay Chandra Das[1], Sanuja Paul[2], Jain Prateek Vijay[3], Kapila Manikantan[3], Guru Charan Sahu[3], Vikram Dilip Kekatpure[3], Pattatheyil Arun[3]

[1]Tata Medical Center, Surgical Oncology, Kolkata, India. [2]Tata Medical Center, Emergency Medicine, Kolkata, India. [3]Tata Medical Center, Head and Neck Surgery, Kolkata, India

Topic

Multidisciplinary management

Keywords

Analysis, Outcome, Contralateral, nodal metastasis

Purpose/Objective

Contralateral lymph node metastasis (CLNM) is a poor prognostic factor in patients with oral squamous cell carcinoma (OSCC). There is limited data from India on this topic. The aim of this study was to evaluate the outcomes of contralateral positive cancer patients undergoing neck dissection in a tertiary hospital in India.

Material/Methods

We retrospectively reviewed the electronic medical records of 180 patients who had bilateral lymph nodes dissection for OSCC. Demographic, clinico-pathological and follow up data was abstracted directly from patients' electronic medical records. We analyzed the disease-free survival (DFS) and overall survival (OS) of these patients using a log-rank test (univariate) and cox proportional hazards model (multivariate).

Results

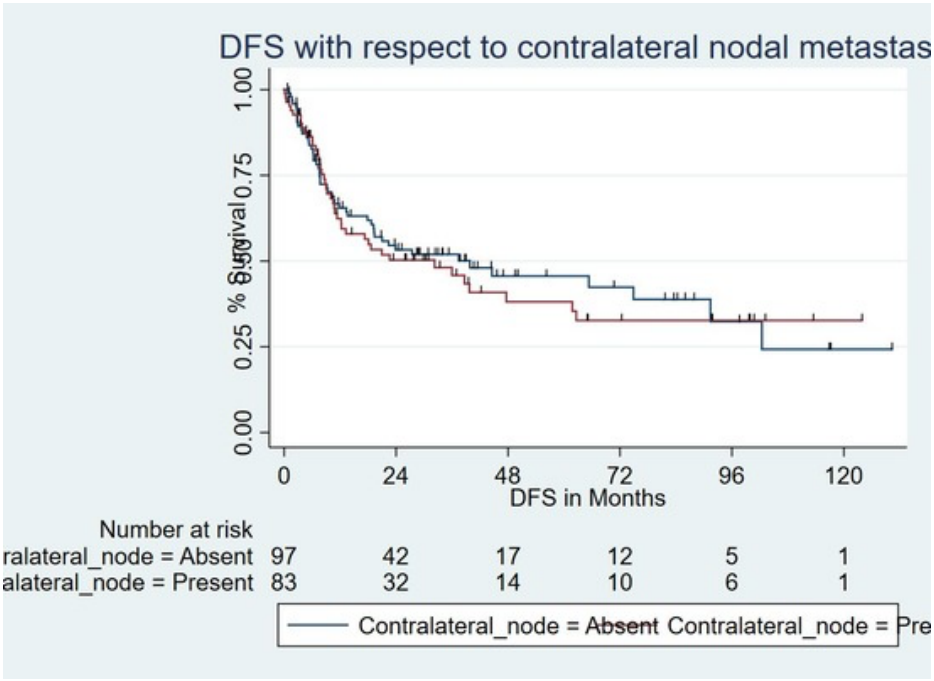
The median age of the cohort was 52 years (21-78 years) and comprised 125 males (69.4%). 83 (46.1%) patients had nodal metastasis on the contralateral side. Median follow up for patients who were alive at the time of analysis was 25.6 months (0.1- 130.1 months). Deeper lesion (depth 2.15 cm vs 1.70 cm, p=0.01), presence of lymphovascular invasion (LVI) (51.9% vs 31.4%, p=0.01), extranodal extension (ENE) (54% vs 34.4%, p=0.01) and nodal metastasis to ipsilateral level IV (83.3% vs 33.1%, p<0.01) predisposed to contralateral nodal metastasis.

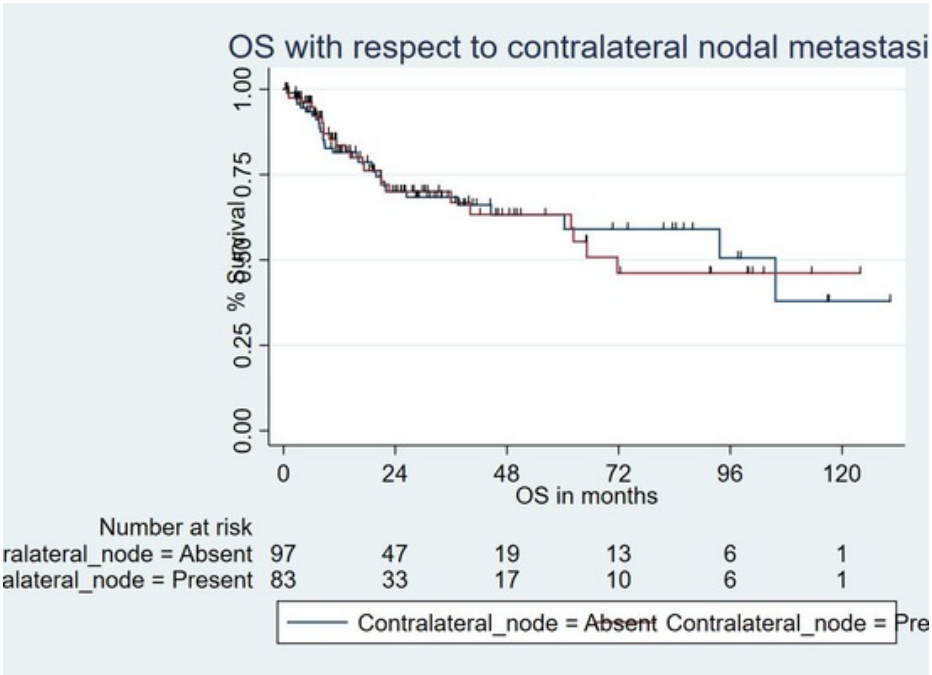
There were 92 disease failures in this cohort with 2 year DFS of 52%. Depth of invasion (DoI) [Hazard ratio (HR) 1.21, 95% confidence interval (CI) 1.02- 1.44, p=0.03), involved margins (HR 3.49, CI 1.83- 6.64, p<0.01), presence of perineural invasion (PNI) (HR 2.64, CI 1.54- 4.53, p <0.01), masticator space invasion (HR 2.10, CI 1.01- 4.08, p= 0.03) and presence of extranodal extension (ENE) in contralateral node (HR HR 2.29, CI 1.00- 5.29, p= 0.04) predicted poorer DFS on univariate analysis. On multivariate analysis, tongue as primary site(HR 0.49, CI 0.28- 0.85, p=0.01), involved margins (HR 2.66, CI 1.30- 5.43, p<0.01) and PNI (HR 2.62, CI 1.36- 4.99, p<0.01) affected the DFS significantly. There were 54 deaths in this cohort with a 2-year OS of 70.1%. Involved margins (HR 4.89, CI 2.17- 11.05, p<0.01), PNI (HR 3.11, CI 1.47- 6.61, p<0.01) and ENE (HR 1.77, CI 1.01- 3.07, p=0.04) were associated with a poorer OS on

univariate analysis. On multivariate analysis, involved margins (HR 2.91, CI 1.22- 6.97, p=0.02) and PNI (HR 2.25, CI 1.02- 4.98, p=0.04) resulted in patients having poorer OS.

Conclusion

This study provides valuable insights into the outcomes of patients with contralateral lymph nodal metastasis for patients who underwent curative intent surgery for oral squamous cell carcinoma. Deeper lesions, presence of lymphovascular invasion, extranodal extension and nodal metastasis to ipsilateral level IV predisposed to contralateral nodal metastasis. Primary site, involved margins and perineural invasion predicted the disease free survival, whereas involved margins and perineural invasion predicted overall survival in this cohort of patients.





149

A novel approach for improving the quality and deliverability of VMAT plans in head and neck cancer

Salwa Fathy[1,2], Omar Kalantan[1], Baderaldeen Altazi[1], Umme Salma Mohamed[1], Elham Rashaidi[1], Maha Alidrisi[1]

[1]King Abdullah Medical City, Radiation Oncology, Jeddah, Saudi Arabia. [2]South egypt Cancer Institue, Radiotherapy and nuclear department, Assiut, Egypt

Topic

Innovative treatments

Keywords

Triple Arc, VMAT, Head & Neck cancer

Purpose/Objective

Advanced radiation techniques are frequently used in the treatment of squamous cell carcinoma of the head and neck (H&N). Volumetric modulated arc therapy (VMAT) is currently the standard treatment across the world. It provides good target volume coverage and enhanced conformal dose distributions while sparing the organs at risk (OARs). However, this may result in a considerable volume of low-dose region in the surrounding normal tissue. In the clinical practice, our oncology center has implemented the Triple Arc (TA) VMAT approach in head and neck cancer treatment planning using three full arcs to enhance the radiation outcomes and effectively spare midline structures. This dosimetric study was performed to verify Triple Arc Volumetric Modulated Arc Therapy (TA-VMAT) in head and neck cancer treatment planning using the simultaneous integrated boost (SIB) technique by proving its deliverability and dosimetric accuracy when compared to Dual Arc (DA)VMAT.

Material/Methods

Thirteen head and neck cancer cases were randomly enrolled in this comparative study. The planning target volumes(PTVs) and OARs were defined using RTOG 0225/0615. Additionally, we identified the thyroid and trachea as well. For each case, two treatment plans TA and DA were generated by the Varian Eclipse planning system yielding a total of 26 treatment plans. Both plans have full arcs that span an angle between 179-181 CW and CCW using a collimator angle of 330 and 30 degrees for the CW, and CCW, respectively. However, in TA arc plans, a third arc with an 80-degree collimator angle was added. Doses of 70Gy, 63Gy, and 54 Gy were delivered to PTV high, intermediate, and low risk, respectively in 35 fractions using the SIB technique. All these treatment plans are assessed in terms of dosimetric quality, OARs sparing, and delivery efficiency.

Results

According to RTOG 0225/0615; both Triple Arc and Dual Arc plans provided appropriate target coverage while lowering OAR doses. However, TA-VMAT effectively managed the dose hotspot and maintained a consistent gantry speed for precise radiation delivery yielding a significantly enhanced target homogeneity and dose conformity in comparison to DA-VMAT (P=0.02 and 0.002 respectively). Moreover, it provides superior dosage reduction to the brain stem, larynx, esophagus, trachea, and spinal cord. A paired-sample t-test was conducted to assess the value of using Triple-arc VMAT over Dual-arc VMAT in terms of the dose coverage, conformity index(CI), and homogeneity index(HI) for

targets as well as the mean and maximum dosage for OARs. Treatment delivery time (min), monitor units (MUs) per fraction, and normal tissue integral dose(NTID) were also evaluated. The maximum dosage (Dmax) to the brain stem in TA-VMAT was significantly lower than in DA-VMAT (p=0.001). The spinal cord maximum dosage (Dmax) was significantly low in TA-VMAT as compared with DA-VMAT (p=0.002).TA-VMAT produced a significantly lower mean dose to the larynx (p=0.027) than DA-VMAT. The mean doses to the esophagus and trachea were significantly lower in TA than in DA treatment plans(p=0.008 and 0.001 respectively). Both treatment plans had almost the same mean treatment delivery time. There were no significant changes in the number of monitor units MU/ fraction or normal tissues integral dose NTID(p=0.057). These results suggest that the Triple Arc VMAT approach is unique, precise, and highly effective in reducing the dose of the OARs during radiation therapy among head and neck cancer patients.

Conclusion

In terms of target coverage and OAR sparing, radiation therapy treatment planning using TA-VMAT outperformed DA-VMAT, resulting in superior treatment outcomes without compromising delivery efficiency in patients with head and neck cancer. It has the potential to be a very effective, and high-quality radiation therapy approach.

References

1. Lee, N, Harris, J, Garden, AS et al. Intensity-modulated radiation therapy with or without chemotherapy for nasopharyngeal carcinoma: radiation therapy oncology group phase II trial 0225. J Clin Oncol 2009; 27: 3684–3690.CrossRefGoogle ScholarPubMed

2. Lee, NY, Zhang, Q, Pfister, DG et al. Addition of bevacizumab to standard chemoradiation for locoregionally advanced nasopharyngeal carcinoma (RTOG 0615): a phase 2 multi-institutional trial. Lancet Oncol 2012; 13: 172–180.CrossRefGoogle ScholarPubMed

3. White, P, Chan, KC, Cheng, KW, et al. Volumetric intensity-modulated arc therapy vs conventional intensity-modulated radiation therapy in nasopharyngeal carcinoma: a dosimetric study. J Radiat Res 2013; 54: 532–545.CrossRefGoogle ScholarPubMed

4. Lee, TF, Ting, HM, Chao, PJ, Fang, FM. Dual arc volumetric-modulated arc radiotherapy (VMAT) of nasopharyngeal carcinomas: a simultaneous integrated boost treatment plan comparison with intensity-modulated radiotherapies and single arc VMAT. Clin Oncol (R Coll Radiol) 2012; 24: 196–207.CrossRefGoogle ScholarPubMed

5. Wagner, D, Christiansen, H, Wolff, H, Vorwerk, H. Radiotherapy of malignant gliomas: comparison of volumetric single arc technique (RapidArc), dynamic intensity-modulated technique and 3D conformal technique. Radiother Oncol 2009; 93: 593–596.CrossRefGoogle Scholar

6. Wolff, D, Stieler, F, Welzel, G et al. Volumetric modulated arc therapy (VMAT) vs. serial tomotherapy, step-and-shoot IMRT, and 3D-conformal RT for the treatment of prostate cancer. Radiother Oncol 2009; 93: 226–233.CrossRefGoogle ScholarPubMed

150

The real world outcome of non-HPV head and neck cancer patients treated with definitive radiotherapy at a tertiary centre

Kevin Chiu Chiu[1], Swarna Arumugam[1], Ashitha Ashraf[1], Shagun Juneja[1], Chrysostomos Tornari[2]

[1]Mount Vernon Cancer Centre, Clinical Oncology, London, United Kingdom. [2]Bedfordshire Hospitals NHS Trust, Head and neck surgery, Luton, United Kingdom

Topic

Quality of life and outcomes

Keywords

Outcomes, staging, head neck cancer

Purpose/Objective

The assessment of cancer patient outcomes is important for any oncology departments. In head and neck cancer, not all patients are suitable for clinical studies. Unfortunately not all oncology centres are well resourced to undertake all available head and neck cancer trials. As a tertiary oncology unit with catchment radius of 50 miles and diverse patient demographics, it remains vital to assess outcomes of patients not included in formal studies. The aim of this study was to gather real world survival data of patients treated with definitive (chemo) radiotherapy.

Material/Methods

As standard of care, head and neck cancer patients are referred from 7 district general hospitals via 2 regional supra-multidisciplinary teams (sMDT). The data of patients demographics, and the clinical details of the head and neck cancer, are as routine collected prospectively for the institution electronic database. The date of disease recurrence on any patients is prospectively recorded at the sMDT.

Non-HPV mucosal head and neck cancer patients who received definitive radiotherapy outside clinical trials between Jan 2018 and May 2022 were retrospectively reviewed. All advanced stage patients (Stages III & IVa/b) were considered concomitant chemotherapy. Radiotherapy volume quality assurance was standard prior to radiation [1]. HPV-mediated oropharynx patients, as well those treated with post-operative or adjuvant radiation, were excluded. The progression free survival (PFS) were calculated from the prospective database, and the overall survival (OS) retrospectively from the institution main death register.

Results

A total of 267 patients were identified: 122 (46%) Larynx, 68 (25%) p16- Oropharynx, 34 (13%) Hypopharynx, 33 (12%) Nasopharynx, and 10 (4%) Nasal Cavity/Paranasal sinus patients. In terms of UICC 8th edition staging, there were 33 Stage I (12%) , 55 Stage II (21%) , 71 Stage III (27%) , and 108 Stage IVa/b (40%) cases across all tumour sites.

The median age was 65 (range 58 - 72). The male to female ratio was 3.2 to 1. Ninety percent (n = 240) of the patients had performance status of 0 or 1. Majority of the patients (n = 209, 78%) had had exposure to tobacco: 122 (46%) ex-smokers and 87 (33%) current smokers. The median smoking pack years for the tobacco exposed patients was 30 (range 10 - 40). As for alcohol consumption, 130 (49%)

patients consumed at least 14 units per week, with 30 (11%) being non-drinkers. All patients received 65Gy in 30 fractions (f) over 6 weeks, unless they were T1/2N0M0 glottic cancer for which they received 55Gy in 20f over 4 weeks. A total of 107 patients (40%) had at least 1 cycle of concomitant chemotherapy with their radiation.

The median follow up was 3 years. Across all tumour sites, the 2 and 3 year PFS was 60% and 55% respectively, while the 2 and 3 year OS was 74% and 65% respectively. The OS probability according to the UICC staging across all disease sites is shown in Figure 1.

For the Larynx subsite, there were 26 Stage I (21%), 30 Stage II (25%), 51 Stage III (42%), and 15 Stage IVa/b (12%) patients. The 2 and 3 year PFS for larynx patients were 70% and 65% respectively, with the 2 and 3 year OS being 82% and 75% respectively.

For the p16- oropharynx cohort, there were 3 Stage I (4%), 12 Stage II (18%), 3 Stage III (4%), and 50 Stage IVa/b (74%) patients. In comparison to the larynx cohort, there were higher proportion of advanced stage patients in the Oropharynx cohort. As a result, the 2 and 3 year PFS for the p16- Oropharynx was 44% and 40% respectively, while the 2 and 3 year OS was 60% and 50% respectively.

As for the hypopharynx group, there were no Stage I (0%) but 3 Stage II (9%), 8 Stage III (24%), and 23 Stage IVa/b (68%) cases. The 2 and 3 year PFS was 40% and 25% respectively, while the 2 and 3 year OS was 55% and 42% respectively.

Separately, there were 2 Stage I (6%), 8 Stage II (24%), 8 Stage III (24%), and 15 Stage IVa (45%) Nasopharynx patients. The 2 and 3 year PFS for nasopharynx cohort was 75% and 60% respectively, with the 2 and 3 year OS being 78% and 70% respectively.

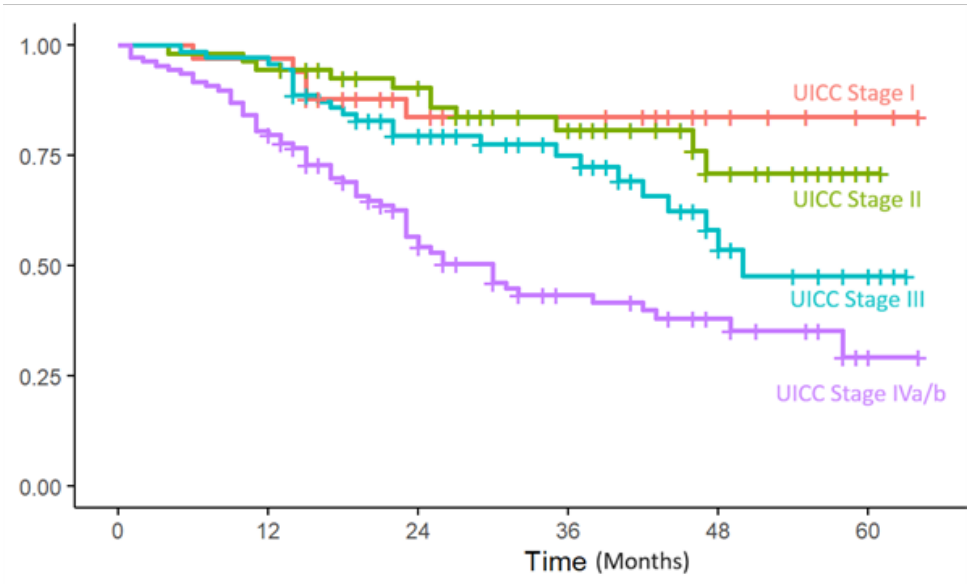


Figure 1 - Overall survival probability according to stages

Conclusion

Despite varying tumour sites, the OS of patients overall corresponded to the UICC Stage of their disease, indicating the importance of accurate initial staging as part of prognostication.

References

[1] Chiu K, Hoskin P, Gupta A, Butt R, Terparia S, Codd L, Tsang Y, Bhudia J, Killen H, Kane C, Ghoshray S, Lemon C and Megias D 2021 The quantitative impact of joint peer review with a specialist radiologist in head and neck cancer radiotherapy planning Br. J. Radiol. 20211219

153

Prognosis and treatment strategies of primary B-cell nasopharyngeal non Hodgkin lymphoma: A series of 12 cases

Cyrine Mokrani, Rim Abidi, Alia Mousli, Mohamed Souissi, Khadija Ben Zid, Amani Yousfi, Chiraz Nasr

Salah Azaiz Institue, Radiotherapy, Tunis, Tunisia

Topic

Multidisciplinary management

Keywords

Nasopharyngeal, Lymphoma, Prognosis

Purpose/Objective

Primary non-Hodgkin's lymphoma of the nasopharynx is a rare tumor that represents less than 10% of head and neck lymphomas (1). This localization is seen at any age. Treatment is based on polychemotherapy and radiotherapy. We describe the diagnostic, therapeutic and prognostic aspects of 12 cases of nasopharyngeal lymphoma.

Material/Methods

Retrospective study including 12 patients diagnosed with large B-cell non-Hodgkin's lymphoma of the nasopharynx treated between 2005 and 2022 at the Salah Azaiz Institute in Tunisia.

Results

The average age at diagnosis was 60.5 years (18 - 76 years). Half of the patients (53.8%) were 60 years or older with male predominance. Nasal obstruction was the most frequent symptom (n=8) followed by cervical adenopathy (n=4). The majority (75%) were classified as stage IIE according to the Ann Arbor classification and only 25% as stage IE. Seven patients had a low intermediate risk (age > 60 years). Only one patient had two unfavorable risk factors (age > 60 years and LDH above normal). Nasopharynx MRI was initially performed in only 16.7%. PET CT was not available. All patients received chemotherapy: 6 R-CHOP in 6 cases, 6 CHOP in 2 cases and 6 CEOP in 4. Among the 7 patients in complete response after chemotherapy, 6 had had the 6 R-CHOP protocol. The median period between the end of chemotherapy and radiotherapy was 3.5 months. All patients had Waldeyer’s ring radiotherapy at a dose of 54 to 36 Gy with conventional fractionation. Supraclavicular irradiation was performed in patients classified as stage IIE. The response to treatment was considered complete in 6 patients. Node recurrence was observed in 50% of the population after a mean delay of 3 years, regardless of chemotherapy and the dose received in radiotherapy. Patients with recurrence were treated with chemotherapy. No

correlation was found between age > 60 years and recurrence. Stage IIE did not correlate with a higher recurrence rate. Overall survival at 2 years was 85%.

Conclusion

There is no therapeutic standard for nasopharyngeal lymphoma. Their prognosis is similar to other non-Hodgkin's lymphomas and remains generally good.

References

(1) Non-Hodgkin lymphoma of the cavum: prognostic factors and therapeutic protocols Saloua Ouraini, Ismail Nakkabi, Fouad Benariba

154

Is adjuvant radiotherapy necessary for early-stage oral cavity cancer patients with the worst pattern of invasion-V?

Beste Atasoy[1], Gulsah Ozden[1], Leyla Cinel[2], Ali Cemal Yumusakhuylu[3], Zeynep Akdeniz Dogan[4], Dilek Gul[5], Cagatay Oysu[3], Bulent Sacak[4], Necati Enver[3], Ahmet Sakarya[4], Yavuz Gundogdu[3], Orhan Asya[3]

[1]Marmara University School of Medicine, Department of Radiation Oncology, Istanbul, Turkey. [2]Marmara University School of Medicine, Department of Medical Pathology, Istanbul, Turkey. [3]Marmara University School of Medicine, Department of Ear Nose Throat, Istanbul, Turkey. [4]Marmara University School of Medicine, Department of 4 Plastic, Reconstructive and Aesthetic Surgery, Istanbul, Turkey. [5]Marmara University Hospital, Radiation Oncology Clinic, Istanbul, Turkey

Topic

Multidisciplinary management

Keywords

oral cavity tumors, worst pattern of invasion

Purpose/Objective

We aimed to investigate the impact of the worst pattern of invasion (WPOI-V), an indicator of biological aggressiveness, on survival outcomes, as well as the potential need for adjuvant radiotherapy in squamous cell oral cavity cancers.

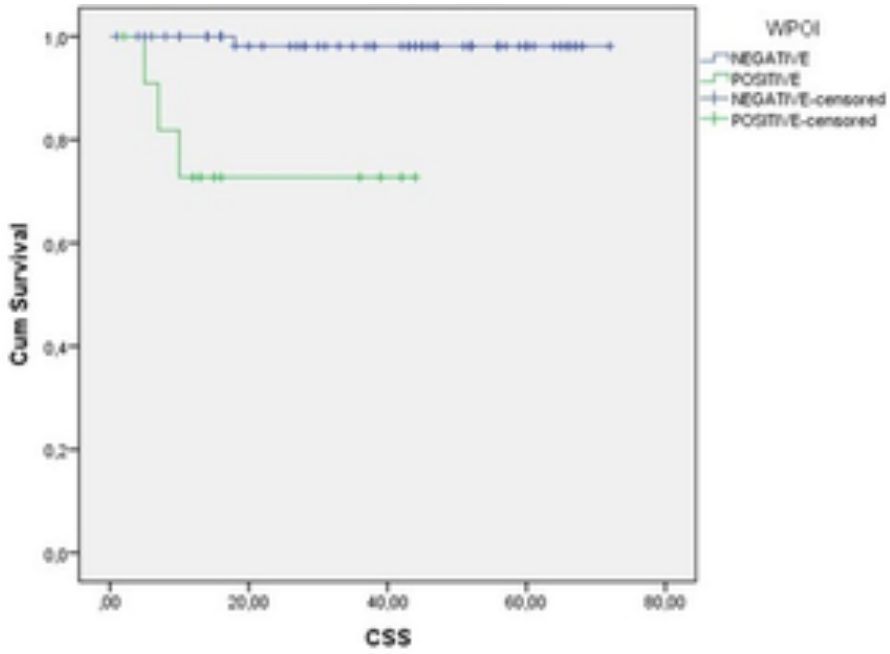
Material/Methods

A total of 162 patients who underwent surgical procedures at our center between 2017 and 2023 were included in the study. The median age of the patients was 65 years (range, 18-91 years). Tumor locations encompassed the lip (n=60), tongue (n=49), gingiva and buccal mucosa (n=23), and other sites (n=30). Patients were categorized into two groups: those with early-stage disease (T1-2 or N0) (n=80) and those with locally advanced disease (T3-4 or N+) (n=82). Cancer-specific survival (CSS) was defined as the time to local, regional, or systemic progression, while overall survival (OS) was defined as the time to death

from any cause following the date of surgery. The Kaplan-Meier method was employed for survival analysis, and statistical significance was set at $p<0.05$.

Results

The median follow-up duration was 36 months, with a range from 0 to 72 months. Local, regional, and/or systemic progression was observed in 26 patients, resulting in distant metastasis in 13 cases, local regional relapse in 8 cases, and second primary lung cancer in 2 cases. The three-year Cancer-Specific Survival (CSS) was significantly worse in patients with the presence of WPOI-V (63% vs. 86.9%, p=0.000) (see Figure 1). The difference was notably more pronounced in early-stage or younger patients. In multivariate analysis, the only significant factor influencing CSS in the early stage was WPOI-V (p=0.008) (Figure 1).There was no significant difference observed in OS.



Conclusion

The presence of WPOI-V in both early-stage and locally advanced patients serves as an indicator of a poor prognosis. This finding may represent a novel factor that warrants consideration for the inclusion of adjuvant therapy in the treatment of early-stage patients.

References

•Brandwein-Gensler M, Teixeira MS, Lewis CM, Lee B, Rolnitzky L, Hille JJ, Genden E, Urken ML, Wang BY. Oral squamous cell carcinoma: histologic risk assessment, but not margin status, is strongly predictive of local disease-free and overall survival. Am J Surg Pathol. 2005 Feb;29(2):167-78. doi: 10.1097/01.pas.0000149687.90710.21. PMID: 15644773.

•Tan A, Taskin T. Tumor Budding Should Be in Oral Cavity Cancer Reporting: A Retrospective Cohort Study Based on Tumor Microenvironment. Cancers (Basel). 2023 Aug 1;15(15):3905. doi: 10.3390/cancers15153905. PMID: 37568721; PMCID: PMC10416929.

•Fonseca D, Khemani R, Pasam MK, Tagore R, Rao BV, Kodandapani S, Rao C, V N Raju KV, Rao TS. Histological risk score and its role in predicting recurrence in early-stage oral squamous cell carcinomas. Indian J Pathol Microbiol. 2023 Jul-Sep;66(3):444-448. doi: 10.4103/ijpm.ijpm_514_21. PMID: 37530322.

•Kopecká K, Pink R. Pattern of invasion of oral squamous cell carcinoma and its relation to the presence of nodal metastases - a review. Acta Chir Plast. 2023 Spring;65(1):28-33. English. doi: 10.48095/ccachp202328. PMID: 37211421.

•Lakhera KK, Nama Y, Maan P, Jindal R, Patel P, Singh S, Hussain A, Sharma RG. Worst Pattern of Invasion as a Predictor of Nodal Metastasis in Early-Stage Oral Squamous Cell Carcinoma. Indian J Surg Oncol. 2023 Mar;14(1):160-168. doi: 10.1007/s13193-022-01639-y. Epub 2022 Sep 10. PMID: 36891424; PMCID: PMC9986178.

155

Treatment of oropharyngeal cancer during lockdown – outcomes for patients treated during the pandemic

Niall O'Dwyer, Liam O'Connell, Darragh Browne, Mary Dunne, Sinead Brennan, Frances Duane, John Armstrong, Alex Boychak, Orla McArdle

St Luke's Radiation Oncology Network, SLRON, Dublin, Ireland

Topic

HPV or EBV related cancers

Keywords

Oropharynx, COVID-19, survival

Purpose/Objective

The onset of the COVID-19 outbreak caused major interruptions to the entire healthcare network affecting most oncological referral, diagnosis and treatment pathways. Oropharyngeal cancer patients were a particularly vulnerable group during this period as many were reluctant to present to hospital due to their concerns of contracting the virus. This created a potential for delayed presentation in keeping with more advanced disease with potential for worsened outcomes.

We designed a retrospective study to analyse differences in patient presenting stage, treatment encountered, delays encountered and treatment outcomes for patients with oropharyngeal cancer treated before and during the COVID pandemic.

Material/Methods

All patients receiving radical radiotherapy for oropharyngeal cancer pre-COVID (July 17– July 18= GROUP 1) and during COVID (Mar 20–Mar 21= GROUP 2) in a large Irish tertiary referral network were included. Patient and disease characteristics, diagnostic timelines, treatment delays and disease outcomes were extracted from patient records. Patients were excluded if performance status was not suitable for curative treatment, if evidence of metastatic disease or if any history of prior head and neck radiotherapy.

Results

	GROUP 1 N=76 (%)	GROUP 2 N=83 (%)	P value
Sex	M=52 F=24	M=73 F=10	
Age at diagnosis	Median= 59yrs (27-82yrs)	Median=60yrs (36-83yrs)	P=0.498
P16 positive	52 (68%)	59 (71%)	P=0.795
TUMOUR CHARACTERISTICS			
T stage			
Tx	2 (2.6%)	2 (2.4%)	
T1	11 (14.5%)	9 (10.8%)	
T2	22 (28.9%)	41 (49.4%)	
T3	24 (31.6%)	19 (22.9%)	
T4	17 (31.4%)	12 (14.5%)	
N stage			
N0	4 (5.3%)	13 (15.7%)	
N1	35 (46.1%)	48 (57.8%)	
N2	30 (39.4%)	20 (24%)	
N3	7 (9.2%)	2 (2.4%)	
Overall stage			
1	19 (25%)	38 (45.8%)	
2	22 (28.9%)	15 (18%)	P=0.268 (grouped)
3	16 (21%)	13 (15.7%)	
4	19 (25%)	17 (20.5%)	

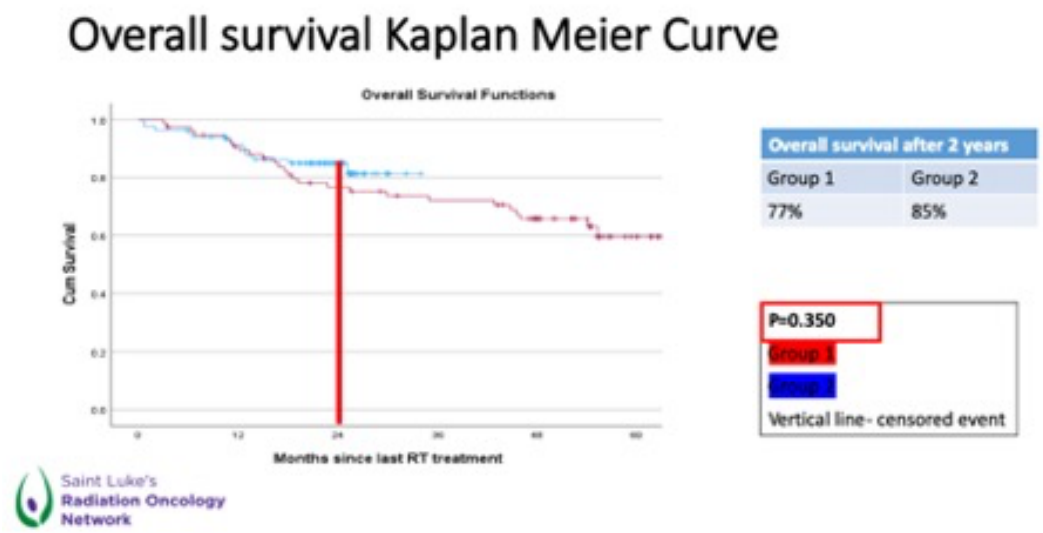
Saint Luke's Radiation Oncology Network

159 patients were suitable for assessment, 76 in Group 1 and 83 in Group 2. Median follow up was 48 months in Group 1 and 23 months in Group 2. When comparing Group 1 and 2: TNM overall stage were as follows: Stage 1: (25% vs 45.8%), Stage 2: (28.9% vs 18%), Stage 3:(21% vs 15.7%), Stage 4:(25% vs 20.5%). When grouped by stage we found no statistically significant difference in presentation stage between Group 1 and 2 (p=0.268).

Use of hypofractionated regimen (65Gy/30fr) increased during the pandemic (2.6% to 10.8%) in keeping with international guidelines. There was no change in numbers of patients experiencing significant treatment delays between groups, with COVID related sepsis accounting for one significant delay and one death during treatment.

There was a small but non-significant reduction in the use of concomitant chemotherapy from 93.4% in group 1 to 85.5% in group 2 (p=0.269).

Overall survival assessed at 2 years was 77% in Group 1 and 85% in Group 2 (p=0.350). Disease free survival assessed at 2 years was 69% in Group 1 and 76% in Group 2 (p=0.567).



Conclusion

In spite of challenges related to the COVID-19 pandemic, this study has demonstrated that oropharyngeal cancer patients' treatment standards and outcomes were maintained within a large tertiary referral centre in Ireland. This study is one of the largest assessing the impact of the COVID-19 pandemic on head and neck radiotherapy patients. We did not demonstrate any difference in overall survival and disease free survival at 2 years when compared to a similar group prior to the pandemic. Furthermore we did not demonstrate any worsening of presenting stage related to delayed presentations during the pandemic.

157

Adaptive radiation therapy

Jean Repha Adhiambo

JKUAT, Radiography, Nairobi, Kenya

Topic

RTT

Keywords

Adaptive radiation therapy

Purpose/Objective

The management of head and neck malignancy requires a multidisciplinary team approach, with an understanding that this disease can produce significant morbidity. Reduction of deformity and restoration of function are important to the management of head and neck cancer. The cure of cancer, with preservation of structure and function (with good cosmetic results), has become more evident with advances in modern radiation oncology because of technologic gains in radiation physics and insights into radiation biology.

Treatment that causes the permanent loss of vision, smell, taste, or hearing should be evaluated concerning its effect on quality of life and survival. Maintenance of food passageways and airways is essential. Treatment decisions should also consider the patient's ability to speak. The loss of speech results in significant changes in the patient's lifestyle and therefore lowers the patient's quality of life. With early detection techniques, head and neck cancers treated with radiation therapy allow for greater preservation of voice and swallowing. Head and neck cancer has witnessed various innovative approaches that include diagnosis and treatment.

The innovative approaches in head and neck oncology involve use of adaptive radiation therapy for large lesions to aid in optimizing treatment plans and improve dose distribution in 3DCRT and IMRT plans.

Material/Methods

A study case example of adaptive radiotherapy involves a male patient who presented to the radiation therapy department with buccal mucosa tumor, a large lesion protruding in the cheek. A 3dimensional conformal radiation therapy plan was made with right and left lateral opposing beams and an anterior neck beam for the nodes. After 4000cGy, it was noted that there was considerable decrease in the size of the tumor. The thermoplastic mask did not correctly immobilize the site of interest.

Results

A CT scan for simulation was performed on the patient and the thermoplastic mask was remoulded to fit into the individual site of interest and consecutively a treatment plan was optimized with reduced margins. This is a form of adaptive radiotherapy. With systematic monitoring of treatment variations, adaptive RT allows reoptimization of the treatment plan during the course of treatment. This process adjusts field margins and treatment dose with routine customization to each individual patient to achieve a safe dose escalation.

Conclusion

Scanning the patient between treatments may guide the treatment strategy in terms of changing the treatment field, escalating dose without overdosing critical structures such as the parotid and spinal cord, and guiding modulation of dose delivery based on tumor growth. These are the few benefits of integrating adaptive radiotherapy in head and neck oncology. The preservation of salivary function with sparing of at least one parotid gland has been a primary objective of head and neck radiotherapy.

Adaptive radiotherapy is also a form of corrective strategy in IGRT. Whereby after a set number of fractions have been completed and there is considerable decrease in the tumor size, prior to the next fraction a more suitable plan is made for tumor control and to minimize dose to critical organs at risk. This is crucial in head and neck oncology. Modification of the treatment plan is done or an appropriate plan is chosen afterwards. IGRT aids in the detection of changes in patient or tumor size. Tumors shrink, we can't use one plan for the patient the same everyday and especially for head and neck cancer which has significantly more fractions.

References

1.Washington,C.M,Leaver,D.T and Megan,T.5th ed.(2020)Principles and Practice of Radiation Therapy Elsevier:Elsevier.

2. Murat,B.,Gokhan,O. and Cuneyt E.2010.Basic Radiation Oncology.Springer-Verlag Berlin Heidelberg.

158

PET CT response outcomes in curatively treated oropharyngeal SCC with bulky N3 neck disease

Fiona Williams[1], Nicholas Morley[2], Webster Richard[1], Rackley Thomas[1], Evans Elin[1], Mererid Evans[1], Nachi Palaniappan[1]

[1]Velindre Cancer Centre, Oncology, Cardiff, United Kingdom. [2]Velindre Cancer Centre, Radiology, Cardiff, United Kingdom

Topic

HPV or EBV related cancers

Keywords

PET-CT, Oropharynx, N3

Purpose/Objective

PET CT scans are used to assess the response following curative intent chemoradiotherapy (CRT) or radiotherapy (RT) for oropharyngeal SCC (OPSCC) 12 weeks after completion of treatment. In the practice changing PETNECK randomised controlled trial, there were 17 patients with N3 neck disease (9 who underwent PET CT surveillance and 8 had planned neck dissections) and in another study (Beyond PETNECK) there were 10 patients. There is little data regarding outcomes following treatment for bulky N3 neck disease. We reviewed our experience of treating patients with bulky N3 neck disease (nodes >6cm, as per TNM7 staging) and their outcomes.

Material/Methods

Patients who had PET CT scans following definitive treatment for OPSCC between 2016 – 2022 in South East Wales were reviewed. 260 patients fulfilled the criteria, of which there were 20 patients with N3 neck disease. Patient demographics, treatment details and PET CT outcomes were collated and analysed.

PET CT response for nodes were categorised as complete response (CR), equivocal response (EQR) and incomplete response (ICR). We analysed the biopsy and salvage surgery results, recurrence rates, 2-year survival data and the impact of neo-adjuvant chemotherapy (NACT) for those with N3 disease.

Results

Of the 20 patients with N3 disease, 17 were male, median age at diagnosis was 60, 17 were P16 positive. Fifteen had NACT, of which 13 went on to have concurrent CRT, 1 patient had concurrent CRT alone without NACT and 6 had RT alone.

PET CT response assessments were performed at a median of 14.4 weeks after completion of treatment. Seventeen patients (85%) had CR at the nodes, 1 (5%) had EQR and 2 (10%) had ICR. Median follow up was 41 months, median overall survival was 47 months and median disease free survival was 42 months.

At last follow up, of the 17 patients with CR, 13 are alive and disease free, 1 developed a primary recurrence and distant metastases but remains alive and undergoing immunotherapy and 3 developed distant metastases and died. The one patient who had EQR underwent a nodal biopsy which was

negative, they remain alive and disease free. Of the 2 patients who had ICR, 1 underwent a salvage neck dissection which was negative and they remain alive and disease free whilst the other developed nodal and distant metastases and died.

Five (25%) developed distant metastatic disease, at a median time from completion of treatment to distant metastases was 4.33 months and mean 5.63 months. Of these, one also developed a primary recurrence and is still alive, while the remaining four died.

Conclusion

The complete nodal response rate in this cohort of patients receiving curative treatment is 85%, which is higher than the 56% reported in PETNECK, however PETNECK includes both N2 and N3 neck disease. In our cohort, fifteen patients received NACT and most were P16 positive. The data regarding the use of NACT in N3 neck disease in PETNECK was not available, so it was not possible to directly compare the outcomes.

Fifteen patients are alive and disease free at a median follow up of 41 months. It is difficult to know the reasons for higher response rates in this cohort of patients, but it could be due to the majority being P16 positive and/or the addition of NACT. Patients who developed distant metastases developed them within 6 months of completion of treatment. More work needs to be done to understand the role of NACT and its potential benefit in bulky N3 disease.

References

[1] Mehanna H et al. PET-CT Surveillance versus Neck Dissection in Advanced Head and Neck Cancer. The New England Journal of Medicine 2016; 374:1444-1454. DOI: 10.1056/NEJMoa1514493.

[2] Zhou S et al. Positron Emission Tomography-Computed Tomography Surveillance after (Chemo)Radiotherapy in Advanced Head and Neck Squamous Cell Cancer: Beyond the PET-NECK Protocol. Clinical Oncology 32 (2020) 665e673.

159

Patient-oriented, individualized follow-up in head and neck cancer (DeIntensiF randomized trial NCT05388136)

Roland Giger[1], Simon A. Mueller[2], Thomas Stadler[2], Gunesh P. Rajan[3], Gregoire B. Morand[3], Sara-Lynn Hool[1], Daniel H. Schanne[4], Timo Nannen[4], Panagiotis Balermpas[5], Andreas Limacher[6], Samantha Chan[6], Sven Trelle[6], Olgun Elicin[4]

[1]Inselspital, Bern University Hospital, University of Bern, Otorhinolaryngology, Head and Neck Surgery, Bern, Switzerland. [2]Zurich University Hospital, Otorhinolaryngology, Head and Neck Surgery, Zurich, Switzerland. [3]Lucern Cantonal Hospital, Otorhinolaryngology, Head and Neck Surgery, Lucern, Switzerland. [4]Inselspital, Bern University Hospital, University of Bern, Radiation Oncology, Bern, Switzerland. [5]Zurich University Hospital, Radiation Oncology, Zurich, Switzerland. [6]University of Bern, Clinical Trials Unit, Bern, Switzerland

Topic

Quality of life and outcomes

Keywords

head and neck cancer, follow-up care, outcome

Purpose/Objective

Approximately 70% of head and neck cancer (HNC) patients present with locoregionally advanced disease. The curative rate for early disease is 80-95%; for advanced tumors, locoregional recurrence rate remains at about 50-60% despite advances in treatment, and 20-30% will have distant metastases. Further, patients will develop a second primary malignancy (SPM) with a rate of 2-4% per year.

Follow-up (FU) is important to detect recurrence (REC) and SPM at an early stage, to enable effective salvagetherapy, manage treatment-related sequelae, and provide functional rehabilitation and psychosocial support.

In the absence of high-level evidence, there is no clear international consensus in FU regimens. There are only retrospective studies addressing this topic, mostly showing no difference in overall survival between patients with REC detected during routine FU and symptom-driven self-referral visits. The value of imaging is also subject of debate. Moreover, many of the hitherto published studies did not include the logistical, psychological and financial consequences and the relevant cost evaluations in today's healthcare systems facing increasing financial pressure.

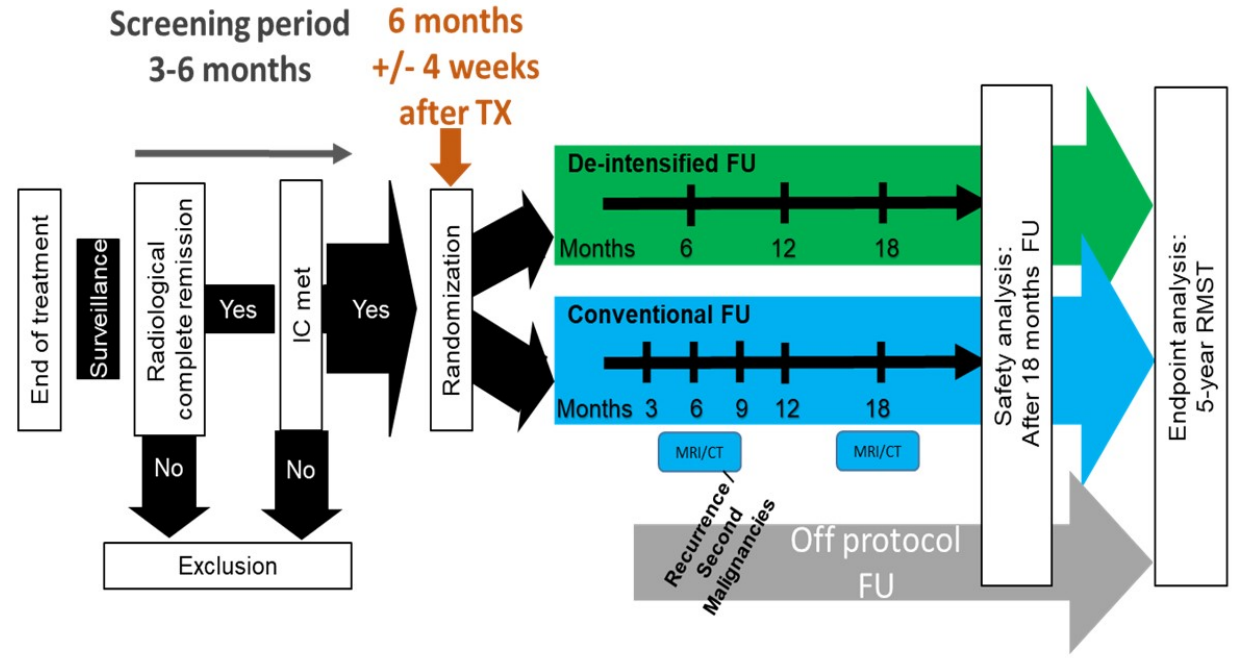
We propose a large multicenter, randomized prospective trial in HNC patients with complete remission 6 months after curative treatment to compare two FU schemes differing in frequency of scheduled clinical examinations and imaging. We hypothesize that implementing an individualized de-intensified FU with active patient involvement does not differ from a conventional regular FU in terms of death from any cause up to 5 years (=primary endpoint). We also hypothesize that symptom-driven self-referral FU visits have a higher diagnostic yield in detection of REC/SPM than regular scheduled clinical and radiological examinations. Consequently, we assume that fewer scheduled exams in well-instructed patients will not lead to worse outcome. The secondary objectives are the comparison of death from HNC and any cancer, detection of first REC/SPM, health-related quality of life, fear of recurrence, compliance with FU assessments, number of visits and HNC-specific health-care utilization.

The objective of the herein presented Pilot 1 study was to assess the feasibility of patients' recruitment, motivation for trial participation and compliance in completing a monthly, paper-based symptoms' monitoring (patient-reported outcome [PRO], symptom tracker). This Pilot is supported by Swiss Cancer Research.

Material/Methods

The study design is shown in Figure 1 (RMST: restricted mean survival time).

Figure 1



The main study is a randomized-controlled combined non-inferiority and superiority trial with explicit Pilot 1 and 2. After curative treatment, participants are randomized to an individualized de-intensified FU with monthly symptoms' monitoring (Figure 2) (experimental arm) or to standard FU.

Figure 2

		Answers				
1.	**Weight** Insert the current weight on the left (use always the same scale at home and under the same conditions) and check on the right whether the weight loss was desired or undesired	(kg)		Weight loss ☐ Unintentional ☐ Intentional ☐ No		
Signs / Symptoms Please indicate severity of signs that have been present **for at least 3 weeks**.		None	Mild	Moderate	Severe	Very severe
2.	**Wound, sores or lump in mouth or throat?**	0	1	2	3	4
3.	**Blood in saliva or sputum?**	0	1	2	3	4
4.	**Ear pain on one or both sides?**	0	1	2	3	4
5.	**Palpable new lump in the neck?**	0	1	2	3	4
6.	**Hoarseness?**	0	1	2	3	4
7.	**Pain or burning sensation in mouth or throat?**	0	1	2	3	4
8.	**Difficulty swallowing?**	0	1	2	3	4
9.	**Difficulty opening the mouth?**	0	1	2	3	4
10.	**Foul smelling breath?**	0	1	2	3	4
11.	**Chest pain?**	0	1	2	3	4
12.	**Shortness of breath?**	0	1	2	3	4
13.	**Cough?**	0	1	2	3	4
14.	**Noisy breathing?**	0	1	2	3	4
15.	**Fatigue or weakness?**	0	1	2	3	4
16.	**Loss of appetite?**	0	1	2	3	4
17.	**Persistent skin lesion (whole body)?**	0	1	2	3	4
18.	**Fear of the cancer coming back?** How would you describe your worst-case fear? 0. I have no fear of recurrence 1. I have a little fear, with occasional thoughts but they don't really bother me 2. I am sometimes having fearful thoughts but I can usually manage these 3. I get a lot of fears of recurrence and these can really preoccupy my thoughts 4. I am fearful all the time that my cancer might return and I struggle with this	0	1	2	3	4

Alerting symptoms possibly indicating REC/SPM or non-completion of the PROs will result in an urgent clinical FU appointment in the experimental arm. Minimal FU within Pilot 1 is 12 months (as opposed to 60 months in the main trial). Recruitment was done in three Swiss tertiary referral centers, which committed to enroll at least 20 patients during one year.

Results

The primary aim of Pilot 1, evaluating the feasibility of patient recruitment, has been confirmed faster than expected (20 committed patients randomized after 7 and 29 patients randomized after 11 months accrual time, respectively). Six unscheduled visits were triggered by our paper-based PRO. Within Pilot 1, a prescreening survey was conducted to better understand the specific motivation of patients to participate in the trial or not. We surveyed 41 potential participants of which 27 (66%) agreed to participate. The potential reduction in imaging was the main reason for the patients to participate in the trial (52%). Additionally, we collected feedback on the design of the paper-based PRO questionnaire at the 6-month FU visit when participants had already gained some experience. Participants expressed that the PRO questionnaire was easy to understand and comprehensive, thus facilitating them to communicate with their corresponding study center. The completion time for the PRO was between 5-10 minutes in 63% of the participants. In addition, 63% of the patients were in favor of transitioning the

paper-based PRO to an electronic version (ePRO), the other 37% felt unsure about using an ePRO. Interim compliance data will be presented.

Conclusion

The recruitment and symptoms' monitoring for HNC patients have been proofed as feasible. Pilot 2 is in planning to allow for a smooth continuation of Pilot 1 with following specific goals: 1) to expand the trial to 12 Swiss and 4 European sites; 2) to recruit up to 200 participants; 3) to implement a web-based version of the symptom tracker (ePRO); 4) to develop an enhanced training strategy for HNC patients; 5) to evaluate the usability of the ePRO; and 6) to assess the safety of omitting systematic lung imaging.

References

Nguyen NA, Ringash J. Head and Neck Cancer Survivorship Care: A Review of the Current Guidelines and Remaining Unmet Needs. Curr Treat Options Oncol. 2018;19:44.

160

Review of oropharyngeal cancer recurrences- how do they present?

Niall O'Dwyer, Darragh Browne, Sinead Brennan, Frances Duane, John Armstrong, Alex Boychak, Orla McArdle

St Lukes Radiation Oncology Network, SLRON, Dublin, Ireland

Topic

HPV or EBV related cancers

Keywords

Oropharynx, Recurrence, presentation

Purpose/Objective

Oropharyngeal squamous cell cancers have a locoregional recurrence rate range of 17.3-32.5% and a distant metastatic rate of 6.5-17% at 3 years (ref1). Structured follow up is of paramount importance to facilitate early diagnosis and salvage treatment. We examined a cohort of patients with oropharyngeal cancer treated radically within a large Irish tertiary referral centre with diagnosed recurrence in order to better understand the clinical presentation and to optimise outpatient follow up following radical treatment.

Material/Methods

An existing database of 259 new oropharynx cancer patients treated radically between 2012 and 2020 was assessed to identify any patient with established recurrence. For those with recurrence: details of clinical presentation and diagnosis were recorded.

Results

Of the 259 patients assessed 70 experienced recurrence: 12 with locoregional failure, 12 with both local and distant failure, 25 with distant only failure and 21 with persistent disease post treatment.

Of the 12 locoregional failures- 92% were symptomatic: pain (83%) and neck lump (8%). One recurrence was identified during routine outpatient review, the remainder following patient contact after onset of symptoms. 75% of the patients with locoregional failure had non-HPV related cancers, and 85% of the group were stage 3 or stage 4 at initial presentation. In terms of timeline to presentation, 50% had been identified within 9 months and 80% within 2 years following treatment.

Of the 12 local + distant failures- 75% were symptomatic: pain (67%) and neck lump (8%). 2 patient recurrences were identified during routine outpatient review, the remainder following patient contact. 50% of the patients in this group had HPV related tumours and 50% of this group were stage 3 or stage 4 at initial presentation. 80% of these recurrences had been identified within 2 years following treatment.

Of the 25 distant failures: 61% were identified on post treatment imaging, 15% presented with respiratory symptoms, 12% presented with pain or palpable lump and 12% were identified on routine imaging. 70% of the patients in this group had HPV related tumours and 57% of this group were stage 3 or 4 at presentation. 80% of these recurrences has been identified within 2 years following treatment.

21 patients were found to have persistent disease following treatment- all were identified on post treatment imaging.

Conclusion

Locoregional recurrence of oropharynx cancer is associated with patient symptoms in over 90% of cases, most commonly pain. These symptoms are rarely discovered during routine review. Of the 12 patients found to have locoregional recurrence, 75% of the group were non HPV related tumours, 85% were stage 3 or 4 at initial presentation and 80% of the recurrences were identified within 2 years of treatment.

This study highlights the importance of both patient and staff education and the importance of outpatient communication pathways that facilitate prompt review and investigation of new symptoms.

References

T. Guo et al: Current perspectives on recurrent HPV-mediated oropharyngeal cancer: Front. Oncology, 18 August 2022. Head and Neck Cancer. Vol 12-2022

161

14-day Pathway from Decision to Treat to Radiotherapy for Head and Neck Cancer in the National Health Service: An Evaluation of Feasibility and Outcomes at Torbay Hospital.

Victoria Cope, Jonathan Chambers, Sarah Kingdon, Naomi Cole

Torbay Hospital, Clinical Oncology, Torquay, United Kingdom

Topic

Quality of life and outcomes

Keywords

Multidisciplinary management

Purpose/Objective

In squamous cell carcinoma of the head and neck there is significant evidence that a prolonged time to treatment initiation results in worse overall survival and loco-regional control[1-6]. This is also evidenced in the adjuvant setting: Patients receiving radiotherapy within 11 weeks of surgery had significant improvement in loco-regional control, compared to those who waited more than 13 weeks[7-11]. This is reflected in NHS England and JCCO guidance[12].

The primary objective of this audit was to evaluate compliance to a 14-day pathway from decision to treat (DTT) to radical radiotherapy, over a 5-year period at Torbay Hospital, UK [13]. We also evaluated compliance for patients receiving postoperative radiotherapy: aiming for all patients to start adjuvant treatment within 35 days of surgery. Our secondary objective was to review survival and recurrence rates within these patients.

Material/Methods

A 14-day pathway from DTT to start of radiotherapy was developed following a quality improvement project which identified common causes of delay. Key preparatory steps are scheduled to enable timely radiotherapy delivery. The pathway is demonstrated in Figure 1.

Mon	Tues	Wed	Thurs	Fri	Sat	Sun
MDT	Clinic	CT Planning Scan	Outlining **Latest Date Dental Extractions**			
Peer r/v and volumes finalised			Plan Approved (am)	QA completed		
RT start						

From January 2017 to December 2022, data on DTT date, site of disease, radiotherapy start date, date of surgery, date of recurrence and date of death was prospectively collected for all patients undergoing definitive radiotherapy or post-operative radiotherapy with curative intent for squamous cell carcinoma of the head and neck. Patients undergoing radiotherapy with palliative intent, patients with non-squamous cell cancers, benign pathologies and patients receiving neoadjuvant chemotherapy or targeted systemic treatment were excluded. 187 patients were included in total over the period.

Results

117 (62.6%) patients underwent radical radiotherapy within 14 days of DTT, 55 (29.4%) patients started within 15 to 21 days and 15 (8.0%) patients started after more than 22 days. Of the 75 patients receiving radiotherapy adjuvantly, 39 (52%) received radiotherapy within 35 days of surgery and 49 (65%) patients received radiotherapy within the national target of 42 days.

158 (84.5%) patients of the 187 treated within the 5-year period were alive at the end of the study period. 9 (4.8%) patients had had a local recurrence of their disease only, 17 (9.1%) patients had metastatic disease. Recurrence by site was; Larynx: 3 of 25 (12%), P16 positive oropharynx: 5 of 84 (6%), P16 negative oropharynx: 4 of 10 (40%), Oral Cavity: 7 of 26 (26.9%), Nasopharynx: 2 of 4 (50%), Parotid: 4 of 15 (26.7%), CUP: 1 of 12 (8.3%). 10 (38.4%) of the 26 patients who developed loco-regional recurrence or metastatic disease had a treatment time of more than 14 days. There was one treatment-related death due to neutropenic sepsis.

Conclusion

This audit demonstrates that a 14-day pathway for the radical treatment of squamous cell cancers of the head and neck is achievable for the majority of patients. Whilst local recurrence and survival data is not mature it is thus far in-keeping with published outcomes. Adherence to the pathway has been maintained over a prolonged period despite workload pressures within the NHS, at no extra financial cost and throughout the Covid-19 pandemic. We therefore believe this would be transferrable to other treatment centres.

References

1. Fortin A, Bairati I, Albert M, Moore L et al. Effect of treatment delay on outcome of patients with early-stage head-and-neck carcinoma receiving radical radiotherapy. Int J Radiat Oncol Biol Phys. 2002 Mar 15;52(4):929-36.

2. van Harten MC, Hoebers FJ, Kross KW et al. Determinants of treatment waiting times for head and neck cancer in the Netherlands and their relation to survival. Oral Oncol 2015 Mar;51(3):272-8.

3. Chen Z, King W, Pearcey R, Kerba M et al. The relationship between waiting time for radiotherapy and clinical outcomes: a systematic review of the literature. Radiother Oncol. 2008 Apr;87(1):3-16.

4. Polesel J, Furlan C, Birri S, Giacomarra V et al. The impact of time to treatment initiation on survival from head and neck cancer in north-eastern Italy. Oral Oncol. 2017 Apr;67:175-182.

5. Grønhøj C, Jensen D, Dehlendorff C, Nørregaard C et al. Impact of Time to Treatment Initiation in Patients with Human Papillomavirus-positive and -negative Oropharyngeal Squamous Cell Carcinoma. Clin Oncol (R Coll Radiol). 2018 Jun;30(6):375-381.

6. Dalke et al. Impact of Time Factors on Outcome in Patients with Head and Neck Cancer Treated with Definitive Radio(Chemo)Therapy. Sep-Oct;31(5):949-955. In Vivo. 2017.

7. Byers RM, Clayman GL, Guillamondequi OM et al. Resection of advanced cervical metastasis prior to definitive radiotherapy for primary squamous carcinomas of the upper aerodigestive tract. Head Neck. 1992 Mar-Apr;14(2):133-8.

8. Peters LJ, Goepfert H, Ang KK, Byers RM et al. Evaluation of the dose for postoperative radiation therapy of head and neck cancer: first report of a prospective randomized trial. Int J Radiat Oncol Biol Phys. 1993 Apr 30;26(1):3-11.

9. Ang KK, Trotti A, Brown BW, Garden AS et al. Randomized trial addressing risk features and time factors of surgery plus radiotherapy in advanced head-and-neck cancer. Int J Radiat Oncol Biol Phys. 2001 Nov 1;51(3):571-8.

10. Tribius S, Donner J, Pazdyka H, Münscher A et al. Survival and overall treatment time after postoperative radio(chemo)therapy in patients with head and neck cancer. Head Neck. 2016 Jul;38(7):1058-65.

11. Graboyes EM, Garrett-Mayer E, Ellis MA, Sharma AK et al. Effect of time to initiation of postoperative radiation therapy on survival in surgically managed head and neck cancer. Cancer. 2017 Dec 15;123(24):4841-4850.

12. House of Commons Committee of Public Accounts 'NHS waiting times for elective and cancer treatment' One Hundredth Report of Session 2017–19. HC 1750 Published on 12 June 2019.

13. Cope V, Chambers J, Kingdon S, Cole N. Is a 14-day Pathway From Decision to Treat to Radiotherapy for Head and Neck Cancer Patients Feasible in the National Health Service? The Torbay Experience 5 Years On. Clinical Oncology. 2023:35 (11) 756-758.

164

Pre-operative Radiotherapy for Sinonasal Squamous Cell Carcinoma: outcomes and patient selection

Revadhi C Chelvarajah[1], Shao Hui Huang[1], Jie Su[2], Jolie Ringash[1], Ian Witterick[3], John de Almeida[3], Eric Monteiro[3], Anna Spreafico[4], John Waldron[1], Brian O'Sullivan[1], Ali Hosni Abdalaty[1], Scott Bratman[1], B.C. John Cho[1], Andrew Hope[1], John Kim[1], Andrew McPartlin[1], C. Jillian Tsai[1], Li Tong[1], Wei Xu[2], Ezra Hahn[1]

[1]Princess Margaret Cancer Centre, Radiation Oncology, Toronto, Canada. [2]Princess Margaret Cancer Centre, Biostatistics, Toronto, Canada. [3]Mount Sinai Hospital, Head and Neck Surgical Oncology, Toronto, Canada. [4]Princess Margaret Cancer Centre, Division of Medical Oncology, Toronto, Canada

Topic

Multidisciplinary management

Keywords

Sinonasal SCC, pre-operative radiation

Purpose/Objective

Resectable sinonasal squamous cell carcinoma (SNSCC) is often managed by surgery +/- post-operative radiation (postop-RT), guided by surgical pathology. In our institution, pre-operative radiation (preop-RT) +/- chemotherapy has been used in select cases after multidisciplinary input from radiation, surgical, and medical oncology teams. Preop-RT has the advantages of lower dose and smaller/better defined volumes in non-surgically perturbed tissues, which can be especially important for treatment approximating optic structures. The aim of this study is to evaluate preop-RT, compared to standard postop-RT, in patients with SNSCC, focusing on oncologic outcomes and patient selection.

Material/Methods

All newly diagnosed SNSCC treated with preop-RT or postop-RT from 2005 to 2021 were included. Clinical characteristics and outcomes were compared between preop-RT vs postop-RT cohorts.

Outcome endpoints included overall survival (OS), disease-free survival (DFS), locoregional control (LRC) and distant control (DC). OS and DFS were estimated with Kaplan-Meier method while LRC and DC were calculated with competing risk methods.

Results

A total of 72 patients were eligible: 25 received preop-RT and 47 postop-RT. The preop-RT cohort comprised more origin from the ethmoid sinus (44% vs 0%, p<0.001), and more T3-T4 diseases (versus T1-2) at presentation (96% vs 68%, p<0.01). HPV testing was not performed in the majority of cases; among those tested, two out of 8 (25%) SNSCC tested p16-positive in the preop-RT cohort and 13 out of 18 (72%) in the postop-RT cohort. The remaining baseline characteristics were similar between the preop-RT vs postop-RT cohorts. The documented clinical reasons for pre-operative radiation included minimizing dose to preserve orbital structures and avoidance of orbital exenteration (n=12, 48%), improving resection margin clearance (n=7, 28%), and reducing extent and morbidity of the surgical approach (n=4, 16%). All patients in preop-RT cohort received 50 Gy in 25 fractions (50 Gy/25f) to the primary site, with 7 patients receiving a boost to 60 Gy (6 patients with simultaneous integrated boost, 1 patient with sequential 10 Gy/5f boost). The reasons for boost were treatment of gross/equivocal nodal disease to spare a neck dissection (n=4, 57%), or high-risk surgical regions with a high likelihood of a R1 resection based on a pre-emptive discussion with the surgical team (n=3, 43%). Three patients received concurrent cisplatin chemotherapy. Patients in the postop-RT cohort received 60 Gy/30f (n=11), 66 Gy/33f (n=20), 70 Gy/33-35f (n=11), and other (n=5). Fourteen (56%) preop-RT patients had complete pathological responses. The median follow-up was 5.5 and 5.2 years for the preop-RT and postop-RT cohort, respectively. Oncologic outcomes at 5-years were similar between preop-RT and postop-RT cohorts: OS 76% vs 69% (p=0.799), DFS 66% vs 62% (p=0.892), LRC 78% vs 69% (p=0.313), and DC 92% vs 88% (p=0.919), respectively (Table 1).

Table 1. Oncologic Outcomes

	Postop-RT (n=47)	Preop-RT (n=25)	P value
5-year Outcomes			
OS	69% (57-85)	76% (61-95)	0.799
DFS	62% (50-78)	66% (49-89)	0.892
LRC	69% (52-80)	78% (50-90)	0.313
DC	88% (72-95)	92% (69-98)	0.919

Conclusion

With multidisciplinary decision-making for SNSCC, preop-RT is correlated with pathologic complete response, and lower doses to critical normal tissues. Oncologic outcomes are comparable between the two groups despite more T3-T4 disease in the preop-RT cohort. In the setting of collaborative multidisciplinary care in a high-volume centre, pre-op RT in the management of locally advanced resectable sinonasal SCC is a reasonable, and possibly preferred, option in select patients to minimize dose to optic structures and improve margin clearance.

168

Automated analysis of elective neck radiation therapy patterns in patients with head and neck cancer

Joseph Marsilla[1], Jun Won Kim[2,3], Sejin Kim[1], Mattea Welch[4], Shao Hui Huang[5,1], Brian O'Sullivan[5], Scott Bratman[5,6], Benjamin Haibe-Kains[1], Andrew Hope[6,5]

[1]University of Toronto, Biophysics, Toronto, Canada. [2]Gangnam Severance, Radiation Oncology, Seoul, Korea, Republic of. [3]Yonsei University College of Medicine, Radiation Oncology, Seoul, Korea, Republic of. [4]University Health Network, Cancer Data Informatics, Toronto, Canada. [5]Princess Margaret Cancer Centre, Radiation Medicine, Toronto, Canada. [6]University of Toronto, Radiation Oncology, Toronto, Canada

Topic

Imaging, radiomics and artificial intelligence

Keywords

radiation, elective neck, segmentation

Purpose/Objective

In patients with head and neck cancer treated with radiation therapy, the choice of which neck levels require elective radiation can dramatically influence the risk of regional failure and may contribute to cancer mortality and overall survival. Retrospective evaluation of elective nodal coverage in previously treated patients with head and neck cancer is a time intensive and, in most cases, subjective process. In order to objectively assess the extent of lymph node irradiation in large cohorts of patients, automated objective methods to assess elective lymph node treatment are crucial. In this work, we demonstrate a novel approach using a convolutional neural network (CNN) to autosegment, retrospectively label, and classify the extent of elective neck irradiation in previously treated patients.

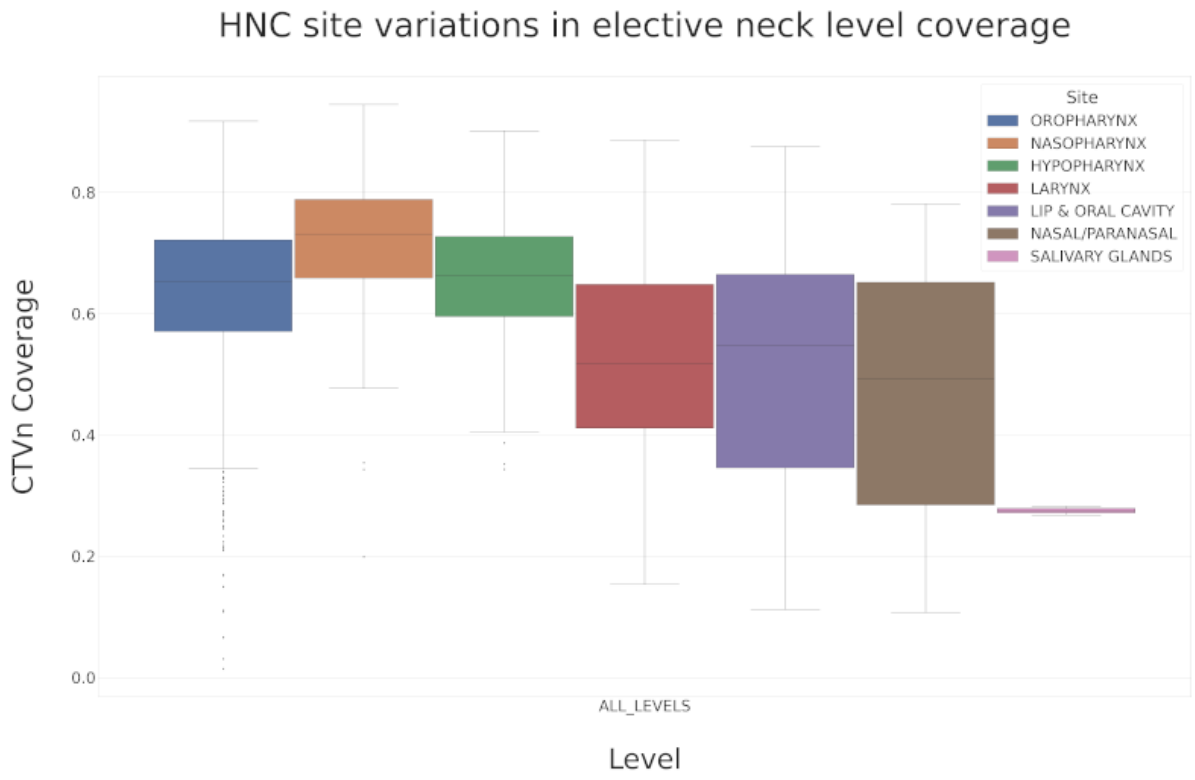
Material/Methods

Initially, 100 patients with head and neck cancer were contoured to identify all elective neck level targets as per standard guidelines[1], including levels IA, IB, II, III, IV, V, VIIA on both left and right necks. These patients were used to train a CNN neck level model (NLM) which was validated on a further 10 patients clinically. After training, the resultant NLM was applied retrospectively to all patients in the RADCURE dataset[2]. Overlap between the autosegmented NLM model contours with existing elective neck CTV targets was assessed using the proportion of voxel overlap of the individual neck structures with the elective CTV which was clinically defined. Primary tumor laterality as assessed in the clinical database was used to normalize right and left neck targets to ipsilateral and contralateral relative to the primary tumor. Neck levels were assumed to be 'treated' if >70% of the auto-segmented volume was overlapped with the clinical elective CTV target in the respective neck. Summary statistics were calculated by disease site, tumor volume, staging information, and clinical variables to evaluate patterns of CTV coverage and associations with tumor or patient factors.

Results

A total of 1,748 patients within the RADCURE dataset were included in the analysis as they had the primary tumor laterality defined clinically. After NLM application, comprehensive neck irradiation (IA-VIIA) occurred in 33%, 55%, 31%, 16%, 14%, and 12% of patients with oropharynx, nasopharynx, hypopharynx, larynx, oral cavity, and paranasal/nasal primary disease sites, respectively. Within primary disease sites, the proportion of the entire elective neck (IA-VII) which was included in the elective target volume varied substantially within sites but also showed expected differences in elective neck treatment (Figure) with nasopharynx representing the most comprehensive approach and nasal and salivary glands the least comprehensive approaches. Important patterns of elective treatment

were visible with variations in specific levels of treatment related to primary site evident in the objective classifications of levels IA, II, and the retropharyngeal (VIIA) nodes. (Table). Specifically, coverage of level IA was rare, but more common in patients with lip/oral cavity or paranasal/nasal primary site. In patients with oropharyngeal primary disease, contralateral level II overlap showed approximately 12% of oropharynx patients were treated with ipsilateral intent only consistent with our previous reports from our institution.[3] Retropharyngeal lymph node coverage was highest in the patients with nasopharyngeal disease, but identified a critical variation in contouring whereby a subset of patients did not have a formal elective VIIA target and instead relied on the overlap of primary site CTVs to ensure coverage of these regions.



	Percentage of patients by site with neck level included in elective CTV					
Neck level	Oropharynx	Nasopharynx	Hypopharynx	Larynx	Lip/Oral	Nasal/Paranasal
Level IA	4%	4%	3%	0%	21%	15%
Level IB (ipsi)	83%	73%	67%	30%	94%	50%
Level IB (contra)	35%	57%	24%	15%	35%	46%
Level II (ipsi)	98%	99%	98%	82%	98%	85%
Level II (contra)	87%	99%	93%	72%	58%	71%
Level VIIA (ipsi)	61%	71%	67%	21%	44%	39%
Level VIIA (contra)	33%	64%	30%	12%	17%	24%

Conclusion

Automatic assessment of elective neck coverage using a neck level auto-segmentation model shows substantial (but anticipated) variation in elective neck coverage based on disease site. Objective

methods to interrogate target volumes and the resultant plan information will allow more detailed analysis and understanding of patterns of failure following radiation therapy.

References

1. Grégoire, V. et al. Delineation of the neck node levels for head and neck tumors: a 2013 update. DAHANCA, EORTC, HKNPCSG, NCIC CTG, NCRI, RTOG, TROG consensus guidelines. Radiother. Oncol. J. Eur. Soc. Ther. Radiol. Oncol. 110, 172–181 (2014).

2. Welch, M et al. Computed Tomography Images from Large Head and Neck Cohort (RADCURE) (Version 1). doi:https://doi.org/10.7937/J47W-NM11.

3. Huang, S. H. et al. Re-evaluation of Ipsilateral Radiation for T1-T2N0-N2b Tonsil Carcinoma at the Princess Margaret Hospital in the Human Papillomavirus Era, 25 Years Later. Int. J. Radiat. Oncol. Biol. Phys. 98, 159–169 (2017).

170

Long term outcomes of the FiGaRO trial: 18F-FDG-PET in Guided Dose-Painting with Intensity Modulated Radiotherapy in Oropharyngeal Tumours

Delali Adjogatse[1,2], Andriana Michaelidou[2], Yae-Eun Suh[3], Lucy Pike[4,2], Christopher Thomas[2,5], Beatriz Sanchez Nieto[6], Mary Lei[1], Sally F Barrington[2], Teresa Guerrero Urbano[1]

[1]Guy's and St Thomas' NHS Foundation Trust, Oncology, London, United Kingdom. [2]King's College London, School of Biomedical Engineering and Imaging Sciences, London, United Kingdom. [3]King's College London, PET centre, London, United Kingdom. [4]King's College London, PET Centre, London, United Kingdom. [5]Guy's and St Thomas' NHS Foundation Trust, Medical physics, London, United Kingdom. [6]Pontificia Universidad Catolica de Chile, Faculty of Physics, Santiago, Chile

Topic

Innovative treatments

Keywords

Dose escalation. Image-guided.

Purpose/Objective

The FiGaRO trial assessed the feasibility and safety of using an FDG-PET-based dose-painting technique to deliver a radiotherapy (RT) boost to the FDG-avid primary tumour in patients with locally advanced high-to-intermediate risk oropharyngeal cancer. Patients were followed up within the study for 2 years. Patients treated at Guy's and St Thomas' hospital subsequently continued with standard clinical follow-up for a minimum of 5 years. The initial survival and toxicity data for all enrolled patients has previously been reported. The purpose of this further evaluation was to report the long-term survival and toxicity outcomes for patients treated within the FiGaRO trial at Guy's and St Thomas' Hospital.

Material/Methods

This study received local institutional approval as a service evaluation. Between April 2014 and October 2017 nineteen patients were treated within the study. Patients underwent a planning 18FDG-PET-CT scan (with contrast enhancement), immobilised in the treatment position, after one cycle of platinum-based induction chemotherapy. The volume of persistent FDG-avidity in the primary tumour, seen after 1 cycle of induction chemo, was escalated to 71.5 Gy in 30 fractions. The dose-escalation was delivered using a simultaneous integrated boost Intensity Modulated RT (SIB-IMRT) technique. Radiotherapy was delivered with concomitant cisplatin following 2 cycles of induction chemotherapy. On completion of trial-specific follow-up, patients were followed up annually until at least 5 years post-completion of radiotherapy. Late toxicity was assessed using Radiation Therapy Oncology Group (RTOG) and European Organization for Research and Treatment of Cancer (EORTC), and Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 toxicity scales.

Results

The median follow-up for living patients treated within the study was 68 months (range 61-101 months). All patients completed RT as prescribed. A median RT dose of 69.9 Gy (range 68.7-70.7) was delivered to ≥95% of the GTV-PET. Eleven patients had T4 primary tumours, three patients had a T3 tumour, and five patients had T2 tumours. All patients had nodal staging N2b or above.

During follow-up there were three local recurrences which all occurred within 12 months of treatment completion. Local control at 5-years was 83.9%. Five-year overall and disease-specific survival was 73.7% and 78.9%, respectively. The 5-year disease-specific survival was superior for intermediate-risk versus high-risk patients: 83.3% versus 71.4%, although this did not reach statistical significance.

Within this cohort there were no cases of persistent grade 3 or more mucosal toxicity, or persistent feeding tube use at 2 or more years post-treatment. Late grade 3 toxicity was limited to CTCAE grade 3 hearing loss (n=2) at 5 years, and RTOG grade 3 osteoradionecrosis of the jaw at 2- and 5 years (n=1). There were no further cases of grade 3 or more toxicity. The predominant toxicities at 2 years were; CTCAE grade 2 dysphagia (n=3) and xerostomia (n=5), and RTOG grade 2 mucosal toxicity (n=3). The predominant toxicities at 5 years were; CTCAE grade 2 dysphagia and xerostomia (n=3, respectively), and RTOG grade 2 mucosal toxicity (n=3).

Conclusion

The long-term outcomes suggest acceptable late toxicity rates and promising local control and disease-specific survival rates for patient treated within the FiGaRO trial. The escalation dose used in FiGaRO may be a suitable dose for further adaptive dose-escalation radiotherapy studies.

References

Michaelidou A, Adjogatse D, Suh Y, Pike L, Thomas C, Woodley O, Rackely T, Palaniappan N, Jayaprakasam V, Sanchez-Nieto B, Evans M. 18F-FDG-PET in guided dose-painting with intensity modulated radiotherapy in oropharyngeal tumours: A phase I study (FiGaRO). Radiotherapy and Oncology. 2021 Feb 1;155:261-8.

173

Return to work after curative radiotherapy in head and neck cancer survivors

Renata Zahu[1,2], Daniela Elena Sturzu[2], Cristina Tiple[3], Stefan Cristian Vesa[4], Magdalena Chirila[3], Gabriel Kacso[1,2]

[1]"Iuliu Hatieganu" University of Medicine and Pharmacy, Department of Oncology-Radiotherapy, Cluj-Napoca, Romania. [2]Amethyst Radiotherapy Center, Department of Radiotherapy, Cluj-Napoca, Romania. [3]"Iuliu Hatieganu" University of Medicine and Pharmacy, Department of Otolaryngology, Cluj-Napoca, Romania. [4]"Iuliu Hatieganu" University of Medicine and Pharmacy, Department 2 Functional Sciences, Discipline of Pharmacology, Toxicology and Clinical Pharmacology, Cluj-Napoca, Romania

Topic

Supportive care, rehabilitation

Keywords

head and neck cancer, return to work

Purpose/Objective

The improvement in survival rates of head and neck cancer patients and the increasing incidence of HPV induced cancers in young people has an important socioeconomic impact. We evaluated the rate of reemployment after having curative radiotherapy for head and neck cancer and tried to identify the barriers of successful return to work in this patient population.

Material/Methods

We performed a cross-sectional, single-institution study including 52 consecutive patients attending followup visits after curative VMAT radiotherapy for head and neck cancer between december 2022-august 2023. Eligible participants were aged 18 to 65 years at diagnosis, employed at or within 3 months before the start of the treatment and had at least 12 months of followup. Participants completed a paper-based survey to assess baseline demographics and lifestyle choices such as smoking and alcohol consumption, employment status.

Results

Mean age was 50 (22-65 years) and 75% were male. Most participants (38.5%) had nasopharynx cancer followed by oropharyngeal cancer in 25%. Successful return to work rate was 55.8%. Only 8 patients (15.4%) returned earlier than 6 months to employment. 22 patients (75.8%) of those who returned, worked full time and one patient was forced to change his profession.

At the time of the analysis 23 cancer survivors (44.2%) were not working. 18 of these choose early retirement and are not planning to return, the rest of 5 patients are still on sick leave and might plan to reemploy. 77.3% reported physical symptoms being the main cause preventing reemployment. The most common physical symptom reported was fatigue in 58.9% cases.

Conclusion

With all technical improvements in treatment delivery with the scope of reducing long term toxicity there is still an important percentage of head and neck cancer survivors not able to return to work after radiotherapy. Professional assistance in their cancer rehabilitation is needed to increase reemployment rates. The high incidence of fatigue in this population warrants further research.

References

1.Kjær T, Bøje CR, Olsen MH, et al. Affiliation to the work market after curative treatment of head-and-neck cancer: a population-based study from the DAHANCA database. Acta Oncol. 2013;52(2):430-439

2.Baxi SS, Salz T, Xiao H, et al. Employment and return to work following chemoradiation in patient with HPV-related oropharyngeal cancer. Cancers Head Neck. 2016;1:4.

3.Verdonck-de Leeuw IM, van Bleek WJ, Leemans CR, de Bree R. Employment and return to work in head and neck cancer survivors. Oral Oncol. 2010;46:56-60.

4.Morales CZ, McDowell L, Lisy K, Piper A, Jefford M. Return to Work in Survivors of Human Papillomavirus-Associated Oropharyngeal Cancer: An Australian Experience. Int J Radiat Oncol Biol Phys. 2020;106:146-156

5.Giuliani M, Papadakos J, Broadhurst M, et al. The prevalence and determinants of return to work in head and neck cancer survivors. Support Care Cancer. 2019;27(2):539-546

6. Miller A. Returning to work after head and neck cancer. Curr Opin Otolaryngol Head Neck Surg. 2020;28(3):155-160

7.Yu J, Smith J, Marwah R, Edkins O. Return to work in patients with head and neck cancer: Systematic review and meta-analysis. Head Neck. 2022;44(12):2904-2924

8.Granström B, Tiblom Ehrsson Y, Holmberg E, et al. Return to work after oropharyngeal cancer treatment-Highlighting a growing working-age population. Head Neck. 2020;42(8):1893-1901

174

Modern Radiotherapy in the Treatment of Laryngeal Adenoid Cystic Carcinoma, a systematic review.

Calogero Casà[1], Domenico Crescenzi[2], Marco Ciaparrone[3], Silvia Di Franco[4], Carlo Guidi[1], Domenico Cristiano Corsi[3], Marco Radici[2], Francesco Miccichè[1]

[1]Ospedale Gemelli Isola, UOC di Radioterapia Oncologica, Rome, Italy. [2]Ospedale Gemelli Isola, UOC di Otorinolaringoiatria, Rome, Italy. [3]Ospedale Gemelli Isola, UOC di Oncologia Medica, Rome, Italy. [4]Università Cattolica del Sacro Cuore, Diagnostica per immagini e radioterapia, Rome, Italy

Topic

Salivary gland, skull base, skin and thyroid cancers

Keywords

Adenoid cystic carcinoma, larynx, radiotherapy

Purpose/Objective

Adenoid cystic carcinoma (ACC) is a rare malignancy of the salivary glands. The larynx is an uncommon site of disease occurrence. This site and histotype pose a particular challenge for management because of the quality of life implications of radical surgery and the radio- and chemo-resistant nature of the tumor. The aim of this systematic review is to assess the role of modern radiotherapy in the treatment of laryngeal ACC and to suggest practical guidelines for a standardized radiotherapy protocol.

Material/Methods

A multidisciplinary team consisting of radiation and medical oncologists and otorhinolaryngologists performed a systematic review on MedLine/pubmed using the terms “carcinoma adenoid cystic” and “larynx” and “radiotherapy”. The inclusion criteria were: original article, paper concerning laryngeal ACC, paper that reported on radiotherapy for laryngeal ACC. The exclusion criteria were: papers not available, editorials/review, papers not focused on ACC radiotherapy.

Results

233 papers were reviewed, 22 paper were included. All included papers were retrospective studies; 9 papers (40.9%) were 1-patient case reports. Radiotherapy was used as adjuvant therapy in 16 papers (72.7%), as definitive therapy in 2 paper (9.1%), both definitive or adjuvant radiotherapy were used in 3 papers (13.6%) and in one paper (4.5%) patient setting was adjuvant, definitive or neoadjuvant. In 15 paper (68.2%) effect of radiotherapy alone, without any concurrent chemotherapy were described, in 6 paper (27.3%) also concurrent chemotherapy was used, in one study (4.5%) the concurrent chemotherapy was not specified.

Conclusion

Based on the scientific literature, which is limited by the lack of strong evidence, a proposal for management in terms of indication and prescription of radiotherapy and chemoradiation treatment in different clinical scenarios was proposed.

175

Induction radiochemotherapy with low dose fractionation XRT in patients with advanced HNSCC.

Urszula Kacorzyk[1], Marek Kentnowski[1], Katarzyna Drosik - Rutowicz[1], Dorota Słonina[2], Gabriela Winiarska[2], Adam Gądek[3], Wojciech Fidyk[4], Jolanta Mrochem - Kwarciak[5], Natalia Amrogowicz[1], Andrzej Wygoda[1], Bolesław Pilecki[1], Dominika Leś[1], Paweł Polanowski[1], Agata Bieleń[1], Piotr Paul[6], Ewa Chmielik[6], Anna Hebda[7], Monika Pietrowska[2], Paulina Leszczyńska[3], Małgorzata Oczko-Wojciechowska[2], Agnieszka Mazurek[2], Barbara Bobek-Billewicz[8], Krzysztof Składowski[1], Tomasz Rutkowski[1]

[1]National Research Institute of Oncology, Gliwice branch, Radiation and Clinical Oncology Department, Gliwice, Poland. [2]National Research Institute of Oncology, Gliwice branch, Center for Translational Research and Molecular Biology of CancerRadiation and Clinical Oncology Department, Gliwice, Poland.

[3]National Research Institute of Oncology, Gliwice branch, Radiotherapy Planning Department, Gliwice, Poland. [4]National Research Institute of Oncology, Gliwice branch, Department of Bone Marrow Transplantation and Oncohematology, Gliwice, Poland. [5]National Research Institute of Oncology, Gliwice branch, Analytics and Clinical Biochemistry Department, Gliwice, Poland. [6]National Research Institute of Oncology, Gliwice branch, Tumor Pathology Department, Gliwice, Poland. [7]National Research Institute of Oncology, Gliwice branch, Radiotherapy Department, Gliwice, Poland. [8]National Research Institute of Oncology, Gliwice branch, Radiology and Diagnostic Imaging Department, Gliwice, Poland

Topic

Innovative treatments

Keywords

ICHRTL , HRS, HNSCC

Purpose/Objective

Supported by the National Science Centre, Poland, 2020/39/O/NZ5/02625.

Induction chemotherapy (iCH) although is not a standard approach, is often used in clinical practice for patients with advanced head and neck cancer (HNSCC). Tumor regression is a potential goal of induction treatment to reduce target volume in the second stage of treatment – radiochemotherapy or radiotherapy.

In this study the most common iCH, TPF (docetaxel, cisplatin, and 5-fluoruracil) has been replaced with two-drugs regimen combined with low-dose radiation. Complementary mechanisms of action and excellent radiation sensitization of drugs together with hyperradiosensitivity (HRS) phenomenon of low-dose fractionated radiation therapy may be beneficial for patients with bulky disease. Additionally, lower toxicity could be expected for two-drugs modality. Preliminary results on effectiveness and toxicity has been presented.

Material/Methods

The group consisted of 27 patients treated due to advanced HNSCC in National Research Institute of Oncology, Gliwice branch between 2020 and 2023. There were 23 (85%) men and 4 (15%) women in the median age of 60 years. In most cases primary tumor site was oropharynx followed by hypopharynx and CUP in 17 (63%), 7 (26%) and 3 (11%) cases respectively. All patients presented advanced stage - III stage in 16 cases (59%) and IV stage in 11 cases (41%). HPV- positive tumors were found in 13 (48%) patients. There were 2 cycles of iCHT consisting of carboplatin (AUC 6) and paclitaxel (75 mg/m2) combined with low-dose radiotherapy 2 x 0.5 Gy on days 1, 8 and 15. Additionally, two doses of 0.5 Gy was given on day 2. CT ,MRI and PET-CT scans were performed to estimate the staging of the cancer, all according to the 8th edition of the TNM classification for malignant tumors.

The volume of the primary tumor and metastatic lymph nodes were estimated in cm3 before and after induction radiochemotherapy with low dose fractionation radiotherapy to analyze the potential value of tumor volume regression . After ICHRTL, all patients were qualified for the second stage of treatment - radiochemotherapy in 24 cases and radiotherapy in 3 cases, respectively. To investigate the presence of HRS effect, fibroblasts were irradiated in vitro with doses ranging from 0.1 to 4 Gy (6-MV X-ray beam) and cell radiosensitivity was estimated by flow cytometry-based clonogenic survival assay and RIANS test (pATM and H2AX foci assays).

Results

Clinical and experimental data will be presented.The mean volumes of tumor and metastatic lymph nodes among 27 patients before ICHRTL were 32.5 cm3 (Vt) and 45.1 cm3 (Vn) , respectively. After ICHRTL, these mean values were 17.2 cm3 (Vt) and 22.2 cm3 (Vn). Wilcoxon test analize showed significant decrease in T volume (Vt) and N volume (Vn) before and after iCHRTL (p=0.003) and p=0.00008) respectively. Due to complications 16 patients (60%) did not receive the full dose of chemotherapy and radiotherapy (ICHRTL). Leukopenia and neutropenia occurred in 12 (44%) and 11 (40%) patients respectively. Poor drug tolerance (vomiting, nausea, abdominal pain) was observed in 3 (11%) patients, and renal failure in 1 (4%) patient. Among normal skin fibroblasts assessed from 21 patients two demonstrated HRS effect.

Conclusion

The use of ICHRTL in patients with advanced HNSCC is a low-toxicity and effective method. The obtained regression of tumor volume (Vt) and metastatic lymph nodes (Vn) in most patients managed to reduce the high dose area in the second stage of treatment (radiotherapy/radiochemotherapy). Further observations are needed to estimate the potential role of decrease in T volume (Vt) and N volume (Vn) after ICHRTL on the expected survival of patients.

References

1.Posner MR, Haddad RI, Wirth L, Norris CM, Goguen LA, Mahadevan A, Sullivan C, Tishler RB. Induction chemotherapy in locally advanced squamous cell cancer of the head and neck: evolution of the sequential treatment approach. Semin Oncol. 2004 Dec;31(6):778-85. doi: 10.1053/j.seminoncol.2004.09.007. PMID: 15599855.

2. Gleason JF Jr, Kudrimoti M, Van Meter EM, Mohiuddin M, Regine WF, Valentino J, Kenady D, Arnold SM. Low-dose fractionated radiation with induction chemotherapy for locally advanced head and neck cancer: 5 year results of a prospective phase II trial. J Radiat Oncol. 2013 Mar 1;2(1):35-42. doi: 10.1007/s13566-012-0074-3. PMID: 26052405; PMCID: PMC4457337.

3. Dey S, Spring PM, Arnold S, Valentino J, Chendil D, Regine WF, Mohiuddin M, Ahmed MM. Low-dose fractionated radiation potentiates the effects of Paclitaxel in wild-type and mutant p53 head and neck tumor cell lines. Clin Cancer Res. 2003 Apr;9(4):1557-65. PMID: 12684432.

4. Arnold SM, Kudrimoti M, Dressler EV, Gleason JF Jr, Silver NL, Regine WF, Valentino J. Using low-dose radiation to potentiate the effect of induction chemotherapy in head and neck cancer: Results of a prospective phase 2 trial. Adv Radiat Oncol. 2016 Jul 14;1(4):252-259. doi: 10.1016/j.adro.2016.06.003. PMID: 28740895; PMCID: PMC5514161.

176

Dysphagia After Swallowing Sparing RadioTherapy: results from a prospective trial (NCT 03448341)

Stefano Ursino[1], Giulia Malfatti[2], Francesca De Felice[3], Pierluigi Bonomo[4], Isacco Desideri[4], Pierfrancesco Franco[5], Francesca Arcadipane[6], Caterina Colosimo[7], Rosario Mazzola[8], Marta Maddalo[9], Daniela Musio[2], Fabiola Paiar[1]

[1]University of Pisa, Department of Translational Research and New Technologies in Surgery and Medicine, Pisa, Italy. [2]Radiation Oncology Unit, University Hospital Campus Biomedico, Roma, Italy. [3]Radiation Oncology Unit, University Hospital La Sapienza, Roma, Italy. [4]Radiation Oncology Unit, University Hospital Careggi, Firenze, Italy. [5]University of Eastern of Piedmont, Department of Translational Medicine, Novara, Italy. [6]Radiation Oncology University of Turin, Department of Oncology, Turin, Italy. [7]Radiation Oncology, University Hospital Santa Chiara, Pisa, Italy. [8]IRCCS Sacro Cuore-Don Calabria Hospital Cancer Care Center, Advanced Radiation Oncology Department, Verona, Italy. [9]Radiation Oncology Unit, Department of Medical and Surgical Specialties, Brescia, Italy

Topic

Quality of life and outcomes

Keywords

Swallowing; IMRT

Purpose/Objective

To prospectively investigate changes in objective deglutition scores and to correlate them with MDADI scores in patients (pts) affected by naso and oropharynx cancer after definitive radiochemotherapy using SWOARs-sparing IMRT (Clinical Trial ID NCT03448341)

Material/Methods

Pts underwent objective evaluation by means of Fiberoptic Endoscopic Evaluation of Swallowing (FEES) and Videofluoroscopy (VFS) together with subjective evaluation by means of MDADI questionnaire at baseline and at 6 and 12 months after treatment.
Pts were categorized in two groups based on baseline MDADI-C value: MDADI-C≥80 and MDADI-C<80.
The amount of pharyngeal residue (PR) and the occurrence of penetration and/or aspiration (P/A) were considered as surrogate of dysphagia. Specifically, PR was categorized as 0: absence; 1: mild; 2: moderate; 3: severe and dichotomized as 0-1 vs 2-3.

Results

Between August 2015 and November 2021 we enrolled 75 pts of whom 40 (53%) were MDADI-C >80 and 35 (47%) were MDADI-C<80 at baseline.
Among MDADI-C≥ 80 pts group the mean baseline PR-score at FEES was 0,42 rising to 1,36 at 6 months (p=0,001) and stabilizing to 1,15 at 12 months (p= 0,21); indeed, the mean baseline PR-score at VFS was 0,55 rising to 1 at 6 months (p=0,069) and slightly dropping to 0,7 at 12 months (p=0,069).
Among MDADI-C <80 pts group the mean baseline PR-score at FEES was 0,56 rising to 1,07 at 6 months (p=0,012) and stabilizing to 1,07 at 12 months (p=0,99); indeed the mean baseline PR-score at VFS was 0,67 rising to 1,19 at 6 months (p=0,04) and dropping to 0,78 at 12 months (p=0,04).
No correlation was found between baseline dichotomized MDADI-C group and PR-score both at FEES and VFS at the 3 different time intervals. Indeed, a statistical significant correlation was found between PR-score and P/A at VFS at 12 months after treatment (p<0,001).

Conclusion

Our results suggest objective deglutition benefit of dose optimization to SWOARs by means of mean low objective scores after treatment both in MDADI-C ≥ 80 and MDADI-C<80 pts group. This means that subjective referred dysphagia is likely not to be associated to a major functional deglutition impairment in our daily clinical practice.

References

1) Ursino S, Calistri E, De Felice F et al. Patient-Reported Outcomes After Swallowing (SWOARs)-Sparing IMRT in Head and Neck Cancers: Primary Results from a Prospective Study Endorsed by the Head and Neck Study Group (HNSG) of the Italian Association of Radiotherapy and Clinical Oncology (AIRO) Dysphagia (2023) 38:159–170

2) Nutting C, Finneran L, Roe J, et al. Dysphagia optimized intensity modulated radiotherapy in patients with head and neck cancer (DARS): a phase III, multicenter randomised controlled trial Lancet Oncol 2023; 24: 868–80

3) Hutcheson KA, Portwood M, Lisec A et al. What is a clinically relevant diference in MDADI scores between groups of head and neck cancer patients? Laryngoscope. 2016;126:1108–13

4) Christianen ME, Langendijk JA, Westerlaan HE, et al. Delineation of organs at risk involved in swallowing for radiotherapy treatment planning. Radiother Oncol. 2011;101:394–402

178

Implementation challenges of artificial intelligence-based radiomics in head and neck oncology: A systematic review

Rasheed Omobolaji Alabi[1], Alhadi Almangush[1], Mohammed Elmusrati[2], Ilmo Leivo[3], Antti A Mäkitie[1]

[1]University of Helsinki, Research Program in Systems Oncology, Helsinki, Finland. [2]University of Vaasa, School of Technology and Innovations, Vaasa, Finland. [3]University of Turku, Institute of Biomedicine, Turku, Finland

Topic

Imaging, radiomics and artificial intelligence

Keywords

Radiomics, AI, Challenges, Head and Neck Cancer

Purpose/Objective

Purpose/Objectives: Artificial intelligence (AI) and its subfields such as machine learning (ML) and deep learning (DL) have been reported to show high performance, particularly in the diagnosis and prognosis of various cancers [1–3]. Despite the promising results obtained from these studies, advancements in technology have increased the availability of medical images in different formats such as computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and ultrasound images [1,2]. Interestingly, these image formats are more than pictures, they are in fact, data [4]. As a result, several approaches such as radiomics have been recently used to extract information that is not visible to the human eye during routine examination from these images [5]. Hence, radiomics is an emerging field in radiology that provides a non-invasive approach for extracting quantitative features from medical cancer images such as CT, PET, MRI, or a combination of these image formats [5]. Traditionally, the extracted features are processed using statistical approaches. However, due to the large amount of extracted features, statistical approaches can no longer effectively handle these features [6,7]. Therefore, in recent years, several studies exploring the potential of AI or its subfields such as ML and DL in handling the extracted features to produce a predictive model have shown promising results that are capable of revolutionizing HNC management [8]. However, in actual everyday clinical practice, the use of AI-based radiomics models remains limited [5]. This is due to several implementation challenges [5]. **Objectives:** This study provides a systematic review of the challenges, concerns, and limitations of AI-based models in head and neck cancer (HNC) oncology. Furthermore, we suggest possible solutions to these challenges.

Material/Methods

We searched OvidMedline, PubMed, Scopus, and Web of Science databases for articles that examine the challenges of AI-based models in HNC oncology. The quality of included studies and their risk of biases were evaluated using the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) and Prediction Model Risk of Bias Assessment Tool (PROBAST).

Results

A total of 11 studies examined the challenges of these models in HNC oncology. These challenges have been summarized into 5 themes. These include data, science of machine learning, model generalizability, model maintenance and performance improvements, and ethical and regulatory concerns. The data concerns include data management, data imbalance and heterogeneity, privacy, and confidentiality. The concerns relating to the science of machine learning include model and result interpretability, explainability, and model performance. The model's generalizability encompasses internal and external independent geographic validation of the models. Some of the ethical and regulatory concerns were as follows: model-clinician disagreement (contradictory diagnostic or prognostic opinion between the model and clinician), workflow and user-design challenges, patient's liberty to decide the type of treatment to follow may be violated, patient–clinician relationship may change, standardized reporting guidelines of AI model development, and outdated regulatory and legal frameworks.

Conclusion

Stakeholders such as the governments, medical institutions, hospital management, clinicians, physicians, regulatory agencies, technological companies, politicians, ethicists, philosophers, legal experts, patient representatives, data scientists, and machine learning experts need to be deeply involved in the development of internationally standardized and structured reporting guidelines for the AI-based model to be beneficial in daily clinical practice. The envisioned guidelines should define solutions to data issues by defining a robust data economy framework. Model interpretability and explainability can be handled using explainability techniques by providing both local and global interpretations of the predictions made by the model. Independent external geographic validation of the model should be a standard procedure. A federated learning paradigm can enhance continuous model improvement and generalizability. The guidelines should also include a defined ethical and regulatory framework for the development and reporting of AI-based radiomics models.

References

1. Alabi, R. O. et al. Utilizing Deep Machine Learning for Prognostication of Oral Squamous Cell Carcinoma—A Systematic Review. Frontiers in Oral Health 2, (2021).

2. Alabi, R. O., Almangush, A., Elmusrati, M. & Mäkitie, A. A. Deep Machine Learning for Oral Cancer: From Precise Diagnosis to Precision Medicine. Front. Oral. Health 2, 794248 (2022).

3. Alabi, R. O. et al. Application of artificial intelligence for overall survival risk stratification in oropharyngeal carcinoma: A validation of ProgTOOL. International Journal of Medical Informatics 175, 105064 (2023).

4. Gillies, R. J., Kinahan, P. E. & Hricak, H. Radiomics: Images Are More than Pictures, They Are Data. Radiology 278, 563–577 (2016).

5. Zhang, Y.-P. et al. Artificial intelligence-driven radiomics study in cancer: the role of feature engineering and modeling. Military Med Res 10, 22 (2023).

6. Kocak, B. et al. Radiomics with artificial intelligence: a practical guide for beginners. Diagn Interv Radiol 25, 485–495 (2019).

7. Alabi, R. O. et al. Machine learning in oral squamous cell carcinoma: Current status, clinical concerns and prospects for future—A systematic review. Artificial Intelligence in Medicine 115, 102060 (2021).

8. Haider, S. P., Burtness, B., Yarbrough, W. G. & Payabvash, S. Applications of radiomics in precision diagnosis, prognostication and treatment planning of head and neck squamous cell carcinomas. Cancers Head Neck 5, 6 (2020).

179

Contralateral Neck Recurrence Following Unilateral Treatment for Oral Tongue Squamous Cell Carcinoma

Rebecca John, Richard Webster, Mererid Evans, Thomas Rackley, Elin Evans, Nachi Palaniappan

Velindre Cancer Centre, Clinical Oncology, Cardiff, United Kingdom

Topic

Multidisciplinary management

Keywords

Radiotherapy, oral tongue, neck recurrence

Purpose/Objective

Carcinoma of the oral cavity is rare, however oral tongue carcinoma has been associated with worse prognosis when compared to other oral cavity subsites.

A retrospective study of oral cavity cancer treated with both surgery and radiotherapy, demonstrated a contralateral relapse rate of 25% in patients with ipsilateral pN2b disease.

Irradiation of the contralateral neck in oral tongue carcinoma has been a topic of controversy and debate. We set out to analyse our experience of contralateral neck recurrence in oral tongue squamous cell carcinoma (SCC).

Material/Methods

Electronic patient records were reviewed of patients diagnosed from 2010-2020 with oral tongue SCC. All patients underwent surgery to primary and or neck followed by adjuvant radiotherapy with or without chemotherapy. Patient demographics, tumour characteristics, treatment details and outcomes were collated.

Results

A total 86 patients were identified during this period who underwent unilateral treatment. Median age 61 years; 55 Male, All patients had lateral oral tongue tumours; 44 on the right side. Surgery included wide local excision (WLE) and primary closure without treatment for neck (26 patients); or WLE, flap reconstruction and modified or selective neck dissection (Levels 1 to 4) in 60 patients. Majority were early stage (I & II) in 59 patients; Stage III in 4 and Stage IVa in 23 patients. 23 patients received post-operative radiotherapy, of which 8 patients received concurrent chemotherapy. Median follow up of 7.1 years.

Recurrence was seen in 18 patients (21%). Four patients developed local recurrence alone, 6 patients developed local and nodal recurrence, nodal recurrence alone in 6 patients and distant metastases in 3 patients. The contra lateral nodal recurrence occurred in 7 (8.1%) patients. Of these, three patients had local recurrence along with neck recurrence and 2 patients had neck and distant metastases. Median time to recurrence was 9 months. Five of the 7 patients had Stage IVa disease.

Conclusion

Our contralateral neck recurrence rate following unilateral treatment for oral tongue cancer is 8.1%. Two patients developed contra lateral neck recurrence alone and underwent salvage neck dissection.

In our experience, unilateral treatment for early lateralised oral tongue tumours results in good loco regional control.

References

1. Vergeer M. Ipsilateral irradiation for oral and oropharyngeal carcinoma treated with primary surgery and postoperative radiotherapy. *Int J Radiat Oncol Biol Phys* 2010; 78: 682-688

2. Chan AK, Huang SH, Le W et al. Postoperative intensity-modulated radiotherapy following surgery for oral cavity squamous cell carcinoma: patterns of failure. *Oral Oncol* 2013; 49: 255-260.

3. The Royal College of Radiologists. *Head and neck cancer. RCR consensus statements*. London: The Royal College of Radiologists, February 2022.

180

Long Term Outcomes following Unilateral Treatment for Squamous Cell Carcinoma of Unknown Primary

Sarah Emma Walters, Richard Webster, Jessica Randall, Thomas Rackley, Elin Sian Evans, Mererid Evans, Nachi Palaniappan

Velindre Cancer Centre, Oncology, Cardiff, United Kingdom

Topic

Quality of life and outcomes

Keywords

Unknown primary, unilateral, outcomes

Purpose/Objective

Squamous cell carcinoma of unknown primary (SCCUP) accounts for up to 5%[1-4] of cancers in the head and neck region and are defined as “metastatic disease in the lymph nodes of the neck without any evidence of a primary tumour of the upper aerodigestive tract”[5]. It typically presents as a painless neck lump and, as a diagnosis of exclusion, requires extensive investigation.

Due to the rarity of SCCUP, management is largely determined by individual institutions depending on local experience and expertise. Much debate in the literature currently centres on management of the ipsilateral versus bilateral adjuvant neck and irradiation of the site of potential primary.

Current practice is evolving nationally due to improved radiotherapy techniques and knowledge of long-term outcomes of dysphagia and aspiration at risk structures (DARS) irradiation. In addition, the integration of procedures such as Transoral Robotic Surgery (TORS) mucosectomy into the pathway

with a view to addressing the diagnostic void is emerging. It is anticipated that updated US ASCO guidelines and RCR consensus statement when published will assist.

In our centre, treatment typically involves surgery to neck followed by adjuvant radiotherapy to the cervical nodal regions and ipsilateral oropharynx with or without chemotherapy. This study reports our long term outcomes following this treatment.

Material/Methods

Electronic notes were reviewed retrospectively of patients diagnosed from 2007-2019 with SCCUP. All patients included were staged as Tx M0, (TNM 7), and treated with radical intent and neck dissection. Patient demographics, tumour characteristics, treatment details and outcomes were collated.

Results

Eighty two patients were identified, 75 patients underwent unilateral neck dissection, one patient had excision biopsy of the neck and 6 patients underwent bilateral neck dissection. Median age at presentation was 60 years, 71 were male; p16 status was available for 41 patients, 32 positive and 9 negative. The commonest staging was Tx N2b M0 in 40 patients. Median follow up of 6.5 years.

Sixty three patients received adjuvant treatment; 32 patients with radiotherapy and concurrent chemotherapy and 31 patients with radiotherapy alone. Loco-regional control rate was 76%. Four patients (6.3%) developed mucosal emergence, 8 patients (13%) developed nodal recurrence and 6 patients developed distant metastases (9.5%).

Nineteen patients had no adjuvant treatment. Loco-regional control rate was 42%. Nine patients (47%) developed mucosal emergence, most common site was ipsilateral tongue base in 6 patients (67%). Of these 9 patients, 6 also developed neck recurrence. One patient developed neck recurrence alone and underwent further surgery followed by post-operative radiotherapy. Two patients developed distant metastases.

Neck recurrence rate was higher when patients had no adjuvant treatment following surgery (37% vs 12%). Primary mucosal emergence was also higher in patients who did not receive adjuvant treatment (47% vs 6.3%). Contra lateral neck recurrence occurred in 2 patients (3.1%) following ipsilateral adjuvant treatment.

Conclusion

Surgery to neck followed by adjuvant radiotherapy with or without chemotherapy to neck and ipsilateral oropharynx in patients with SCCUP offers excellent rates of loco regional control. Our data supports the use of ipsilateral neck radiotherapy, showing low rates of contra-lateral recurrence.

Radiotherapy to potential primary was associated with low rates of mucosal emergence. The high rate of primary mucosal emergence and local neck failure in patients without adjuvant radiotherapy supports its integral role in long-term loco-regional control.

More work needs to be done to establish the role of TORS in the management of these patients.

References

1. Grau C, Johansen LV, Jakobsen J, Geertsen P, Andersen E, Jenson BB. Cervical lymph node metastases from unknown primary tumours: Results from a national survey by the Danish Society for Head and

Neck Oncology. Radiother Oncol. 2000;55(2):121-129. Doi: https://doi.org/10.1016/S0167-8140(00)00172-9

2. Jereczek-Fossa BA, Jassem J, Orecchia R. Cervical lymph node metastases of squamous cell carcinoma of an unknown primary. Cancer Treat Rev. 2004;30(2):153-164. Doi: 10.1016/j.ctrv.2003.10.001

3. Waltonen JD, Ozer E, Hall NC. Metastatic Carcinoma of the Neck of Unknown Primary Origin Evolution and Efficacy of the Modern Workup. Arch Otolaryngol Head Neck Surg. 2009;135(10):1024-1029. Doi: 10.1001/archotol.128.1.58

4. Strojan P, Ferlito A, Langendijk JA, Corry J, Woolgar JA, Rinaldo A, Silver CE, Paleri V, Fagan JJ, Pellitteri PK, Haigentz M Jr, Suarez C, Robbins KT, Rodrigo JP, Olsen KD, Hinni ML, Werner JA, Mondin V, Kowalski LP, Devaney KO, de Bree R, Takes RP, Wolf GT, Shaha AR, Genden EM, Barnes L. Contemporary management of lymph node metastases from an unknown primary to the neck: II. A review of therapeutic options. Head Neck. 2013;35(2):286-293. Doi: 10.1002/hed.21899

5. Galloway TJ, Ridge JA. Management of Squamous Cancer Metastatic to Cervical Nodes With an Unknown Primary Site. J Clin Oncol. 2015;33(29):3328-3337. Doi: 10.1200/JCO.2015.61.0063

181

Baseline Hemoglobin as an independent marker for survival outcome in squamous cell carcinoma of head and neck- An institutional review from tertiary cancer centre

Preetha Umesh, Sarthak Tandon, Sandeep Purohit, Parveen Ahlawat

Rajiv Gandhi Cancer Institute and Research Centre, Radiation Oncology, New Delhi, India

Topic

Radiobiology

Keywords

anemia, survival predictor, head and neck cancer

Purpose/Objective

Anemia is a common obstacle encountered in almost 30% cancer patients during the course of their disease[1,2]. Impact of hypoxia on radio-sensitivity of tumor tissue is a well documented radiobiological phenomenon[3]. The presence of oxygen during exposure to radiation is proven to "fix" the damage caused by hydroxyl free radicals which is necessary to prevent the repair of sublethal damage (the underlying mechanism of tumor cell kill). Head and neck cancers (HNC) are well known to harbour high proportions of hypoxic cell fractions ranging between 1-50% of total tumor volume and are also notorious for having high preponderance for local failures[4-6]. Thus, this combination makes HNC, an ideal site to evaluate the role hypoxia related factors that could impact disease outcomes. Subsequently various treatment strategies have been directed at increasing the oxygenation of tumor ecosystem in head and neck cancers in order to improve loco regional control[7]. This review aims to evaluate the role of baseline Hemoglobin (Hb) in its impact on Overall survival (OS) and Relapse free survival (RFS) in HNC patients treated with radiotherapy.

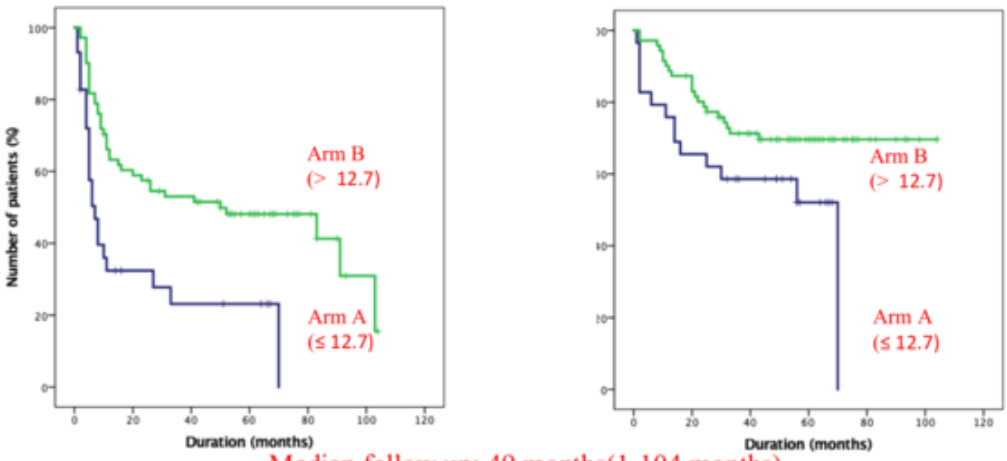
Material/Methods

The institutional database was reviewed from 2020 to 2022 for head and neck cancer patients undergoing definitive Radiotherapy with or without chemotherapy. A total of 100 patients fulfilling inclusion criteria and complete data sets were analyzed. Using 12.7g/dl as a cutoff (using historical evidence) for baseline hemoglobin, the entire cohort was divided into two groups - A (≤ 12.7 g/dl) and B (> 12.7g/dl). The groups were analyzed for Overall survival (OS) and relapse free survival(RFS), taking into account factors such as T stage (</=T2 vs >T2), N stage(</=N2b vs >N2b), smoking, tobacco use and gender

Results

The baseline and treatment characteristics were comparable between two groups except for clinical nodal staging, smoking and gender. The median follow-up was 49 months (range 1 – 104 months) for the entire cohort. The median OS was 70 months for patients in arm A whereas it was not reached for arm B (p = 0.044). The median RFS was 7 (95% CI 3.92 - 10.08) months and 50 (95% CI 6.36 - 93.64) months, respectively (p = 0.001). A logistic regression analysis was performed to ascertain the effect of Hb on the likelihood of the patients that were surviving. The results showed, for each unit reduction in the Hb level, the odds of surviving decrease by a factor of 0.231 (Odd Ratio 0.794; CI = 0.680 - 0.926; p = 0.003). On univariate analysis , T staging ,N staging, tobacco usage, smoking and Hb groups were significant predictors for RFS. However, only Hb group and N staging were significant predictors for OS on univariate analysis.

Characteristics	Number of patients with Hemoglobin </=12.7 in n=29 (%)	Number of patients with Hemoglobin >12.7 I in n=71 (%)	P value
Site			0.083
OralCavity	6	5	
Oropharynx	15	27	
Larynx	4	26	
Hypopharynx	3	10	
Nasopharynx	1	3	
Sex			<0.001
Male	18	71	
Female	11	0	
Clinical Tumor stage			0.072
</=T2	3	19	
>T2	26	52	
Clinical Nodal stage			0.009
</=N2b	17	59	
>N2b	12	12	
Comorbidities			0.259
Absent	20	55	
Present	9	16	
Tobacco use			0.163
Absent	20	58	
Present	9	13	
Alcohol consumption			0.051
Absent	22	39	
Present	7	32	
Smoking			0.001
Absent	12	9	
Present	17	62	

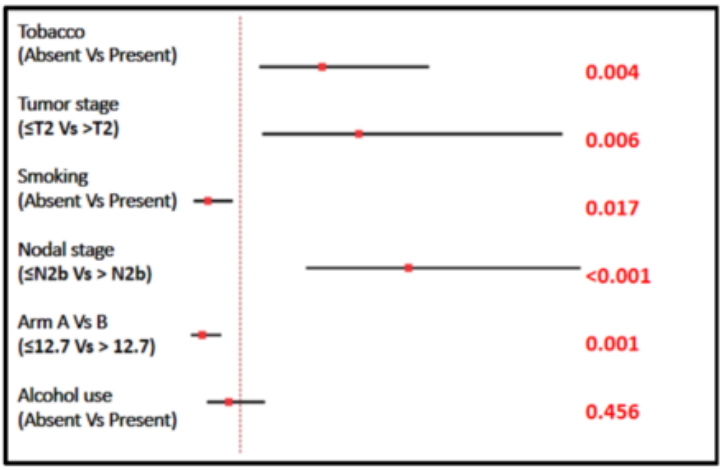


Median follow up: 49 months(1-104 months)

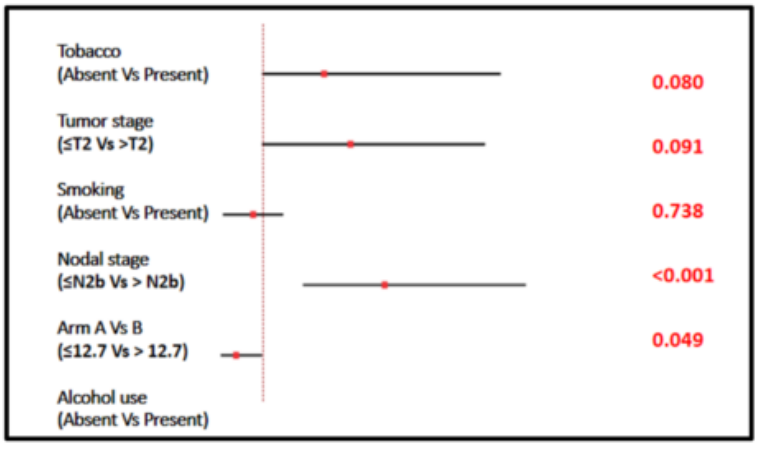
RFS	
A	7 months
B	50 months
pvalue	0.001

OS	
A	70 months
B	-
p Value	0.044

Univariate analysis for RFS



Multivariate analysis for RFS



Conclusion

Low baseline Hb (less than 12.7 g/dl) is a poor prognostic marker for overall survival and relapse free survival in HNC patients treated with definitive RT with or without chemotherapy. Low Hb is an easily accessible and affordable marker of systemic inflammation capable of guiding clinical decisions regarding survival and recurrence among locally advanced HNSCC patients. Correction of low hemoglobin should be strongly considered in HNC patients as it is a low cost, low effort way of contributing towards improved local control.

References

1.Caro JJ, Salas M, Ward A, Goss G. Anemia as an independent prognostic factor for survival in patients with cancer: a systematic, quantitative review. Cancer. 2001 Jun 15;91(12):2214-21.

2.Murphy GP, Lawrence W, Lenhard RE. American Cancer Society textbook of clinical oncology. The Society; 1995.

3.Douglass M. Eric J. Hall and Amato J. Giaccia: Radiobiology for the radiologist: Wolters Kluwer, Philadelphia, PA, 2019, 624 pp, ISBN: 978-1496335418.

4.Kumar P. Impact of anemia in patients with head and neck cancer. The oncologist. 2000 Jun 1;5(S2):138.

5.Molls M, Stadler P, Becker A, Feldmann HJ, Dunst J. Relevance of oxygen in radiation oncology. Mechanisms of action, correlation to low hemoglobin levels. Strahlentherapie und Onkologie: Organ der Deutschen Rontgengesellschaft...[et al]. 1998 Dec 1;174:13-6.

6.Fein DA, Lee WR, Hanlon AL, Ridge JA, Langer CJ, Curran Jr WJ, Coia LR. Pretreatment hemoglobin level influences local control and survival of T1-T2 squamous cell carcinomas of the glottic larynx. Journal of Clinical Oncology. 1995 Aug;13(8):2077-83.

7.Overgaard J, Horsman MR. Modification of hypoxia-induced radioresistance in tumors by the use of oxygen and sensitizers. InSeminars in radiation oncology 1996 Jan 1 (Vol. 6, No. 1, pp. 10-21). WB Saunders.

182

Artificial Intelligence-Driven Radiomics in Head and Neck Cancer: Current Status and Future Prospects

Rasheed Omobolaji Alabi[1], Mohammed Elmusrati[2], Ilmo Leivo[3], Alhadi Almangush[1], Antti A Mäkitie[1]

[1]University of Helsinki, Research Program in Systems Oncology, Helsinki, Finland. [2]University of Vaasa, School of Technology and Innovations, Vaasa, Finland. [3]University of Turku, Institute of Biomedicine, Turku, Finland

Topic

Imaging, radiomics and artificial intelligence

Keywords

AI, Radiomics, Head and Neck Cancer

Purpose/Objective

Background: Radiomics is a rapidly growing field used to leverage medical radiological images by non-invasively extracting quantitative features [1]. These are supposed to characterize a patient's phenotype, and when combined with artificial intelligence techniques, to improve the accuracy of diagnostic models and clinical outcome prediction [2]. **Objectives:** This review aims at examining the application areas of artificial intelligence-based radiomics (AI-based radiomics) for the management of head and neck cancer (HNC). It further explores the workflow of AI-based radiomics for personalized and precision oncology in HNC. Finally, it examines the current challenges of AI-based radiomics in daily clinical oncology and offers possible solutions to these challenges.

Material/Methods

Comprehensive electronic databases (PubMed, Medline via Ovid, Scopus, Web of Science, and Institute of Electrical and Electronics Engineers (IEEE)) were searched following the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines. The quality of included studies and their risk of biases were evaluated using the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) and Prediction Model Risk of Bias Assessment Tool (PROBAST).

Results

A total of 45 articles fulfilled the inclusion criteria. Our review revealed that the application of AI-based radiomics model as an ancillary tool for improved decision-making in HNC management includes radiomics-based cancer diagnosis and radiomics-based cancer prognosis. The radiomics-based cancer diagnosis includes tumor staging, tumor grading, and classification of malignant and benign tumors. Similarly, radiomics-based cancer prognosis includes prediction for treatment response, recurrence, metastasis, and survival. In addition, the challenges in the implementation of these models for clinical evaluations include data imbalance, feature engineering (extraction and selection), model generalizability, multi-modal fusion, and model interpretability.

Conclusion

Considering the highly subjective and interobserver variability that is peculiar to the interpretation of medical images by expert clinicians, AI-based radiomics seeks to offer potentially useful quantitative information, which is not visible to the human eye or unintentionally often remains ignored during clinical imaging practice. By enabling the extraction of this type of information, AI-based radiomics has the potential to revolutionize HNC oncology, providing a platform for more personalized, higher quality, and cost-effective care for HNC patients.

References

1. Zhang, Y.-P. et al. Artificial intelligence-driven radiomics study in cancer: the role of feature engineering and modeling. Military Med Res 10, 22 (2023).

2. Fh, T., Cyw, C. & Eyw, C. Radiomics AI prediction for head and neck squamous cell carcinoma (HNSCC) prognosis and recurrence with target volume approach. BJR|Open 3, 20200073 (2021).

184

Comparative analysis of hematological parameters and protein markers in human papillomavirus-positive versus -negative oropharyngeal cancers.

Jolanta Mrochem-Kwarciak[1], Andrzej Wygoda[2], Tomasz Rutkowski[2], Magdalena Prokop[1], Krzysztof Składowski[2]

[1]Maria Skłodowska-Curie, National Research Institute of Oncology, Gliwice Branch, ANALYTICS AND CLINICAL BIOCHEMISTRY DEPARTMENT, Gliwice, Poland. [2]Maria Skłodowska-Curie, National Research Institute of Oncology, Gliwice Branch, I RADIATION AND CLINICAL ONCOLOGY DEPARTMENT, Gliwice, Poland

Topic

HPV or EBV related cancers

Keywords

hematological parameters, protein markers

Purpose/Objective

HPV-positive cancer is strongly immunogenic tumor which induces cell type response in surrounding microenvironment. Systemic inflammation is generally accompanied by cancer disease and it weakens cell response and negatively influences organism reaction to cancer

The aim of present study was to compare laboratory parameters of the immune system: leukocyte count (WBC), neutrophil count (Neut) and lymphocyte count (Lym), monocyte count (Mono), C-reactive protein (CRP), Interleukine 6 (Il-6), in patients with HPV-positive and HPV-negative OPC.

Material/Methods

75 patients were treated with curative intent with radiotherapy alone (32 %) or combined with platinum-based chemotherapy (68%). There were 47% patients with T1/2 and 53% with T3/4 of primary tumor stage and 44% and 56% of patients with N0 and N+ nodal stage disease, respectively. Complete blood counts (CBC), C-reactive protein (CRP) and Il-6 were estimated in blood or serum before and after the treatment. HPV DNA was determined in plasma by QPCR method.

Results

In patients with HPV-negative OPC WBC count (p=0,006 median: 6,88 vs 5,69), Lym count (p=0,02 median: 1,96 vs 1,49) and CRP (p=0,0001 median: 5,88 vs 1,35 mg/dl) was higher than for HPV-positive OPC before treatment. Additionally, in patients with HPV-negative OPC WBC count (p=0,03 median: 5,53 vs 4,17), Lym count (p=0,02 median: 0,69 vs 0,44), Mono count (p=0,003 median: 0,58 vs 0,43) and Il-6 (p=0,05 median: 25,53 vs 11,65 pg/ml) was higher than for HPV-positive OPC after therapy. Before treatment significantly longer overall survival (OS) for patients with low WBC count (p=0,001)(Fig.1), low concentration of CRP (p=0,0001) (Fig. 2) and Il-6 (p=0,01) was also found.

Conclusion

Inflammation processes are more severe in HPV-negative OPC. Low levels of inflammatory indicators like WBC count, Lym count, CRP, Il-6 may be associated with longer OS in this group of patients. Systemic inflammation reflects host reaction on cancer, characterized by a significant weakness of cellular immunity. It is more characteristic for patients with HPV–negative OPC

186

Early mortality following induction chemotherapy and concurrent chemoradiotherapy for nasopharyngeal cancer

Amine Lachgar, Rania El Gueddari, Imane Haddnaoui, Sara Abdou, Mouna Taouchikht, Tatiana Edith, Houda Fares, Karima Nouni, Hanan El Kacemi, Tayeb Kebdani, Khalid Hassouni

National Institute of Oncology, Radiotherapy, Rabat, Morocco

Topic

Multidisciplinary management

Keywords

Nasopharynx, Chemoradiotherapy, Death

Purpose/Objective

Induction chemotherapy followed by concurrent chemoradiotherapy is a standard in the treatment of advanced, nonmetastatic nasopharyngeal carcinoma. This approach significantly improve survival, and it is accepted as a standard of care for stage III-IVA disease. However, this strategy is associated with considerable acute toxicity and a risk of short-term mortality.

The aims of this study were to determine the rate and to characterize the causes of early death, in order to define the subset of patient with higher risk of early mortality.

Material/Methods

We conducted a single-center retrospective study including patients, diagnosed with locally advanced non-metastatic undifferentiated carcinoma of the nasopharynx treated with induction chemotherapy followed by concurrent chemoradiotherapy, in the National Institute of Oncology in Morocco, from 1 January 2018 until 31 December 2021.

Early death was defined as any death during the course of therapy or within 6 months following the end of chemoradiotherapy.

Clinicopathological characteristics was collected, and their prognostic value affecting early mortality was tested using univariate and multivariate Cox proportional hazards models.

Results

A total of 263 patients were included (median age 55, range 21-77 years, 61.5% male). Disease were predominately stage III (68.2 %) and 31.8% were stage IVA in the AJCC 8th edition.

Induction chemotherapy consisted of 3 cycles of cisplatin-based chemotherapy followed by concurrent chemoradiotherapy (Volumetric-modulated arc therapy plus platinum weekly chemotherapy).

22 patients (8.4%) did not complete all three cycles of induction chemotherapy, and only 195 of 263 patients (74.1%) received concurrent chemoradiotherapy with the full planned course of chemotherapy.

Early death occurred in 18 patients (6.8%), of these 15 (83.3%) patients died of a treatment-related cause. The incidence of acute adverse events of grade ≥ 3 was 78.5%.

Age, low performance status, and low body mass index before treatment were significantly correlated with the occurrence of early death in multivariate analysis.

At a median follow-up of 41.5 months, the 2-year relapse-free survival and overall survival rates were 76.1% and 82% respectively.

Conclusion

Almost 7% of patient with advanced, nonmetastatic nasopharyngeal carcinoma will die within the 6 months following the end of treatment.

Identification of patients who are at risk may help in minimizing the risk of early death, by optimizing performance and nutritional status before therapy, along with the proposition of a less aggressive treatment strategy in older patients.

187

Transcriptomic and tumor microenvironment landscape of Epstein-Barr virus related Nasopharyngeal Carcinoma in endemic and non-endemic areas.

Deborah Lenoci[1], Carlo Resteghini[2], Mara S Serafini[1], Federico Pistore[1], Brigette Ma[3], Stefano Cavalieri[2,4], Annalisa Trama[5], Lisa Licitra[2,4], Loris De Cecco[1]

[1]Fondazione IRCCS Istituto Nazionale dei Tumori, Department of Research, Integrated biology of rare tumors, Milan, Italy. [2]Fondazione IRCCS Istituto Nazionale dei Tumori, Head and Neck Medical Oncology Department, Milan, Italy. [3]The Chinese University of Hong Kong, Department of Clinical Oncology, Hong Kong SAR, China. [4]University of Milan, Department of Oncology and Hemato-Oncology, Milan, Italy. [5]Fondazione IRCCS Istituto Nazionale dei Tumori, Evaluative Epidemiology Unit, Milan, Italy

Topic

HPV or EBV related cancers

Keywords

Nasopharyngeal cancer, EBV, Transcriptomics

Purpose/Objective

Epstein-Barr virus (EBV)-related nasopharyngeal carcinoma (NPC) is an epithelial malignancy arising from the nasopharyngeal mucosal lining. A high incidence was recorded in EBV-endemic areas (EA) such as East and Southeast Asia [1] while in Europe, a non-endemic area (NEA), is low (1/105/year); however, the estimated survival rate is much lower than that recorded in Asian EA (5-year age-standardized relative survival = 54–57% vs. 74%) [2]. Risk factors of NPC include genetic, ethnic and environmental factors [3]. Differences in incidence and survival rates between EA and NEA NPCs could involve several factors, including EBV-related factors, genetic susceptibility of the population to EBV infections, and environmental factors such as diet and pollution [4-7]. Nevertheless, all proposed models of NPC pathogenesis are based on data derived from EA in Asia. Furthermore, clinical, pathogenic, and microenvironmental characteristics may play additional roles. EBV-related NPC in EA has already been characterized using genomic and transcriptomic data analysis [8-9]. However, gene expression analysis data [10] of NEA NPC is limited. Comparing gene expression data from EA and NEA diseases allows the recognition of similarities and differences in incidence and outcome among diseases arising in different geographical areas. We investigated the transcriptomic patterns of genes involved in EA NPC to interpret these differences and verifying them to an Italian cohort with available tumor tissue and clinical data. The immune and biological/functional characterization of EA and NEA NPC could improve the identification of new therapeutic strategies. Currently, the treatment for localized NPC includes radiotherapy, which is often combined with platinum-based chemotherapy, especially for locally advanced cancer. Neoadjuvant chemotherapy with cisplatin and gemcitabine was administered in the case of high-risk disease [11-12]. Immunotherapy with checkpoint inhibitors has shown clinical efficacy in recurrent/metastatic advanced NPC and is currently under evaluation to define its mechanism of action [13]. Our study aimed to dissect the gene expression (GE) and microenvironment of NPC, leading to the identification of the molecular subtypes of EA and NEA NPC. We also aimed to elucidate the biological and functional differences within EA NPC and between EA NPC and NEA NPC to eventually provide new insights into novel treatment strategies.

Material/Methods

Six GE datasets of NPC-EA transcriptomic repositories, including tumor and normal samples (GSE12452, GSE34573, GSE132112, GSE53819, GSE68799, GSE102349) and one validation dataset including both EA and NEA (https://doi.org/10.5281/zenodo.5347891) were retrieved. Four GE signatures associated to EBV related NPC prognosis (PMID: 24297049, 35262435, 32596151, 33096113), genes/pathways and gene sets (PMID: 35846746, 35394843, 35105963) were applied on EA and NEA NPC cohorts (Liu_NPC, Wood EBV EBNA1 Targets Down, Sengupta NPC_with LMP1 UP, REACTOME DNA Repair; Hallmarks). A bioinformatic meta-analysis approach was used to integrate the six EA datasets, and the classifier method was applied to the validation dataset in order to identify the subtype with worst prognosis. Moreover, RNA sequencing was performed on 50 Italian NEA NPC samples (study number: INT188/19; GSE208281). Biological and functional profiling of EA and NEA were performed using xCell, Gene set enrichment analyses, and treatment prediction methods (radiosensitivity index PMID: 16103067, pRRophetic R package, Immunophenoscore PMID: 28052254).

Results

Through the meta-analysis of EA-NPC datasets, four clusters (Cl) were identified. Prognostic analyses revealed that Cl3 had the worst prognosis (P=0.0476), confirmed by three of the four prognostic signatures and in the validation dataset (P=0.0368). The biological and functional characterization of these clusters disclosed the relative GE subtypes: Cl1, Immune-active; Cl2, Defense-response; Cl3,

Proliferation; Cl4, Perineural-interaction/EBV-exhaustion. According to the treatment prediction methods, the sensitivity of each cluster was radiotherapy and immunotherapy for immune-active, radiochemotherapy and immunotherapy for defense-response, chemotherapy for proliferation, and cisplatin treatment for perineural-interaction/EBV-exhaustion. Only three clusters ,excluding perineural-interaction/EBV-exhaustion, were expressed in our NEA cohort. Immune/biological characterization and treatment prediction analyses of NEA partially replicated the EA results.

Conclusion

Our study provides a relevant biological overview of EBV-related NPC in both EA and NEA. The immune microenvironment plays a critical role in NPC owing to the viral etiology of this malignancy. The presence of a perineural-interaction/EBV-exhaustion cluster in EA suggests an inactive EBV infection according to the viral related "hit and run theory". Evaluation of miRNAs is ongoing along with miRNA/gene expression integration. Well characterized EA- and NEA-NPC retrospective and prospective cohorts are needed to validate the obtained results and can help designing future clinical studies.

References

1.Chen YP, Chan ATC, Le QT, Blanchard P, Sun Y, Ma J. Nasopharyngeal carcinoma. Lancet. 2019 Jul 6;394(10192):64-80. doi: 10.1016/S0140-6736(19)30956-0. Epub 2019 Jun 6. PMID: 31178151.

2. Gatta G, Capocacia R, Botta L, et al. Burden of centralised treatment in Europe of rare tumours: results of RARECAREnet-a population-based study. Lancet Oncol 2017; 18: 1022-39

3. Lo KW, To KF, Huang DP. Focus on nasopharyngeal carcinoma. Cancer Cell. 2004 May;5(5):423-8. doi: 10.1016/s1535-6108(04)00119-9. PMID: 15144950.

4. Russo A, Crosignani P, Berrino F, et al. Incidence of cancer in migrants: data of the Lombardy tumor registry. Epidemiol Prev. 1994;18:125-32.

5. Murata T, Sato Y, Kimura H. Modes of infection and oncogenesis by the Epstein-Barr virus. Rev Med Virol. 2014.

6. Farrow DC, Vaughan TL, Berwick M, Lynch CF, Swanson GM, Lyon JL. Diet and nasopharyngeal cancer in a low-risk population. Int J Cancer. 1998 Dec 9;78(6):675-9. doi: 10.1002/(sici)1097-0215(19981209)78:6<675::aid-ijc2>3.0.co;2-j. PMID: 9833758.

7.Wang Y, Zhang Y, Ma S. Racial differences in nasopharyngeal carcinoma in the United States. Cancer Epidemiol. 2013 Dec;37(6):793-802. doi: 10.1016/j.canep.2013.08.008. Epub 2013 Sep 12. PMID: 24035238; PMCID: PMC3851929.

8. Tsao SW, Tsang CM, Lo KW. Epstein-Barr virus infection and nasopharyngeal carcinoma. Philos Trans R Soc Lond B Biol Sci. 2017 Oct 19;372(1732):20160270. doi: 10.1098/rstb.2016.0270. PMID: 28893937; PMCID: PMC5597737.

9. Islam KA, Chow LK, Kam NW, Wang Y, Chiang CL, Choi HC, Xia YF, Lee AW, Ng WT, Dai W. Prognostic Biomarkers for Survival in Nasopharyngeal Carcinoma: A Systematic Review of the Literature. Cancers (Basel). 2022 Apr 24;14(9):2122. doi: 10.3390/cancers14092122. PMID: 35565251; PMCID: PMC9103785.

10. Fountzilas G, Psyrri A, Giannoulatou E, Tikas I, Manousou K, Rontogianni D, Ciuleanu E, Ciuleanu T, Resiga L, Zaramboukas T, Papadopoulou K, Bobos M, Chrisafi S, Tsolaki E, Markou K, Giotakis E, Koutras A, Psoma E, Kalogera-Fountzila A, Skondra M, Bamia C, Pectasides D, Kotoula V. Prevalent somatic BRCA1 mutations shape clinically relevant genomic patterns of nasopharyngeal carcinoma in Southeast

Europe. Int J Cancer. 2018 Jan 1;142(1):66-80. doi: 10.1002/ijc.31023. Epub 2017 Sep 30. PMID: 28857155.

11. Bossi P, Chan AT, Licitra L, Trama A, Orlandi E, Hui EP, Halámková J, Mattheis S, Baujat B, Hardillo J, Smeele L, van Herpen C, Castro A, Machiels JP; ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org; EURACAN. Nasopharyngeal carcinoma: ESMO-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up†. Ann Oncol. 2021 Apr;32(4):452-465. doi: 10.1016/j.annonc.2020.12.007. Epub 2020 Dec 25. PMID: 33358989.

12. Zhang Y, Chen L, Hu GQ, et al. Gemcitabine and cisplatin induction chemotherapy in nasopharyngeal carcinoma. N Engl J Med. 2019;381(12):1124-1135.

13. Xu JY, Wei XL, Wang YQ, Wang FH. Current status and advances of immunotherapy in nasopharyngeal carcinoma. Ther Adv Med Oncol. 2022 May 7;14:17588359221096214. doi: 10.1177/17588359221096214. PMID: 35547095; PMCID: PMC9083041

190

hypofractionated radiotherapy in elderly/frail head and neck cancer patients: our experience from COVID-19 pandemic.

Ilaria Benevento[1], Angela Pia Solazzo[2], Antonella Bianculli[1], Antonietta Montagna[1], Giovanni Castaldo[1], Luciana Rago[1], Barbara D'Andrea[1], Raffaele Maria Tucciariello[1], Valentina Pirozzi Palmese[1], Vito Metallo[1], Grazia Lazzari[1]

[1]IRCCS-CROB, Radiation Oncology, Rionero in Vulture, Potenza, Italy. [2]IRCCS_CROB, Radiation Oncology, Rionero in Vulture, Potenza, Italy

Topic

Management of elderly or frail patients

Keywords

Hypofractionated RT/ Locally Advanced HN Cancer

Purpose/Objective

Head and neck cancer (HNC) remains a significant health concern worldwide. Approximately 50% of HNC occur in the elderly patients and this rate is destined to increase over time, due to the aging of the population. The treatment of HNC poses unique challenges, as it often requires a combination of surgery, chemotherapy, and radiotherapy (RT). Additionally, age-related comorbidities and frailty may complicate the management of HNC in this setting of patients. RT alone has been one of the treatment options for patients with locally advanced HNC squamous cell carcinoma (SCC) with contraindications to chemotherapy, such as cardiac risk, renal or hepatic impairment, frailty or advanced age, and patient choice. In recent years, hypofractionated RT (HFRT) has emerged as an alternative treatment approach, offering the potential to reduce the overall treatment duration while maintaining or even improving treatment outcomes. Several clinical studies have investigated the efficacy and safety of HFRT in HNC. However, robust data are lacking and mainly concern oropharyngeal and laryngeal carcinoma or palliative treatments. The emergence of the COVID-19 pandemic in late 2019 had a profound impact on healthcare systems worldwide. One significant consequence was the need to adapt cancer

treatment protocols to minimize patient exposure to the virus while maintaining treatment efficacy. HFRT, with its potential to shorten treatment duration, became an attractive option during this time. The purpose of this study is to report our preliminary retrospective experience on elderly/frail locally advanced HNC patients treated with HFRT, and to assess how the COVID-19 pandemic influenced treatment duration.

Material/Methods

We conducted a retrospective analysis of locally advanced HNC patients aged 70 years and older, not candidate to surgery nor chemotherapy and treated with HFRT alone at our Institution from 2021 to 2022. Gross tumor volume (GTV) was determined according to clinical examination, computed-tomography scan (CT), magnetic resonance imaging (MRI), or positron emission tomography scan (PET). Two clinical target volumes (CTV) were identified (high and low risk). HFRT was delivered with a Linear Accelerator (Trilogy, Varian, Palo Alto, CA, USA) with intensity-modulated (IMRT) or volumetric-modulated (VMAT) RT technique and daily image guidance. HFRT regimens included 60 Gy in 25 fractions over 5 weeks (2.4 Gy per fraction) for CTV-high risk and 50 Gy in 25 fractions over 5 weeks (2.0 Gy per fraction) for CTV-low risk. Patients were evaluated by clinical/endoscopic examination and CT or MRI imaging every 3 months after the completion of HFRT. Response to treatment on imaging (complete or partial response, stable disease), overall survival (OS) and Radiation Therapy Oncology Group (RTOG) Toxicity Criteria were assessed.

Results

A total of five elderly/frail locally advanced HNC patients were included. The median age was 78 years (range 72-82 years). Patients were staged according to seventh edition of TNM system. Of five patients, three patients had cT3-4 cN2-3 oral cavity SCC, one patient had cT4 parotid gland cancer with cutaneous ulceration and one patient had cT3 cN3b (ipsilateral large lymph node with extracapsular invasion) oropharyngeal SCC. All patients completed the full planned course of HFRT. Acute toxicities according to RTOG scale were grade 2/3 skin toxicity, grade 1/2 dryness of mouth and grade 2 oral mucositis. After a median follow-up of 6.3 months, four patients were alive, one patient with complete response (patient with oropharyngeal SCC), one patient with partial response and two patients with stable disease on imaging. Late toxicities sec. RTOG scale were grade 1/2 skin toxicity and grade 1/2 salivary gland toxicity.

Conclusion

In conclusion, HFRT is an evaluable option in the management of elderly/frail HNC patients. With a growing elderly population and the challenges posed by the COVID-19 pandemic, there is a need to explore new treatment strategies that optimize clinical outcomes in this subgroup of patients. This experience has recently been adopted in our daily clinical practice to treat very selected elderly/frail HNC patients not fit to chemo-radiotherapy or access difficulties to our radiation unit center. Future research should focus on HFRT protocols to assess long-term survival and quality of life in elderly/frail HNC patients.

References

1. Smith BD, Smith GL, Hurria A, et al. Future of cancer incidence in the United States: burdens upon an aging, changing nation. J Clin Oncol. 2009 Jun 10;27(17):2758-65. doi: 10.1200/JCO.2008.20.8983. Epub 2009 Apr 29. PMID: 19403886.

2. Huang SH, O'Sullivan B, Su J, et al. Hypofractionated radiotherapy alone with 2.4 Gy per fraction for head and neck cancer during the COVID-19 pandemic: The Princess Margaret experience and proposal. Cancer. 2020 Aug 1;126(15):3426-3437. doi: 10.1002/cncr.32968. Epub 2020 Jun 1. PMID: 32478895; PMCID: PMC7300809.

3. Belgioia L, Bacigalupo A, Missale F, et al. Individualized treatment of head neck squamous cell carcinoma patients aged 70 or older with radiotherapy alone or associated to cisplatin or cetuximab: impact of weekly radiation dose on loco-regional control. Med Oncol. 2019 Mar 29;36(5):42. doi: 10.1007/s12032-019-1264-2. PMID: 30927146.

4. Caudell JJ, Torres-Roca JF, Gillies RJ, et al. The future of personalised radiotherapy for head and neck cancer. Lancet Oncol. 2017 May;18(5):e266-e273. doi: 10.1016/S1470-2045(17)30252-8. Epub 2017 Apr 26. PMID: 28456586; PMCID: PMC7771279.

5. Psycharis SS, Salameh S, Turkdogan S, et al. Prioritization of head and neck cancer patient care during the COVID-19 pandemic: a retrospective cohort study. J Otolaryngol Head Neck Surg. 2023 Feb 14;52(1):15. doi: 10.1186/s40463-023-00625-w. PMID: 36782236; PMCID: PMC9925359.

6. Prajoko YW, Supit T. Radiotherapy service amidst COVID-19: Experience from Tertiary Referral Hospital in Semarang, Indonesia. J Public Health Res. 2023 Sep 12;12(3):22799036231197189. doi: 10.1177/22799036231197189. PMID: 37711727; PMCID: PMC10498704.

7. Jackson SM, Hay JH, Flores AD. Local control of T3N0 glottic carcinoma by 60 Gy given over five weeks in 2.4 Gy daily fractions. One more point on the biological effective dose (BED) curve. Radiother Oncol. 2001 May;59(2):219-20. doi: 10.1016/s0167-8140(01)00286-9. PMID: 11325452.

8. Corry J, Peters LJ, Costa ID, et al. The 'QUAD SHOT'--a phase II study of palliative radiotherapy for incurable head and neck cancer. Radiother Oncol. 2005 Nov;77(2):137-42. doi: 10.1016/j.radonc.2005.10.008. Epub 2005 Nov 2. PMID: 16260054.

9. Ferris RL, Flamand Y, Weinstein GS, et al. Evaluation of response and quality of life with palliative single-fraction radiation therapy in patients with head and neck cancer. JAMA Otolaryngol Head Neck Surg. 2016;142(10):974-981. doi:10.1001/jamaoto.2016.1674.

10. Pfister DG, Spencer S, Brizel DM, et al. Head and Neck Cancers, Version 2.2020, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2020;18(7):873-898. doi:10.6004/jnccn.2020.0023.

191

Dose prescription variability in Oropharynx Cancer Radiotherapy

Christian R Hansen[1,2,3], Tony Tadic[4], Andrea McNiven[4], Jens Petersen[5,6], Sharma Manju[7], Gareth Price[8], Mohamed A Naser[9,10,11], Pernille Lassen[12,13], Jens Overgaard[12], Lachlan McDowell[14], Clifton David Fuller[9,10,11], David Thomsen[8], Sue S Yom[7], Jørgen Johansen[15], Jeppe Friborg[5], Andrew Hope[16]

[1]Laboratory of Radiation Physics, Odense University Hospital, Odense, Denmark. [2]Institute of Clinical Research, University of Southern Denmark, Odense, Denmark. [3]Danish Center of Particle Therapy, Aarhus University Hospital, Aarhus, Denmark. [4]Department of Medical Physics, Princess Margaret Cancer Centre, Toronto, Canada. [5]Department of Oncology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark. [6]Department of Computer Science, University of Copenhagen, Copenhagen, Denmark. [7]Department of Radiation Oncology, University of California San Francisco, San Francisco, USA. [8]Division of Cancer Sciences, University of Manchester, The Christie NHS Foundation Trust, Manchester, United Kingdom. [9]Department of Radiation Oncology, Baylor College of Medicine, Houston, USA. [10]Department of Radiation Oncology, The University of Texas MD Anderson Cancer

Center, Houston, USA. [11]Medical Physics Program, The University of Texas Graduate School of Biomedical Sciences, Houston, USA. [12]Department of Experimental Clinical Oncology, Aarhus University Hospital, Aarhus, Denmark. [13]Department of Oncology, Aarhus University Hospital, Aarhus, Denmark. [14]Department of Radiation Oncology, Princess Alexandra Hospital, Brisbane, Australia. [15]Department of Oncology, Odense University Hospital, Odense, Denmark. [16]Department of Otolaryngology-Head Neck Surgery, Princess Margaret Cancer Centre, Toronto, Canada

Topic

HPV or EBV related cancers

Keywords

Dose prescription, Treatment planning, Trials

Purpose/Objective

Radiotherapy treatment planning hinges on a critical factor: the prescribed dose. Surprisingly, no consistent, standardised global approach to interpreting this prescription exists. This study aimed to examine and illustrate the variations in prescribed doses for the same treatment across North European and North American centres.

Material/Methods

The study analysed consecutively treated oropharynx cancer patients from six globally recognised radiotherapy departments. The criteria for inclusion encompassed curative IMRT or VMAT radiotherapy administered in 2017 or later. These centres were divided into three North American and three North European centres.

Dose-volume histogram (DVH) data were extracted from the local treatment planning system for the Gross Tumour Volume (GTV), the high-dose Clinical Target Volume (CTV), and Planning Target Volume (PTV) for each patient. The DVH was sampled in 1 cGy dose bins across the 0 to 100 Gy range.

All DVHs were scaled to a standard prescription of 70 Gy delivered in 35 fractions to facilitate straightforward comparisons across centres. No biological corrections were applied.

For the three target volumes (GTV, CTV, PTV), we extracted and compared metrics such as D95% (Dose to 95% of the volume), D98%, D99%, V95% (Volume receiving 95% of the prescription dose), V105%, and V107%. We visually compared these metrics and conducted statistical testing using the Mann-Whitney U-test.

Results

Our study encompassed 1,375 patients treated across six centres, revealing a spectrum of 38 different dose prescriptions, ranging from 55 Gy in 20 to 70 Gy in 35 fractions.

When normalised to 70 Gy, the median mean CTV dose exhibited a 4% difference, ranging from 70.12 Gy to 72.93 Gy across centres. Notably, the three European centres showed a high consistency, deviating by only 0.4%, while the three North American centres showed a slight variation within 2%. Figure 1 presents the mean CTV dose and the D98% boxplots. The interquartile range (IQR) for the mean CTV dose from 0.17 Gy to 1.22 Gy, with European centres showing the smallest IQR.

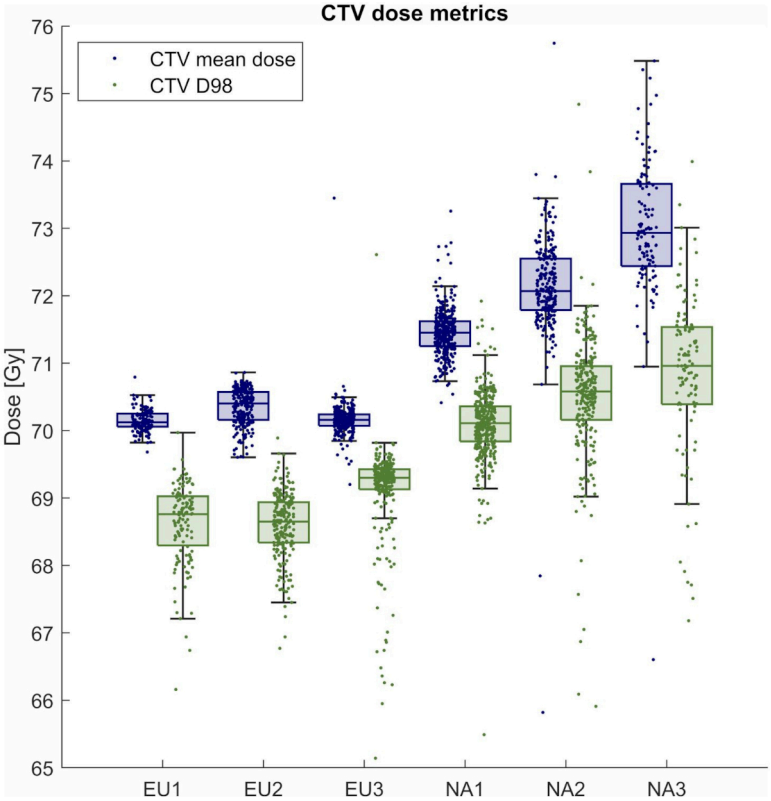


Figure 1. Boxplots of the mean dose and D98 of the high dose CTV. The European centres (EU1-3) show high compliance with the mean dose prescription, whereas the North American centres (NA1-3), to a lesser degree, comply with the near minimum dose prescription.

Examining the near-minimum CTV doses (D98% of CTV), we observed a range from 68.65 Gy to 70.96 Gy, with an IQR from 0.30 Gy to 1.15 Gy. A scatter plot of CTV mean dose against CTV D98% revealed distinct clusters for each of the six centres (Figure 2). Notably, the European centres cluster more densely compared to the North American centres.

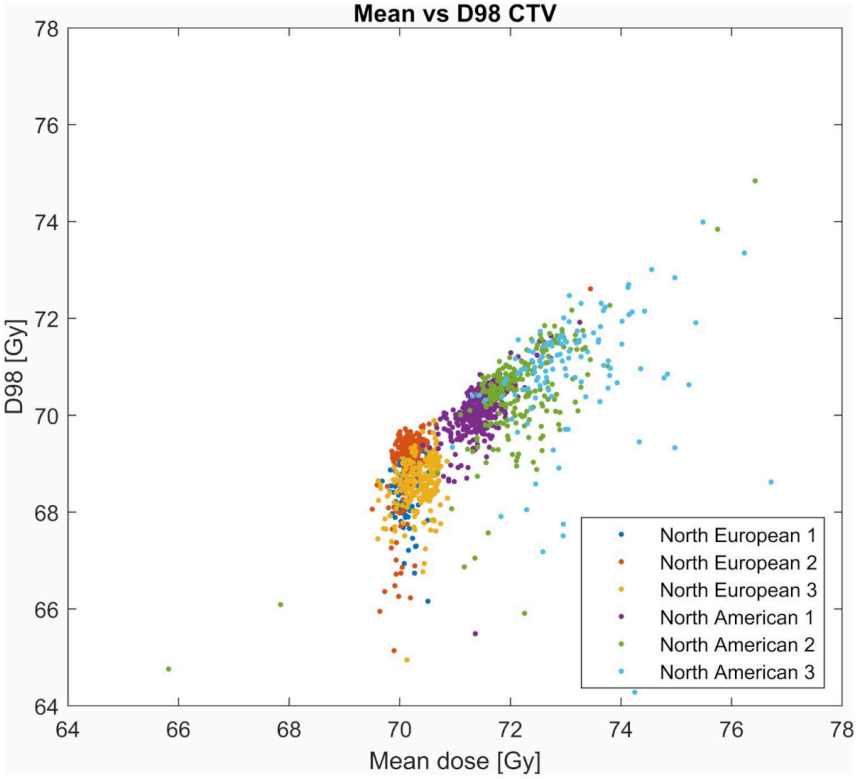


Figure 2. Scatterplot of the mean dose vs D98 of the high dose CTV. The European centres cluster more densely compared to the North American centres

The variation in prescribed doses for the same treatment regimen poses a significant challenge. Clinical interpretation of 70 Gy varies widely between centres and is influenced by each centre's individual experience, which, in turn, impacts the interpretation of published results. European centres primarily adhere to the ICRU dose prescription, targeting the median CTV dose. Conversely, North American centres tend to prescribe based on the minimum dose to the CTV or, in some cases, the PTV, as outlined in various RTOG protocols.

Conclusion

Our study underscores that prescribing a dose of 70 Gy in 35 fractions for standard oropharynx cancer patients results in substantial variations in mean and near-minimum CTV doses. These dose prescription discrepancies significantly impact the interpretation of clinical trial outcomes comparison. Furthermore, this significant dosimetric variability has important implications for dose de-escalation strategies for HPV+ oropharynx cancer treatment.

193

Videofluoroscopy assessment of swallowing following dysphagia-optimised IMRT in head and neck cancer

Anne Weitzenkorn[1], Jane Dunton[1], Teresa Guerrero Urbano[2], Mary Lei[2], Miguel Reis Ferreira[2], Anthony Kong[2], Imran Petkar[2]

[1]Guy's and St Thomas' NHS Foundation Trust, Department of Speech and Language Therapy, London, United Kingdom. [2]Guy's and St Thomas' NHS Foundation Trust, Department of Oncology, London, United Kingdom

Topic

Quality of life and outcomes

Keywords

videofluoroscopy, swallow,dysphagia-optimised IMRT

Purpose/Objective

Primary (chemo) radiotherapy (CRT) for head and neck cancers may have an adverse effect on patients' swallowing function. Minimising RT dose to critical swallowing structures using dysphagia-optimised intensity-modulated RT (DO-IMRT) has been shown to improve post-treatment patient-reported swallowing outcomes. Following the implementation of DO-IMRT as standard of care at our centre for HNC patients treated with primary (C)RT, videofluoroscopy (VFS) as a core monitoring component was piloted for an initial cohort of 30 patients. We present swallowing outcomes based on prospectively collected pre- and post-treatment VFS assessment.

Material/Methods

30 consecutive patients treated with DO-IMRT between March and August 2022 were included. All patients received a radical RT dose of 65 Gy/30 fractions/6 weeks to the tumour and involved nodes, and a prophylactic dose of 54 Gy/30 fractions/6 weeks to regions at risk of microscopic disease – with or without chemotherapy. VFS was performed at baseline and three months following completion of treatment. Analysis of VFS imaging included 1) quantification of depth and response to airway compromise using Penetration-Aspiration Scale (PAS: 1-2 normal, 3-5 penetration, 6-8 aspiration); 2) grading severity of dysphagia with Dynamic Imaging Grade of Swallowing Toxicity (DIGEST: 5-point scale; 0 normal, 4 life-threatening); 3) pathophysiological assessment of swallow using the Modified Barium Swallowing Impairment Profile (MBSImP). PAS was dichotomised in two ways, one to indicate any laryngeal penetration or aspiration (PAS <3 vs PAS ≥3) and one to indicate aspiration not ejected (PAS <7 vs PAS 7-8). For DIGEST and MBSImP, parameters were dichotomised to differentiate normal swallow to mild impairment from moderate-severe impairment (0-1 vs 2+). Dichotomised parameters were compared using McNemar's test. No corrections for multiplicity were made. PAS and DIGEST were scored by two speech and language therapists (SLTs) independently. MBSImP was scored by one certified SLT who was blinded to diagnosis and clinical assessment outcomes as well as baseline results at time of scoring post-treatment VFS.

Results

Patient, disease and treatment characteristics are presented in Table 1. One patient died before completion of the post-treatment VFS, therefore final analyses were based on complete data for 29 patients. There was no significant increase in the rates of aspiration not ejected (PAS 7-8) following treatment ($p = 0.125$), though the prevalence of laryngeal penetration/aspiration (PAS 3-8) increased from 17% at baseline to 45% at three months following treatment completion ($p = 0.038$) (Table 2:A). 7% of patients had baseline moderate-severe dysphagia as per DIGEST; this increased to 21% following treatment and was not statistically significant ($p =0.125$) (Table 2:A). All DIGEST scores and subscores remained predominantly stable following treatment. (Table 2:B; Figure 1). There was no statistically significant increase in prevalence of moderate-severe impairment for any analysed MBSImP components of swallowing between pre- and post-treatment VFS (Table 2:A); the most frequent outcome for 9 out of 10 MBSImP components was stability, while initiation of swallow (MBSImP component 6) most frequently showed improvement (Table 2:B; Figure 1).

Table 1: Patient, disease and treatment characteristics

Characteristics	**n (%)**
Sex	
Male	26 (87)
Female	4 (13)
Age at diagnosis	
Range 39-74 years	
Mean 61 years	
Smoking status	
Current	3 (10)
Previous	21 (70)
Never	6 (20)
Smoking history	
Never	6 (20)
<10 pack years	5 (17)
>10 pack years	19 (63)
Tumour staging	
T1	4 (13)
T2	6 (20)
T3	9 (30)
T4	11 (37)
Nodal staging	
N0	13 (43)
N+	17 (57)
Disease stage (AJCC 7th edition)	
I	1 (3)
II	5 (17)
III	6 (20)
IV	18 (60)
Primary site	
Nasopharynx	2 (7)
Oropharynx	16 (53)
- Oropharynx HPV+	10 (33 of total)
- Oropharynx HPV-	6 (20 of total)
Larynx	7 (23)
Hypopharynx	5 (17)
Treatment	
RT	7 (23)
CRT	20 (67)
Induction chemotherapy + CRT	3 (10)
RT neck treatment	
Unilateral neck	1 (3)
Bilateral neck	29 (97)

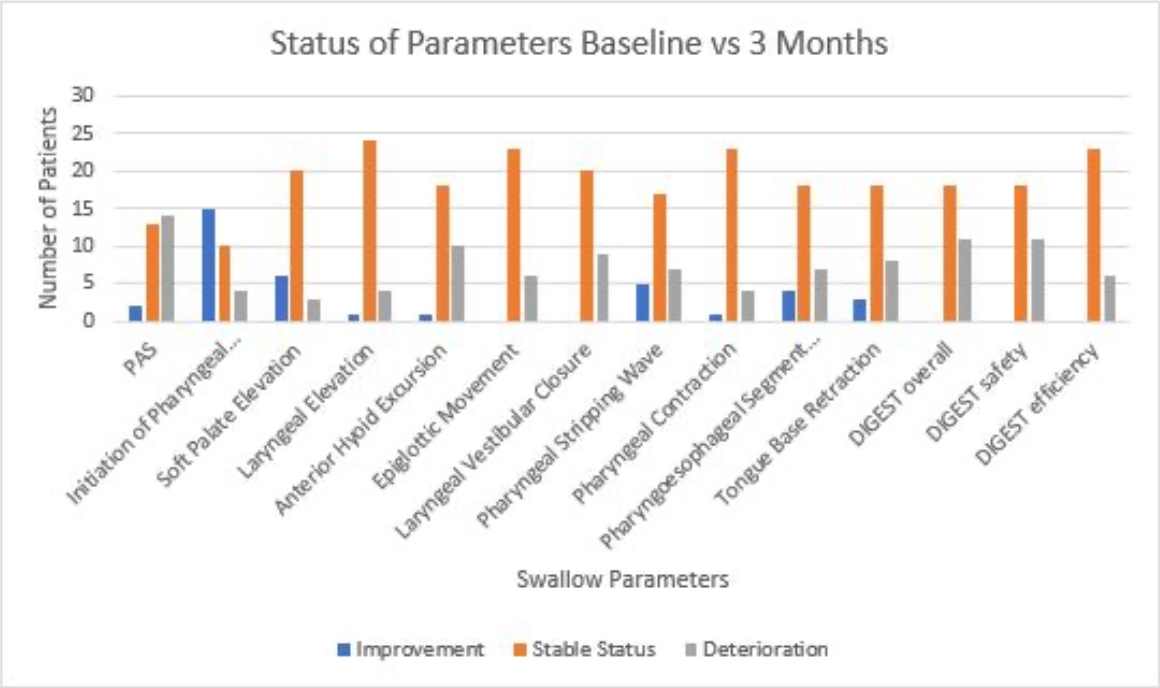
VFS assessment	
Baseline	30 (100)
3 months post-treatment	29 (97)

Table 2: Results of VFS at baseline and three months post-treatment

		A			B		
		Baseline prevalence of moderate/severe impairment n (%)	3 month prevalence of moderate/severe impairment n (%)	P value (McNemar's test – two tailed)	Improvement (3 months vs baseline) n (%)	Stable status (3 months vs baseline) n (%)	Deterioration (3 months vs baseline) n (%)
Penetration-Aspiration Scale	Penetration/aspiration (PAS 3-8)	5 (17)	13 (45)	0.038	2 (7)	13 (45)	14 (48)
	Aspiration (PAS 7-8)	2 (7)	6 (21)	0.125	0 (0)	2 (7)	4 (14)
MBSImP	Initiation of pharyngeal swallow (Component 6)	23 (79)	17 (59)	0.109	15 (52)	10 (34)	4 (14)
	Soft palate elevation (Component 7)	0 (0)	0 (0)	1	6 (21)	20 (69)	3 (10)
	Laryngeal elevation (Component 8)	1 (3)	0 (0)	1	1 (3)	24 (83)	4 (14)
	Anterior hyoid excursion (Component 9)	1 (3)	1 (3)	1	1 (3)	18 (62)	10 (34)
	Epiglottic movement (Component 10)	1 (3)	2 (7)	1	0 (0)	23 (79)	6 (21)
	Laryngeal vestibule closure (Component 11)	0 (0)	0 (0)	1	0 (0)	20 (69)	9 (31)
	Pharyngeal stripping wave (Component 12)	0 (0)	0 (0)	1	5 (17)	17 (59)	7 (24)
	Pharyngeal contraction (Component 13)*	6 (21)	8 (29)	0.625	1 (4)	23 (82)	4 (14)
	Pharyngoesophageal segment opening (Component 14)	1 (3)	1 (3)	1	4 (14)	18 (62)	7 (24)
	Tongue base retraction (Component 15)	18 (62)	20 (69)	0.727	3 (10)	18 (62)	8 (28)
DIGEST	DIGEST overall	2 (7)	6 (21)	0.125	0 (0)	18 (62)	11 (38)
	DIGEST safety	2 (7)	4 (14)	0.5	0 (0)	18 (62)	11 (38)
	DIGEST efficiency	1 (3)	4 (14)	0.25	0 (0)	23 (79)	6 (21)

*Analysis for this component based on 28 patients as anterior-posterior (A-P) view not captured for one patient in error

Figure 1: Rates of change of swallow parameters



Conclusion

In this small pilot cohort, prospective instrumental evaluation of swallowing function using validated assessment tools showed that functional outcomes following DO-IMRT did not significantly deteriorate at three months post-treatment in comparison to baseline and supports the implementation of this toxicity-sparing RT delivery technique. The prevalence of laryngeal penetration/aspiration (PAS 3-8) did increase statistically significantly over time, but rates of aspiration not ejected (PAS 7-8) specifically did not, which may be of more pertinent clinical importance. Further longitudinal assessment with a larger cohort is required to determine the longer-term benefits of DO-IMRT.

References

1. Nutting C, Finneran L, Roe J, Sydenham MA, Beasley M, Bhide S, et al. Dysphagia-optimised intensity-modulated radiotherapy versus standard intensity-modulated radiotherapy in patients with head and neck cancer (DARS): a phase 3, multicentre, randomised, controlled trial. The Lancet Oncology [Internet]. 2023 [cited 2023 Aug 15];24(8):868–80. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1470204523002656

2. Rosenbek JC, Robbins JA, Roecker EB, Coyle JL, Wood JL. A penetration-aspiration scale. Dysphagia [Internet]. 1996 Mar 1 [cited 2023 Oct 9];11(2):93–8. Available from: https://doi.org/10.1007/BF00417897

3. Hutcheson KA, Barrow MP, Barringer DA, Knott JK, Lin HY, Weber RS, et al. Dynamic Imaging Grade of Swallowing Toxicity (DIGEST): Scale development and validation. Cancer [Internet]. 2017 [cited 2023 Oct 9];123(1):62–70. Available from: https://acsjournals.onlinelibrary.wiley.com/doi/10.1002/cncr.30283

4. Hutcheson KA, Barbon CEA, Alvarez CP, Warneke CL. Refining measurement of swallowing safety in the Dynamic Imaging Grade of Swallowing Toxicity (DIGEST) criteria: Validation of DIGEST version 2. Cancer [Internet]. 2022 [cited 2023 Oct 9];128(7):1458–66. Available from: https://acsjournals.onlinelibrary.wiley.com/doi/10.1002/cncr.34079

5. Martin-Harris B, Brodsky MB, Michel Y, Castell DO, Schleicher M, Sandidge J, et al. MBS Measurement Tool for Swallow Impairment—MBSImp: Establishing a Standard. Dysphagia [Internet]. 2008 [cited 2023 Oct 9];23(4):392–405. Available from: http://link.springer.com/10.1007/s00455-008-9185-9

6. Gawryszuk A, Bijl HP, Van Der Schaaf A, Perdok N, Wedman J, Verdonck-de Leeuw IM, et al. Relationship between videofluoroscopic and subjective (physician- and patient- rated) assessment of late swallowing dysfunction after (chemo) radiation: Results of a prospective observational study. Radiotherapy and Oncology [Internet]. 2021 [cited 2023 Jun 16];164:253–60. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0167814021067402

7. Barbon CEA, Yao CMKL, Alvarez CP, Goepfert RP, Fuller CD, Lai SY, et al. Dysphagia profiles after primary transoral robotic surgery or radiation for oropharyngeal cancer: A registry analysis. Head & Neck [Internet]. 2021 [cited 2023 Aug 15];43(10):2883–95. Available from: https://onlinelibrary.wiley.com/doi/10.1002/hed.26768

194

Do all roads lead to Speech and Language Therapy? Evaluation of a pilot waiting-list initiative for radiation-oncology head and neck cancer patients to enhance access to Speech and Language Therapy

Katie Higgins[1], Susan Lawson[1], John Armstrong[2], Oleksandr Boychak[2], Fran Duane[2], Sinead Brennan[2]

[1]SLRON, Speech and Language Therapy, Dublin, Ireland. [2]SLRON, Radiation Oncology, Dublin, Ireland

Topic

Multidisciplinary management

Keywords

SLT radiation-oncology patient education

Purpose/Objective

All head and neck cancer (HNC) patients receiving radiotherapy should have access to Speech and Language Therapy (SLT) for management of speech and swallowing(1).

A pilot SLT education group programme, was delivered over a 10-week-period in a radiation-oncology (RO) service in 2023 as part of a waiting-list initiative. The purpose was to increase timely access to SLT for HNC patients.

We aimed to evaluate the SLT pilot education group and make recommendations for future service delivery models.

Material/Methods

HNC patients receiving radical radiotherapy (n=22) prioritised as low-risk SLT patients, attending for RO, were identified and invited to attend an SLT education session. High-risk patients requiring intensive SLT intervention e.g. hypo-pharyngeal cancer, advanced laryngeal cancer and T4 tumours were excluded.

Topics covered included an introduction to eating, drinking and swallow (ED&S) mechanisms, side-effects of radiotherapy and potential impact on ED&S, management strategies and prophylactic swallowing exercises. Sessions were interactive and patient information leaflets were provided. Invitations to attend additional sessions were extended; individual appointments were available on patient request.

Swallowing outcomes (The MDADI global score, EAT-10) and patient satisfaction levels were completed at the time of attendance.

Data was collected on patient demographics, treatment plans, attendance rates, admissions, patient self-report of dysphagia and impact on quality of life. Waiting-list times and cost savings were calculated.

Results

The results demonstrated that 14 patients attended (64%) the offered education session (9 males; mean age 66.5, range 46-84 years)

The majority of patients had disease staging as ≤T2 (57%; 8/14). Attendees were heterogeneous with regard to tumour location (Table 1).

No patients requested individual appointments.

Of 14 attendees, 5 required inpatient admission (36%), compared to 6 (75%) patients who were invited and did-not-attend the education session.

Reason for admission analysis revealed all 5 attendees required admission for symptom control, chiefly pain management, nausea, constipation and weight loss. Requirement for NG feeding was stated in 3/5 (60%) cases. Inpatient NG insertion requirement in the non-attender cohort was 67% (4/6).

Treatment for pneumonia was required in 0% of cases.

Attendees were admitted later into their treatment (mean fraction at time of admission 32; range 28-35) when compared to non-attendees (mean fraction at time of admission 23.5; range 13-35).

The presence of oropharyngeal dysphagia as per self-report was identified in 8 (57%; EAT-10 score ≥3) attendees. However, the majority of attendees did not consider dysphagia as affecting quality-of-life (Mean MDADI global-question score of 3).

All attendees reported the education session as helpful, they planned to implement advice given and would recommend attendance to fellow-patients.

Seven patients received SLT input within local departmental standards (KPI of by 5 fractions). An additional 7 patients accessed SLT who would not have been seen due to service constraints. A further 8 patients would have received SLT guidance if they had attended the education session offered.

When comparing costings for individual versus group interventions, a saving of €482.46 could be made per group programme for a similar patient cohort(2).

Tumour Location	Overall Invitees	Attendees
Parotid	3	3
Tonsil	5	4
Neck	3	2
Tongue	3	1
Soft Palate	2	1
Larynx	1	1
Other	4	2
Total	22	14

Table 1

Conclusion

This waiting-list group initiative provided access to SLT for a cohort of low-risk HNC patients who would not have received guidance due to departmental service constraints.

This pilot study has shown that group interventions can be an effective way to introduce the role of SLT, deliver general patient education and introduce swallowing rehabilitation to this specific client group.

Preliminary findings suggest that this pilot waiting-list initiative was an effective medium to enhance patient experience and encourage patient autonomy and empowerment for HNC patients during their radiation-oncology journey.

However, this pilot programme was delivered to a low-risk HNC patient cohort and a similar approach may not be appropriate for HNC patients with more extensive disease where an individualised treatment programme is the gold-standard (3).

Group intervention can be a necessary solution to address service delivery demands in the existence of resource constraints. Nevertheless, the value, impact and effectiveness of tailored face-to-face SLT interventions with HNC patients who present with acute, chronic and complex ED&S needs cannot be underestimated(4, 5).

This initiative will continue and facilitate further analysis regarding admission avoidance, alternative feeding requirement and swallow function outcomes. Further analysis exploring rationale for non-attendance will assist with future programme design.

Data will also be used to assist with future service development, resource allocation and staff planning.

References

1 Baijens, L. W. et al (2021) European white paper: oropharyngeal dysphagia in head and neck cancer. European Archives of Oto-Rhino-Laryngology https://doi.org/10.1007/s00405-020-06507-5

2 HIQA (2018) Guidelines for the Economic Evaluation of Health Technologies, Dublin

3 Clarke, P. et al (2016) Speech and swallow rehabilitation in head and neck cancer: United Kingdom national multidisciplinary guidelines. The Journal of Laryngology and Otology 130, S176-S180

4 Patterson J, Wilson JA. The clinical value of dysphagia preassessment in the management of head and neck cancer patients.Curr Opin Otolaryngol Head Neck Surg. 2011;19:177–81. doi:10.1097/MOO.0b013e328345aeb0.

5 Govender, R. et al (2019) Helping Patients with Head and Neck Cancer Understand Dysphagia: Exploring the Use of Video-Animation.American Journal of Speech-Language Pathology Vol 28 697-705

195

epidemiological, clinical, and evolutionary features of nasopharyngeal squamous cell carcinoma

Mona Taouchikht[1,2], Houda Fares[1,2], Sara Abdou[1,2], Rania El Gueddari[1,2], édith Tatiana Ngbwa[1], Imane Hassnaoui[1,2], Karima Nouni[1,2], Amine Lachgar[1,2], Hanan Elkacemi[1,2], Tayeb Kebdani[1,2], Khalid Hassouni[1,2]

[1]National Oncology Institute, Radiotherapy, Rabat, Morocco. [2]Faculty of Medicine and Pharmacy, Medicine, Rabat, Morocco

Topic

Epidemiology and prevention

Keywords

Nasopharyngeal carcinoma, Squamous Cell Carcinoma

Purpose/Objective

Nasopharyngeal carcinoma (NPC) is one of the most frequent cancers in Morocco, with 5-7 cases per 100,000 persons annually.

The most common histological type is undifferentiated carcinoma of nasopharyngeal type (UCNT), while squamous cell carcinoma represents only 5 to 10% of cases.

The aim of this study is to characterize the epidemiological, clinical, and evolutionary features of nasopharyngeal squamous cell carcinoma.

Material/Methods

Data were collected from the records of 61 patients with non metastatic nasopharyngeal cancers treated in the Radiotherapy department at the National Oncology Institute in Rabat, Morocco, between January 1st, 2019, and December 31, 2019.

Results

Among the 61 cases of nasopharyngeal carcinoma, only 7 were squamous cell carcinomas. The majority of patients were male (70%), with an average age of 49 years (range 18-61), and 70% were chronic smokers.

Stage at diagnosis was III and II According to the TNM classification (UICC 8th edition 2017), in 58% and 42% of cases respectively.

Neoadjuvant chemotherapy was indicated in 85% of cases, followed by curative concurrent chemo-radiotherapy, using the VMAT (Volumetric Modulated Arc Therapy) technique, delivering 70 Gy in 33 fractions, along with cisplatin-based chemotherapy (40mg/m2/week) with an average of 5 cycles.

At 4-year follow-up, local relapses were observed in 2 patients (28% of cases), while metastatic relapses in the lungs and bones were observed in 3 patients (42% of cases), and a complete response was observed in 2 patients (28%).

Conclusion

Our study shows that squamous cell carcinoma of the nasopharynx remains a relatively rare histological form of nasopharyngeal cancers, strongly associated with chronic smoking, and exhibits an unfavorable outcome compared to UCNT.

196

Evaluation and implementation of open face masks with surface-guided radiotherapy (SGRT)

Rayk Nachtigall[1], Sebastian Exner[2], Nicholas Seeto[3], Fabian Fehlauer[2]

[1]Strahlenzentrum Hamburg MVZ, medical physics, Hamburg, Germany. [2]Strahlenzentrum Hamburg MVZ, specialists, Hamburg, Germany. [3]Strahlenzentrum Hamburg MVZ, radiationtherapists, Hamburg, Germany

Topic

Innovative treatments

Keywords

SGRT, open mask, patient movement

Purpose/Objective

Since the installation of the SGRT-system AlignRT by VisionRT at the “Strahlenzentrum Hamburg MVZ” there is a unique possibility to evaluate the patient movement during the treatments, and the therapy as a whole. With the experience of SGRT for thoracic and pelvic treatments in out clinic, we approached the reduction of the h&n mask coverage of the patients face.

Material/Methods

This analysis uses finished h&n treatments of each 20 patients with conventional closed (cM) and open masks (oM). The direct comparison of the mask modifications is done by the shifts of the initial positioning CBCTs at the beginning of each treatment fraction. Furthermore, the open masks were used in combination with the SGRT (350+ fractions) gathering surface data. The evaluation comprises all treatments as a whole, and is focused on the three translation dimensions: superior-inferior, left-right, and anterior-posterior. As well as the spanned vectors of the surfaces. The amount of data entries of the SGRT data justifies a Gaussian analysis.

Results

The couch shifts after the CBCT reduce with the usage of SGRT from σ_{cM}(lng/lat/vrt)=6.8/2.4/5.8 (in mm) to σ_{oM}(lng/lat/vrt)=2.7/1.7/2.3 (in mm). The patient movement monitoring of the SGRT shows a mean deviation of σ_{SGRT}(lng/lat/vrt)=0.44/0.44/0.39(in mm). The resulting deviation of the spatial vector is σ_{vec}=0.38 mm, which results in an integrated patient movement coverage of 99% within 1 mm margin.

Conclusion

The use of open masks and SGRT is a step forward in patient safety, and comfort. It helps to reduce the errors in the initial positioning, and therefore increases the accuracy of the repositioning from fraction to fraction. This allows the evaluation of PTV to smaller margins around the GTV, which also can increase the accuracy of stereotactic treatments. Noteworthy is the ability to monitor the patient during the treatment, and to react to the smallest movements. Furthermore, the open mask helps the patients to relax, and not backing off or nod, like indicated in the close mask CBCTs.

197

Time from surgery to commencing adjuvant radiotherapy does not affect survival in patients with head and neck squamous cell carcinoma

James M Price[1,2], Alexandra Ferrera[1], Kate Garcez[1], Christopher Hughes[1], LipWai Lee[1], Golnoosh Motamedi-Ghahfarokhi[2], Gareth Price[2], Catharine West[2], David Thomson[1,2]

[1]The Christie NHS Foundation Trust, Clinical Oncology, Manchester, United Kingdom. [2]The University of Manchester, Division of Cancer Sciences, Manchester, United Kingdom

Topic

Multidisciplinary management

Keywords

Adjuvant, radiotherapy, modelling

Purpose/Objective

Studies have reported inferior outcomes when adjuvant radiotherapy starts more than 6-8 weeks post-surgery for locally-advanced head and neck squamous cell carcinoma (HNSCC). However, the applicability of these studies may be limited due to the dichotomisation of time variables (e.g.,'on time' vs 'delayed' radiotherapy) either arbitrarily or based on the sample median[1-3]. In clinical practice, oncologists may omit radiotherapy when delays extend beyond this time and instead advocate for observational approaches only.

This study aimed to assess the relationship between survival and the time interval between surgery and radiotherapy as a continuous variable. We hypothesised there would be no significant change in survival around either six or eight weeks post-surgery.

Material/Methods

An institutionally approved, retrospective review of prospectively collected data. Inclusion criteria: all patients with HNSCC who underwent curative-intent surgery followed by post-operative (chemo)radiotherapy at The Christie NHS Foundation Trust (UK) between Jan 2014 and Dec 2020. Patient, cancer and treatment data were collected. Time intervals of interest included (i) days from surgery to radiotherapy start and (ii) overall treatment time (OTT; days from surgery to radiotherapy completion).

Demographic and cancer details were summarised using descriptive statistics. A multiple linear regression model was fitted to assess associations between patient / tumour characteristics and time from surgery to radiotherapy. The primary endpoint was overall survival (OS). A multivariable Cox Proportional Hazards (PH) model was fitted. Missing values were handled by multiple imputation using chained equations.

Results

386 patients were included. Patient characteristics are shown in the Table.

Characteristic	**N = 386**[1]
Age (median, IQR)	65 (56-71)
Gender	
Female	120 (31%)
Male	266 (69%)
ECOG performance status	
0	94 (24%)
1	193 (50%)
2	79 (21%)
3	19 (4.9%)
ACE-27 score	
0	166 (43%)
1	133 (35%)
2	64 (17%)
3	21 (5.5%)
Smoking history	
Current	70 (19%)
Ex	214 (59%)
Never	80 (22%)
H&N subsite	
Larynx	45 (12%)
Oral cavity	214 (55%)
Pharynx	103 (27%)
Nose / sinuses	24 (6.2%)
Surgical margin status	
<1mm	164 (44%)
1-5mm	149 (40%)
>5mm	59 (16%)
Tumour stage	
T1	53 (14%)
T2	111 (24%)
T3	57 (15%)
T4	157 (42%)
Nodal stage	
N0	130 (34%)
N1	77 (20%)
N2	44 (11%)

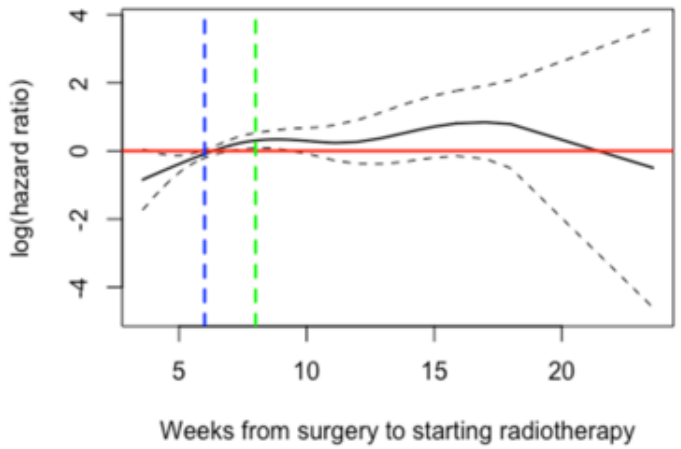
N3	135 (35%)
Treatment modality	
Chemo-RT	110 (28%)
RT alone	276 (72%)
Radiotherapy schedule	
4 weeks	75 (19%)
6 weeks	310 (81%)

The median time between surgery and radiotherapy start was 44 days (IQR: 14 days). 175 patients (45.3%) commenced radiotherapy within six weeks of surgery, and 317 (82.1%) within eight weeks. The median OTT was 83 days (IQR: 14 days).

On multivariable linear regression, the time interval between surgery and radiotherapy start was not associated with any candidate covariate (as listed in Table). The multiple R-squared value for the model was 0.07 (i.e., the model accounted for only 7% of variability in the time between surgery and radiotherapy start).

There were 154 OS events at a median of 1.65 years (IQR 2.46 years) For surviving patients (n = 232), the median follow-up was 4.57 years (IQR 2.59 years).

To explore the relationship between OS and days from surgery to starting radiotherapy, the two variables were plotted (Figure). While log(hazard) for OS increased around 6 weeks post-surgery, the increase was small before falling again at 8 weeks post-surgery. The risk only increased again at ~ 12 weeks post-surgery, although inferences become difficult at this point due to small patient numbers.



On multivariable Cox regression, the time interval between surgery and radiotherapy start was not associated with OS (HR 1.00; 95% CI 0.99 - 1.01; p=0.5). A further Cox model was fitted, with OTT as an alternative covariate; this too was not prognostic (HR 1.01; 95% CI 0.94 - 1.09; p=0.7).

Conclusion

In this study, neither an increasing time interval between surgical resection and commencing post-operative radiotherapy nor increasing OTT was associated with inferior OS for patients with resected HNSCC, when adjusted for demographic, clinical and treatment-related covariables. We recommend

that patients are still considered for adjuvant radiotherapy even in the presence of a delay post-surgery of > 6-8 weeks.

References

1. Vikram, B. Importance of the time interval between surgery postoperative radiation therapy in the combined management of head & neck cancer. International Journal of Radiation Oncology*Biology*Physics 5, 1837–1840 (1979).

2. Rosenthal, D. I. et al. Importance of the treatment package time in surgery and postoperative radiation therapy for squamous carcinoma of the head and neck. Head Neck 24, 115–126 (2002).

3. Tribius, S. et al. Survival and overall treatment time after postoperative radio(chemo)therapy in patients with head and neck cancer: Overall treatment time and survival after postoperative radio(chemo)therapy in head and neck cancer. Head Neck 38, 1058–1065 (2016).

198

treatment tolerance and toxicity in elderly nasopharyngeal cancer patients and implication on outcomes

Sara Abdou[1,2], Rania El Gueddari[1,2], Mouna Taouchikht[1,2], Houda Fares[1,2], Imane Hassnaoui[1,2], Edith Tatiana Ngbwa[1,2], Karima Nouni[1,2], Amine Lachgar[1,2], Hanan ElKacemi[1,2], Tayeb Kebdani[1,2], Khalid Hassouni[1,2]

[1]national oncology institute, radiotherapy, RABAT, Morocco. [2]faculty of medicine and pharmacy, medicine, RABAT, Morocco

Topic

Management of elderly or frail patients

Keywords

Nasopharyngeal ,elderly,Radiotherapy

Purpose/Objective

Nasopharyngeal cancer is common in Morocco. It is a clinicobiological and histological entity that differs from other head and neck cancers, notably in its geographical distribution and evolutionary profile.

The aim of our work was to evaluate the impact of treatment tolerance and toxicity in nasopharyngeal cancer in elderly (age at diagnosis ≥ 60 years).

Material/Methods

This was a retrospective study of patients with nasopharyngeal cancer treated by VMAT technique in the radiotherapy department at the Institute of Oncology RABAT between January 2018 and December 2021.

Patients received radiotherapy with or without concomitant systemic therapy.

Results

We identified 257 patients: 21% elderly and 79% young, with no differences in AJCC stage 8th edition,

Tumors were classified as T1 in 11 %, T2 in 33%, T3 in 24 %, and T4 in 32 %.

Median age in elderly group was 66 years, Sex repartition: 79% men and 21% women. Comorbidities were observed in 14% cases.

The predominant histological type was undifferentiated nasopharyngeal carcinoma (UCNT) in 87% of cases.

Median total duration was 45 days, with 3% patient who did not complete the prescribed RT course with no differences across age groups.

31% patient received radiotherapy alone and 69% received concomitant radio-chemotherapy to a total dose of 69.96 Gy, combined with weekly Cisplatin at a dose of 40 mg/m2/week.

Patients underwent weekly clinical and tomographic monitoring. The dominant side effect was radiomucositis: 55% G1, 20% G2, 22% of patients presented G3 , and 3% were hospitalized for G4 .

In terms of evolution, locoregional control was found in 75% of patients treated, with 11% of recurrence and 4% metastatic progression. 6% of patients died of their cancer and 4% were lost to follow-up.

Conclusion

Nasopharyngeal Cancer presents a particular evolutionary profile, which partly explains the therapeutic failures despite high radiosensitivity. For the age group studied, this evolutionary profile is compounded by a high delay in consultation and a terrain already weakened by age.

199

Disease characteristics, treatment and two-years overall survival for non-metastatic nasopharyngeal carcinoma: real world data from the national oncology institute, Morocco.

Edith Tatiana D NGBWA[1,2], Imane Hassnaoui[1,2], Houda Fares[1,2], Abdou Sara[1,2], Gueddari Rania[1,2], Taouchikht Mona[1,2], Nouni Karima[1,2], Amine Lachgar[1,2], Hanan Elkacemi[1,2], Tayeb Kebdani[1,2], Khalid Hassouni[1,2]

[1]National oncology institute, Radiotherapy, Rabat, Morocco. [2]Faculty of Medecine and Pharmacy, Radiotherapy, Rabat, Morocco

Topic

HPV or EBV related cancers

Keywords

nasopharyngeal,cancer,morroco

Purpose/Objective

Nasopharyngeal cancer is one of the most common aero-digestive cancers in Morocco. His treatment is essentially based on radiotherapy combined with chemotherapy (1,2).

In addition to investigating disease characteristics and pattern of treatment, the main objective of this study is to evaluate locoregional, distant control and 2 years overall survival in patients with non-metastatic nasopharyngeal carcinoma.

Material/Methods

This is a retrospective study involving 254 patients collected in the National Institute of Oncology (INO) in Morocco. The study period extends from January 1, 2018 to December 31, 2021.

For this study, we included patients suffering from nasopharyngeal cancer based on histological and radiological evidence. We collected data through hospital records and during patient follow-up consultations.

The statistical analysis was carried out using SPSS software version 18.0.

Results

During the four years of the study, we identified a total of 254 patients. The series finds 154 men and 100 women. Sex-ratio was 1,54. The median age was 47,07 years with extremes of 12 and 86 years. Undifferenciated Carcinoma of Nasopharyngeal type (UCNT) was the most represented histological type, i.e 82,22 % of the population. Squamous cell carcinoma was found in 17,78%.

We had 5 stages I patients, 35 stages II patients, 81 stage III patients, 133 stage IVa patients.

In the majority of our patients therapeutic approach was based on concomitant chemoradiation (205 patients); 157 of these patients underwent neoadjuvant chemotherapy. Doxorubicin combined with cisplatin was the most frequently used protocol (35.66%) as neoadjuvant chemotherapy.

All patients received weekly cisplatin during concomitant chemoradiation.

Overall survival at 2 years was 84,56% for stage I and II patients and 62,03% for stage III and IVA patients.

Conclusion

In view of our data and those of the literature, cisplatin-based chemotherapy and head and neck radiotherapy at curative doses, as well as neoadjuvant chemotherapy with concomitant radio-chemotherapy, allowed local control of overall survival at two years. However, certain toxicities can interfere with the successful completion of treatment.Future trials should therefore offer less toxic molecules for therapeutic purposes.

References

(1): Blanchard P,Lee A,Marguet S et al.MAC-NPC Collaborative group. Chemotherapy and Radiotherapy in nasopharyngeal carcinoma:an update of the MAC-NPC méta-analyse. Lancet Oncologies 2015;114(suppl):6-7.

(2): Yoshizaki T, Kondo S, Murono S et al. Progress and controverse for the rôle of chemothérapy in nasopharyngeal carcinoma. Jpn J Clin Oncologies 2015,45(3)244-47.

200

cigarette smoking and risk of nasopharyngeal carcinoma

Mona Taouchikht[1,2], Houda Fares[1,2], Sara Abdou[1,2], Rania El Gueddari[1,2], édith Tatiana Ngbwa[1,2], Imane Hassnaoui[1,2], Karima Nouni[1,2], Amine Lachgar[1,2], Hanan Elkacemi[1,2], Tayeb Kebdani[1,2], Khalid Hassouni[1,2]

[1]National Oncology Institute, Radiotherapy, Rabat, Morocco. [2]Faculty of Medicine and Pharmacy, Medicine, Rabat, Morocco

Topic

Epidemiology and prevention

Keywords

nasopharyngeal carcinoma, cigarette smoking

Purpose/Objective

Nasopharyngeal carcinoma (NPC) is one of the most important cancers in Morocco , with 5-7 cases/ 100,000 persons a year . Its etiology is not well known, but cigarette smoking has been implicated in some epidemiologic studies.

This is a retrospective epidemiological study of the NPC in the North-West of Morocco , to evaluates the impact of the consumption of tobacco on the risk of development of NPC.

Material/Methods

In this retrospective study, we identified 194 patients with nasopharyngeal cancers, treated in the Radiotherapy department at the National Oncology Institute in Rabat between January 1st, 2019 and December 31, 2021 by curative concurrent chemo-radiotherapy.

We compared the number of patients using cigarettes with the number of non-smokers patients.

Results

The study show that this cancer was predominant in men, particularly in the population between 40- and 59-years-old.

The percentage of patients who smoked was 33% (63 patients) compared with 67% of non-smokers patients (131 patients).

Conclusion

Based on the information provided earlier, we can conclude that our findings indicate there is no association between long-term cigarette smoking and the risk of developing Nasopharyngeal carcinoma.

202

Concurrent chemoradiotherapy in the treatment of nasopharyngeal Carcinoma: data from 2018 to 2022

IMANE I HASSNAOUI[1,2], RANIA R EL GUEDDARI[3,2], SARA S ABDOU[4,2], EDITH E TATIANA[1,2], MONA M TAOUCHIKHT[1,5], HOUDA H FARES[6,2], KARIMA K NOUNI[7,5], AMINE A LACHGAR[8,2], HANAN H ELKACEMI[1,2], Tayeb T KEBDANI[1,9], KHALID K HASSOUNI[8,2]

[1]national oncology institute, Radiotherapy, Rabat, Morocco. [2]Faculty of Medicine and Pharmacy, Medicine, RABAT, Morocco. [3]national oncology institute, radiotherapy, Rabat, Morocco. [4]national oncology i, Radiotherapy, Rabat, Morocco. [5]Faculty of Medicine, Medicine, RABAT, Morocco. [6]national oncology institute, Radiotherapy, rabat, Morocco. [7]national oncology institute, Radiotherapy, RABAT, Morocco. [8]national oncology institute, radiotherapy, rabat, Morocco. [9]Faculty of medicine, Medicine, RABAT, Morocco

Topic

RTT

Keywords

chemoradiotherapy, nasopharyngeal, Carcinoma

Purpose/Objective

Nasopharyngeal carcinoma is a malignant tumor that differs from other head and neck, it has a remarkable radiosensitivity and chemosensitivity, making concurrent chemoradiotherapy the standard treatment. Nasopharyngeal carcinoma is endemic in Morocco and North Africa.

The aim of this work is to evaluate the efficacy concomitant chemotherapy and conformational radiotherapy with intensity modulation in the treatment of patients with carcinoma of nasopharyngeal.

Material/Methods

The present retrospective study is an experience of the National Institute of Oncology in the curative treatment of nasopharyngeal carcinoma.

The study carried out 253 patients treated for non-metastatic nasopharyngeal cancer from January 2018 to December 2021.

We include in our study, patients who were histologically and radiology proven nasopharyngeal carcinoma disease and treated with only a concurrent chemoradiotherapy.

Results

In our study, we included 80 patients who were only treated by a concurrent chemoradiotherapy.

The median age of our patients was 53.6 years with extremes between 19 years and 83 years.

33 patients were male and 45 were female.

25% of patients had co-morbidities, including 32 % with hypertension, 25 % with diabetes and two patients with a history of ischemic stroke. In our studies, 51% have been smoking for the last 10 years and the rest have never been smoking.

Thanks to pre-treatment IRM data, we were able to categorize patients according to the TNM classification.

11 patients had a T1 stage, 32 patients had a T2 stage, 20 had a T3 stage and 17 had a T4 stage.

Regarding to lymph nodes 16 patients had N0 stage, 31 had a N1 stage, 29 had a N2 stage and 4 patients had a N3 stage. 35% of the patients had a stage I, 38,75% had a stage II and 20 patients had stage III, respectively.

Patients were irradiated with a Volumetric Modulated Arc Therapy at the dose of 69.96 Gy, -70 Gy, 2.12 Gy-daily/fractions, 5 fractions per week. The average number of radiotherapy sessions was 33,3.

Concurrent Chemotherapy was administered weekly type cisplatin at a dose of 40 mg/m2.

The average dose of treatments was 4,75 sessions.

Both radiotherapy and chemotherapy have their share of toxicities.

Chemotherapy is mainly responsible for digestive toxicity, 70% of the patient reported nausea and emesis. Regarding to hematologic toxicity, 10 patients reported anemia, 20 patients developed a neutropenia and 5 patients developed a leucopenia.

Radiotherapy, on the other hand, 20% of the patient related a trismus, 50 % a hypoacusis and 2 patients presented a total deafness.

A complete tumor response was obtained in 68 patients, assessed by IRM DATA.

Only four patients presented a partial local response, then a progression. Two patients had a local relapse 2 years after the end of treatment and only 6 had a distant metastatic disease after the end of treatment.

Two patients died before starting their treatment, 3 others died one month after the end of the therapeutic protocol.

With a median follow up of 20 months, the overall survival and progression-free survival rates were 91.25% and 86.25 %, respectively.

Conclusion

Radiotherapy with modulated intensity and concurrent chemotherapy are effective, and well tolerated in the treatment of nasopharyngeal cancer.

To improve on current results, efforts are needed to evaluate and develop new therapeutic strategies

more effective and less toxic.

204

impact of tumor volume in radiotherapy for nasopharyngeal cancer treatment

Sara Abdou[1,2], Rania El Gueddari[1,2], Mouna Taouchikht[1,2], Houda Fares[1,2], Imane Hassnaoui[1,2], Edith Tatiana Ngbwa[1,2], Karima Nouni[1,2], Amine Lachgar[1,2], Hanan Elkacemi[1,2], Tayeb Kebdani[1,2], Khalid Hassouni[1,2]

[1]national oncology institute, radiotherapy, RABAT, Morocco. [2]faculty of medicine and pharmacy, medicine, RABAT, Morocco

Topic

RTT

Keywords

volume , radiotherapy, nasopharyngeal

Purpose/Objective

Nasopharyngeal cancer is a challenging malignancy with unique characteristics, and its management often involves a combination of radiotherapy, chemotherapy, and targeted therapies.

This abstract discusses the significant influence of tumor volume assessment on radiotherapy strategies for treating nasopharyngeal cancer.

Material/Methods

Tumor volume measurement has become a critical aspect of nasopharyngeal cancer treatment planning. We conducted a retrospective study of 257 patients treated with the VMAT technique in the external radiotherapy department at the National Institute of Oncology RABAT between January 2018 and December 2021, using various imaging modalities, such as MRI and CT scans, to assess tumor volumes accurately.

Results

We identified 257 patients. Sex repartition: 82% men and 18% women. Comorbidities were observed in 15% cases.

Tumors were classified as T1 in 7 %, T2 in 21 %, T3 in 29 %, and T4 in 43 % 21% based on AJCC stage 8th edition.

The GTV mensuration was mentioned in 32% cases (n=83), median GTV was 77 mm (14mm-140mm)

The predominant histological type was undifferentiated nasopharyngeal carcinoma (UCNT) in 87% of cases.

86% patient received NAC-CCRT, and 14 % patient received CCRT ($p < 0.001$).

Toxicities were reported at 42% of the patients with a higher incidence of radiomucositis Grade 3 and 4 in important GTV size 25%.

At a Median follow-up of 48 months, locoregional control was found in 75% of patients treated, with 11% of recurrence and 4% metastatic progression. 6% of patients died of their cancer and 4% were lost to follow-up

Conclusion

Our analysis reveals a strong correlation between tumor volume and treatment response in nasopharyngeal cancer patients undergoing radiotherapy. Larger tumor volumes often lead to increased treatment resistance, local recurrence, and distant metastasis. Moreover, high tumor volumes are associated with higher rates of treatment-related toxicity.

205

nasopharyngeal cancer in children: understanding, diagnosing and treating

Houda Fares[1,2], Mona Taouchikht[1,2], Sara Abdou[1,2], Rania El Gueddari[1,2], édith Tatiana Ngbwa[1,2], Imane Hassnaoui[1,2], Karima Nouni[1,2], Amine Lachgar[1,2], Hanan Elkacemi[1,2], Tayeb Kebdani[1,2], Khalid Hassouni[1,2]

[1]National Oncology Institute, Radiotherapy, Rabat, Morocco. [2]Faculty of Medicine and Pharmacy, Medicine, Rabat, Morocco

Topic

RTT

Keywords

Nasopharyngeal cancer ,children

Purpose/Objective

Nasopharyngeal cancer presents clinical, therap,eutic and progressive particularities; it is a chemo- and radiosensitive disease, its management is complex due to the lack of specific trials for children. Primary aim was evaluating the role of radiotherapy in the management of nasopharyngeal cancer in children. And describing the epidemiological, clinical assecondary aims.

Material/Methods

A retrospective analysis of patients aged under 15 years, and treated for nasopharyngeal cancer between January 2017 and december 2020 in the radiotherapy department of the National Institute of Oncology in Morocco ; data were collected from medical records.

Results

Twenty patients were collected, the median age was 13 years, the tumors were classified as stage III in 9 cases (45%) and stage IVA in 11 cases (55%). One patient (5%) was metastatic at the time of diagnosis, 13 patients (65%) received induction chemotherapy with TPF (docetaxel, cisplatin, 5FU), 2 (10%) with ECF (epirubicin, cisplatin,5FU). After a median follow-up of 24 months, 4 patients (20%) presented with a metastatic relapse, and one patient (5%) presented with local regional or distant . Overall survival at 2 years was is 90%. In subgroup analysis, a number of courses greater than 4 or greater than 5 and a cumulative dose of cisplatin greater than 380 mg/m2 were associated with better OS. No grade 3-4 late toxicity was observed; the most common late toxicity was grade 1-2 xerostomia in 9 patients (45%), grade 1 skin fibrosis in 15% of patients.

Conclusion

Childhood nasopharyngeal cancers treated with induction chemotherapy followed by concomitant radiotherapy and chemotherapy have a better prognosis than that of older patients, however metastatic relapses remain frequent and determine the prognosis. The number of chemotherapy courses as well as the cumulative dose of cisplatin seem to largely influence the therapeutic results.

206

neo adjuvant chemotherapy followed by concurrent chemoradiotherapy in locally advanced nasopharyngeal carcinoma

Sara Abdou[1,2], Ouail Benzerouale[3,2], Rania El Gueddari[1,2], Mouna Taouchikht[1,2], Houda Fares[1,2], Imane Hassnaoui[1,2], Edith Tatiana Ngbwa[1,2], Karima Nouni[1,2], Amine Lachgar[1,2], Hanan Elkacemi[1,2], Tayeb Kebdani[1,2], Khalid Hassouni[1,2]

[1]national oncology institute, radiotherapy, RABAT, Morocco. [2]faculty of medicine and pharmacy, medicine, RABAT, Morocco. [3]national oncology institute, oncology, RABAT, Morocco

Topic

RTT

Keywords

nasopharyngeal,chemotherapy,radiotherapy

Purpose/Objective

Neoadjuvant chemotherapy followed by concurrent chemoradiotherapy (NAC-CCRT) is an alternative strategy for decreasing tumor size and controlling micrometastases before main treatment. The aim of this study was to investigate

Material/Methods

This retrospective study included consecutive histologically confirmed Locally Advanced Nasopharyngeal cancer patient treated with NAC-CCRT at the Institute of Oncology RABAT Hospital during the January 2018 to December 2021.

CCRT protocols consisted of 3-week cycles of cisplatin 100 mg/m2 with concurrent radiotherapy. NAC consisted of 3-week cycles of cisplatin on day 1 and, 5 fluorouracil on days 1–4, or Doxorubicine on day 1 for a maximum three cycles.

Results

Of the 257 patients that received treatment during the study period,

86% patient received NAC-CCRT, and 14 % patient received CCRT ($p < 0.001$).

Median follow-up was 36 months. Significantly more patients with advanced clinical stage (stage IVA-IVB).

Toxicities were reported at 42% of the patients, with a higher incidence of neutropenia ,anemia, nausea and vomiting ,renal toxicity and radiomucositis Grade 3 and 4.

At a Median follow-up of 48 months, locoregional control was found in 75% of patients treated, with 11 % of recurrence and 4% metastatic progression. 6% of patients died of their cancer and 4% were lost to follow-up

Conclusion

In patients that received neo adjuvant chemotherapy, locoregional relapse should be of concern. High-risk distant metastasis patients (N3 stage) that could achieve survival advantage from NAC-CCRT is an interesting and important topic for further study.

208

Key concerns raised by patients in the post- radiotherapy/chemoradiotherapy head and neck cancer patient group as identified through the use of the electronic Holistic Needs Assessment (HNA) in the nurse-led post-treatment clinic.

Hannah E Millar, Xiaoying Wang, Audrey B Scott

Mount Vernon Cancer Centre, East and North Hertfordshire NHS Trust, Cancer Services, Northwood, United Kingdom

Topic

Supportive care, rehabilitation

Keywords

eHNA, patient concerns, rehabilitation

Purpose/Objective

To identify the key concerns of head and neck cancer patients in post radiotherapy/chemoradiotherapy period in order to ensure adequate support and appropriate onward referral.

Material/Methods

From 2010, Macmillan have developed the eHNA for use with cancer patients, advising that these should be undertaken at diagnosis and at strategic points throughout the patient journey (Macmillan, 2014). The HNA is a means of discussing, gathering and recording information with the patient and/or caregiver. It allows for an assessment that is focused on the patient's entire well-being and enables the development of a care plan that encompasses spiritual, emotional, mental, physical, social and environmental needs (National Cancer Action Team, 2007). This care plan is a document produced as a result of the discussion between the CNS (clinical nurse specialist) and the patient, is agreed jointly, and can be shared with primary care providers. The NHS Long Term Plan envisions personalised care for all patients, with HNAs as a key component in the cancer patient's journey (National Health Service

(NHS), 2019). As a result of this initiative, the eHNA has been implemented within the East and North Hertfordshire NHS Trust, due to its accessibility and ease of use for both patients and staff members.

The Macmillan Electronic Holistic Needs Assessment (eHNA) was utilized for this study. Patients score their concerns from 1 to 10, with 1 being low level of patient perceived concern, and 10 being high level of concern. Patients are able to pick more than one area of concern, and these are each scored individually. The eHNAs were offered to patients at the start of treatment and again at six weeks post-treatment. Over the four month period, 105 eHNAs were offered in total, with 9 patients declining the assessment and 10 assessments expiring before completion. 48 patients of the 105 were in the post-treatment setting, which will be the scope of this study. Data from this period was extracted and reviewed from the Macmillan My Care Plan web platform. Assessments were emailed out to patients to be completed in their own time at home; these were then discussed with the Clinical Nurse Specialists (CNSs) at their next clinic review (usually 2 weeks later). Patients without access to the internet or who were unable to complete these electronically for other reasons were able to complete with the help of the CNS in clinic.

Results

109 concerns were raised by the 48 patients; these are subdivided into 22 different concerns. The three highest scoring concerns were 'Eating, appetite or taste' with 22 patients identifying this with some level of concern, 'Swallowing' with 18 patients identifying concern, and 'Pain' with 11 patients identifying concern. These three concerns were not only most frequently selected by patients, but were also scored as being of high level of concern, with 16 of the 22 (73%) scoring 'Eating, appetite or taste' at a 5/10 or higher; 12 out of 18 (67%) patients scored 'Swallowing' as 5/10 or higher; 'Pain or discomfort' was graded over 5/10 by 8 of the 11 patients (73%). Infrequently selected concerns included 'Hot flushes or sweating', 'Nausea or vomiting', and 'Taking care of others'. Of the 48 patients, 7 selected the 'I have questions about my diagnosis, treatments or effects' (15%). Further concerns and outcomes will be displayed within the poster.

Conclusion

As expected, this study has highlighted eating, swallowing and pain to be of highest level of concern for head and neck cancer patients in the post-treatment setting. Patients are currently supported by a multi-disciplinary team including dieticians and speech and language therapists (SLTs) throughout their treatment and the recovery period. The use of the holistic needs assessment during this period has allowed the patients the opportunity to be open about their concerns, which can sometimes be challenging for patients to raise in a clinic setting. It has also allowed the CNS team the opportunity to assess these needs and to start to think about what changes can make in practice to adequately support patient with their rehabilitation. Further audit of onward referrals will be carried out as a result of the highlighted concerns.

References

Macmillan (2014) Electronic Holistic Needs Assessment and Care Planning (eHNA). https://www.macmillan.org.uk/documents/aboutus/health_professionals/macvoice/sharinggoodpractice-electronicholisticneedsassessmentandcareplanning.pdf (Accessed: 10/10/2023).

National Cancer Action Team (2007) Holistic Common Assessment of Supportive and Palliative Care Needs for Adults with Cancer. NCAT, London.

National Health Service (NHS) (2019) The NHS Long Term Plan. https://www.longtermplan.nhs.uk/online-version/ (Accessed: 10/10/2023).

209

Generating change through collaboration - a clinician-led IGRT framework for head and neck radiotherapy

Katie McNamara[1], Imogen Griffiths[1], John Rodgers[1], Lip Lee[2], James Price[2], Kate Garcez[2], Christopher Hughes[2], David Thomson[2], Philip Whitehurst[3], Clare Triffitt[1]

[1]The Christie NHS Foundation Trust, Radiotherapy, Manchester, United Kingdom. [2]The Christie NHS Foundation Trust, Clinical Oncology, Manchester, United Kingdom. [3]The Christie NHS Foundation Trust, Medical Physics, Manchester, United Kingdom

Topic

RTT

Keywords

IGRT, radiotherapy, framework

Purpose/Objective

Image guided radiotherapy (IGRT) in head and neck cancer treatment can be challenging due to complexities presented by variable target and organ at risk (OAR) position. In the authors department an audit of 178 consecutive patients found primary target baseline shifts occurred in 17% of patients (30/178). When baseline shifts are detected by radiographers (RTTs) initial referral online is to departmental IGRT advanced practitioner radiographers (IGRT APRTT). Decision making by IGRT APRTTs can be subjective, introducing a level of uncertainty during the online IGRT process. It also increases the time taken for treatment to take place.

Departmental protocol is to image first three days and then weekly (eNAL). Audit data demonstrated that 54.3% of all head and neck fractions were imaged, a significant increase upon the expected 24% for an eNAL protocol. This imaging workload provided an impetus to consider daily imaging for head and neck treatment. The clinical head and neck team within the authors department acknowledged this and wanted to provide robust protocols that would aid decision making and establish a clinician approved scope of practice for both RTTs and IGRT APRTTs. The aim of this report is to detail the project pathway and evaluate the effectiveness of the developed framework.

Material/Methods

The intent was to apply principles of project management planning and develop the framework within a systematic framework. The project pathway steps are illustrated in figure 1. A timeframe of 6 months was established for completion. Using the 178 patients included within the audit, relevant CBCT images with primary target baseline shifts were reviewed by an interdisciplinary team. The members consisted of the head and neck consultant group (5 clinicians), head of treatment planning, radiotherapy technical lead, pre-treatment RTT, IGRT APRTT team representative, and two RTTS. Images were discussed and consideration for optimising online and offline interventions was made. Based on consensus judgements thematic trends were categorised. A decision making framework was constructed to cover various scenarios with recommended actions dependent on thresholds. Established actions levels were based on severity:

- Green - proceed to treat
- Amber- proceed to treat with required intervention online/offline
- Red - do not treat

Prior to implementation a dual registration methodology for glottis treatments was validated (described in a supporting abstract), training materials were developed and a pilot timing study was carried out to determine if implementation would lead to improvements in efficiency. 20 glottic, hypopharyngeal and tongue base patients were included in the timing study. Two RTTs involved in the development of the project employed the scope of practice outlined by the framework to online image reviews. In order to capture the complete IGRT process timing began at the start of CBCT acquisition and was recorded when the first treatment VMAT arc was initiated. Although no further changes within the department were made that might have influenced IGRT review the timing study included timing for online image review from other RTTs without use of the framework scope of practice. This allowed comparison for scenarios where escalation to IGRT APRTTs was needed and where no escalation was required.

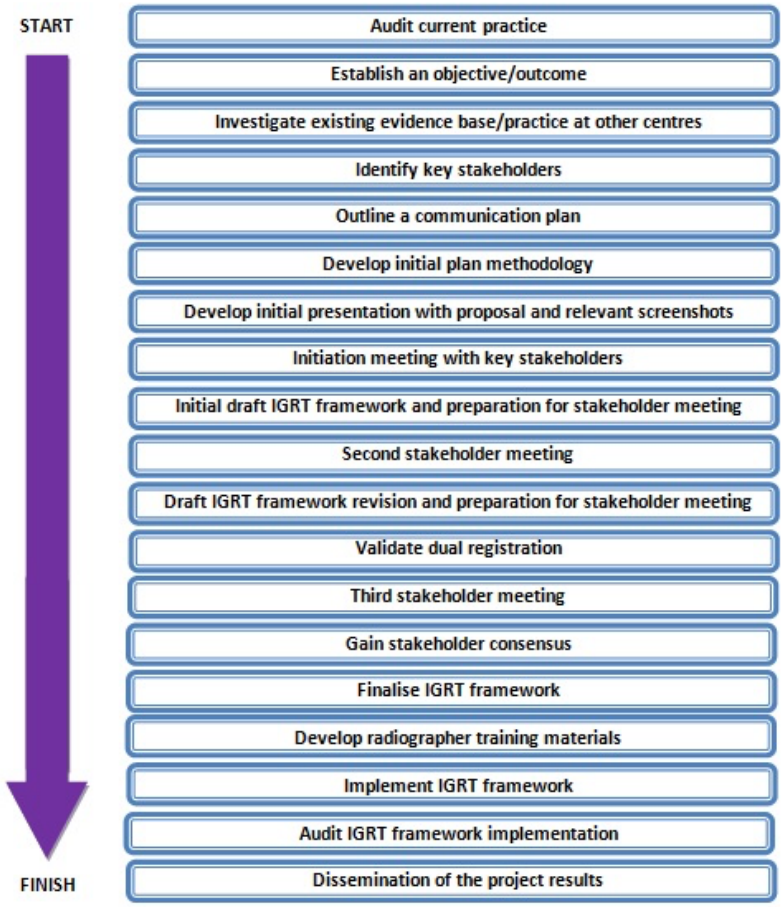


Fig 1. Head and neck clinician-led IGRT framework project pathway

Results

The head and neck IGRT framework (figure 2) project pathway was completed in 146 days and within the projected 6 months (153 days). The process began 18th May 2023 (audit results completed and disseminated/project outcome established) and was finalised 11th October 2023 (dissemination of project results).

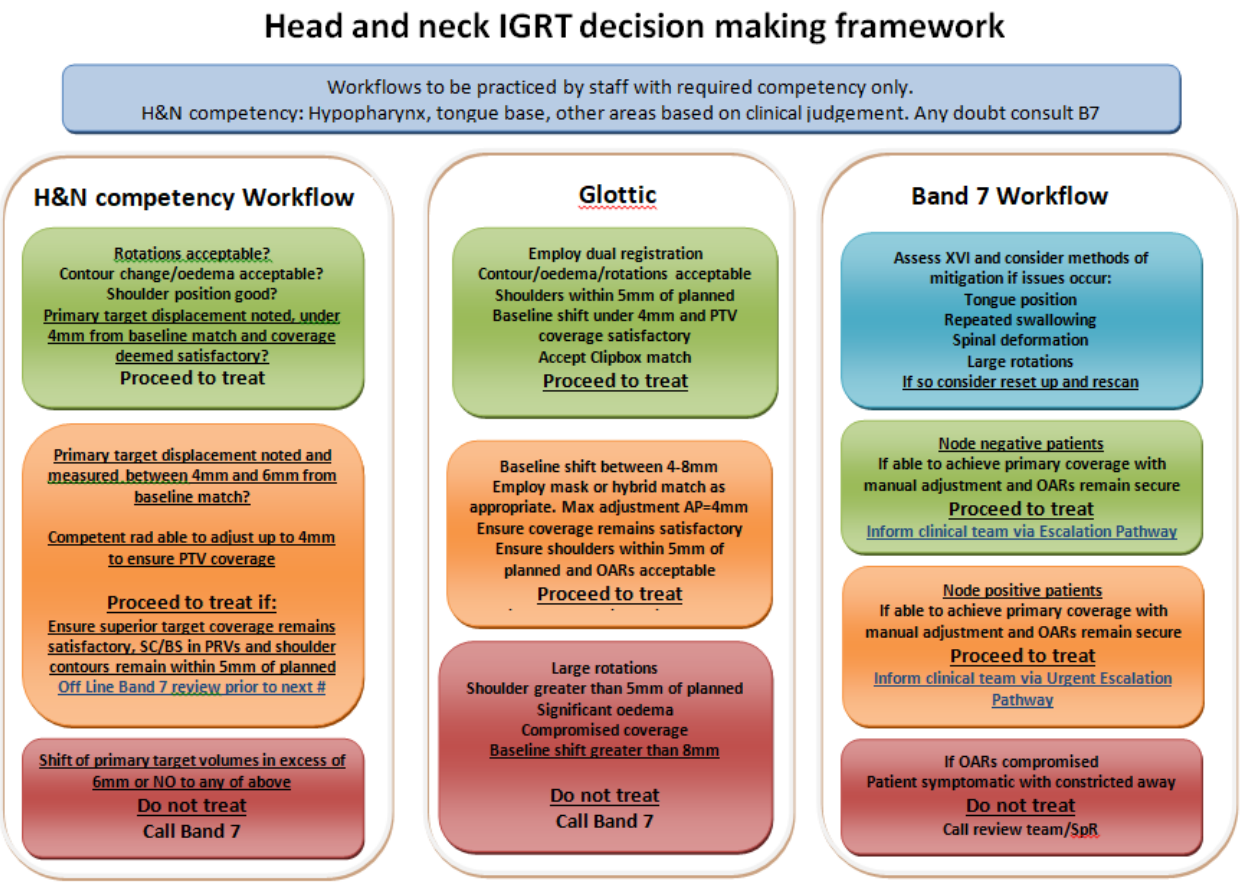


Fig 2. Completed head and neck clinician-led IGRT framework

20 patients and 60 images were included within the pilot timing study. Images that required no escalation resulted in a mean time of 3:08 minutes calculated as from start of CBCT acquisition until the first treatment VMAT arc was initiated. For image reviews which required escalation to an IGRT APRTT the mean time taken was 7:08 minutes. For a subset of twenty images reviewed by RTTs under the decision-making framework, which would have otherwise been escalated to IGRT ARPTTs, the mean image review time was 4:08 minutes. This represents a 42% reduction in image workflow time compared to the department's standard method of escalation to IGRT ARPTTs.

Conclusion

Employing a collaborative interdisciplinary approach using project management principles in the development of an IGRT decision making framework for head and neck radiotherapy lead to a successful and efficient outcome. It encouraged the establishment of a consensus approach and has allowed scope and opportunity to develop creative solutions in managing primary target displacement, such as the use of dual registration. Furthermore it has augmented and expanded the RTT IGRT scope of practice, helped standardise actions and reduce uncertainty, and improved on-treatment efficiency in preparation for adoption of daily imaging.

211

Plasma EBV estimation in Nasopharyngeal carcinoma from a nonendemic region: Impact of probe assay type, EBV copy numbers as a predictive and prognostic marker.

Sarbani Ghosh Laskar[1], Shwetabh Sinha[1], Anuj Kumar[1], Samarpita Mohanty[1], Kumar Prabhash[2], Anuradha Chougule[2], Omshree Shetty[3], Aarushi Singla[1], Naziba Karim Khondekar[4], Monali Swain[1], Ashwini Budrukkar[1]

[1]Tata Memorial Hospital, Radiation Oncology, Mumbai, India. [2]Tata Memorial Hospital, Medical Oncology, Mumbai, India. [3]Tata Memorial Hospital, Molecular Pathology, Mumbai, India. [4]Apollo Hospita, Radiation Oncology, Kolkata, India

Topic

HPV or EBV related cancers

Keywords

Nasopharyngeal cancer, EBV estimation

Purpose/Objective

Nasopharyngeal carcinomas (NPC) are non-endemic in most parts of India except in the northeastern region. We aimed to evaluate the use of estimation of plasma EBV (Epstein Bar Virus) DNA copy numbers on epidemiology and its impact on survival in NPC at a tertiary cancer center in India.

Material/Methods

In this ambispective study, we included treatment naïve biopsy-proven NPC treated at our institute between December 2013 and March 2023. Estimation of plasma EBV DNA was done at baseline, and at first follow-up, 3 months post-treatment completion. Plasma EBV analysis was done using the EBNA probe (n= 240) till September 2019 and the BAMH1 (n= 76) probe thereafter. The endpoints estimated were baseline EBV positivity rates, response rates based on EBV positivity/ EBV copy numbers, and correlation of EBV positivity/ EBV copy numbers with clinicoradiologic stage, FDG-PETCT parameters, and survival endpoints: Loco-regional Control (LRC), Distant Control (DC), Event Free Survival (EFS) and Overall Survival (OS). The study was approved by the Institutional Ethics Committee.

Results

Three hundred and sixteen patients were accrued in the study. The median age of patients was 43 (IQR: 28-54) years, and the majority were males (n=222, 70.3%). Sixty-two (19.6%) patients were from Endemic (Northeast India) regions out of which only 24 (36.1%) were plasma EBV positive. The most common histology was non-keratinizing or undifferentiated (WHO Types IIA & B) {n=248, (78.5%)}. T1/T2 and T3/T4 were equally distributed among the entire cohort (n=158, 50%) and N2/N3 (n=234, 74.1%) was the most common nodal classification. Metastatic disease (M1) was present in 25 (7.9%) patients. Most of the patients had stage III (n=105, 33.2%) or stage IV (n=169, 53.5%) disease. One hundred and seventeen (37%) patients were EBV-positive at baseline {n=82, (34.1%) with EBNA and n=35, (46.1%) with BAM H1}. Tissue diagnosis by IHC was available for 91 out of these patients. Out of these, there was a discordance in EBV status between EBV status by DNA copy number and tissue diagnosis in 36 (39.6%). The median copy numbers in those with detectable EBV (EBV positive) with EBNA was 712 copies/ml (IQR:332-1989), and BAM H1 was 425 copies/ ml (IQR:162-1210). A high baseline EBV DNA copy number with BAMH1 (but not EBNA) was associated with a higher T stage (p=0.02). At the first

follow-up, 283 (89.5%) patients had a complete response, and 33 (10.5%) patients had residual disease. Higher baseline EBV DNA copy numbers with BAMH1 (but not EBNA) correlated with an inferior complete response rate at the first follow-up (p=0.05).

The median follow-up was 63.2 (IQR:33.5–87.4) months. At the last follow-up, 90 patients had failed, 27 (30%) locoregional (LR), 45 (50%) distant, and 18 (20%) combined locoregional and distant relapses. The 5-year LRC, DC, EFS, and OS for the entire cohort were 83.2% (95%CI:78.4-88), 77.5% (95% CI:72.3-82.7), 68.2% (95%CI: 62.6-73.8), 74.5 (95% CI:68.9-80.1).

There was no significant difference in LRC, DC, EFS, and OS rates based on the overall EBV positivity vs negativity at baseline. None of the survival outcomes correlated with EBV positivity or EBV DNA copy number using the EBNA probe.

The median follow-up of patients with BAMH1 probe analysis was 21 (IQR:13.1-33.5) months. There was no difference in survival outcomes based on EBV positivity vs negativity with the BAMH1 probe. However, in the patients with detectable EBV DNA with BAMH1, a higher DNA copy number/ml was associated with an inferior EFS (p=0.05). A cut-off value of 335 copies/ml (BAMH1) was most sensitive for predicting an inferior EFS.

Conclusion

EBV positivity remained low in this nonendemic NPC population with both EBNA and BAMH1 probes, even amongst patients from the northeast. Hence, EBV DNA estimation cannot be routinely used as a screening, predictive, or prognostic marker uniformly for NPC patients in India. However, in those patients who have measurable EBV DNA copies, we found that the BAMH1 probe assay at baseline has a better predictive and prognostic value than the EBNA probe. The BAM H1 DNA copy number values may be incorporated as a baseline evaluation tool into routine clinical practice for further validation as a treatment decision aid in NPC in nonendemic regions. However, we would also like to further strengthen this estimation in a larger number of patients.

212

It takes two... validating a novel use of dual registration for Glottic radiotherapy treatment

Imogen Griffiths, Katie McNamara, John Rodgers, Clare Triffitt

The Christie NHS Foundation Trust, Radiotherapy, Manchester, United Kingdom

Topic

RTT

Keywords

IGRT, dual registration, laryngeal

Purpose/Objective

Contemporary external beam photon head and neck radiotherapy is characterised by highly conformal delivery techniques that allow high doses to complex target areas. This demands commensurate

accuracy and precision due to reduced expansion margins, steep dose gradients and proximity to critical organs OARs.

IGRT is essential to ensure optimal radiotherapy delivery and requires robust, reliable registration of both target volumes and OARs. Automated rigid registration algorithms provide rapid alignment however one of the most challenging scenarios in IGRT is the potential for primary target volume displacement.

A recent audit in the authors department involving 172 patients found that 17% of those experienced primary target baseline shifts, mainly in the longitudinal plan, at some time during their treatment. The majority were systematic and the most common site was glottic cancer.

Our department wanted to evaluate the accuracy of image registration using the XVI system (Elekta, Stockholm, Sweden) dual registration tool (DRT) for use in glottic radiotherapy. DRT allows an assessment of baseline registration (usually to proximal bony anatomy) and a soft tissue region of interest (mask) sequentially and quantifies differences between them. Dual registration has previously been investigated for prostate [1], inferior neck nodes [3] and chest wall [2] .

We wanted to validate DRTs accuracy and reliability prior to its integration within a departmental IGRT head and neck guidance framework. This framework contains stipulated action levels based on thresholds that would be augmented by DRTs ability to quantify the magnitude of primary tumour baseline shifts. The first objective was to establish the accuracy of DRTs soft tissue mask registration algorithm to primary glottis tumour targets; the second was to assess inter-observer consistency of agreement between RTTs.

Material/Methods

This retrospective study used 36 randomly selected XVI images from 18 glottic patients. To establish the accuracy of DRT mask soft tissue registration algorithm with glottis primary lesions it was compared to a gold standard registration (GSR). This registration was defined by a departmental IGRT specialist RTT with 18 years' experience of online head and neck image review. Proposed couch shifts for both matches were recorded in the right/left (RL), superior/inferior (SI) and anterior/posterior (AP) directions.

To assess inter-observer reliability of DRT between RTTs, three RTTs with varying levels of experience in image registration were asked to performed a dual registration on all images and select the most appropriate match (baseline, mask or hybrid) using the head and neck IGRT framework as guidance. Proposed couch shifts were recorded in the RL, SI and AP directions.

Bland-Altman 95% Limits of Agreement (LoA) were used to assess agreement between the DRT and GSR matchings. To analyse agreement between RTT's a modified Bland-Altman process described by Jones et al [4] was utilised.

A clinical threshold of 3 mm was predetermined for both statistical methods. This threshold was deemed appropriate as our department has an action level of 3 mm for these patients.

Dual registration baseline registration was defined through a cuboidal region of interest around the cervical spine adjacent to PTVs. The mask region of interest was defined as the planned GTV structure with a margin of 0.5cm.

Results

For the comparison between the soft tissue mask-GSR a total of 72image registrations were performed (36 per method). The 95% LoA in the left/right, superior/inferior and anterior/posterior directions were

−1.40 to +1.66 mm, −2.07 to +2.54 mm, and −2.17 to +2.67 mm, respectively. One mask CBCT match (2.8%) was beyond the 3-mm threshold in the anterior/posterior direction.

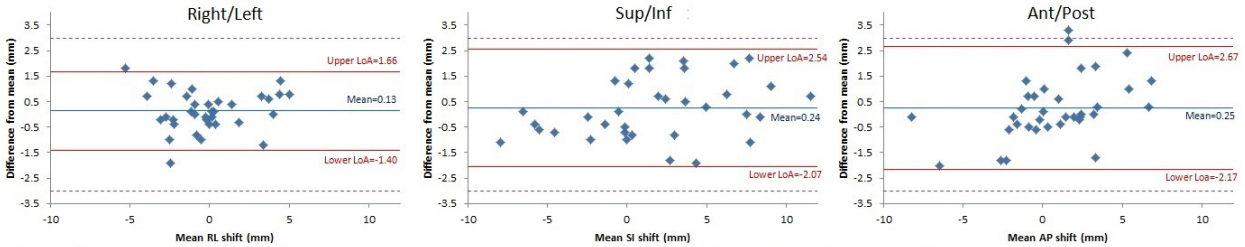


Fig 1. Bland-Altman plots showing the difference in registration between mask match versus gold standard registration in all three translational planes. Red lines show Limits of Agreement. Purple dashed lines illustrate the threshold of clinical acceptability (3mm)

108 image registrations were performed for the assuming of inter-observer reliability of DRT between RTTs (36 image registration per RTT). The 95% LoA between RTTs in the left/right, superior/inferior and anterior/posterior directions were −1.21 to +1.30 mm, −2.39 to +2.90 mm and −1.46 to +1.81 mm, respectively. Three RTT CBCT matches (2.8%) were outside the 3-mm threshold. All matches beyond 3mm were in the superior/inferior direction.

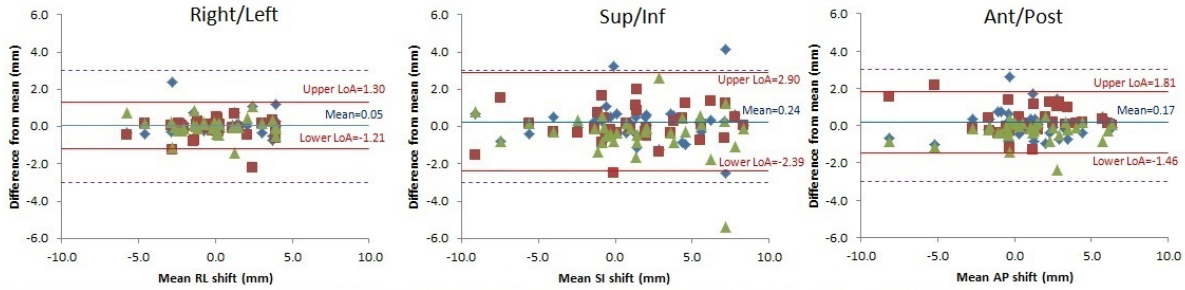


Fig 2. Modified Bland-Altman plots showing the difference in registration for each observer compared to the mean of all observers in all three translational plans. Red lines show Limits of Agreement. Purple dashed lines illustrate the threshold of clinical acceptability (3mm)

Conclusion

This is the first work to investigate a novel use of XVI DRT during image registration for glottis head and neck radiotherapy. The findings of this study demonstrate that DRTs mask functionality provides accurate registrations to primary target volumes and are considered clinically acceptable when compared with an expert GSR for this cohort of patients. The use of DRT was also considered reliable when used by RTTs operating under the guidance of a clinician-led IGRT framework. The introduction of DRT allows accurate quantification of primary target baseline shifts, identifying cases for rapid escalation to clinicians whilst extending and standardising RTT IGRT scope of practice.

References

1. Campbell A, Owen R, Brown E, Pryor D, Bernard A, Lehman M. Evaluating the accuracy of the XVI dual registration tool compared with manual soft tissue matching to localise tumour volumes for post-prostatectomy patients receiving radiotherapy. J Med Imaging Radiat Oncol. 2015;59:527–34

2. Goldsworthy S, Leslie-Dakers M, Higgins S, Barnes T, Jankowska P, Dogramadzi S, et al. A pilot study evaluating the effectiveness of dual-registration image-guided radiotherapy in patients with oropharyngeal cancer. J Med Imaging Radiat Sci. 2017;48:377–84

3. Mohandass P, Khanna D, Kumar TM, Thiyagaraj T, Saravanan C, Bhalla NK, Puri A. Study to Compare the Effect of Different Registration Methods on Patient Setup Uncertainties in Cone-beam Computed

Tomography during Volumetric Modulated Arc Therapy for Breast Cancer Patients. J Med Phys. 2018 Oct-Dec;43(4):207-213

4. Jones M, Dobson A, O'Brien S. A graphical method for assessing agreement with the mean between multiple observers using continuous measures. Int J Epidemiol 2011; 40: 1308–13

213

Radiotherapy fraction delivery time does not affect survival outcomes in patients with oropharynx cancer, unselected for chronotype

James M Price[1,2], Matthew Beasley[3], Kate Garcez[1], Christopher Hughes[1], Zsuzsanna Iyizoba-Ebozue[4], LipWai Lee[1], Hitesh Mistry[2], Robin Prestwich[4], Gareth Price[2], Catharine West[2], David Thomson[1,2]

[1]The Christie NHS Foundation Trust, Clinical Oncology, Manchester, United Kingdom. [2]The University of Manchester, Division of Clinical Sciences, Manchester, United Kingdom. [3]Leeds Cancer Centre, Radiotherapy Physics, Leeds, United Kingdom. [4]Leeds Cancer Centre, Clinical Oncology, Leeds, United Kingdom

Topic

Quality of life and outcomes

Keywords

Oropharynx, circadian, radiotherapy

Purpose/Objective

The rhythmic expression of clock genes generates circadian rhythms that affect cell cycle progression[1]. As different stages of the cell cycle correlate with sensitivity to radiation, it has been postulated that the time of day that radiotherapy is delivered can influence treatment outcomes[2]. Prior studies, including randomised trials, suggest that earlier vs later radiotherapy times are associated with superior outcomes, but these are limited by dichotomisation of treatment times, small patient numbers and cohort heterogeneity[3,4].

In this study, we aimed to assess the relationship between radiotherapy time and outcomes for a large, contemporary cohort of oropharynx squamous cell carcinoma (OPSCC) treated at a tertiary cancer centre.

Material/Methods

Design: a retrospective review of prospectively-collected data. Eligibility criteria: all newly-diagnosed cases of non-metastatic OPSCC treated with curative-intent (chemo)radiotherapy at The Christie Hospital between 2012 and 2019. Patient-, cancer- and treated-related information was extracted, including the time of day that each radiotherapy fraction was delivered. The average radiotherapy fraction delivery time per patient was calculated and considered as a continuous variable.

Relationships between average fraction delivery time and other variables were assessed. The primary endpoint of interest was overall survival (OS). Progression-free survival (PFS) was a secondary endpoint. Kaplan-Meier plots were created to show estimated OS according to average fraction delivery time quartile. A multivariable Cox Proportional Hazards (PH) model was fitted, adjusting for relevant patient- and cancer-factors, along with average fraction delivery time, the need for hospital transport (% of

fractions), distance of patients' address from the treating centre and the Index of Multiple Deprivation (IMD) decile as a marker of socio-economic deprivation.

Results

32742 fractions of radiotherapy were delivered for 1119 patients. Patient characteristics are shown in the Table.

Characteristic	**N = 1,129[1]**
Age (years)	59 (52 - 66)
Gender	
Female	249 (22%)
Male	870 (78%)
ECOG performance status	
0	651 (59%)
1	334 (30%)
2	104 (9.4%)
3	23 (2.1%)
ACE-27 co-morbidity index	
0	492 (44%)
1	351 (31%)
2	197 (18%)
3	75 (6.7%)
Weight (kg)	76 (65 - 89)
Body mass index (kg/m^2)	26.0 (22.7 - 29.2)
Smoking history	
Current	465 (42%)
Ex	306 (28%)
Never	331 (30%)
Distance from radiotherapy centre (km)	22 (13 - 34)
Surgery (yes)	264 (24%)
Tumour stage (TNMv7)	
T1	201 (18%)
T2	448 (40%)
T3	210 (19%)
T4a	221 (20%)
T4b	39 (3.5%)
Nodal stage (TNMv7)	
N0	189 (17%)
N1	167 (15%)
N2a	97 (8.7%)
N2b	429 (38%)
N2c	198 (18%)
N3	39 (3.5%)
Tumour p16 status	
Negative	234 (25%)

Positive	713 (75%)
Not known	172 (15%)
Induction chemotherapy (yes)	169 (15%)
Concurrent chemotherapy (yes)	507 (45%)
Radiotherapy fractionation schedule	
4 weeks	75 (6.7%)
6 weeks	1044 (93%)

Average fraction delivery time did not correlate with patient age or the distance the patient lives from the radiotherapy centre. On average, married patients were treated earlier in the day than single / separated patients (average fraction delivery time 12:30 *vs* 13:22). Other patients with an earlier average fraction delivery time were those with superior ECOG performance status (ECOG PS 0-1 *vs* 2-3, 12:53 *vs* 13:43), less co-morbidity (ACE-27 score 0-1 *vs* 2-3, 13:02 *vs* 13:23) or p16-positive disease (p16-positive vs negative, 12:56 *vs* 13:46).

The Figure shows estimated OS according to mean fraction delivery time quartile (quartile 1 = earliest, quartile 4 = latest); mean fraction delivery time quartiles seem to stratify for OS.

On Cox PH regression, when adjusted for relevant patient- (e.g., age, ECOG PS, ACE-27 score, smoking status, IMD decile), cancer- (tumour p16 status, tumour stage, nodal stage) and treatment- factors (radiotherapy fractionation, use of cisplatin chemotherapy) mean fraction delivery time was not prognostic for OS (HR 0.97; 95% CI 0.91 - 1.04; p=0.4) or PFS (HR 1.00; 95% CI 0.93 - 1.07; p>0.9).

Conclusion

When assessing mean fraction delivery time as a continuous variable and adjusting for relevant factors, mean fraction delivery time is not prognostic for patients with OPSCC treated with radical (chemo)radiotherapy. Observations of improved outcomes for patients treated earlier in the day (prior to adjusting for covariates) can be explained by such patients typically being fitter, having less co-morbidity and being more likely to have p16-positive disease.

There is no evidence that circadian rhythm affects survival outcomes in patients with OPSCC, unselected for chronotype.

References

1. Farshadi, E., Van Der Horst, G. T. J. & Chaves, I. Molecular Links between the Circadian Clock and the Cell Cycle. Journal of Molecular Biology 432, 3515–3524 (2020).

2. Harper, E. & Talbot, C. J. Is it Time to Change Radiotherapy: The Dawning of Chronoradiotherapy? Clinical Oncology 31, 326–335 (2019).

3. Jiang, D. et al. Does Time of Daily Treatment Matter in Radiation Therapy for Head and Neck Cancer? International Journal of Radiation Oncology*Biology*Physics 93, E348 (2015).

4. Elicin, O. et al. The prognostic impact of daytime and seasonality of radiotherapy on head and neck cancer. Radiotherapy and Oncology 158, 293–299 (2021).

214

Assessment of patient's quality of life after total laryngectomy vs. concomitant chemoradiotherapy for laryngeal preservation

Rachida Laraichi[1,2], Amine Lachgar[1,2], Chadia Ezzouitina[1,2], Imane Hassnaoui[1,2], karima Nouni[1,2], Hanan Elkacemi[1,2], Tayeb Kebdani[1,2], Khalid Hassouni[1,2]

[1]National Institute of Oncology, radiotherapy, Rabat, Morocco. [2]Mohamed V University, Faculty of Medicine and Pharmacy, Rabat, Morocco

Topic

Quality of life and outcomes

Keywords

larynx, quality of life

Purpose/Objective

The treatment of head and neck cancers, especially that of the larynx, causes late effects and can affect negatively the patient's quality of life.

For locally advanced laryngeal cancer, clinical response outcomes such as locoregional control and survival were similar in patients treated with concomittent chemoradiotherapy and those treated with total laryngectomy (TL).

The aim of this work was to compare the quality of life of patients treated by concomitant radio-chemotherapy with those treated by total laryngectomy (TL) followed by adjuvant radiotherapy.

Material/Methods

Thirty-six patients treated for locally advanced laryngeal cancer (stage III or IV) were included in this study. These patients were treated with concomitant chemoradiotherapy or TL with adjuvant radiotherapy. Patients had to be without evidence of recurrence and have completed treatment at least 3 months before study inclusion.

The European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Core Questionnaire (QLQ-C30) and Head and Neck (H&N35) questionnaires were used for the assessment of quality of life.

An interrogation took place during the post-therapeutic monitoring consultation during the period from January 1, 2023 to August 1, 2023.

Results

On the baseline questionnaire (QLQ-C30), there was a difference in the overall quality of life score between the 2 groups, with a higher score in the group treated with concomitant chemoradiotherapy meaning a better quality of life in this group.

Analysis of functional subscales revealed a tendency for patients in the surgery followed by radiotherapy group to experience greater difficulty in social functioning compared to the chemoradiotherapy group.

On the QLQ-H&N35, surgical patients reported significantly greater difficulties with sensory disturbances (smell and taste), analgesic use, and cough. On the other hand, patients treated with chemoradiotherapy reported significantly more problems with dry mouth and ageusia.

Conclusion

We found better overall quality of life scores in patients undergoing concomitant chemoradiotherapy for laryngeal preservation compared to patients treated with LT and postoperative radiotherapy for advanced laryngeal cancer. This appears to be primarily caused by better physical health, functioning, and social contact scores and fewer problems with pain, speech, senses, and sleep disturbances in this group.

216

Head and neck re-irradiation: retrospective single institution study of 60 patients treated with curative intention.

Raquel Granado Carrasco[1], Enar Recalde Vizcay[1], Sergi Benavente Norza[1], Savannah Pie Padro[2], Marcelino Hermina Lopez[2], Blanca Peregrin[1], Juan Sebastian Parada[1], Juan David Assaf Pastrana[3], Irene Braña Garcia[3], Jordi Giralt Lopez de Sagredo[1]

[1]Hospital Vall d'Hebron, Radiation Oncology, Barcelona, Spain. [2]Hospital Vall d'Hebron, Physics, Barcelona, Spain. [3]Hospital Vall d'Hebron, Medical Oncology, Barcelona, Spain

Topic

Innovative treatments

Keywords

Re-irradiation, head and neck cancer

Purpose/Objective

Radiotherapy (RT) plays a fundamental role in the definitive treatment of carcinoma of the head and neck cancer, but loco regional relapse happens up to 40% of the patients despite optimal initial multidisciplinary treatment, as well as second neoplasmstumors. Management of these scenarios is challenging, as re-treating an already irradiated field has a narrow balance between disease control benefit and toxicity risk. We aimed to provide data of outcomes in terms of disease control, survival and toxicity of re-irradiated patients, to facilitate selection and stratification of those who could benefit more.

Material/Methods

Retrospective analysis of patients with loco-regional relapse or second primary head and neck carcinomastumor who were re-irradiated between 2009 and-2023 in a previously irradiated field (≥50

Gy) using 3D or IMRT/VMAT, and conventional fractionation. Data about event-free survival (EFS), overall survival (OS), acute and chronic toxicity according to CTCAEv54 wereas collected from clinical reports.

Results

Sixty patients were re-irradiated. Most of them (78%) were male and 98% were ECOG 1-0. Mean age at diagnosis was 60 years (median 59y, range 51-67y). First diagnosis tumor histology was SCC in 94% of the patients, and was alsowas the most frequent histology (98%) for the second primary alsotumor. Most common site for both, first and second tumortumor was oral cavity (49% and 38%, respectively). Time between two RT treatments was at least 2 years in 63% of the patients, with no patients treated with less than 6 month6-month period (mean time to second RT 40.4 months, median 30.5 months, range range 19.5-54.5 months).

Most of the patient retreated underwent adjuvant RT (n=32, 58%), reaching a mean dose of 59.95Gy (70.00-48.40) in addition to concomitant chemotherapy (67%).

Re-irradiation was more mostly used in an adjuvant context (55%). Systemic concomitant treatment was 65%, with preference for triweekly regimens (34%). After second treatment, 58% of the patients had complete response, 40% had a partial response or stable disease, and only one patient progressedhad progression. Mean total dose for re-irradiation was 60 Gy (median 60 Gy, range 54-70 Gy). Only 22 of the re-irradiation treatment volumes included cervical areas. IMRT/VMAT was the preferred treatment technique (76%). All treatments were normo-fractionated treatments.

Mean follow up is was 2.7 years from the end of RT. All patients had at least a 6-months follow up. Acute toxicity after re- irradiation was very common (95%), occurring in 70% of the patients presented mucositis and 67% epithelitis. Long- term toxicity consisted of dysphagia (45 patients74), osteonecrosis (6 patients), fistula (5 patients), trismus (5 patients G3-4). Carotid rupture happened in one patient.

Mean time to progression was 20.4 months. Kaplan Kaplan-Meier analysis for event- free survival (EFS) shows better outcomes in patients who received re-irradiation at least 2 years after the first irradiation, with a median time to event of 9.59 6 months (95%CI 4.14-9.92m) compared with 4.94 months in patients who had earlier re-irradiation (95%CI 6.14-22.11m), with no statistically significant differences (Figure 1). No statistically significant differences in time to event according to total dose of re-irradiation were seen, as well as between patients with adjuvant or radical intention.

Median overall survival (OS) was 18.2 months (95%CI 14.061-40.1m) (Figure 2). At 51 months, 15 patients are still alive. OS is better in patients receiving RT more than 2 years after the first treatment (22.67 months vs 18.23 months), with differences maintained over the follow up. Patients who were treated with more than 50 Gy seem to have better median OS (19.7m vs 13.37m4m) without statistically significant differences.

Kaplan Meier

Time between RT1 and RT2

Factor	n	median IC95%	HR IC95%	p.value
< 2 years between RT1 and 2	22	4.94m [4.14 ; 9.92]	Ref. [Ref. ; Ref.]	-
> 2 years between RT1 and 2	38	9.59m [6.14 ; 22.11]	0.64 [0.36 ; 1.14]	0.13

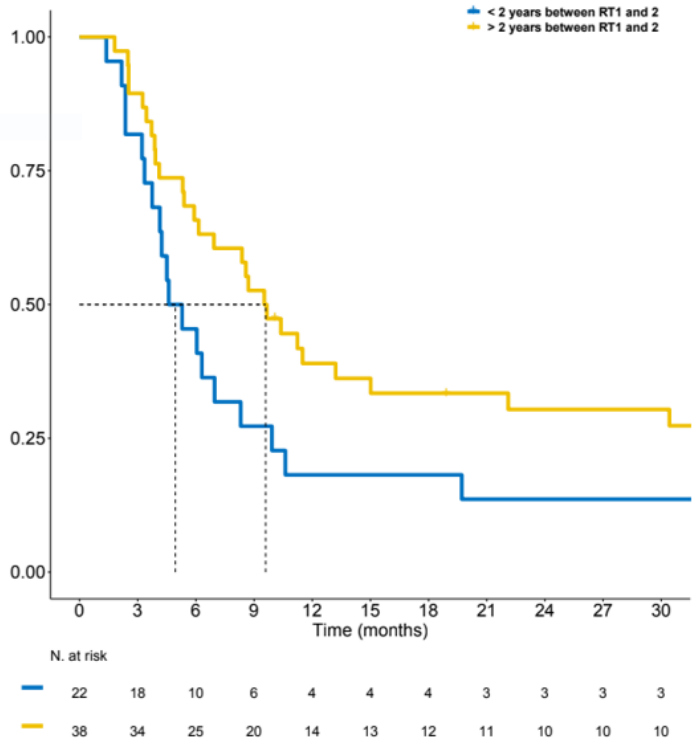


Figure. 1. Kaplan Meier curve for Event Free Survival. Patients treated 2 years or later after the first irradiation (blue) vs Patients treated earlier (yellow).

Kaplan Meier

Global

n	median IC95%	6 months	12 months	24 months	36 months
60	18.23m [14.06 ; 40.11]	86.7%m [78.5% ; 95.7%]	65.7%m [54.6% ; 79.2%]	42.4%m [31.3% ; 57.5%]	38.7%m [27.8% ; 53.8%]

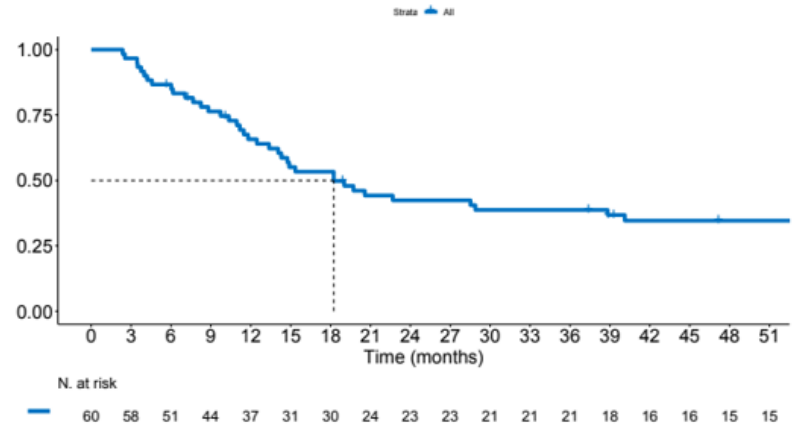


Figure. 2. Kaplan Meier curve for Overall Survival (all patients n=60).

Conclusion

Our analysis shows that patients with head and neck cancer with good performance status who undergo a re-irradiation treatment with curative intent present prolonged survival and disease control after the treatment, which seems benefited when second irradiation happens later than 2 years after the first course of RT, for both adjuvant and radical RT strategies.

References

1. Andratschke et al. European Society for Radiotherapy and Oncology and European Organisation for Research and Treatment of Cancer consensus on re-irradiation: definition, reporting, and clinical decision making. Lancet Oncol 2022; 23: e469–78.

2. Ward et al. Refining Patient Selection for Reirradiation of Head and Neck Squamous Carcinoma in the IMRT Era: A Multi-institution Cohort Study by the MIRI Collaborative. Int J Radiation Oncol Biol Phys 2018; 100 (3): 586-594.

3. Ward et al. Retreatment of Recurrent or Second Primary Head and Neck Cancer After Prior Radiation: Executive Summary of the American Radium Society (ARS) Appropriate Use Criteria (AUC). Int J Radiat Oncol Biol Phys 2022; 15, 113 (4): 759-786.

217

Quality of life after radiation therapy for laryngeal cancer in the North of Morrocco

Sami M Amraoui, Nabila Sellal, Amine Tantaoui, Mohamed El Hfid

University Hospital Mohamed 6, Radiotherapy, Tangier, Morocco

Topic

Quality of life and outcomes

Keywords

laryngeal cancer - radiotherapy - quality of life

Purpose/Objective

To evaluate the quality of life in patients treated for locally advanced laryngeal cancer with surgery, radiation therapy or both

Material/Methods

A retrospective study conducted at the radiation therapy department of Mohamed 6 University Hospital of Tangier. This study included patients treated for non-metastatic laryngeal cancer between April 2017 and April 2023, who received radiation therapy during their course of treatment. Treatment modalities included either surgery followed by radiotherapy or laryngeal preservation (LP) strategy by concomitant chemoradiotherapy (CRT) or induction chemotherapy (IC) followed by CRT. Clinical data, treatment and follow-up results were gathered using the digitalized hospital network. All patients answered the EORTC QLQ H&N 35 questionnaire for quality of life in its approved Arabic version.

Results

40 patients were included in the study. Mean age was 62 +/- 12 years old. 50% of the patients had a stage IVA disease and 30% had a stage III cancer. Radiation therapy was administered in adjuvant setting for 75% of the patients. Amongst patients treated with surgery + radiotherapy, 50% had a stage IV disease.

Regarding dysphonia, 80% of patients considered they had a poor quality of voice. 45% of the patients found difficulties communicating with others. 66.7% of them described these difficulties as severe. In the LP group, 3 patients reported severe difficulties and they were all treated for a stage IVA disease: the choice of treatment modality was due to patients' refusal of surgery for 2 of them. Voice restoration surgery was performed for 3 patients.

Pain issues were reported by 3 patients and nearly half of patients (45%) had dysphagia: 13 of them had surgery and 5 were treated following a LP strategy. A feeling of an abnormal rate of mucus secretion was found in 11.5% of the patients. Regarding sensory disorders (taste and odor), there was 1 case of dysgueusia reported: the patient was treated with IC + CRT.

Sexual life was worsened in 12.5% of patients (4 men and a woman), all of whom had a definitive tracheostomy. Issues reported were dyserection, lack of libido and a poorer quality of physical relations.

Conclusion

Quality of life is an important factor to consider in the choice of treatment setting, which has to be done according to the stage and international guidelines. Our study found that quality of voice is the main altered function after treatment according to patients, even when they have recovered their voice. Same results were found in the literature. Despite the mutilating treatment and the toxicity of irradiation, and as shown in the study, a decent quality of life can still be obtained for our patients, thus avoiding a poorer outcome of the cancer. Research in laryngeal cancer these days tends towards the improvement of quality of life without compromising survival results.

References

Guibed M. and al. "Quality of Life in patients treated for advanced hypopharyngeal ot laryngeal cancer." *Eur Ann Otorhinolaryngology, Head Neck Dis. 2011, 128, 218-223*

Sadoughi B. and al. "Quality of life after conservative surgery for laryngeal cancer." *Otolaryngology Clin North Am. 2015 Aug; 48, 665-65*

Babin E. and al. "Sex-related quality of life after total laryngectomy for cancer." *Eur Ann Otorhinolaryngology, Head Neck Dis. 2023 May; 140: 121-126*

218

The experience of ENT cancer : how does it impact the social life of the spouse ?

Rachida Laraichi[1,2], Amine Lachgar[1,2], Fatima zahra Chraa[1,2], Sara Smiti[1,2], Karima Nouni[1,2], Hanan El kacemi[1,2], Tayeb Kebdani[1,2], Khalid Hassouni[1,2]

[1]national oncology institute, radiotherapy, Rabat, Morocco. [2]Mohamed V university, faculty of medecine and pharmacy, Rabat, Morocco

Topic

Quality of life and outcomes

Keywords

sociability, spouse, ENT cancer

Purpose/Objective

Sociability is defined as the set of experiences connecting the individual to other people. It brings together the analysis of five different environments: the friendly environment, the solitary environment, the known environment, the unknown environment, and the necessary environment

The aim of this study is to assess the impact of ENT cancer and its treatment on the sociability of spouses.

Material/Methods

The collection was carried out via an original questionnaire sent to the patient's spouses. The main outcome criterion used was the spouse's self-assessment of the influence or otherwise of the illness on their daily life.

We included the spouses of patients treated for squamous cell carcinoma of the larynx, hypopharynx, the oropharynx, and the oral cavity between 1er january 2022 and 30 septembre 2023. A informed consent of patients and their spouses has been collected.The spouses of the selected patients were asked to answer the questionnaire assessing their social relationships .

Results

Sixty spouses responded to the questionnaire with a clear predominance of female spouses (51F/9M). Their daily activities were influenced by the disease in 85% of cases.

The friendly environment was considered to have deteriorated in % 51,7%. The number of solitary activities increased in 66,7% of cases. The unfamiliar environment was judged altered in 70% of cases. Social activities linked to the known external environment decreased among 63,3% of spouses. The necessary environment including relationships within the couple was judged to be altered in 48,3% of spouses.

Conclusion

The quality of life of spouses of patients with head and neck cancer is known to be deteriorated. Our study explored more specifically the sociability of spouses showing a real deterioration in all its areas, which underlines the importance of psychologically supporting spouses.

220

Head and Neck Re-Irradiation: Toxicity Analysis and Correlation between Toxicity and Dosimetric Parametres

Raquel Granado Carrasco[1], Enar Recalde Vizcay[1], Sergi Benavente Norza[1], Marcelino Hermida Lopez[2], Savannah Pie Padro[2], Blanca Peregrin[1], Juan Sebastian Parada[1], Juan David Assaf Pastrana[3], Irene Braña Garcia[3], Jordi Giralt Lopez de Sagredo[1]

[1]Hospital Vall d'Hebron, Radiation Oncology, Barcelona, Spain. [2]Hospital Vall d'Hebron, Physics, Barcelona, Spain. [3]Hospital Vall d'Hebron, Medical Oncology, Barcelona, Spain

Topic

Innovative treatments

Keywords

Re-irradiation, toxicity, dose sum

Purpose/Objective

As radiotherapy (RT) is fundamental for definitive treatment of head and neck carcinomas and novel modulated techniques permit more selected patients to be re-irradiated, we aimed to collect data about chronic and acute toxicity after second irradiation and evaluate correlation with dosimetric parameters, for future specification of organ at risk constraints.

Material/Methods

Retrospective analysis of 60 patients treated at our institution for loco-regional relapse or second primary head and neck tumor, re-irradiated between 2009 and 2023 to a previously irradiated location (>50Gy) using 3D or IMRT with a total dose of 60Gy (mean 60Gy, range 54-70Gy) at 2-2.1Gy/Fx. Data about acute and chronic toxicity was collected from clinical reports, according to CTCAEv5.

We were able to evaluate dosimetric data about 59 patients. For data extraction, rigid registration was made with TPS Eclipse. Sum plan of both treatments was created (dose distribution were not converted to EQD2 because of TPS limitations) on the most recent CT scan. Dosimetric data were extracted using homemade script from API Eclipse. Planning and calculation system: Eclipse (v10-v15.6). Calculation algorithm: AAA for IMRT plans, Acuros XB for VMAT plans.

Results

Acute toxicity after re-irradiation was very common (95%). 70% presented mucositis (28 out of 32 were G1-2) and 67% epithelitis (35 out of 40 were G1-2). Chronic toxicity after second RT consisted of dysphagia (74,5% of the patients, with 23 patients requiring use of nasogastric tube (NGT) or Percutaneous Endoscopic Gastrostomy (PEG), of which 16 were attributed to RT toxicity and not to prior treatment sequelae), osteonecrosis (6 patients), fistula (5 patients), trismus (24% G1-2, 3.3% G3-4). Carotid rupture happened in one patient.

Of 6 patients presenting osteonecrosis, 3 were grade 3, with no patients with grade 4 toxicity. Looking at the plan sum, these all three patients had received a total D0.035 > 100Gy to the mandible bone, and received a higher mean dose (113.7Gy vs 100.8Gy) to the mandible compared with patients who presented milder or no toxicity (Figure 1).

For dysphagia, we analysed mean dose to pharynx constrictor muscles. We can see that those needing PEG/NGT (G3 toxicity) receive a higher mean dose (61Gy vs 53Gy) than those who don't need it. Of the 16 patients who required these interventions due to RT toxicity (not because of surgery sequelae or similar), the received dose is still higher (60.4Gy) than the mean dose received in patients without PEG or NGT (Figure 2).

Univariate model showed that those who required NGT or PEG after re-irradiation because of RT toxicity present higher risk of events, with HR of 3.05 (1.57-5.92, p<0.001). No statistically significant differences were seen for treatment technique (IMRT vs 3D) or other variables, also for the multivariable analysis.

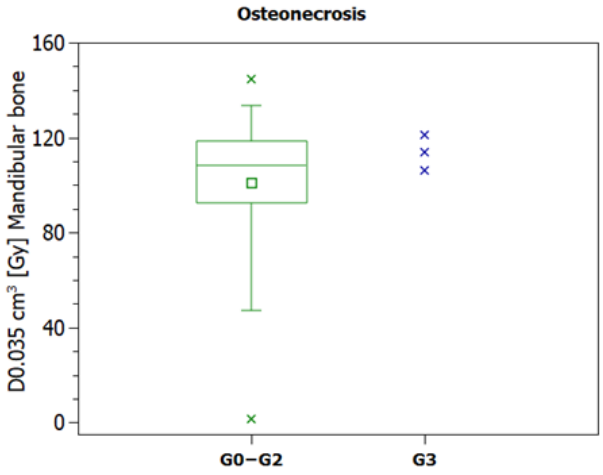


Figure 1. Osteonecrosis according to toxicity grade (G0,1,2 vs G3). D0.035cm3 summation (First RT treatment and re-RT) in Gy to the mandibular bone.

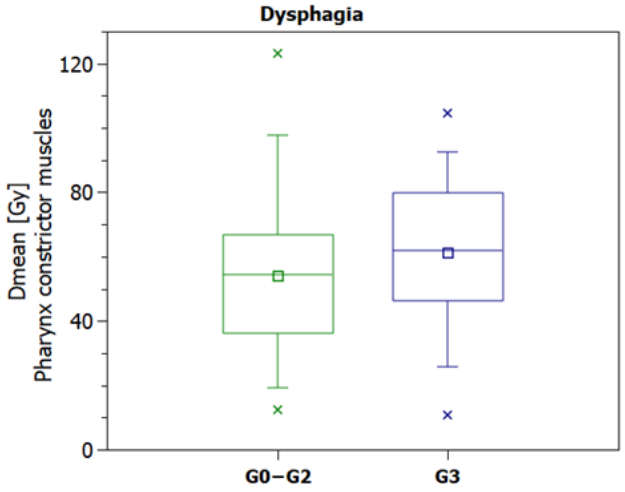


Figure 2. Dysphagia according to toxicity grade (G0,1,2 vs G3). Dmean summation (First RT treatment and re-RT) in Gy to the pharynx constrictor muscles.

Conclusion

Toxicity after re-irradiation in head and neck càncer patients is not negligible. Despite acute effects are the most frequent ones, regarding long term toxicity, dysphagia is the most frequent and the one with more impact in the quality of life of the patient, but this, as well as the other toxicities are rare to have a severe presentation (G3 or more). Our data seems to show a correlation between dose to the mandible bone and G3 osteonecrosis, but interpretation must be cautious, as the limitations of this analysis include the rigid dose registration instead of deformable, no EQD2 dose summation and the

relevance of anatomic variations due to surgeries and tumor growth. Further investigations regarding these issues could help to improve the management of re-irradiation dosimetry evaluation.

References

1. Andratschke et al. European Society for Radiotherapy and Oncology and European Organisation for Research and Treatment of Cancer consensus on re-irradiation: definition, reporting, and clinical decision making. Lancet Oncol 2022; 23: e469–78.

2. Vargo JA, Moiseenko V, Grimm J, et al. Head and Neck Tumor Control Probability: Radiation Dose-Volume Effects in Stereotactic Body Radiation Therapy for Locally Recurrent Previously-Irradiated Head and Neck Cancer: Report of the AAPM Working Group. Int J Radiat Oncol Biol Phys. 2021;110(1):137-146. doi:10.1016/j.ijrobp.2018.01.044

3. Ward et al. Retreatment of Recurrent or Second Primary Head and Neck Cancer After Prior Radiation: Executive Summary of the American Radium Society (ARS) Appropriate Use Criteria (AUC). Int J Radiat Oncol Biol Phys 2022; 15, 113 (4): 759-786.

221

Sexual quality of life two years after Head and neck cancer diagnosis.

Loriguet Lea[1,2], Almont Thierry[3], Iacob Mariana[1], Fouilloux Antoine[1], Gorzo Alecsandra[1], Goada Dragos[1], Even Caroline[1], Huyghe Eric[4]

[1]gustave roussy, head and neck, villejuif, France. [2]Centre intercommunal hospitalier, oncologie, Creteil, France. [3]CHU martinique, epidemiologie, martinique, France. [4]CHU Toulouse, urologie, toulouse, France

Topic

Quality of life and outcomes

Keywords

Sexuality, Head and neck cancer,

Purpose/Objective

Head and neck cancers and their treatments can impact a patient's sexuality and body image. However, healthcare providers often fail to distribute information regarding this particular and sensitive issue.

The aim of this retrospective study was to evaluate the sexual quality of life in patients 2 years after a diagnostic of a head and neck cancer, to determine clinical factors associated with sexual or body image disorders, and moreover, to identify the information received from the healthcare providers.

Material/Methods

This retrospective and transversal study selected the patients with head and neck cancers among the 4349 patients from the « ViCAN 2 » study, performed in France. The analysis started 2 years after the initial diagnosis.

The patients were interrogated about marital status, libido, frequency and satisfaction of sexual act, and medical information received on the subject. The interrogation was conducted by phone call or by filling a questionnaire.

Results

284 patients were included, with a median age of 55 years, and a predilection of male population (230 males, 54 females). More than 1/3 of patients were 60 years old.

Regarding the marital status, 75% of patients were in couple before diagnosis, with no significant change 2 years after diagnosis.

Half of the patients had decreased libido (M : 49%, W : 48%).Also, sexual satisfaction, frequency of sexual act and tenderness decreased. Among all, 45% of males and 40.7% of females were satisfied with their sexual activity.

It was noted a tendency for depression in the female population, without statistical significance (14.5% vs 8.2%).

Less than 10% of patients received information about this subject. Among the 10%, the majority received the information at their own request. Only 1% of patients were informed at the initiative of healthcare providers

Conclusion

There are few data on sexuality in head and neck cancer patients. However, they are just as affected as other cancer patients and need detailed information on these specific issues. Therefore, the information about the impact of cancer on sexuality should come from healthcare professionals. The latter should be better trained in this field to improve the quality of the medical act and ensure a holistic perspective.

References

Low a, M. Fullarton b, E. Parkinson b, K. O'Brien c, S.R. Jackson a, D. Lowe d, S.N.Rogers Issues of intimacy and sexual dysfunction following major head and neck cancer.TreatmentOral Oncology 45 (2009).

Bethany A. Rhoten, PhD, RN, Amanda J. Davis, MSN, Breanna N. Baraff, MSN, KellyH. Holler, BS, Mary S. Dietrich, PhD. Priorities and Preferences of Patients With Head and Neck Cancer for Discussing and Receiving Information About Sexuality and Perception of Self-Report Measures. J Sex Med. August 2020.

Bethany Andrews Rhoten and al.Head and Neck Cancer and Sexuality: A Review of theLiterature. Cancer Nurs Jul-Aug 2016;39

222

Consistency and Prognostic Value of NI-RADS Scoring in Early Post-operative C.E. CT for Oral Cavity Cancer: Implication for Clinical Practice

Mariangela Massaccesi[1], Silvia Longo[1], Marco Panfili[2], Rosalinda Calandrelli[2], Stefano Settimi[3], Dario Mele[3], Francesco Pastore[1], Francesco Miccichè[4], Carlo Lajolo[5], Alessandro Moro[6], Giovanni Almadori[3], Jacopo galli[3], Luca Tagliaferri[1], Maria Antonietta Gambacorta[1]

[1]Fondazione Policlinico Universitario A. Gemelli IRCCS, Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia, Roma, Italy. [2]Fondazione Policlinico Universitario A. Gemelli IRCCS, UOC Radiologia e Neuroradiologia, Dipartimento Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia, Roma, Italy. [3]Fondazione Policlinico Universitario A. Gemelli IRCCS, UOC Otorinolaringoiatria, Dipartimento di Scienze dell'Invecchiamento, Neurologiche, Ortopediche e della Testa-Collo, Roma, Italy. [4]Gemelli Isola, Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia, Roma, Italy. [5]Fondazione Policlinico Universitario A. Gemelli IRCCS, UOC Odontoiatria Generale e Ortodonzia, Dipartimento di Scienze dell'Invecchiamento, Neurologiche, Ortopediche e della Testa-Collo, Roma, Italy. [6]Fondazione Policlinico Universitario A. Gemelli IRCCS, Chirurgia Maxillo-Facciale,, Roma, Italy

Topic

Imaging, radiomics and artificial intelligence

Keywords

NI-RADS, Oral cavity cancer, prognostic value

Purpose/Objective

The Neck Imaging Reporting and Data System (NI-RADS) is a valuable tool for post-operative imaging evaluation in head and neck cancer patients. Yet, its specific utility in oral cavity cancer, especially in early post-operative contrast-enhanced computed tomography (C.E. CT), remains underexplored, despite potential therapeutic implications. This retrospective study aims to assess frequency of observations at both Primary and Regional levels, evaluate inter-reviewer concordance, and explore whether NI-RADS scores in early post-operative C.E. CT scans correlate with patient survival outcomes.

Material/Methods

This study involved a cohort of consecutive patients who had undergone surgical treatment for oral cavity squamous cell carcinoma (OSCC). Early post-operative contrast-enhanced computed tomography (CE-CT) scans, conducted within less than 90 days from surgery, were included for analysis. Two experienced radiologists (RC and MP) independently reviewed the CE-CT scans and assigned NI-RADS scores to different findings. NI-RADS scores ranged from 1 (indicating no suspicion of recurrence) to 3 (indicating a high suspicion of recurrence). The Kaplan-Meier survival analysis was employed to evaluate the correlation between NI-RADS scores and patient overall survival.

Results

In this study, 42 CE-CT scans were reviewed. One patient couldn't be evaluated for the primary tumor due to metal artifacts. NI-RADS scores at the primary site were: RC - 25 cases (NI-RADS 1), 9 cases (NI-RADS 2a), 5 cases (NI-RADS 2b), and 2 cases (NI-RADS 3); MP - 24 cases (NI-RADS 1), 7 cases (NI-RADS 2a), 5 cases (NI-RADS 2b), and 2 cases (NI-RADS 3).At the regional level: RC - 37 cases (NI-RADS 1), 2 cases (NI-RADS 2), 3 cases (NI-RADS 3); MP - 38 cases (NI-RADS 1), 1 case (NI-RADS 2), 3 cases (NI-RADS 3). The Cohen's kappa statistic indicated substantial inter-reviewer agreement for the primary tumor (kappa = 0.91, 95%CI 0.79-1.00) and regional lymph nodes (kappa = 0.92, 95%CI 0.77-1.00), confirming reliable NI-RADS score assignment.

Patients with a NI-RADS score of 3 at the primary tumor level had a shorter median OS of 7 months compared to those with NI-RADS scores of 1, 2a, and 2b, who had a median OS of 68 months. This difference was statistically significant with a p-value of 0.006.

Conclusion

The study demonstrates that NI-RADS scores in early post-operative contrast-enhanced computed tomography (CE-CT) scans can provide valuable insights into patient outcomes. Further research and validation of NI-RADS in OSCC management are warranted to solidify its clinical relevance. Additionally, exploring the utility of NI-RADS in larger patient populations can provide more robust evidence for its integration into clinical practice.

224

MuciLight trial: phase 2 of LED photobiomodulation for treatment of mucositis in oral cavity or oropharyngeal cancer.

Xavier Liem[1], Sophie Maiezza[1], Jennifer Wallet[2], Séverine Lals[1], Marriane Darrou[1], Marie Vanseymortier[2], Véronique Belot-Cheval[1], Arnaud Felin[1], Marie-Cécile Le Deley[2], Xavier Mirabel[1]

[1]Oscar Lambret Center, Radiotherapy and Brachytherapy, Lille, France. [2]Oscar Lambret Center, Biostatistique, Lille, France

Topic

Supportive care, rehabilitation

Keywords

mucositis, radiotherapy, photobiomodulation

Purpose/Objective

monocentric prospective phase 2 trial to evaluate the photobiomodulation with LED (PLED) lamp for curative treatment of mucositis in a high risk population without nutritionnal support: oral cavity or orophayngeal cancer treated by radiotherapy (RT) or radiochemotherapy in a postoperative or exclusive situation. PLED is a easy and fast technic to realize photobiomodulation with nurse or paramedical staff, with the whole oral cavity treated at once, and the exposable part of the oropharynx.

Material/Methods

Inclusion criteria were as follow: oral cavity or oropharyngeal cancer treated by radiation therapy or radiochemotherapy with at least one criteria of risk of grade 3 mucositis (G3M) : concomittant chemotherapy, activ tabagism, denutrition or diabetes ; grade 1 ou 2 mucositis (G1M G2M) ; age above 18 years old. PLED has to begin during week 2 or 3 during RT, and PLED scheme constited of a daily session of 13 min of 630 nm with 75 J/cm3 of PLED with Medisol® lamp. Clinical evaluation (pain, nutrition, PS) were performed daily with a nurse, and every week with the radio-oncologist until the end of RT and one month after the end of RT. Primary objective was the non occurrence of G3M, scored by CTCAE v5 during the beginning of PLED and the end of RT. The non occurrence of G3M was defined as a success of the PLED. Secondary objectives were pain evaluation, type of pain killers prescribed, quality of life (QoL), safety of PLED, weight variation and indication of enteral nutrition. 50 % of G3M was considered as the null hypothesis, and, with a proportion of success anticipated at 75 %, 26 patients were needed.

Results

26 patients were included from mars 2021 to august 2022. Median age was 63, 85 % were active smokers and 15 % have already opiods prescription at the inclusion. 56 % received surgery before the radiation, 50 % of the patients had chemotherapy and all of the patients were prescribed more than 60 Gy. PLED was initated at 23 Gy in median, 85 % of patients had grade 1 mucositis (G1M) of the inclusion. 19 PLED session were realized (median) per patient, 2 patients stopped the PLED. 57 % had at least one temporary interruption of one session. At the end of the RT, 7 patients had G3M (27%), 11 G2M (42%), 6 G1M (23%) et 2 G0M (8%). Non occurend of G3M was 73 % (IC : 52 – 88 %, p = 0.019) at the end of RT and 72.2 % (IC 95 % 50.2 – 85.7% p <0.05). One patient had nasogastric tube one months after the end of RT. We observed a median weight variation of – 4 kg at the end of RT, which is below the threshold of denutrition definition. PS and Qol with QLQC30 and HN35 were statistically lower compared to baseline, in relation with the RT. 38 % of the patients had a new prescription of opoids. All patients experienced dry mouth, and 39 % had tingling sensation. No patient had G2 or more adverse effect of PLED.

Conclusion

With a 73 % of success (non occurrence of G3M) in a population of patients with high risk of severe oral mucositis without nutritional support, Mucilight trial reached his primary objective. Weight variation was below the 5 % variation theshold of denutrtion defined by the French health authorities. PLED is a safe and efficient technic of curative treatment of mucositis, and it's easily feasible by nurse or paramedical staff.

225

Skin toxicity predictive factors in cervical radiotherapy treatement

Alia Mousli[1,2], Lina KCHAOU[1], Emna Boudhina[1], Alia Methnani[3,2], Emir Kouti[1], Ben Zid Khadija[1,2], Semia Zarraa[1,2], Safia Yahiaoui[1,2], Abidi Rim[1,2], Chiraz Nasr[1,2]

[1]Salah Azaiez Institut, Radiation Oncology, Tunis, Tunisia. [2]University of Tunis El Manar, Faculty of Medecine, Tunis, Tunisia. [3]Salah Azaiez Institut, Otorhinolaryngology, Tunis, Tunisia

Topic

Quality of life and outcomes

Keywords

Skin toxicity, Cervical radiotherapy

Purpose/Objective

Head and neck cancer requires a comprehensive multimodal approach involving surgery, chemotherapy, and radiotherapy. As effective as these treatment modalities may be, they are not without drawbacks. In particular, during radiotherapy, skin toxicities are frequently encountered, ranging from mild erythema to severe ulceration, necrosis or hemorrhage. The aims of this study were to assess cumulative skin doses and to identify potential factors that may contribute to skin reactions.

Material/Methods

We selected 20 patients treated for head and neck cancer in the Radiotherapy Oncology Department at Salah Azaiez Institute, in Tunisia. Patient data was collected from medical records and dosimetric data from our server (Eclipse). All patients were treated with conformational radiotherapy (RT) and were clinically monitored weekly. Acute radiation dermatitis was recorded based on the Common Terminology Criteria for Adverse Events (CTCAE v5.0) criteria. A 5 mm skin contour was delineated on the treatment plan for each patient.

Results

There were 15 males and 5 females (sex ratio=3). Median age was 58 years old (25 to 79). Seven patients had a smoking habit, while 4 have a past history of immunodepression (Diabetes, autoimmune hepatitis). Tumor localizations were in the nasopharynx (n=11), in the larynx (n=4) in the oral cavity (n=3), in the nasal fossa (n=1) and in the thyroid (n=1). First line treatment was chemotherapy (3 cycles of TPF: docetaxel; cisplatin; fluorouracil) in 63% of nasopharyngeal cancer patients. Only 20% patients (n=4) underwent previous surgery for the primary tumor with neck dissection. Fifty percent of patients recieved concomitant chemotherapy. Volumetric Arctherapy (VMAT) technique was Performed in 17 cases (85%). On average, radiodermatitis grade 1 (G1) or 2 (G2) appeared after a period of respectively 30 and 37 days, after the first day of RT treatment. Median dose when noticing G1-dermatitis was 34 Gy, correlated with median cumulative mean (Dmean) and maximal (Dmax) doses in the skin, respectively of 17,19 Gy and 32,32 Gy. G2-dermatitis was observed in 6 patients, median dose when noticing G2-dermatitis of 42 Gy, at Dmean of 42 Gy. Median cumulative Dmean and Dmax in the skin were respectively, 23,3 Gy and 43,13 Gy for G2 radiodermatitis. Among the G2-subgroup, median age was 59 years old, there were 3 smokers, 2 cases of immunodepression medical history, 3 underwent previous surgery with neck dissection, 3 had nasopharyngeal cancer with locally advanced tumor. No cases of G3-toxicity were reported in our population study.

Conclusion

The neck skin should be identified as a sensitive structure for dose optimisation. Skin-sparing techniques should be considered in cervical irradiations for head and neck cancer.

226

Clinical and dosimetric predictors of primary hypothyroidism in nasopharyngeal carcinoma patients following intensity-modulated radiotherapy

Alia Mousli[1,2], Amir Kouti[1], Alia Methnani[3,2], Lina Kchaou[1], Emna Boudhina[1], Samia Zarraa[1,2], Khadija Ben Zid[1,2], Safia Yahiaoui[1,2], Rim Abidi[1,2], Chiraz Nasr[1,2]

[1]Salah Azaiez Institute, Radiation Oncology, Tunis, Tunisia. [2]University of Tunis El Manar, Faculty of medecine, Tunis, Tunisia. [3]Salah Azaiez Institute, Otorhinolaryngology, Tunis, Tunisia

Topic

Quality of life and outcomes

Keywords

Hypothyroidism , nasopharyngeal cancer , toxicity

Purpose/Objective

Advances in the treatment of nasopharyngeal carcinoma (NPC) have led to improved clinical outcomes in terms of tumor control and toxicities mainly through the widespread use of intensity-modulated radiotherapy (IMRT). However, hypothyroidism (HT) remains a frequent late complication observed in half of patients who have undergone cervical irradiation. The aim of our study was to identify clinical and dosimetric factors predictive of primary HT in patients irradiated for NPC with IMRT at the Salah Azaiez Institute in Tunisia.

Material/Methods

Data were collected retrospectively from hospitalization registers and medical records. We included a total of 50 patients treated for NPC with curative intent by IMRT between January 2017 and January 2019. Patients with thyroid dysfunction prior to treatment were excluded from the study. The mean dose (Dmean), the percentage of thyroid volume exposed to specific dose levels denoted V30-V50, and the absolute volume of thyroid tissue spared from particular dose levels, denoted VS45-VS60 were studied.

Results

The median follow-up was 60 months. Primary hypothyroidism had cumulative incidence rates of 45.2% and 58.1% at 3- and 5-year intervals, respectively, highlighting the progressive nature of thyroid dysfunction over time. Among the factors examined, young age, female sex, and reduced thyroid volume (less than 16 cc) emerged as the most influential predictors of susceptibility to primary hypothyroidism in univariate analysis. In the dosimetric study specific thresholds have been established. Patients were classified into high-risk and low-risk groups based on these thresholds, improving our ability to identify individuals at greater risk for primary hypothyroidism. The threshold values defined were 45 Gy for average dose. The volume receiving 40 Gy in more than 80 % of the total thyroid volume appear as a significant risk factor of HT in the univariate analalysis. In term of sparing volume, the 5 cm3 and 10 cm3 were identified factors for the VS 45Gy an VS 60Gy respectively.

Conclusion

Given the prevalence of primary hypothyroidism in our study, we recommend the use of IMRT treatment optimisation targets aimed at limiting Dmean < 45 Gy, V40 < 80%, VS45 ≥ 5 cm3 or VS60 ≥ 10 cm3 for the thyroid gland.

227

Early outcomes for a single-arm, single-stage phase I/II trial of Selective Avoidance of nodalVolumEs at minimal Risk (SAVER) in the contralateral neck of patients with p16-positiveoropharynx cancer

Matthew E Witek[1], Jason K Molitoris[1], Ranee Mehra[2], Rodney J Taylor[3], William Regine[1], Kyle M Hatten[3]

[1]University of Maryland, Radiation Oncology, Baltimore, USA. [2]University of Maryland, Medical Oncology, Baltimore, USA. [3]University of Maryland, Otolaryngology - Head and Neck Surgery, Baltimore, USA

Topic

Innovative treatments

Keywords

HPV, de-intensification, elective nodal volumes

Purpose/Objective

Most patients with p16-positive oropharynx cancer (p16+OPC) receive elective nodal radiation therapy that improves regional control but increases acute and long-term toxicity. We evaluated the efficacy and toxicity profile of a reduced contralateral elective nodal volume in patients with p16+OPC receiving definitive or adjuvant radiation therapy.

Material/Methods

Patients with newly diagnosed p16+OPC without contralateral nodal involvement treated with primary proton or photon-based (chemo)radiation therapy or adjuvant (chemo)radiation therapy following transoral robotic surgery (TORS) were eligible for enrollment. The reduced contralateral nodal volume included high-risk regions of levels II and III[1]. The primary endpoint was elective out-of-field contralateral nodal failure. Dosimetric studies comparing standard versus reduced elective nodal volumes were analyzed with the t-test. Acute toxicity was collected using CTCAE v4.0.

Results

Fifty-two patients were enrolled of which 36 (69.2%) received definitive (chemo)radiation therapy. Sixteen (30.8%) patients underwent adjuvant radiation therapy following TORS of which 5 (31.2%) received concurrent chemotherapy. Proton therapy was used in 38 (73.1%) of patients. There were no elective nodal failures at a median follow up of 15 months (range 1-24 months). For the first 20 patients enrolled, dosimetric comparison of the reduced contralateral elective nodal volume to a consensus elective nodal volume demonstrated a decrease in mean dose (14.1 Gy to 18.5 Gy [$p<0.05$]) and V30 Gy (11.6% to 21.3% [$p<0.01$]) of the contralateral parotid gland. Significant differences were independent of radiation modality or technology. Acute grade 3 toxicity was observed in 13 (25%) patients including 6 (11.5%) who received a gastrostomy tube during treatment. There were no grade 4-5 acute toxicities, and no patients with 6 months of follow up retained gastrostomy tube.

Conclusion

Precise delivery of radiation therapy to high-risk areas for contralateral nodal disease results in excellent regional control regardless of treatment approach. Dose to contralateral organs at risk and toxicity profile were favorable. Longer follow-up is needed to further support this de-intensification strategy.

References

1. Defining High-Risk Elective Contralateral Neck Radiation Volumes for Oropharynx Cancer. *Matthew E. Witek, MD, Neil M. Woody, Hima B. Musunuru, Patrick M. Hill, Poonam Yadav, Adam R. Burr, Huaising C. Ko, MD, Richard B. Ross, MD, Randall J. Kimple, MD, PhD, Paul M. Harari, MD. Head Neck, 2021, November 11. DOI: 10.1002/hed.26924. PMID: 34761832, PMCID: PMC9723806.

228

Adjuvant radiation therapy for anaplastic thyroid cancer: single center experience of 12 patients with advanced and not completely resected disease: toxicity and treatment complications

Nikita Kataev[1], Natalia Timofeeva[2], Alexei Mikhaylov[1], Vorobyov Nikolay[3], Berezina Natalia[4], Michael Cherkashin[5], Kirill Suprun[5]

[1]MIBS - Dr. Berezin Medical Institute, Radiation oncology, Saint Petersburg, Russian Federation. [2]Saint Petersburg state university clinic, Endocrine surgery, Saint Petersburg, Russian Federation. [3]MIBS - Dr. Berezin Medical Institute, Proton therapy, Saint Petersburg, Russian Federation. [4]MIBS - Dr. Berezin Medical Institute, Administrative, Saint Petersburg, Russian Federation. [5]MIBS - Dr. Berezin Medical Institute, Surgery, Saint Petersburg, Russian Federation

Topic

Salivary gland, skull base, skin and thyroid cancers

Keywords

Radiation therapy, anaplastic, thyroid cancer

Purpose/Objective

To evaluate acute toxicity and treatment complications in patients receiving adjuvant radiation therapy for advanced anaplastic thyroid cancer in cohort of patients who have not underwent complete R0 surgery. Find correlations between incompletment of radiation therapy, doses to organs at risk and completeness of surgical treatment.

Material/Methods

We retroactively analysed plans, medical records, CT and MR scans of patients before and after surgical treatment. In our analysis were included total 12 patients between 2021 and 2023. Median age of patients was 72 (+/-7,1).

4/12(33,3%) were male, other 8/12 (66,6%) were female.

3(25,0%) patients had R1 resection and 9(75,0%) had R2 resection.

3(25,0%) had not completely respected nodes. 5(41,7%) had part of primary tumor not removed. And 1(8,4%) had vertebra involved which wasn't completely respected.

9(75,0%) had involved regional nodes by pathology report. 4(33,3%) were metastatic patients.

All of them were tested for BRAF mutation and 5(41,7%) were positive for this mutation.

All patients had underwent radiation therapy in 30 fractions: 60,0Gy for subclinical disease and regional nodes with boost dose up to 66,3Gy for gross disease. Acute toxicity toxicity was assessed according to NCI CTCAE v5,0.

9/12(75,0%) of them completed therapy without interruptions and one(8,4%) have received full dose due aspiration pneumonia. We analysed dose at organs at risk such as: mucosa, larynx, pharynx, major

salivary glands, skin and oral cavity. We searched correlation between surgery treatment attributes, volume and type of gross disease, loads on organs at risk.

Results

1 We found strict correlation between development of acute toxicity grade 2 and greater (CTCAE v5,0) and loads on organs at risk.

2 We also found that patients older 75 years old had more grade 2 mucosal toxicity (CTCAE v5,0).

3 Medicinal therapy before radiation treatment did not affect on toxicity and interruptions of radiation course.

4 We also found that volume of gross disease and boost volume strictly connect with radiation course interruptions.

5 Concurrent therapy for metastatic patients caused greater toxicity.

All correlations reported are statistically reliable with $p<0,05$.

Conclusion

For those patients volume of gross disease after surgery can affect on completeness of radiation treatment. We also found that age, concurrent therapy and doses on organs at risk can affect on treatment tolerance and toxicity.

229

Weekly vs 3-weekly cisplatin: a retrospective cohort study

Michael Saerens[1,2], Alexander Van den Broeck[2], Geertrui Van de Weghe[2], Huvenne Wouter[3,4], Tomassen Peter[3,4], Bauters Wouter[5], Tijl Vermassen[1,2], Deschuymer Sarah[6,7], Sylvie Rottey[1,8,2], Fréderic Duprez[6,7]

[1]Ghent University Hospital, Medical Oncology, Ghent, Belgium. [2]Ghent University, Basic and Applied Medical Sciences, Ghent, Belgium. [3]Ghent University Hospital, Head and neck surgery, Ghent, Belgium. [4]Ghent University, Head and skin, Ghent, Belgium. [5]Ghent University Hospital, Radiology, Ghent, Belgium. [6]Ghent University Hospital, Radiotherapy, Ghent, Belgium. [7]Ghent University, Human structure and repair, Ghent, Belgium. [8]Ghent University Hospital, Drug Research Unit, Ghent, Belgium

Topic

Quality of life and outcomes

Keywords

Chemoradiotherapy, cisplatin, toxicity

Purpose/Objective

To investigate the differences in outcome of CRT with three-weekly cisplatin (100mg/m², cis100) versus weekly (40mg/m², cis40) cisplatin in the treatment of locally advanced (LA) HNSCC in a real-world setting.

Material/Methods

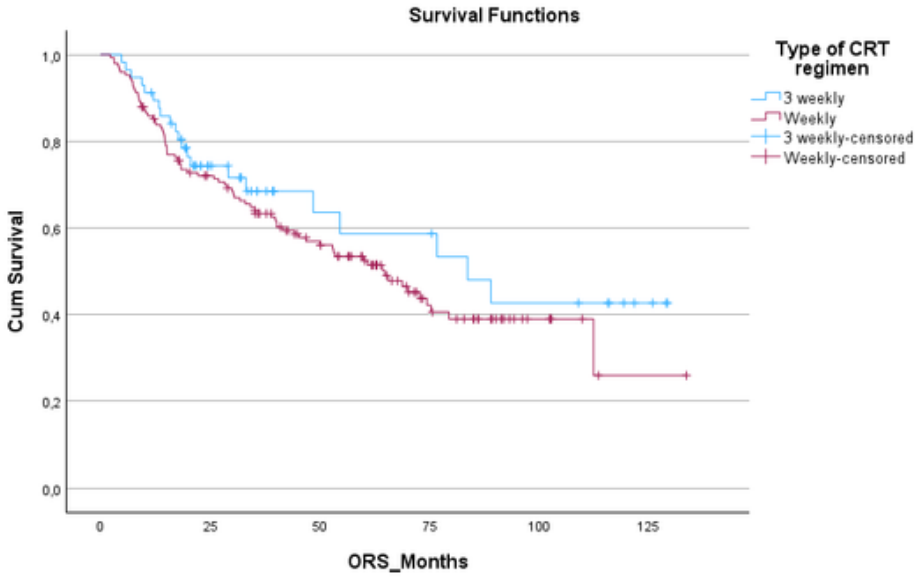
A retrospective chart review in a tertiary care facility in Ghent, Belgium, including all patients with LA HNSCC treated with concurrent cisplatin-based CRT, whether adjuvant or definite, from 2011-2022. Patients were treated with intensity-modulated radiotherapy (IMRT) or volumetric-arc radiotherapy (VMAT) using simultaneous integrated boost. Definite treatment comprised 32x2.16 Gy to the primary tumor and involved lymph nodes, and 56 Gy to elective neck nodes. Adjuvant treatment comprised 32x2.16 Gy (after R1 or R2 resection or ENE) or 33x2Gy on tumor bed and 56 Gy on elective neck nodes. Patients who underwent neoadjuvant chemotherapy, had other histologic subtypes or who received prior irradiation for HNSCC were excluded. The primary outcomes were disease-free survival (DFS) and overall survival (OS). Secondary outcomes were 3-month locoregional control (LRC) measured as first response evaluation, treatment completion and grade 3-5 toxicity according to the CTCAE v5.0. Survival analyses were performed via the Kaplan-Meier method using the log-rank test. Independent outcomes were assessed at the 0.05 significance level.

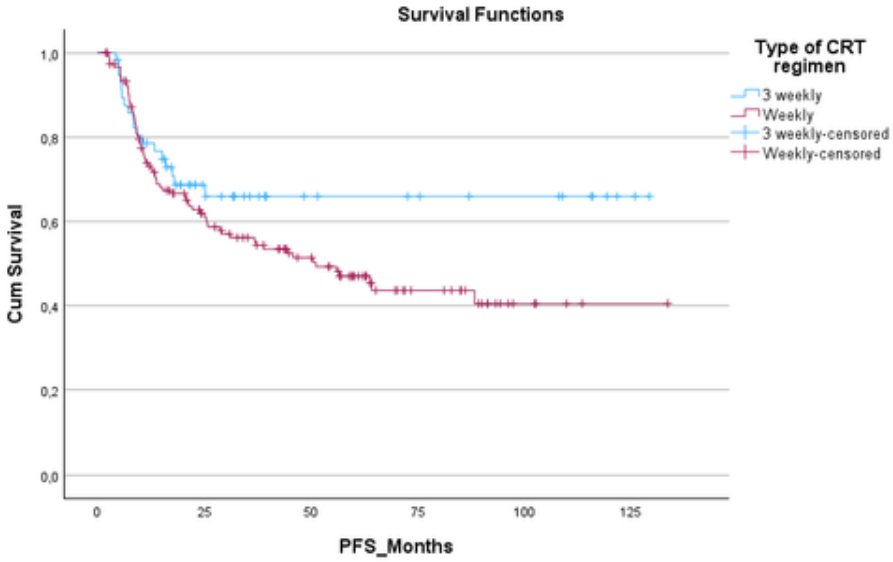
Results

220 patients were included (162 cis40, 58 cis100). Median duration of follow-up was 66 months. Patient characterstics and outcomes are summarized in Table 1. Median OS and DFS were numerically longer in the cis100 group, although this difference was not statistically significant (mOS 83.6m vs 64.7m, p=0.316; mDFS NR vs 50.3m, p=0.125). First response evaluation showed no significant differences between the two groups (see table 1). Less patients completeted the full dose of prescribed radiotherapy in the cis40 group (93% vs 100%, p=0.07) although this was not significant. Mean cumulative dose of cisplatin was similar between groups. Toxicity analysis showed higher rates of ototoxicity (29 vs 7%, p<0.001) and gr 3-4 acute kidney failure (15.6vs 4.9%, p<0.05) and in the cis100 group, although this did not translate into increased chronic kidney impairment in the cis100 group. We observed more hematologic toxicity in the cis40 group (see table 1).

	Cisplatin 3-weekly (100mg/m²) N=58	**Cisplatin weekly (40mg/m²)** N=162	**P value**
Mean age	57.9 (SD 6.36)	59.7 (SD 7.12)	
ECOG			
0-1	16 (27%)	148 (91%)	P=0.19
2	33 58%)	12 (7%)	
NA	0	2 (2%)	
Disease stage			
III	16 (27%)	28 (17%)	P=0.24
IVa	33 (58%)	103 (63%)	
IVb	9 (16%)	31 (19%)	
Primary Site			P=0.96
oral cavity	14 (24%)	45 (28%)	

oropharynx	24 (41%)	65 (40%)	
P16+	9/24	19/65	
P16-	9/24	24/65	
unknown	6/24	22/65	
hypopharynx	9 (16%)	27 (17%)	
larynx	7 (12%)	17 (10%)	
CUP	4 (7%)	8 (5%)	
Indication for CRT			
adjuvant	8 (14%)	36 (22%)	P=0.16
definite	50 (86%)	126 (78%)	
Mean cumulative cisplatin dose	233.4 mg/m² (IQR 100-300)	231.7 mg/m² (IQR 200-280)	
Completion of prescribed RT	58/58 (100%)	151/162 (93%)	P=0.07
mDFS	NR	51.1 months [95%CI 30.4-71.7]	P=0.125
mOS	83.6 months [95%CI 40.8-125.1]	64.7 [95%CI 49.5-79.9]	P=0.32
First response evaluation			
CR	42/58 (72%)	110162 (67%)	P=0.52
PR	6/58 (10%)	26/162 (17%)	P=0.29
PD/metastasis	5/58 (8%)	11/162 (7%)	P=0.64
death	1/58 (2%)	3/162 (2%)	P=0.95
NE	4/58 (7%)	12/162 (7%)	P=0.89
Toxicity analysis			
Gr 3-4 acute kidney injury	9/58 (15.6%)	8/162 (4.9%)	P<0.05
Chronic kidney disease (≥CKD gr3)	1/58 (1.7%)	5/162 (3%)	P=0.65
Anemia (any grade)	46/58 (79%)	149/162 (92%)	P<0.05
Anemia (gr 3-4)	1/58 (1.6%)	10/162 (6.1%)	P<0.05
Neutropenia (gr 3-4)	4/58 (7.8%)	37/162 (22%)	P=0.16
Febrile neutropenia	1/58 (1.7%)	4/162 (2.4%)	P=0.77
Thrombocytopenia (gr 3-4)	2/58 (3.4%)	15/162 (9%)	P<0.05
Mucositis gr 3-4	14/58 (24.1%)	28/162 (17.2%)	P=0.172
Acute hearing impairment (any grade)	17/58 (29%)	12/162 (7%)	P<0.001
Acute hearing impairment (gr 3-4)	9/58 (15%)	5/162 (3%)	P<0.001
Hospitalization during CRT	21/58 (36%)	76/162 (47%)	P=0.214





Conclusion

In this retrospective single-centre study, high dose cisplatin was associated with a trend to improved survival outcomes compared to weekly cisplatin. We observed an increase in Gr 3-4 acute kidney injury and ototoxicity in the cis-100 group, and more hematotoxicity in the cis40 group.

230

Body image seen by patients with nasopharyngeal cancer

Houda Fares[1,2], Mona Taouchikht[1,2], Sara Abdou[1,2], Rania El Gueddari[1,2], édith Tatiana Ngbwa[1,2], Imane Hassnaoui[1,2], Karima Nouni[1,2], Amine Lachgar[1,2], Hanan Elkacemi[1,2], Tayeb Kebdani[1,2], Khalid Hassouni[1,2]

[1]National Oncology Institute, Radiotherapy, Rabat, Morocco. [2]Faculty of Medicine and Pharmacy, Medicine, Rabat, Morocco

Topic

RTT

Keywords

nasopharyngeal cancer; Body image

Purpose/Objective

nasopharyngeal cancer often involves heavy treatment based on radio-chemotherapy which can affect the body image of patients, however,this parameter is often neglected by health professionals and its impact can be devastating.

Evaluate body image in patients with cavum cancers at different times during treatment.

Material/Methods

This is a descriptive cohort study assessing body image that included 30 patients treated between January and March 2022. For cavum cancer. The Body Image Scale (BIS) was used for this assessment.

A high score reflected an alteration in body image. The average age was 45 years (20-65 years) with a sex ratio of 2.5. The majority of patients were married, of urban origin (17 patients; 56%) and of primary education level (15 patients; 50%). The tumor stage (III) was the most represented (24 patients; 80%); the questionnaire was carried out during treatment for 20 patients (66%) Before treatment for 5 patients (16%) and in the first 6 months of follow-up for 5 patients (16%); 2 patients had a recurrence of the disease (6%).

Results

Patients presented functional symptoms related to cancer or treatments in 90% (27 patients). The most common symptoms were: dysphagia (15 patients), xerostomia (8 patients), hair loss and dysgeusia (6 patients) and fatigue, pain and burning sensations in 5 patients.

These symptoms bothered the patients in 90% of cases (27 patients) and had caused a negative psychological impact in 66% of cases (20patients); 8 patients (26%) expressed an avoidance of the mirror, felt less attractive and believed they were victims of mutilating treatment.

10 patients (33%) expressed social avoidance and discomfort with themselves and 7 patients expressed a lack of self-confidence (23%) and discomfort with their partner (20%). 13 patients felt depressed (43%), however 17 patients felt optimistic (56%) and no patients expressed suicidal thoughts. All patients claimed to have a containing family and 13 patients (43%) complained of a negative impact on the profession. 14 patients used camouflage objects (46%), the most frequent of which: a scarf in 8 patients and a cap or hat in 6 patients, the average BSI score was 17 (10-37).

Conclusion

Screening for altered body image in patients with cavum cancer seems to be essential by all health professionals, which helps improve the quality of life of patients.

231

Gross Tumour Volume predicts survival in HPV related Oropharyngeal Squamous Cell Carcinoma

Darragh Patrick Browne[1], Niall O'Dwyer[1], Mary Dunne[2], Emma Connolly[1], Jane Burns[1], Megan McNamara[1], Oleksandr Boychak[1], John Armstrong[1], Fran Duane[1], Sinead Brennan[1], Orla McArdle[1]

[1]St Luke's Radiation Oncology Network, Radiation Oncology, Dublin, Ireland. [2]St Luke's Radiation Oncology Network, Clinical Trials, Dublin, Ireland

Topic

HPV or EBV related cancers

Keywords

OPSCC, p16, GTV

Purpose/Objective

To investigate if tumour volume (primary, nodal and combined) predicts recurrence free (RFS) and overall survival (OS) in p16+ oropharyngeal squamous cell carcinoma.

Material/Methods

Study design

We conducted a retrospective analysis of patients with OPSCC treated with curative radiotherapy in SLRON from 2013 - 2021. TNM 8th edition definition of stage was applied.

Participants

Eligible participants had OPSCC and received radiotherapy as definitive, radical treatment. Diagnosis was based on clinical assessment, histological sampling and PET imaging. p16 status was available for all patients. Clinical examination and PET imaging were used to assess response to treatment.

Treatment

Patients received 65-70Gy over 30-35 fractions, delivered using Intensity-Modulated Radiotherapy (IMRT).

Endpoints

Primary endpoints:

1. To investigate if GTVp predict RFS & OS in p16+ OPSCC
2. To investigate if GTVn predict RFS & OS in p16+ OPSCC
3. To investigate if GTVcomb predict RFS & OS in p16+ OPSCC

Secondary endpoints:

1. To investigate if GTVp &/or GTVn predict RFS & OS in p16- OPSCC

2. To investigate if GTVp &/or GTVn predict RFS & OS in OPSCC
3. To investigate if use of concomitant chemotherapy improves outcomes in OPSCC in this cohort
4. To estimate RFS and OS

Statistical Analysis

All analyses were performed in IBM SPSS Statistics ver 29.0, and involved descriptive statistics, survival analyses by Kaplan-Meier method, and linear regression by Cox Proportional Hazards (univariate & multivariate). OS was evaluated from date of final RT. RFS was evaluated from date of final RT to the date of first local or distant recurrence, death, or last clinical assessment/investigation.

Results

Baseline Characteristics

From January 2013 to April 2021, 246 patients were eligible for this review. Median age at first RT was 59.6. 187 (76%) were male. 179 (73%) had p16+ disease. 218 (88.6%) received chemotherapy. Median follow up was 25.5 months (0.5 - 96).

Disease stage & Tumour volumes

Patients with p16+ disease were diagnosed with earlier stage disease (86% stage 1 or 2), in comparison with those with p16- disease (3% stage 3 or 4; p< .001).

Treatment

Treatment was delivered using IMRT. 235 (95.5%) received 70Gy in 35 fractions and 11 (4.5%) received 65Gy in 30 fractions.

Overall Survival

61 out of 246 patients (25%) died. Median survival for the total population was not reached. 3, 4 and 5 year overall survival was 75% (95%CI: 69 to 81%), 69% (95%CI: 61 to 76%) and 64% (95%CI: 55 to 73%) respectively.

There was a significant difference in OS between those with P16- and P16+ (p<.001).

Median survival for the P16- population was 34.9 months (95%CI 13 to 56 months).

Median survival for the P16+ population was not reached.

Recurrence Free Survival

Median recurrence free survival for the total population was not reached.3, 4 and 5 year RFS survival was 65% (95%CI: 59 to 72%), 63% (95%CI: 56 to 70%) and 58% (95%CI: 49 to 66%) respectively.

There was a significant difference in RFS between those with P16- and P16+ (p<.001).

Median survival for the P16- population 23.6 months (95%CI 11 to 37 months).

Median survival for the P16+ population was not reached.

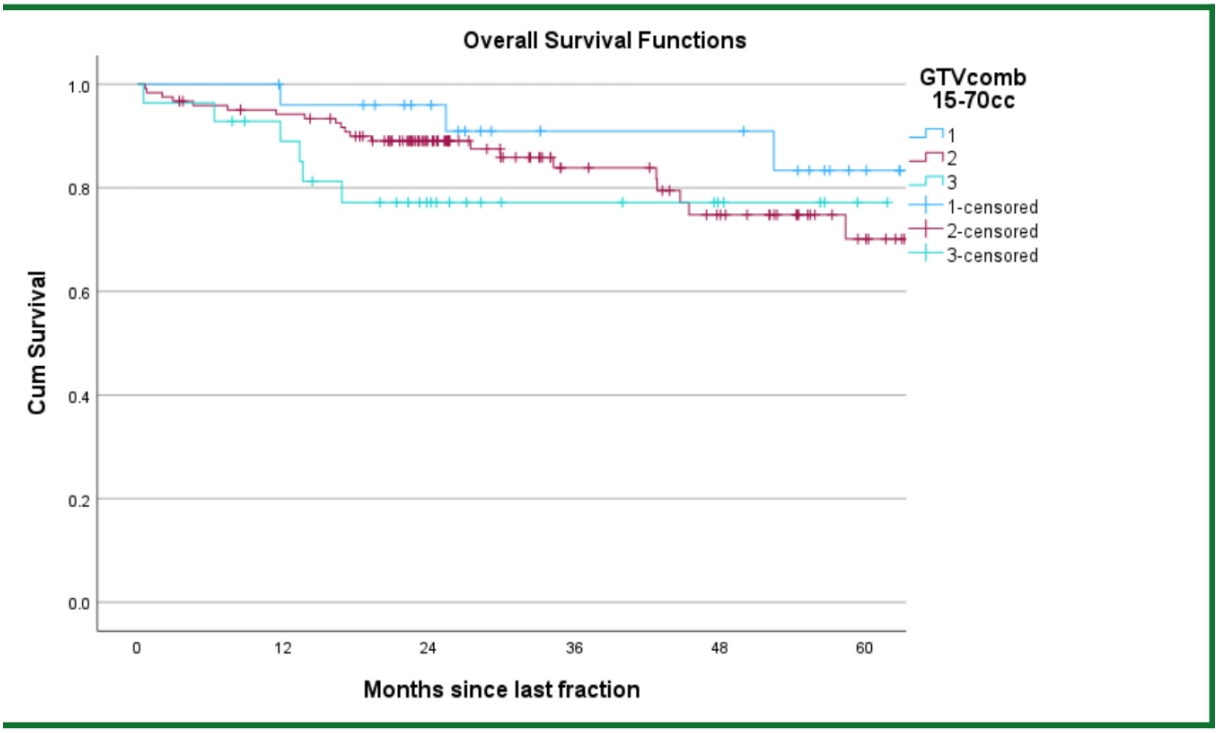
Survival based on Gross Tumour Volume

For the total population (p16+ & p16-):

- GTVp greater or less than median GTVp (dichotomized) was a statistically significant predictor of OS (p= .004)
- GTVp based on Adrian et al volume brackets <6 cm^3, 6–12 cm^3, 12–24 cm^3, 24–48 cm^3, 48–96 cm^3, and>96cm^3 (as suggested by Adrian et al, 2022) was a statistically significant predictor of OS (p<.001)
- GTVp greater or less than 40cm^3 (as suggested by Adrian et al, 2022) was a statistically significant predictor of OS (p<.001)
- GTVcomb based on volume brackets <15cc, 15-70cc, >70cc (as suggested by Panje et al, 2017) was a statistically significant predictor of OS and RFS (p= .001 and p<.001 respectively).

When looking only at those with P16+, neither age, gender nor stage 1-2, were predictive of OS. The following variables were predictive of OS: GTVp, GTVp >18.3cc, GTV as per Adrian et al volume brackets, GTVp 15-70cc, GTVp>40cc, GTVn, GTVcomb and total dose.

	p16 - n = 67 (27%)	p16 + n = 179 (73%)	n = 246
Stage (TNM 8th) 1 2 3 4A 4B	 0 (0%) 2 (3%) 17 (25%) 43 (64%) 5 (8%)	 78 (44%) 76 (42%) 25 (14%) 0 (0%) 0 (0%)	 78 (32%) 78 (32%) 42 (17%) 43 (17%) 5 (2%)
GTVp (cm3) median (range) missing data (n)	 24.3 (0 - 153) 0	 16.2 (0 - 150) 10	 18.3 (0 - 153) 10
GTVn (cm3) median (range) missing data (n)	 6.0 (0 - 137) 2	 15.0 (0 - 178) 12	 12.9 (0 - 178) 14
GTVcomb (cm3) median (range) missing data (n)	 37.4 (0 - 173) 0	 38.2 (3 - 298) 3	 37.9 (0 - 298) 3



Conclusion

We demonstrate that GTV (primary, nodal and combined) predict outcome in p16+ OPSCC. This metric is readily available to the Radiation Oncologist at tumour delineation, and therefore may aid dose de-escalation decision making, without added delay.

Future work may investigate cautious dose de-escalation in a cohort with smaller GTVs.

References

1. Fakhry C. Improved survival of patients with human papillomavirus-positive head and neck squamous cell carcinoma in a prospective clinical trial. Journal of the National Cancer Institute : JNCI. 2008;100(4):261–9.

2. Masterson, L., et al. "De-Escalation Treatment Protocols for Human Papillomavirus-Associated Oropharyngeal Squamous Cell Carcinoma: A Systematic Review and Meta-Analysis of Current Clinical Trials." European Journal of Cancer, vol. 50, no. 15, 2014, pp. 2636-2648.

3. Adrian, G., Carlsson, H., Kjellén, E. et al. Primary tumor volume and prognosis for patients with p16-positive and p16-negative oropharyngeal squamous cell carcinoma treated with radiation therapy. Radiat Oncol 17, 107 (2022).

4. Gabani, P., et al. "Radiation Therapy Dose De-Escalation Compared to Standard Dose Radiation Therapy in Definitive Treatment of HPV-Positive Oropharyngeal Squamous Cell Carcinoma." Radiotherapy and Oncology, vol. 134, 2019, pp. 81-88.

5. Lee, N., et al. "Strategy of using Intratreatment Hypoxia Imaging to Selectively and Safely Guide Radiation Dose De-Escalation Concurrent with Chemotherapy for Locoregionally Advanced Human Papillomavirus–Related Oropharyngeal Carcinoma." International Journal of Radiation Oncology Biology Physics, vol. 96, no. 1, 2016, pp. 9-17.

6. Swisher-McClure, S., et al. "A Phase 2 Trial of Alternative Volumes of Oropharyngeal Irradiation for De-Intensification (AVOID): Omission of the Resected Primary Tumor Bed After Transoral Robotic Surgery for Human Papilloma Virus–Related Squamous Cell Carcinoma of the Oropharynx." International Journal of Radiation Oncology Biology Physics, vol. 106, no. 4, 2020, pp. 725-732.

232

The impact of tracheostomy on the course of radiotherapy.

Asmae Hamdan[1,2], Salma El Baz[1,2], Oumaima Eddarif[1,2], Karima Nouni[1,2], Amine Lachgar[1,2], hanan El kacemi[1,2], Tayeb Kebdani[1,2], Khalid Hassouni[1,2]

[1]The National Institute of Oncology, Radiotherapy, Rabat, Morocco. [2]Faculty of medicine and pharmacy, Medicine, Rabat, Morocco

Topic

RTT

Keywords

laryngeal, cancer, tracheostomy

Purpose/Objective

The aim of this study is to assess the impact of tracheostomy on radiotherapy in patients with laryngeal cancer.

Material/Methods

This is a prospective qualitative study conducted in the year 2022, including 49 patients undergoing radiotherapy for laryngeal cancer. Patients were interviewed using a questionnaire with several items during their weekly follow-up consultations. They were required to rate each step of radiotherapy (in the supine position, the application and maintenance of the thermoformed mask, positioning, dosimetric CT scan, and the treatment session) on a scale from 0 to 10, with 0 representing no discomfort and 10 representing extreme discomfort. Patients were also asked to report their level of anxiety during each step. Correlations were explored using the Pearson coefficient.

Results

The age of patients ranged from 42 to 84 years with a median of 63 years. The most common histological type was squamous cell carcinoma. Tracheostomy was performed urgently in 34 patients, accounting for 69.38%, and scheduled in 15 patients, accounting for 30.61%.

According to our surveyed patients, the application and maintenance of the thermoformed mask were the most unpleasant moments, with an average discomfort rating of 8.5/10 and an average anxiety level of 9/10. The averages for other items varied between 3/10 and 8/10. In response to the question "What do you fear the most during the session?", 11 patients, or 22.44%, believed that the thermoformed mask could cause them asphyxiation. No significant correlations were found.

Conclusion

To ensure the smooth progress of radiotherapy in tracheostomized patients, it is essential to provide prior explanations for all stages of radiotherapy, its benefits, and its side effects. Adequate management of specific situations and a trusting relationship between medical personnel and the patient are also necessary.

234

Anterior frontal vertical partial laryngectomy: Oncological results and voice quality

Alia SA Methnani[1], RIM Braham[1], Jihen Gharssalli[1], Alia Mousli[2], Mohamed Dhaha[1], Souhail Jbali[1], Sawsen Dhambri[1], Skander Kedous[1]

[1]Salah Azaiez institute, Cervico-facial surgery department, Tunis, Tunisia. [2]Salah Azaiez institute, Radiothérapy, Tunis, Tunisia

Topic

Supportive care, rehabilitation

Keywords

partial laryngectomy.voice quality

Purpose/Objective

To Study the oncological and functional results of Anterior frontal vertical partial laryngectomy (Tucker).

Material/Methods

Retrospective study conducted over a period of 10 years [2013-2022] collecting 19 patients treated with Tucker partial laryngectomy for laryngeal cancer.

Results

All patients were male. Mean age was 58 years. Three patients were diabetic and four were hypertensive. Seventeen patients had glottic limited tumor. Two patients had a subglottique extension. No lymph-nodes and no distant metastatic extension were noted. Fifteen patients had the two arytenoids preserved. The histological type was in all cases squamous cell carcinoma. Resection limits were healthy in 17 cases and cramped in 2 cases. Postoperative complications were surgical site infection (2 cases) and lung infection (2 cases). The mean postoperative decannulation time was 11 days [4-22 days]. The mean time to remove the nasogastric tube was 15 days [7-24 days]. The mean duration of hospitalization was 17 days [13-28 days]. Eight patients benefited from speech therapy rehabilitation. The average time to resume an audible voice was 10 days. For a mean follow-up of 3 years, one patient presented recurrenceand was treated with total laryngectomy.

Conclusion

Anterior frontal vertical partial laryngectomy allows to have good oncological and fuctional results for selected early stage of laryngeal cancers.

235

Nasopharyngeal cancer chemotherapy – before or after curative chemoradiation?

Sara Magno[1], Rita Freitas[2], Inês Dunões[3], Inês Vicente[1], Madalena Machado[1], Margarida Pereira[1], Fátima Vaz[1], Isabel Sargento[1]

[1]Instituto Português de Oncologia de Lisboa Francisco Gentil, Medical Oncology, Lisbon, Portugal. [2]Hospital Professor Dr Fernando Fonseca, Medical Oncology, Lisbon, Portugal. [3]Hospital do Espirito Santo, Medical Oncology, Évora, Portugal

Topic

HPV or EBV related cancers

Keywords

nasopharyngeal, adjuvant, induction

Purpose/Objective

Nasopharyngeal carcinomas (NPC) are endemic in southeast Asia and rare in Europe with an incidence of 0.07/100.000 persons. Five-year survival is about 50%. Diagnosis is provided by histological findings and staging classification is done according to AJCC. EBV DNA serum levels should be determined before and after local treatment, carry prognostic significance and can be used in the active surveillance of cancer survivors. The best method for serum determination of EBV DNA is still under discussion.

Advanced locoregional disease carries a greater risk of distant spread, highlighting the need of treatment intensification in higher risk patients. The best treatment plan is still under discussion: concurrent chemoradiation followed by adjuvant chemotherapy (ACT) or induction chemotherapy (ICT) followed by chemoradiation. ACT/ICT regimens should consist of two-/three-drug regimens, including a platinum agent and the best drug regimen is still under investigation. ACT carries great toxicity (50% require dose reductions, 60% complete treatment) and has a relatively low PFS and OS benefit. ICT is better tolerated, but may compromise cisplatin cumulative dose in concomitant chemoradiation and delay radiation start, possibly compromising the effectiveness of local treatment. Nonetheless, ICT improves PFS and OS when compared to chemoradiation alone, mostly because of better metastasis free survival (MFS), making this a promising strategy in properly selected high risk patients.

Most NPC trials were conducted in countries where NPC is endemic, primarily non-queratinizing and EBV-related. Data in non-endemic countries are lacking.

Our study aims to compare ACT and ICT in locally advanced and oligometastatic NPC patients treated in a European reference centre.

Material/Methods

Retrospective, observational study of patients with NPC diagnosis between January 2017 and September 2023 and disease stage III-IVb. Data were collected from patient records and included patient characteristics (gender, age, smoking history, ECOG performance status), tumor characteristics (T, N, staging, histology, EBV-status) and treatment characteristics (ACT, ICT, toxicities). PFS and OS were analyzed. Toxicity grading is according to CTCAE 5.0 and statistical analysis is descriptive.

Results

A total of 69 patients were included. Most patients were male (56.5%, n=39) with a median age of 53.0 years (18-75). Most patients had a good performance status (0 or 1 in 98.5%, n=68). Stage IVa was the most frequent initial staging (50.7%, n=35), with a majority of patients having T4 (33.3%, n=23) and N3 (39.1%, n=27) tumours. All tumours were undifferentiated queratinizing carcinomas and 86.9% (n=60) were EBV-positive. EBV DNA was rarely determined.

Characteristics	Total (68)	ACT (58) % (n)	ICT (11) % (n)
Sex			
Male	57.4% (39)	56.9% (33)	54.5% (6)
Age			
Median, SD	53.0, 13.5	53.0, 12.2	54.0, 20.4
Max	75	74	75
Min	18	18	18
Smoker			
Yes	39.7% (27)	37.9% (22)	54.5% (6)
No	57.4% (39)	58.6% (34)	45.4% (5)
Missing	2.9% (2)	3.4% (2)	-
ECOG performance status			
0	64.7% (44)	67.2% (39)	54.5% (6)
1	33.8 (23)	32.8% (19)	36.3% (4)
2	1.5% (1)	-	0.9% (1)
Tumor category (T)			
1	36.8% (25)	41.4% (24)	0.9% (1)
2	8.8% (6)	8.6% (5)	0.9% (1)
3	22.1% (15)	20.7% (12)	27.2% (3)
4	32.4% (22)	29.3% (17)	54.5% (6)
Missing	-	-	-
Nodal status (N)			
0	1.5% (1)	1.7% (1)	-
1	27.9% (19)	31.0% (18)	18.1% (2)
2	30.9% (21)	32.8% (19)	18.1% (2)
3	39.7% (27)	34.5% (20)	63.6% (7)
TNM staging			
II	14.7% (10)	17.2% (10)	-
III	23.5% (16)	27.6% (16)	-
IVa	50.0% (34)	53.4% (31)	36.3% (4)
IVb	11.7% (8)	1.7% (1)	63.6% (7)
EBV-tumor			
Positive	86.8% (59)	84.5% (49)	100.0% (11)

Until 2019 the most frequent treatment strategy was ACT with cisplatin-5FU (57.9%, n=40), after which ICT became more frequently used (15.9%, n=11), mostly with cisplatin-gemcitabin (45.4%, n=5). ICT had less acute toxicities that lead to treatment discontinuation (0.9% (n=1) versus 39.7% (n=23)). All patients completed radiotherapy after ICT, but in 4 patients optimal concomitant cisplatin dose (≥200mg/m2) was compromised. Both ICT and ACT showed good response rates, with a complete response in 63.6% versus 79.3%, respectively. Median follow up was 45 months in the ACT group (4-125) and 27 months (1-55) in the ICT group. PFS with ACT was 45.0 months (95%CI 34.8-55.2) and OS was 46.0 months (95%CI 38.5-53.4). The ICT group is small and has a short follow-up time; PFS and OS data will be determined in the future.

Characteristics	ACT % (n)	ICT % (n)
Chemotherapy regimen		
Cisplatin-gemcitabin	-	45.4% (5)
Carboplatin-gemcitabin	-	18.1% (2)
Cisplatin-5FU	69.0% (40)	0.9% (1)
Carboplatin-5FU	27.6% (16)	0.9% (1)
Carboplatin	1.7% (1)	-
Carboplatin-Paclitaxel	1.7% (1)	0.9% (1)
Cisplatin-epirrubicin	-	0.9% (1)
Toxicities		
Hematological	10.3% (6)	63.6% (7)
Nausea	1.7% (1)	0.9% (1)
Nephrotoxicity	-	-
Mucositis	5.2% (3)	36.3% (4)
Ototoxicity	3.4% (2)	0.9% (1)
Peripheral neuropathy	-	0.9% (1)
Led to dose modification	8.6% (5)	0.9% (1)
Led to discontinuation	39.7% (23)	0.9% (1)
Chemoradiation		
Yes	100.0% (58)	63.6% (7)
Isolated RT	-	27.2% (3)
With dose reduction	34.5% (20)	18.1% (2)
Response to ICT		
No response/stable disease	-	0.9% (1)
Partial	-	45.4% (5)
Complete	-	0.9% (1)
No assessment	-	36.3% (4)
Response to treatment (ICT + CRT)		
Complete response	-	63.6% (7)
Partial response	-	18.1% (2)
Stable disease	-	0.9% (1)
Response to treatment (CRT + ACT)		
Complete response	79.3% (46)	-
Partial response	15.5% (9)	-
Stable disease	-	-
No assessment	5.2% (3)	

Conclusion

The best course of treatment of advanced NPC is still unclear - which patients and histologies benefit most from treatment intensification? What is the role of EBV DNA and what is the best method for its determination? Should ACT or ICT be preferred? Which chemotherapy regimen is better? Treatment center expertise and the ability to provide timely treatment may also play a role in treatment decisions.

Our study presents the experience of a European reference centre where ACT was the preferred treatment for a longer period of time and therefore has a significantly larger patient population with longer follow-up time. ACT seems to provide good patient outcomes, despite a worse toxicity profile and more related treatment discontinuations, but group comparison is not yet possible since our centre only recently changed strategies in managing advanced NPC patients, preferring ICT over ACT. ICT patients are still underrepresented in this analysis, with fewer patients and shorter follow-up time. Moreover, the ICT patient group has more advanced disease, including IVb oligometastatic disease (that was not included in the intensification ACT and ICT studies), making head-to-head comparisons difficult.

The management of advanced NPC is a clinical challenge and more data are needed to better select both patients and treatment strategies for treatment intensification, while taking into consideration the differences between endemic and non-endemic NPC.

References

1. Age Standardized (World) Incidence Rates, Nasopharynx, Males, All Ages.; 2020. https://gco.iarc.fr/today

2. Bossi P, Chan AT, Licitra L, et al. Nasopharyngeal carcinoma: ESMO-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology. 2021;32(4):452-465. doi:10.1016/j.annonc.2020.12.007

3. Chen YP, Chan ATC, Le QT, Blanchard P, Sun Y, Ma J. Nasopharyngeal carcinoma. The Lancet. 2019;394(10192):64-80. doi:10.1016/S0140-6736(19)30956-0

4. Bossi P, Chan AT, Even C, Machiels JP. ESMO–EURACAN Clinical Practice Guideline update for nasopharyngeal carcinoma: adjuvant therapy and first-line treatment of recurrent/metastatic disease. Annals of Oncology. 2023;34(3):247-250. doi:10.1016/j.annonc.2022.11.011

5. Haddad RI, Hicks WL, Hitchcock YJ, et al. NCCN Guidelines Version 2.2023 Head and Neck Cancers Continue NCCN Guidelines Panel Disclosures.; 2023. https://www.nccn.org/home/member-

6. Ng WT, Chang ATY, Lee SWM, Sze HCK, Lee AWM. Chemotherapy for Nasopharyngeal Cancer: Neoadjuvant, Concomitant, and/or Adjuvant. Curr Treat Options Oncol. 2015;16(9). doi:10.1007/s11864-015-0361-5

7. Jiromaru R, Nakagawa T, Yasumatsu R. Advanced Nasopharyngeal Carcinoma: Current and Emerging Treatment Options. Cancer Manag Res. 2022;14:2681-2689. doi:10.2147/CMAR.S341472

8. Zhang Y, Chen L, Hu GQ, et al. Gemcitabine and Cisplatin Induction Chemotherapy in Nasopharyngeal Carcinoma. New England Journal of Medicine. 2019;381(12):1124-1135. doi:10.1056/nejmoa1905287

9. Yuan C, Xu XH, Luo SW, et al. Which neoadjuvant chemotherapy regimen should be recommended for patients with advanced nasopharyngeal carcinoma? a network meta-analysis. Medicine (United States). 2018;97(34). doi:10.1097/MD.0000000000011978

236

Evaluating predictive factors for chemoradiotherapy related dysphagia in patients with head and neck cancer.

Margarida Lagarto, Tiago Pina Cabral, Vanessa Duarte Branco, Ana Carolina Vasques, Filipa A.S. Ferreira, Ana Martins

Hospital São Francisco Xavier, Oncology, Lisboa, Portugal

Topic

Quality of life and outcomes

Keywords

head and neck cancer; toxicity predictive factors

Purpose/Objective

The treatment of head and neck cancers has progressed over the years which yields a better chance of long-term survival. Nevertheless, treatment intensification also increases rates of treatment related toxicities. Dysphagia is an underestimated, yet challenging, complain of head and neck cancer patients

undergoing chemoradiotherapy. This retrospective study aims to determine if there are any variables that can be used as predictive factors for this outcome.

Material/Methods

All patients diagnosed with head and neck cancer that underwent treatment with definitive chemoradiotherapy with cisplatin every 3 weeks at our center, between 2018 and 2022, were included. Patients that had dysphagia prior to treatment, who died before the end of treatment and patients that lost follow-up within 6 months after treatment end, were excluded. Considering the latter, we collected a sample of 42 individuals from which we obtained data concerning gender, age (< 65 years old vs. ≥ 65 years old), smoking history, HPV status, cancer type (oropharyngeal vs non-oropharyngeal), treatment radiation dose (< 70Gy vs ≥ 70Gy), number of cisplatin cycles and early and late dysphagia outcomes using the CTCAE scale. To evaluate the association between any of these categorical variables and early/late dysphagia outcomes, we applied Fisher's exact test, given the small counts, using the EasyR® software.

Results

Most of our sample included male patients (N = 37; 88,1%) and heavy smokers (N = 34; 80% with > 10 units pack year); with a mean age of 62 years at the time of diagnosis. The most frequent type of cancer was oropharyngeal (N = 21; 50%) followed by laryngeal cancer (N = 12; 28,6%). For early dysphagia, HPV status (p = 0,0357) was significantly associated with outcome, whereas in later dysphagia treatment radiation dose (p = 0,0291) was significantly associated with outcome.

Conclusion

As far as we know, the association between HPV and treatment related dysphagia has not been established. Our results indicate that HPV status has an influence in the patient's risk of developing early dysphagia while treatment radiation dose influences the risk of developing late dysphagia.

References

- Ray, X., Sumner, W., Sutton, L. et al. Evaluating predictive factors for toxicities experienced by head & neck cancer patients undergoing radiotherapy. J Transl Med 19, 380 (2021). https://doi.org/10.1186/s12967-021-03047-2

- Tengku S, Lohi I, Connelly A, Slaven E, Sloane K, Herity K, McBlain L, Douglas CM, Montgomery J. Late-onset swallowing outcomes post-treatment for head and neck cancer in a UK-based population. J Laryngol Otol. 2023 Mar;137(3):293-300. doi: 10.1017/S0022215122000834. Epub 2022 Mar 23. PMID: 35317872; PMCID: PMC9975761.

- Vidyasagar N, Manur Gururajachar J. Predicting toxicity for head and neck cancer patients undergoing radiation therapy: an independent and external validation of MDASI-HN based nomogram. Rep Pract Oncol Radiother. 2020 May-Jun;25(3):355-359. doi: 10.1016/j.rpor.2020.03.005. Epub 2020 Mar 19. PMID: 32256219; PMCID: PMC7103655.

- Denaro N, Merlano MC, Russi EG. Dysphagia in Head and Neck Cancer Patients: Pretreatment Evaluation, Predictive Factors, and Assessment during Radio-Chemotherapy, Recommendations. Clin Exp Otorhinolaryngol. 2013 Sep;6(3):117-26. doi: 10.3342/ceo.2013.6.3.117. Epub 2013 Sep 4. PMID: 24069513; PMCID: PMC3781223.

237

Role of reirradiation in the management of relapses local nasopharyngeal cancer

Houda Fares[1,2], Mona Taouchikht[1,2], édith Tatiana Ngbwa[1,2], Sara Abdou[1,2], Rania El Gueddari[1,2], Imane Hassnaoui[1,2], Karima Nouni[1,2], Amine Lachgar[1,2], Hanan Elkacemi[1,2], Tayeb Kebdani[1,2], Khalid Hassouni[1,2]

[1]National Oncology Institute, Radiotherapy, Rabat, Morocco. [2]Faculty of Medicine and Pharmacy, Medicine, Rabat, Morocco

Topic

RTT

Keywords

nasopharyngeal cancer; reirradiation

Purpose/Objective

The local control rate of nasopharyngeal carcinomas has increasingly increased since the routine use of intensity-modulated conformal radiotherapy. The treatment of local recurrences is essentially based on reirradiation; but it is limited by the doses previously received by the organs at risk in series. Evaluate the Efficacy and Toxicity of Reirradiation of Local Relapses of Nasopharyngeal Carcinoma

Material/Methods

This is a retrospective study, including 12 patients re-irradiated at the National Institute of Oncology in Rabat for a local or locoregional relapse between 2015 and 2020.

Results

Among 600 irradiated patients, 12 patients had a local or locoregional recurrence for which they received intensity-modulated reirradiation. The average age of patients at the time of initial diagnosis was 40.8 years (range 22 to 52 years). The tumor was initially classified according to the AJCC 2017 classification stage II, stage III and stage IV in 2 cases (16%), 4 cases (34%) and 6 cases (50%) respectively. Initial treatment was based on neoadjuvant chemotherapy followed by concomitant chemoradiotherapy in 9 patients (75%) and concomitant chemoradiotherapy alone in 3 patients (30%). Initial irradiation was using a conventional three-dimensional technique having delivered a total dose of 70 Gy at a rate of 2 Gy per session. All patients were in complete remission. The average time to local relapse was 7 years (range: 3 years – 10 years). The diagnosis was confirmed by a pathological study in all patients. Recurrence was classified stage II, stage III and stage IV respectively in 3 cases (25%), 5 cases (41%) and 4 cases (33%). Therapeutically, 5 patients (50%) received neoadjuvant chemotherapy followed by concomitant chemoradiotherapy; 6 patients (90%) received radiochemotherapy concomitant therapy alone and one patient received exclusive radiotherapy. The reirradiation was with intensity modulation by Arc Therapy, having delivered a total dose of 60 Gy in all patients at a rate of 2Gy per fraction. After a mean follow-up of 19 months (range: 10 months – 34 months), seven patients were in complete remission; two died of the disease after an average follow-up of 10 months and three patients were lost to follow-up. The late toxicity of reirradiation was an increase in hearing toxicity (grade 3 becoming grade 4) in 4 patients, trismus in two patients and cervical fibrosis in two patients.

Conclusion

Reirradiation is the only salvage treatment for recurrences of nasopharyngeal carcinomas, precisely conformal radiotherapy with intensity modulation which makes it possible to deliver sufficient doses to the tumor volume while sparing the organs at risk already irradiated; however, given the associated toxicity, patients must be rigorously selected.

238

The role of PD-L1 and TILsCD8+ in oral cavity and pharyngeal cancers treated with definitive radiation

Natalia Cichowska-Cwalińska[1,2], Ewa Pawłowska[1], Michał Bieńkowski[2], Marta Popęda[2], Renata Zaucha[1]

[1]Medical University of Gdańsk, 1. Department of Oncology and Radiotherapy, Gdańsk, Poland. [2]Medical University of Gdańsk, 2. Early Phase Clinical Trials Centre, Gdańsk, Poland

Topic

Biology and molecular targeting

Keywords

PD-L1, radiotherapy, head and neck cancer

Purpose/Objective

The incidence of head and neck cancer (HNC) which is the seventh most common cancer worldwide, continues to rise due to tobacco-derived carcinogens, excessive alcohol consumption, and common infection with oncogenic strains of human papillomavirus (HPV) [1,2]. The steady increase in the number of HPV-related oropharyngeal cancers makes the landscape of HNC more heterogeneous. Radiation therapy (RT) remains the mainstay of treatment as a sole modality, in combination with chemotherapy (chemoradiotherapy, CRT) or adjuvant after surgery. However, reliable predictive markers of response to conventional RT or CRT have not been found, despite established knowledge about the predictors of checkpoint inhibitors in metastatic disease. In view of the unsatisfactory results of clinical trials using concurrent RT/CRT with immunotherapy, increasing attention is being paid to the local effects of RT on the tumor microenvironment and systemic immune response. We hypothesized that the baseline expression of programmed death 1 ligand (PD-L1) and intratumoral infiltration with CD8+ lymphocytes (TILsCD8+) score in the non-metastatic oral cavity (OC) and oro-/hypopharynx (PX) cancers may correlate with RT response.

Material/Methods

It was a retrospective single-center analysis involving OC and PX patients who underwent radical RT (66Gy prescribed to the primary tumor, given in 30 fx/6 weeks) with or without concurrent chemotherapy (Cisplatin 100 mg/m2 i.v. every three weeks or 40 mg/m2 i.v weekly). We performed analysis of TILsCD8+ and PD-L1 expression status in the archival biospecimens of the treatment-naïve primary tumor. Tissue microarrays (TMA) were prepared using the Manual Tissue Arrayer MTA-1 (Beecher Instruments, Inc., USA). The TMA sections were first stained with hematoxylin and eosin to verify the invasive neoplastic content within each core. Next, consecutive sections were stained with IVD-grade antibodies, anti-PD-L1 (SP263) and anti-CD8 (SP57). PD-L1 expression was assessed in tumor cells, as TPS. For statistical analysis, the patients were divided into three groups: consistently negative (all cores with no positive cells), heterogeneous, and consistently PD-L1 high (const-high, all cores with >30% positive cells). Next, for each patient, the mean number of TILsCD8 per 1.76 mm2 of invasive tumor was calculated and recorded semi-quantitatively. Scores of <5, 6–50, 51–199, and ≥200

lymphocytes per core were rated as immunoscores (IMs) of 0, 1, 2, and 3, respectively. For statistical analyses, patients were divided into two groups: TILsCD8-negative (IM = 0) and TILsCD8-positive (IM ≥ 1).

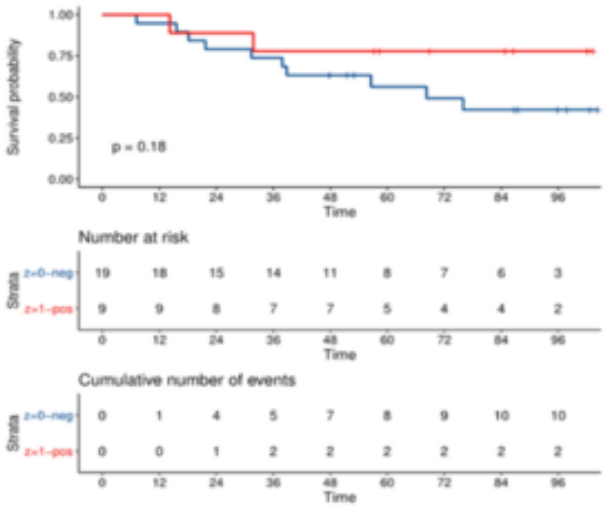
Results

Table 1. Baseline characteristic - OC and PX cancer patients.

		OC (n=33)			Univariate analysis		PX (n=28)			Univariate analysis	
		N	m5yrOS %	m5yrOS (months)	HR (95%CI)	cox p - val	N	m5yrOS	m5yrOS (months)	HR (95%CI)	cox p - val
Sex	Female	17	41.2%	91.3	Ref		9	66.7%	NA	Ref	
	Male	16	50.0%	74.7	0.82 (0.44 – 2.84)	0.713	19	52.6%	76.0	1.54 (0.42 – 5.70)	0.516
Age	< 60yo	18	38.9%	NA	Ref		13	69.2%	NA	Ref	
	≥ 60yo	15	53.3%	74.7	0.80 (0.31 - 2.06)	0.642	15	46.7%	72.1	2.07 (0.62 - 6.88)	0.237
AJCC 8th ed.	T1-2	14	42.9%	57.3	Ref		15	60%	NA	Ref	
T stage	T3-4	17	41.2%	76.1	0.75 (0.29 - 1.97)	0.565	13	53.8%	68.3	1.31 (0.42 - 4.06)	0.644
AJCC 8th ed.	N0	12	58.3%	NA	Ref		8	37.5%	57.4	Ref	
N stage	N1-3	19	31.6%	74.7	1.82 (0.64 - 5.15)	0.262	20	65.0%	NA	0.51 (0.16 - 1.61)	0.252
ECOG	0	11	81.8%	NA	Ref		17	58.8%	NA	Ref	
	≥ 1	22	27.3%	43.0	6.21 (1.42 - 27.24)	0.015	11	54.5%	76.0	1.24 (0.39 - 3.94)	0.711
Treatment	R-RT	16	31.3%	56.9	Ref		19	52.6%	68.3	Ref	
	PORT	17	58.8%	91.3	0.49 (0.19 - 1.27)	0.144	9	66.7%	NA	0.61 (0.16 - 2.27)	0.463
Chemotherapy	No	13	46.2%	91.3	Ref		5	20.0%	31.8	Ref	
	DDP q3w	6	50.0%	49.4	0.80 (0.21 - 3.11)	0.749	11	72.7%	NA	0.25 (0.05 - 1.11)	0.067
	DDP weekly	4	42.9%	76.1	0.89 (0.32 - 2.46)	0.818	12	58.3%	68.3	0.47 (0.12 - 1.77)	0.264
PD-L1	<1%	19	42.1%	91.3	Ref		19	47.4%	57.7	Ref	
	≥1%	14	50.0%	76.1	1.06 (0.41 - 2.74)	0.911	9	77.8%	NA	0.37 (0.08 - 1.70)	0.200
TILsCD8	negative	4	25.0%	70.4	Ref		1	100%	NA		
	positive	29	48.3%	76.1	1.00 (0.21 - 2.61)	0.650	27	55.6%	NA		

The study group was compromised of 61 patients (OC, n=33; PX, n=28). The cumulative 5-year overall survival (5YOS) rate was 57.58% and 64.29%, respectively. Patients were treated between 2012 and 2018, postoperatively (PORT; n=26) or qualified for definitive CRT (n=35). HPV-positive cancers accounted for 3% of OC and 54% of PX. In the OC and PX groups, more patients were PD-L1 negative, 57% and 67%, respectively (Table 1). The univariate analysis showed no influence of PD-L1 expression values on long-term survival. However, the survival curves of patients with PX and PD-L1 expression ≥1% vs. <1% visibly separate (p=0.18) (Figure 1). Most of the examined patients with OC showed a positive TILsCD8 score, with longer 5YOS compared to patients with score 0, however the difference did not reach statistical significance (OC - 48.3% vs 25%; p=0.65).

Figure 1. Survival probability and PD-L1 status in patients with oro/hypopharyngeal cancers



Blue line – PD-L1 negative (<1%), red line – PD-L1 positive (≥1%)

Conclusion

In our analysis, no association of PD-L1 expression and TILsCD8+ score, and patient outcome can be found. In univariate analysis we did not find any predictive factors for RT response. The main limitation of our study was very small group sizes.

References

1. Mody MD, Rocco JW, Yom SS, et al: Head and neck cancer. Lancet 398:2289-2299, 2021

2. https://gco.iacr.fr/overtime/en. Accessed October 10th, 2023

239

Re-irradiation in head and neck cancers: Real-world experience from a tertiary cancer institute

Siddharth Malukar, Satyajeet Rath, Suryanarayana Kunikullaya, Ankita Parikh, Vinay Shivhare, Niranjan Dash, Arun T, Maitrik Mehta, Sonal Patel Shah, Jayesh Singh, Akash Pandya, Viraj Modi, Dhara Patel, Krishna Prajapati

The Gujarat Cancer and Research Institute, Radiation Oncology, Ahmedabad, India

Topic

Multidisciplinary management

Keywords

Head and Neck Cancer, Re-irradiation, IMRT

Purpose/Objective

More than 1/3rd of head and neck cancer patients eventually fail loco-regionally or appear as second primary, despite ever-improving treatment options.1,2 Recommended potentially curative treatment options include salvage surgery if the disease is amenable to surgery, or reirradiation.2 Reirradiation of head and neck cancers presents a dilemma in terms of achieving adequate doses to the target, maintaining the organ-at-risks (OAR) dose constraints within limits, and managing toxicities emerging during and after the treatment.3–5 Intensity-modulated radiotherapy (IMRT) has slowly evolved to be the modality of choice for re-irradiation owing to its ability to improve disease control and reduce treatment-related toxicity.6 We present the data of re-irradiated head and neck cancer patients treated at our centre with IMRT.

Material/Methods

This was a retrospective single-arm observational analysis. Details of head and neck cancer patients treated at our hospital with re-irradiation were retrieved. After reviewing all the treatment records, the follow-up details were assembled.

All the cases were treated with IMRT with or without concurrent chemotherapy. All the patients received radiation and re-irradiation with a dose-per-fraction of 1.8 to 2Gray with adjuvant or definitive intent, for five days a week for six weeks or above. The dose prescribed was preferably 60 – 66Gy in 30-33

fractions. Dose constraints used for OARs were: Spinal cord Dmax <=45Gy, and brainstem and optic apparatus Dmax <=54Gy.3,5 Special care was also taken to limit the cumulative dose of carotid arteries to <120Gy.7 The mean dose of parotid was limited at 23Gy, although target volume coverage was given priority, whenever the two were in proximity.

Patients were immobilised using a 5-clamp head and neck thermoplastic mask. 3 mm slice thickness contrast-enhanced computed tomography (CT) images were obtained from vertex to 2 cm below the carina using Siemens Emotion 6 (Somatom, Germany). The treatment planning was done on MONACO (Version 5.11). The target volumes for definitive treatment were contoured as per ICRU 62.8 The decision to include nodes depended on certain factors: previous history of nodal positivity, nature of irradiation in the first radiotherapy schedule, nature and location of primary during second irradiation, definitive/adjuvant intent of re-irradiation, surgical resection of nodes, duration between the irradiation treatments, dose volumes used and dosimetric parameters achieved for OARs in the first radiotherapy.

Patients were treated by using linear accelerator (Elekta Compact and Synergy; Elekta, Crawley, UK). All patients were followed up on a regular basis. Response assessment scans were done after 3 months of treatment completion.

Overall Survival (OS) was defined time from start date of re-irradiation to the date of death or date of last clinical follow-up. Progression-free survival (PFS) was defined as interval from the start date of RT to any documented recurrence. Analysis was performed with the SPSS statistical (version 23.0; IBM, Armonk, NY, USA). All potential prognostic factors were analysed. the patients were divided into three prognostic subgroups using Multi-Institution Re-irradiation (MIRI) recursive partitioning analysis (RPA).9

Results

Seventy-three cases were included in the final analysis. During the re-irradiation schedule, 34/73 cases were treated with definitive irradiation, whereas 39 cases were treated with postoperative adjuvant radiotherapy. Median interval between both the RT schedules was 55 months (range: 13-197). Median follow-up duration after re-irradiation was 23 months (range: 4-74). Median initial RT dose was 60 Gy (range: 58-66) and median re-irradiation dose was 60Gy (range: 54-66). The median initial RT and re-irradiation dose was 2Gy (range: 1.8-2).

There were 41 events in PFS. The 2-year and 4-year PFS rates were 55.8% and 29.2%. The estimated 4-year DFS definitive re-irradiation versus adjuvant radiotherapy were 28.7 vs 29.3% (p-0.786).

There was no statistically significant difference for 3-year OS of de novo versus post-operative cases (54.7 vs 56.3%, p-0.559). No significant differences in DFS or OS were elucidated for duration of re-irradiation for a 2-year period (48.6 vs 39.7, p-0.648) and 3-year period (3yr DFS – 48 vs 57.5%, p-0.091).

Patients recurring within 2 years of primary radiation had poorer OS than those recurring after 2 years. (57.14 vs 49.25%, p-0.039). Patients with more than 3 high-risk factors during adjuvant reirradiation post-surgery had poor OS. (38.46 vs 31.5%, p-0.043). The number of cases in RPA Class I, II, and III were 16, 49 and 8, respectively. The 2-year DFS for Class I, II and III, were 62.5%, 59.7% and 12.5% (p<0.0001).

Conclusion

Re-irradiation in head and neck cancers is tolerable and toxicities are acceptable. A larger cohort and a longer duration of study will help in discerning the factors that will help in reducing the toxicities and improving outcomes further.

References

1. Bots WTC, van den Bosch S, Zwijnenburg EM, et al. Reirradiation of head and neck cancer: Long-term disease control and toxicity. Head Neck. 2017;39(6):1122-1130. doi:10.1002/hed.24733

2. Kim YS. Reirradiation of head and neck cancer in the era of intensity-modulated radiotherapy: patient selection, practical aspects, and current evidence. Radiat Oncol J. 2017;35(1):1-15. doi:10.3857/roj.2017.00122

3. Benson R, Giridhar P, Venkatesulu BP, Mallick S, Raza MW, Rath GK. Re-irradiation for head and neck squamous cell carcinoma. J Egypt Natl Canc Inst. 2017;29(1):1-9. doi:10.1016/j.jnci.2016.07.002

4. Popovtzer A, Gluck I, Chepeha DB, et al. The pattern of failure after reirradiation of recurrent squamous cell head and neck cancer: implications for defining the targets. Int J Radiat Oncol Biol Phys. 2009;74(5):1342-1347. doi:10.1016/j.ijrobp.2008.10.042

5. Lee N, Chan K, Bekelman JE, et al. Salvage re-irradiation for recurrent head and neck cancer. Int J Radiat Oncol Biol Phys. 2007;68(3):731-740. doi:10.1016/j.ijrobp.2006.12.055

6. Re-irradiation Using Intensity-modulated Radiotherapy for Recurrent and Second Primary Head and Neck Cancer. Anticancer Res. 2018;38(5). doi:10.21873/anticanres.12580

7. Embring A, Onjukka E, Mercke C, et al. Re-Irradiation for Head and Neck Cancer: Cumulative Dose to Organs at Risk and Late Side Effects. Cancers (Basel). 2021;13(13). doi:10.3390/cancers13133173

8. Stroom JC, Heijmen BJM. Geometrical uncertainties, radiotherapy planning margins, and the ICRU-62 report. Radiotherapy and Oncology. 2002;64(1):75-83. doi:10.1016/S0167-8140(02)00140-8

9. Ward MC, Riaz N, Caudell JJ, et al. Refining Patient Selection for Reirradiation of Head and Neck Squamous Carcinoma in the IMRT Era: A Multi-institution Cohort Study by the MIRI Collaborative. Int J Radiat Oncol Biol Phys. 2018;100(3):586-594. doi:10.1016/j.ijrobp.2017.06.012

243

Sarcomatoid carcinoma in Head and Neck cancers: Clinical features and prognosis

Léa Loriguet, Anne Auperin, Randa Chehab, Odile Casiraghi, Antoine Moya-Plana, France Nguyen, Yungan Tao, Francois Bidault, Gabriel Garcia, Mariana Iacob, Antoine Fouilloux, Francois Régis Ferrand, Alecsandra Gorzo, Dragos Goada, Ingrid Breuskin, Caroline Even

Gustave Roussy, Head and neck cancer, Villejuif, France

Topic

Epidemiology and prevention

Keywords

Sarcomatoid carcinoma, head and neck, prognosis

Purpose/Objective

Sarcomatoid carcinoma of head and neck is a rare type of squamous cell carcinoma (SCC) with sarcomatoid features associated with a poor prognosis.

This study aimed to summarize the clinical characteristics, prognosis and treatment options for these patients.

Material/Methods

Patients diagnosed with a sarcomatoid carcinoma of the head and neck between December 2012 to November 2022 were selected from the pathology database of Gustave Roussy. The data (patients, tumor characteristics, treatment, outcomes, etc.) were collected retrospectively. Multivariable prognosis analysis of progression free survival (PFS), and overall survival (OS) were performed.

Results

A total of 57 cases of sarcomatoid carcinoma were included. There were 41 (72%) males and 16 (28%) females. The median age at diagnosis was 64 years. The oral cavity (32%) and the larynx (26%) were the most common tumor sites, followed by the oropharynx (23%), posterior wall of the pharynx and maxillary sinus (5%). 17 patients (30%) were no smokers.

More than half of the patients (65%) presented with advanced-stage disease (T3, T4), 95% of them had no metastatic disease at diagnosis. A total of 37 patients (65%) had no previous history of head and neck cancers (de novo tumors), and 25 (44%) arised in irradiated areas.

Among all, 28 (49%) underwent a surgical treatment, for 9 (32%) the resection was R1, 9 patients had perineural invasion, and 6 of them presented vascular embols. 32% had nodal metastasis.

The other 51 % of patients received radiochemotherapy (n=15), palliative chemotherapy (n=10), or best supportive care (n=4).

The follow-up was 51.8 months. The median [95%CI] OS and PFS were 29.7 months [13.8;49.2] and 9.5 months [7.5;22.8].

The multivariable prognostic analysis showed that age, T stage, site (larynx and oral cavity), no history of head and neck cancer , and the presence of a tumor in irradiated site were significantly correlated with a poor OS. With the exception ofno history of head and neck cancer, all of the above negatively influenced the PFS

Conclusion

Sarcomatoid carcinoma is a different entity from the conventional SCC of head and neck. This type of tumor is very aggressive and has a poor prognosis. Tumors in irradiated site have a significant poor prognostic.

Further clinical trials are needed to establish the best treatment strategy for these tumors.

References

Lin Ding, Zhuo-Fei Bi, Hang Yuan, Xiao-Hui Zhao, Xue-Dan Guan, He-Rui Yao, Yi-Min Liu.Sarcomatoid Carcinoma in the Head and Neck: A Population-Based Analysis of Outcome and Survival. Laryngoscop 2021.

Katie M. Mingo, Adeeb Derakhshan, and Brian B. Burkey. Characteristics and Outcomes in Head and Neck Sarcomatoid Squamous Cell Carcinoma: The Cleveland Clinic Experience. Annals of Otology, Rhinology & Laryngology. 2020

Su H, Chu ST, Hou YY, Chang KP, Chen CJ. Spindle cell carcinoma of the oral cavity and oropharynx: factors affecting outcome. J Chin Med Assoc. 2006

244

weight loss during chemoradiotherapy in patients with nasopharyngeal cancers

Mona Taouchikht[1,2], Houda Fares[1,2], Sara Abdou[1,2], Rania El Gueddari[1,2], édith Tatiana Ngbwa[1,2], Imane Hassnaoui[1,2], Karima Nouni[1,2], Amine Lachgar[1,2], Hanan Elkacemi[1,2], Tayeb Kebdani[1,2], Khalid Hassouni[1,2]

[1]National Oncology Institute, Radiotherapy, Rabat, Morocco. [2]Faculty of Medicine and Pharmacy, Medicine, Rabat, Morocco

Topic

Quality of life and outcomes

Keywords

Weight loss, Concurrent chemoradiotherapy

Purpose/Objective

Concurrent chemo-radiotherapy (CCR) is currently the gold standard treatment for nasopharyngeal carcinoma (NPC). The objective of this retrospective study is to analyze the variations in weight observed in patients with nasopharyngeal cancers under concurrent chemo-radiotherapy, in order to optimize dietary care.

Material/Methods

240 patients with nasopharyngeal cancers, treated in the Radiotherapy department at the National Oncology Institute in Rabat between January 1st, 2018 and December 30, 2021 by curative concurrent chemo-radiotherapy, using the VMAT (Volumetric Modulated Arc Therapy) technique delivering 70 Gy in 33 fractions, with chemotherapy based on cisplatin (40mg / m2 / week) with an average of 5 cures.

Variations in weight were collected at the beginning, the mid, and the end of treatment.

Results

From the beginning to the end of treatment, it can be seen that 85% of patients lost weight (median = 6,05 kg [1,5kg- 13,6kg]), according to a separate distribution: 33% had lost more than 8 kg, 56% had lost between 3 and 8 kg, and only 11% had lost less than 3 kg.

Weight loss from mid to end of treatment (median = 3, 55 kg [1 kg−8,1kg]) was greater than that from baseline to mid-treatment (median = 2,5 kg [0,5 kg−5,5kg]) (P = 0.016).

For the rest of patients (15%) : 7% had kept a stable weight, and 8% gained an average of 2 to 6 kg.

Conclusion

Three-quarters of patients receiving concurrent chemo-radiotherapy lost weight during treatment, despite weekly adverse reaction monitoring.

Early nutrition intervention with dietary advice associated with oral nutritional supplementation is necessary in order to favorably influence the outcome of patients by limiting weight loss.

245

Tongue schwannoma: a clinicopathologic study of a case report with a systematic review

Rim Braham[1], Alia Methnani[1], Malek Driss[1], Alia Mousli[2], Aymen Sifaoui[1], Mohamed Dhaha[1], Souhail Jbali[1], sawsen Dhambri[1], Skander Kedous[1]

[1]Salah Azaiez institute, Cervico-facial surgery department-, Tunis, Tunisia. [2]Salah Azaiez institute, Radiotherapy, Tunis, Tunisia

Topic

Multidisciplinary management

Keywords

Tongue. schwannoma

Purpose/Objective

Schwannomas commonly occur in the head and neck but infrequently involve the oral cavity and rarely afect the tongue. In this observation, the clinical and pathologic characteristics of a rare case of schwannoma of the tongue was evaluated.

Material/Methods

A rare case of schwannoma of the tongue was evaluated.

Results

A 29-year-old man, without any significant medical history was referred to our Department of Otolaryngology and Cervicofacial Surgery at the Salah Azaiez Institute for evaluation of a mass in the tongue. .

Clinically, the patient presented with a lingual mass noted to be slowly increasing in size. He reported associated tongue pain localized to the lesion. The duration of symptoms was 12 months. Examination revealed a 1,5 cm mass on the right lateral part of the tongue.

It had semielastic consistency, is movable, causes pain when touched, and is covered by a nonulcerated mucosa. No radiologic investigations were needed because the mass was easily seen and palpable.

An excisional biopsy was done under general anesthesia by transoral approach. The entire lesion was removed completely from the tongue using blunt dissection.

There were no perioperative and postoperative complications, and there was no need for nasogastric tube insertion postoperatively. Tissue was sent for histopathologic examination.

On gross examination, the histopathologic examination reveals a well-defined neoformation surrounded by fibrous connective tissue in a capsule-like form where remains of nerve endings. There is no mitotic activity. The final diagnosis was a benign schwannoma.

The postoperative outcome was uneventful, with no signs of recurrence even after two years.

Conclusion

Although schwannomas are often asymptomatic, given enough time, they can cause significant health issues such as significant dysphagia, dysarthria, and obstructive sleep apnea. The rarity of lingual schwannoma may explain the limited knowledge concerning these tumours. The treatment is exclusively surgical. The prognosis is excellent after resection, as malignant transformation is exceptional.

248

Cisplatin Head & Neck Chemoradiotherapy: A Real-World Survival & Compliance Analysis of Weekly vs 3-Weekly Regimes

Jennifer Kahan, Gail Povey, Martin Rolles, Russell Banner

Swansea Bay University Health Board, South West Wales Cancer Centre, Swansea, United Kingdom

Topic

Quality of life and outcomes

Keywords

cisplatin, chemoradiotherapy, weekly

Purpose/Objective

Concurrent chemoradiotherapy with 100 mg/m2 cisplatin (Cis100) every 3 weeks has been the standard of care for locoregionally advanced head and neck squamous cell carcinomas (LAHNSCC) for many years (Grégoire). Full compliance with all three cycles is achieved in only around two thirds' cases (Szturz) and interest in alternative regimes has led some clinicians to adopt weekly cisplatin regime in the hope of improved toxicity, compliance and to ease capacity demands.

Low dose cisplatin chemotherapy regimens have been investigated in a number of studies. The use of weekly cisplatin at 40 mg/m2 (Cis40) is supported by a large, randomised phase III trial confirming weekly cisplatin is non-inferior to 3 weekly cisplatin, it was also better tolerated with less toxicity (Chatterjee). Additionally, evidence from the Japan Oncology Group found weekly Cis40 achieved comparable cumulative cisplatin dosing and was associated with a better overall survival (Kiyota).

Here we present a real-world retrospective analysis of 9 years of clinical data comparing weekly cisplatin versus 3-weekly cisplatin in both adjuvant and definitive settings for LAHNSCC. We aim to assess if there is a difference between regimens in terms of overall survival and assess compliance.

Material/Methods

Data was collected via the chemotherapy prescribing software, including all locally advanced head and neck patients registered for radical or adjuvant chemo-radiotherapy. Patients were treated in a single regional cancer centre between 02/09/2009 and 28/02/2018 with treatment was allocated according to clinician preference. Data was censored at date of death or at time of analysis with minimum 5.5yrs follow up.

Results

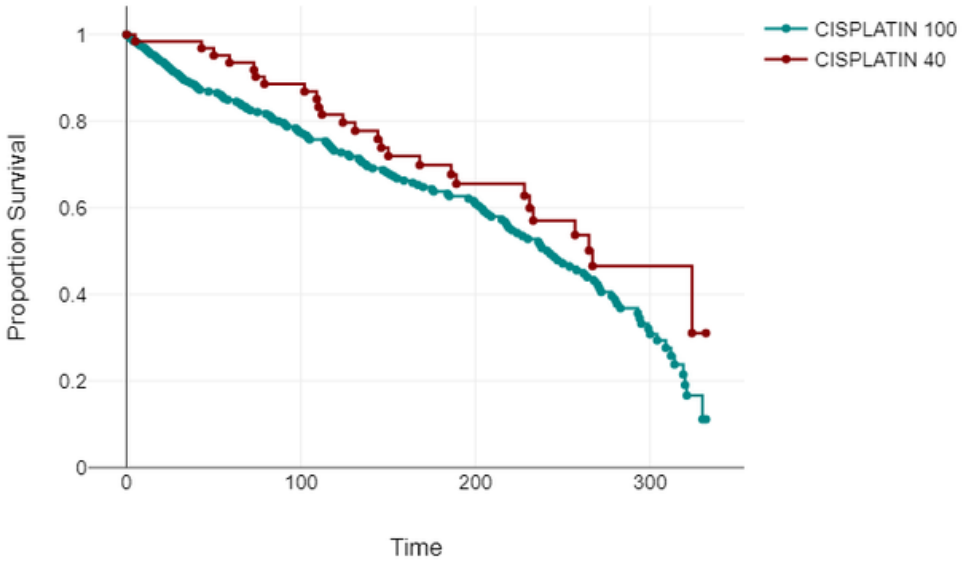
Over the time period 335 patients were treated for locally advanced head and neck cancers with cisplatin + radiotherapy. Three patients within the data set had adenocarcinoma and were removed from analysis. Of 332 patients, 269 received standard dose Cis100 every 3 weeks, 63 patients received Cis40 weekly. The groups were equally balanced; approximately three quarters of patients were male and one quarter female in both regimens. In both groups the average age was 59 years, (range in in Cis100 group was 31-79years and Cis40 was 37-78years).

Event free survival was calculated from the time of first chemotherapy to death or censorship. In the whole cohort of Cis100 median EFS was 82 months, (95% CI 71.95 to 84.96 months). Within the Cis40 group median EFS was 74 months, (CI 53.17 to 74.61 months).

		Frequency	Median	Interquartile Range	95% Confidence interval of Mean
mEFS from 1st Chemotherapy (months)	CISPLATIN 100	269	82	100	71.95; 84.96
	CISPLATIN 40	63	74	66	53.17; 74.61

139 patients in Cis100 group had died at the time of evaluation, 26 within the Cis40 group.

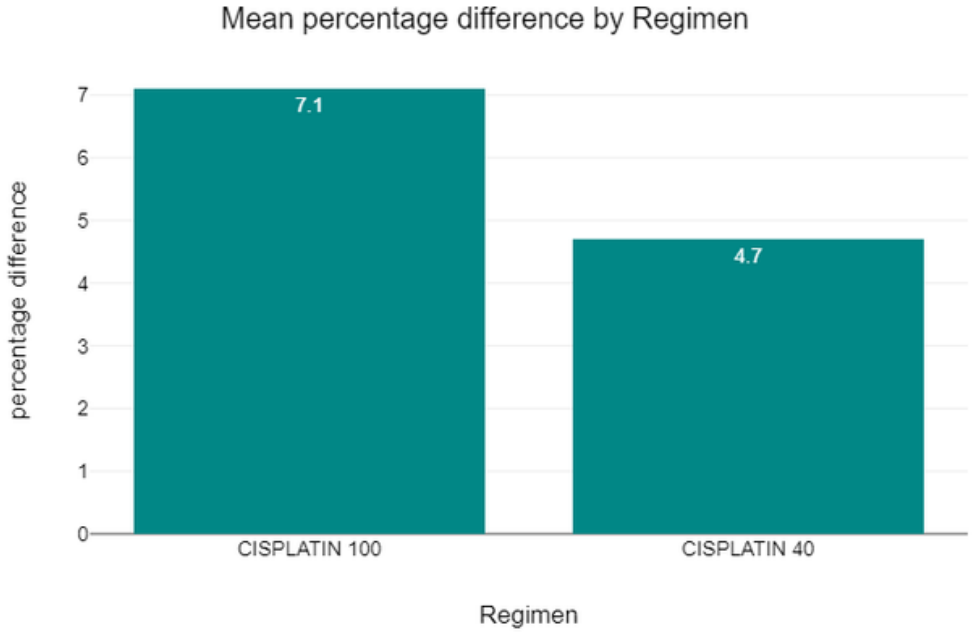
A log-rank test was calculated to see if there was a difference between groups Cis100 and Cis40 in time to event occurrence (death). For the present data, the log-rank test showed that there is no significant difference between the groups in terms of the distribution of time until the event occurs, p=.086. See Graph 1.



We wanted to assess the effect of chemotherapy dosing between the groups. Within the Cis100 group the average prescribed dose was 322mg of cisplatin with average received dose of 301mg, 13.4% of patients (36 of 269) received less than their prescribed dose. 50% or less of the prescribed dose was received by 11.2% (30 of 269).

In the Cis40 group the average prescribed dose was 321mg of cisplatin, with an average of 300mg received, 17.5% patients (11 of 63) received less than their prescribed dose of chemotherapy but only 1.6% (1 patient) received less than half of their prescribed dose.

The mean difference in chemotherapy prescribed to received was 7.1% and 4.7% in the Cis100 and Cis40 groups respectively. This showed a negative correlation which was not statistically significant. This is less than the previously documented reduction of dose within trial setting (Szturz).



The log-rank test was used to assess if a difference in OS existed between the two regimens taking into account the reduction of received chemotherapy. For the present data, there was no difference between the groups in terms of the distribution of time until the event occurs, p=.617.

Conclusion

This is a large real-world retrospective analysis suggesting no difference between Cis40 and Cis100 in terms of OS. There is a difference in percentage of chemotherapy successfully delivered between the regimens, but this does not translate into a difference in OS from our data.

References

Grégoire V, Lefebvre JL, Licitra L, Felip E; EHNS-ESMO-ESTRO Guidelines Working Group. Squamous cell carcinoma of the head and neck: EHNS-ESMO-ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. (2010) 21(Suppl. 5):v184–6. doi: 10.1093/annonc/mdq185

Szturz P, Wouters K, Kiyota N, Tahara M, Prabhash K, Noronha V, et al. Weekly low-dose versus three-weekly high-dose cisplatin for concurrent chemoradiation in locoregionally advanced non-nasopharyngeal head and neck cancer: a systematic review and meta-analysis of aggregate data. Oncologist. (2017) 22:1056–66. doi: 10.1634/theoncologist.2017-0015

Chatterjee, S, Kiyota, N, Vaish, R, et al. Weekly versus 3-weekly cisplatin along with radiotherapy for locoregionally advanced non-nasopharyngeal head and neck cancers: Is the equipoise in literature addressed yet? Head & Neck. 2023; 45(6): 1594-1603. doi:10.1002/hed.27365

Kiyota N, Tahara M, Mizusawa J, et al. Weekly Cisplatin Plus Radiation for Postoperative Head and Neck Cancer (JCOG1008): A Multicenter, Noninferiority, Phase II/III Randomized Controlled Trial. J Clin Oncol. 2022;40(18):1980-1990. doi:10.1200/JCO.21.01293

249

External validation of a predictive model for severe malnutrition developed on a multicenter real-life cohort from UNITRAD

Paul Giraud[1], Sebastien Guihard[2], Sebastien Thureau[3], Philippe Guilbert[4], Amandine Ruffier[5], Remi Eugene[6], Aissa Lamrani-Ghaouti[7], Cyrus Chargari[8], Xavier Liem[9], Jean Emmanuel Bibault[10]

[1]INSERM, UMR 1138, Paris, France. [2]ICANS, Radiation Oncology, Strasbourg, France. [3]Centre Henri Becquerel, Radiation Oncology, Rouen, France. [4]Institut Jean Godinot, Radiation Oncology, Paris, France. [5]Centre Cancerologique de la Sarthe, Radiation Oncology, Le Mans, France. [6]Elekta, Informatics, Paris, France. [7]Unicancer, Research, Paris, France. [8]Pitié Salpêtrière, Radiation Oncology, Paris, France. [9]Oscar Lambret, Radiation Oncology, Lille, France. [10]HEGP, Radiation Oncology, Paris, France

Topic

Imaging, radiomics and artificial intelligence

Keywords

Malnutrition, Head and Neck, AI

Purpose/Objective

Sarcopenia in the context of head and neck cancers is associated with poorer survival. Severe malnutrition resulting from rapid weight loss, aphagia, or anorexia during treatment is difficult to anticipate. Anticipating it would allow for preventive actions, such as the placement of a prophylactic gastrostomy. The goal was to develop an interpretable predictive model using real-life data to predict severe malnutrition.

Material/Methods

Unitrad initiated a standardization effort for routine clinical use of structured forms on MOSAIQ (Elekta) for collecting baseline and acute clinical data during head and neck radiotherapy in three centers. Consequently, baseline data from 410 patients without missing information (the UNITRAD cohort) were split into a training cohort (80%) and a validation cohort (20%). Model performance on the validation sample was compared with performance tested on an external monocentric cohort (CHB cohort) of 230 prospectively collected patients. XGBoost was employed for model development, and interpretation of the model's predictions at the individual patient level was performed using Shapley values.

Results

The predictive performance on the UNITRAD validation cohort showed a positive predictive value (PPV) of 86.36%, a negative predictive value (NPV) of 83.78%, a receiver operating characteristic area under the curve (ROC AUC) of 0.89, and a precision-recall curve AUC of 0.79. Performance on the CHB cohort revealed a PPV of 72.32%, an NPV of 72%, an ROC AUC of 0.75, and a precision-recall curve AUC of 0.74. The clinical variables most frequently calculated with Shapley values were the presence of concurrent chemotherapy, the location, and the T and N stage. For each patient, a diagram can be displayed, showing the factors that contributed to increasing or decreasing the final probability predicted by the model.

Conclusion

Real-world data collected as part of routine clinical practice in the oncology information software were leveraged to develop a predictive model for severe malnutrition. The model performed satisfactorily on the UNITRAD validation cohort and the external validation cohort from CHB, albeit with an increased error rate in the external cohort. The next steps include enhancing the model with dosimetric parameters and conducting a prospective study to assess its impact on clinical decision-making.

252

Impact of Anatomopathological Characteristics on Salivary Gland Carcinoma Prognosis Undergoing Radiotherapy

Alice Manuela Alves, Catarina van der Elzen, Filipa Abreu Martins, Ana Rita Lago, João Casalta Lopes, Lurdes Alves Vendeira, Maria Gabriela Pinto

Centro Hospitalar Universitário São João, Radiotherapy, Porto, Portugal

Topic

Salivary gland, skull base, skin and thyroid cancers

Keywords

Salivary Gland, Radiation therapy

Purpose/Objective

Salivary Gland Carcinomas (SGCs) are a group of rare tumors characterized by their aggressiveness, high recurrence and metastasis rates, and significant heterogeneity. Treatment involves surgery and adjuvant radiotherapy (RT). Systemic therapy is personalized based on immunohistochemical and genetic markers. The main aim of this work was to assess the impact of the immunohistochemical and histological characteristics of SGCs on overall survival (OS) and disease-free survival (DFS) in patients undergoing RT.

Material/Methods

Included cases of SGCs treated at the RT Service of CHUSJ between January 2018 and June 2023, with a total dose of 60-70 Gy in 30/35 fractions. Statistical analysis was performed using IBM SPSS Statistics version 29; survival analysis (OS and DFS) was conducted using the Kaplan-Meier method and Log-Rank test; a type I error of 0.05 was considered.

Results

We included 24 patients with SGCs of the major glands, with a median age at diagnosis of 73 years, and 70.8% were male. The treatment intention was palliative in 16.4%, and among those with curative intent, 25% developed recurrent/metastatic disease. The most frequent histological subtypes were squamous cell carcinoma (37.5%), salivary duct carcinoma (16.7%), and myoepithelial carcinoma (12.5%). With a median follow-up of 10 months, we observed an OS of 94.1% and a DFS of 67.8% at 9 and 20 months. Immunohistochemical expression of Ki67 and cyclin D1 had a positive impact on DFS (p=0.027).

Conclusion

Despite the limitations arising from the sample's size and heterogeneity, this study suggests that the expression of Ki67 and cyclin D1 may have a prognostic impact on patients with SGCs undergoing RT.

References

Lassche, G., et al. Identification of Fusion Genes and Targets for Genetically Matched Therapies in a Large Cohort of Salivary Gland Cancer Patients. Cancers, 14, 4156. (2022). https://doi.org/10.3390/cancers14174156

L. S. Monteiro et al, Epidermal growth factor receptor immunoexpression evaluation in malignant salivary gland tumours. J Oral Pathol Med 38, 508–513. (2009)

Soper, M. S., Iganej, S., Thompson, L. D. R. Definitive treatment of androgen receptor-positive salivary duct carcinoma with androgen deprivation therapy and external beam radiotherapy. PMID: 23720164. DOI: 10.1002/hed.23383.

254

survival outcome of chemotherapy and radiotherapy in patients with metastatic tonsillar cancer(M1)

Amr Aly

Faculty of medicines Suez Canal University, Pathology, Ismailia, Egypt

Topic

Innovative treatments

Keywords

Metastatic tonsillar cancer, Adjuvant therapy,

Purpose/Objective

Tonsillar Cancer is among the rarest types of cancer. However, it constitutes 25% of all oral cavity cancers. Tonsillar Cancer has an overall good prognosis as it causes early symptoms which leads to early diagnosis and treatment. Surgery is the best treatment for early-stage Tonsillar Cancer however, there are some debates whether chemotherapy or radiotherapy are effective treatment modalities for metastatic Tonsillar Cancer. Accordingly, this study aims to evaluate the value of these treatment options for M1 tonsillar cancer.

Material/Methods

We extracted the data of 716 patients from the Surveillance, Epidemiology, and End Results (SEER) database whom were diagnosed between 2000-2020. All of them had Metastatic Tonsillar Cancer (M1). We divided the patients into 4 groups; chemotherapy, radiotherapy, combined chemoradiotherapy and no systemic therapy. We calculated the 5-year relative survival for each group. Kaplan-Meier curve and log rank test were performed using SPSS 25 for survival analysis. We also used the Cox regression hazard model to evaluate age, sex, year of diagnosis, race, months from diagnosis to treatment, chemotherapy, radiotherapy, and laterality as predictors of outcome.

Results

The 5-year overall survival of Metastatic Tonsillar Cancer was 23.7%; $P<0.001$. The 5-year relative survival of chemotherapy, radiotherapy, combined chemoradiotherapy and no systemic therapy were (8.4% ,26.8%, 31.7%, 11.4%; $P<0.001$). Age and Months from diagnosis were significant predictor of outcome both having a hazard ratio (HR) of 1; $P<0.001$. Chemotherapy and radiotherapy were also of significant prognostic value with HR of 0.74; $P<0.005$ and 0.86; $P<0.045$ respectively. Sex, year of diagnosis, race and laterality were of no significant value as predictors; $P>0.05$.

Conclusion

Metastatic Tonsillar Caner had an overall poor prognosis. Our results indicated that combined chemoradiotherapy showed the best survival outcomes followed by radiotherapy. Age and months from treatment were neutral prognostic value as they neither worsen nor improve outcomes. We recommend combined chemoradiotherapy as the first line treatment option for Metastatic tonsillar cancer. We also recommend radiotherapy in patients who can't tolerate chemotherapy. Chemotherapy alone is not recommended as it showed the poorest survival outcome.

256

comparison of clinicopathological and prognostic features of HPV positive and HPV negative head and neck squamous cell carcinoma (HNSCC)

Amr Aly

Faculty of medicines Suez Canal University, Pathology, Ismailia, Egypt

Topic

HPV or EBV related cancers

Keywords

HPV+ versus HPV-, Clinicopathological features

Purpose/Objective

Squamous cell carcinoma accounts for 95% of head and neck cancers (HNSCC). Recently, Human papilloma virus associated HNSCC have shown rising incidence rates specifically caused by HPV-16 subtype. There have been limited data to differentiate the pathological and prognostic behaviors of HPV+ versus HPV- HNSCC. So, that is the aim of our study.

Material/Methods

Data of 8802 HNSCC patients were extracted from the Surveillance, Epidemiological, and End Results (SEER) database diagnosed from 2000-2020. The histopathological classification of HPV+ and HPV- HNSCC were according to WHO ICD-0-3 classification. Cox regression hazard model was performed using SPSS 25 to assess age, race, sex, radiotherapy, chemotherapy and surgery as predictors for outcome.

Results

HPV+ and HPV- HNSCC were found to be more common in males and white race. Increasing age was associated with poorer prognosis in HPV+ with a hazard ratio (HR) of 1.05; $P<0.05$, however it was insignificant predictor for HPV-; $P>0.05$. Surgery, radiotherapy and chemotherapy were all associated with better outcomes for HPV+; HR: 0.21, 0.23, 0.83; respectively; $P<0.05$. For HPV-, having surgery and radiotherapy were significant good prognostic factors; HR: 0.35 and 0.28 respectively; $P<0.05$. while chemotherapy wasn't significant; $P>0.05$. Race and Sex weren't statistically significant for HPV+ and HPV- HNSCC.

Conclusion

HPV+ HNSCC Showed an overall better prognosis than HPV- HNSCC. In terms of demographic characteristics. Increasing age had a poor prognostic outcome for HPV+ but no impact on prognosis for HPV-. Age and Sex were insignificant predictors for both groups. Surgery and Radiotherapy showed better prognostic value for both groups. Our results showed better outcomes of surgery and radiotherapy in HPV+ HNSCC compared to HPV- HNSCC. Chemotherapy showed slightly good prognostic outcomes for HPV+ but had no impact on outcomes for HPV-. We recommend radiotherapy and surgery to be the first line of treatment for both HPV+ and HPV- HNSCC. Chemotherapy can be preserved for selective HPV+ patients while for HPV- it had no value so, we don't recommend and we can avoid unnecessary side effects unless there are other indications.

257

risk of second primary cancer in HPV+ head and neck squamous cell carcinoma (HNSCC)

Amr Aly

Faculty of medicines Suez Canal University, Pathology, Ismailia, Egypt

Topic

HPV or EBV related cancers

Keywords

HPV+ HNSCC, risk of second primary

Purpose/Objective

Human papilloma virus (HPV) was long known to be primarily causing cervical cancers. However, recently, HPV was discovered to be carcinogenic in other regions in the body most predominantly in the head and neck region. We have little information about the nature of HPV caused head and neck SCC and its associations with a second primary cancer in the head and neck region and non-head and neck regions. So, that is the aim of our study.

Material/Methods

Data of 8,547 patients were extracted from the Surveillance, Epidemiology, and End Results (SEER) database diagnosed from 2000-2019. Using MP-SIR seer session, the standardized incident ratio (SIR) was assessed as Observed/Expected (O/E) ratio and Excess Absolute Risk (EAR) is per 10000. Confidence intervals are 95% and P value is significant $P<0.05$. We assessed the risk of a second primary cancer in both head and neck regions and distant regions.

Results

Out of all patients, 652 got a second primary tumor for which 407 were in the head and neck region and 245 were in distant sites. The primary sites at risk for a second primary tumor in the head and neck region were the tonsils and the tongue. The tonsils had the highest risk of a second primary tumor of an EAR=105.6, and O/E= 730.8 ($P<0.05$, 95%CI: 608.3-870.8) with the highest risk being at 12-59 months after the diagnosis of HPV+ HNSCC; EAR=109.3, O/E=741.6 ($P<0.05$, 95%CI: 557.1-967.6). The tongue was found to be at the second highest risk with an overall EAR=97 and O/E=340.19 ($P<0.05$, 95%CI: 280.9-408.4). The highest risk for second primary tongue cancer was at the first 11 months with EAR=101.3, O/E=362.3 ($P<0.05$, 95%CI: 282.5-457.8).

For non-head and neck regions, Sites with the highest risk were the esophagus and the lungs. The esophagus had the biggest risk with an EAR=10, O/E=6.4 ($P<0.05$, 95%CI: 3.5-10.80). The highest risk was at months 12-59 with EAR=12.3, O/E=7.6 ($P<0.05$, 95%CI: 3.1-15.6). Lungs were the second with EAR=8.5, O/E=1.8 ($P<0.05$, 95%CI: 1.1-2.7) and the highest risk was at months 12-59 with EAR=23.3, O/E=3.1 ($P<0.05$, 95%CI: 1.8-5).

Conclusion

These results showed that 7.6% of patient with primary HPV+ HNSCC suffered a second primary cancer. The tonsils showed an overall 730-fold risk to develop a second primary tumor with the highest risk to

be between 12-59 months of HPV+ HNSCC diagnosis. The tongue had a 340-fold risk increase for developing second primary cancer with highest risk at the first 11 months.

Regarding distant region, the esophagus had 6-fold increase in the chances of developing a second primary cancer while it was around 2-fold risk for the lungs. Both had the highest risk at months 12-59

We recommend follow up screening of newly diagnosed patients in the first 11 months for tongue cancer and at months 12-59 for tonsillar cancer. For non-head and neck region, we only recommend screening follow up for high risk patients at months 12-59 for both esophageal and lung cancer.

258

Radiotherapy in the Treatment of Early-Stage Glottic Laryngeal Carcinoma - Experience from a Hospital Center

Alice Manuela Alves, Catarina van der Elzen, Filipa Manuela Martins, Ana Rita Lago, João Casalta Lopes, Lurdes Alves Vendeira, Maria Gabriela Pinto

Centro Hospitalar Universitário São João, Radiotherapy, Porto, Portugal

Topic

RTT

Keywords

Glottic laryngeal, Radiotherapy, Toxicities

Purpose/Objective

Laryngeal carcinoma represents 1-2% of all malignant neoplasms worldwide. Glottic laryngeal carcinoma (GLC) can present with involvement restricted to the vocal cords or extend to the anterior and posterior commissures, with approximately 3/4 of cases being diagnosed in early stages. Radiotherapy (RT) and laser surgery have become the standard of care for the treatment of early-stage GLC, offering high disease control rates and the advantage of organ preservation with maintenance of phonatory function. The primary objective of this study is to evaluate overall survival (OS), disease-free survival (DFS), and treatment-related toxicity in patients with stage cT1-T2N0M0 GLC.

Material/Methods

We retrospectively analyzed 16 cases of cT1-T2N0M0 glottic laryngeal carcinoma diagnosed and treated in our Department of Radiotherapy from January 2018 to June 2023. Radiotherapy regimens applied consisted of 70 Gy in 35 fractions of 2 Gy/day and 63 Gy in 28 fractions of 2.25 Gy/day. Data collection was performed through a review of clinical records. Data were analyzed using IBM SPSS Statistics version 29. We conducted a descriptive analysis of sociodemographic variables, assessed OS and DFS rates, and evaluated treatment-related toxicities based on the RTOG/EORTC toxicity scale. Survival analysis was conducted using the Kaplan-Meier method, and comparisons were made using the Log-Rank test, with a significance level of 0.05 considered for statistical inference.

Results

The median age at diagnosis was 65.5 years, and the mean follow-up time was approximately 25 months. For the time period analyzed, OS was 87.5%, and DFS reached 93.8%. Among the cases analyzed, 50% presented involvement of the anterior commissure of the larynx, and at 5 years, an OS rate of 70% and a DFS of 50% were observed (without statistically significant differences). The most frequent acute toxicity symptoms were odynophagia (n=11/16) and erythema (n=13/16). Odynophagia manifested approximately 16 days after the start of treatment, and erythema appeared after 28 days of treatment. No acute toxicity symptoms led to treatment interruption.

Conclusion

Radiotherapy treatment in patients with cT1-T2N0 glottic laryngeal carcinoma demonstrated favorable OS and DFS results, consistent with the literature. Additionally, RT-related toxicity was well-tolerated in the studied population, as no patients discontinued treatment due to toxicity. The analyzed sample suggests that RT remains an effective treatment option for early-stage GLC patients, offering a promising perspective for disease control and preservation of phonatory function. Nevertheless, it is essential to emphasize the need for long-term follow-up of these patients to evaluate long-term survival and the incidence of late toxicities.

References

Andrew M Coughlin, MD et al, Glottic Cancer,Mesacpe. Dec 03, 2021.

Yamazaki H, et al. Radiotherapy for early glottic carcinoma (t1n0m0): results of prospective randomized study of radiation fraction size and overall treatment time. Int. J. Radiation Oncology Biol. Phys., Vol. 64, No. 1, pp. 77–82, 2006

259

Acute swallowing outcomes in oropharyngeal cancers following clinical introduction of dysphagia-optimised IMRT (DO-IMRT) at a single tertiary centre

Karen Chan, Teresa GuereroUrbano, Anthony Kong, Mary Lei, Miguel Reis Ferriera, Imran Petkar

Guys and St Thomas NHS Trust, Head and Neck Cancer, London, United Kingdom

Topic

Quality of life and outcomes

Keywords

DO-IMRT, dysphagia, oropharyngeal cancer

Purpose/Objective

Swallowing dysfunction following curative (chemo) radiotherapy (RT) for head and neck cancers (HNC) is a significant treatment-related morbidity. Dysphagia-optimised IMRT (DO-IMRT) has recently shown to improve patient-reported swallowing outcomes, by reducing RT dose to dysphagia and aspiration – related structures. We implemented DO-IMRT in HNC patients undergoing primary radical RT-based

treatment at our institution in August 2021. The objective of this retrospective analysis was to evaluate patient-reported and physician-scored acute swallowing toxicities in oropharyngeal squamous cell carcinoma (OPSCC) treated with DO-IMRT.

Material/Methods

Eligibility criteria included newly diagnosed OPSCC, treatment with primary radical DO-IMRT to the oropharynx and bilateral neck, alive and with no evidence of loco-regional recurrence at a minimum of 6 months following treatment completion. All patients received 65 Gy/30 fractions/6 weeks to the planning target volume (PTV1) of the tumour and involved nodes and 54 Gy/30 fractions/6 weeks to regions at risk of microscopic disease (PTV2) +/- chemotherapy as per institutional guidelines. Volumes of extended oral cavity, superior pharyngeal constrictor (PC), middle PC, inferior PC and larynx lying outside the PTVs were set optimal mean dose constraints of < 40 Gy, < 50 Gy, < 50 Gy, < 50 Gy, and < 30 Gy respectively during the optimisation process. Under-dosage of PTVs was not permitted to meet optimal dose constraints. Patients prospectively completed MD Anderson dysphagia inventory (MDADI), a patient-reported swallowing questionnaire, at baseline, week 6 , 3 –, 6 –, 12 – and 24 months following treatment completion and a composite MDADI score for each point was generated. Prospective physician-scored toxicities using CTCAE v5.0 were also recorded at the above timepoints. This analysis evaluated swallowing outcomes measures upto 6 months post-RT. Descriptive statistics were used to report results.

Results

47/56 OPSCC patients treated between August 2021 and February 2023 met the eligibility criteria. Baseline patient and tumour characteristics are presented in table 1. Majority of tumours were stage IV (AJCC 7thedition), human papillomavirus-associated, and treated with concomitant CRT. Mean (SD) composite MDADI scores at baseline, week 6, 3- and 6- months post treatment were 84 (15.0), 55.4 (12.8), 66.1 (18.3) and 73.1 (19.1) respectively (Table 2). Compared to baseline, 7 % and 11 % of patients reported a 10-point (clinically significant) improvement in composite MDADI score at 3 and 6 months respectively. The proportion of patients recording a clinically significant worse score was 87 %, 67 % and 53 % at week 6, and at 3- and 6 – months. 18 (38 %) patients required feeding tube (FT) insertion. 2 (4 %) patients were FT- dependent at 6 months. Majority of patients (81 %) had < grade 2 dysphagia at 6 months.

Table 1 : Baseline characteristics

Characteristics	
Sex	
Male	32 (68 %)
Female	15 (32 %)
Age at diagnosis	
Median	62
Range	51 - 77
Tumour subsite	
Base of tongue	15 (32 %)
Tonsil	27 (57 %)
Soft palate	5 (11 %)
HPV status	
Positive	38 (81 %)

Negative	9 (19%)
Smoking history	
Never	13 (28 %)
< 10 pack year	11 (23 %)
> 10 pack year	21 (45 %)
Unknown	2 (4 %)
Tumour staging	
T1	5 (11 %)
T2	9 (19%)
T3	7 (15 %)
T4	26 (55 %)
Nodal staging (AJCC 7th edition)	
N0	10 (20 %)
N1	6 (13 %)
N2a	6 (13 %)
N2b	13 (28 %)
N2c	7 (15 %)
N3	5 (11 %)
TNM staging	
I	1 (2 %)
II	4 (9 %)
III	3 (6%)
IV	39 (83 %)
Treatment	
CRT	34 (72%)
IC + CRT	4 (9 %)
RT	9 (19 %)

Composite MDADI score	N with data	Mean	SD
Baseline	47	84	15.0
Week 6	45	55.4	12.8
3 months post - RT	42	66.1	18.3
6 months post – RT	46	73.1	19.1
Change – Baseline to week 6	45	-28.5	16.8
Change – Baseline to 3 months	42	-18.3	17.1
Change – Baseline to 6 months	46	-11.1	18.4

Table 2: MDADI composite scores at different timepoints

Conclusion

FT-dependence in this initial cohort of OPSCC patients treated with DO-IMRT at our centre is low and compares favourably to contemporary data. Swallowing-related quality of life outcomes appear

promising, with incremental improvements at 3- and 6-months post treatment. Future work includes assessment of longitudinal toxicity data, and the relationship between RT dose swallowing structures and toxicity.

References

1. Nutting C, Finneran L, Roe J, Petkar I, Rooney K, Hall E, et al. Dysphagia-optimised intensity-modulated radiotherapy versus standard radiotherapy in patients with pharyngeal cancer. Lancet Oncol. 2023;24(10):e398.

261

Radiotherapy as a therapeutic weapon in the adjuvance of nasosinusal adenocarcinoma intestinal-type

Catarina v.d. Elzen, Alice Alves, Filipa Abreu Martins, Ana Rita Lago, João Casalta Lopes, Maria Gabriela Pinto

Centro Hospitalar Universitário de São João, Serviço de Radioterapia, Porto, Portugal

Topic

Multidisciplinary management

Keywords

nasosinusal; adenocarcinoma; radiotherapy

Purpose/Objective

Intestinal-type adenocarcinoma (ITA) is the second most common nasosinusal adenocarcinoma. It occurs mainly in men and has a high incidence in workers exposed to wood dust. If resectable at diagnosis, surgical excision of the lesion plays a decisive role, with radiotherapy (RT) being a very important therapeutic weapon in these lesions, either as an adjuvant treatment or as a radical treatment in inoperable tumors. The objective of this study was to analyze demographic data, clinical presentation, risk factors, the applicability and treatment of radiotherapy and the survival of patients with nasosinusal adenocarcinoma of the intestinal type.

Material/Methods

Retrospective study of patients with nasosinusal adenocarcinoma intestinal-type treated between 2013 and 2022, at the Radiotherapy Service of Centro Hospitalar Universitário de São João. Statistical analysis was performed using IBM SPSS Statistics version 29. Survival analysis was performed using the Kaplan-Meier method and comparisons using the Log-Rank test. Considered a significance level of 0.05.

Results

Nineteen patients were identified, all male. One locksmith and 18 carpenter patients. The average age at diagnosis was 58.7 years and the average follow-up time was 22.9 months. Nasal obstruction with rhinorrhea (73.7%), orbital complaints (13.2%) and epistaxis (13.2%) were the symptoms presented at diagnosis. At diagnosis, 10 patients were T4, 4 patients T3, 2 patients T2 and 2 patients T; 17 N0M0

patients and 2 NxMx patients. In the pathological anatomy of surgical resection, 14 patients had Rx margins, 2 with R0 margins, 2 patients with R1 margins and 1 patient with R2 margin. The most common therapy was surgery with adjuvant radiotherapy. The total dose range used in RT was 56-70Gy with conventional fractionation, 1x/day, 5 days/week, with 2 patients undergoing the 3D-CRT technique and the remaining 17 with VMAT. The most serious toxicity described was G2 enanthema (1 patient), with 5 patients without toxicities. Overall and disease-free survival were 68.4% and 57.9%. Six patients died, 2 due to non-oncological disease, 5 are alive with disease progression, 4 alive with stable disease and 4 with no evidence of recurrence. Distant metastasis was 26.4%. Intracranial invasion influenced both local disease-free survival (p=0.001) and global disease-free survival (p=0.005). Venous invasion had an impact on distant metastasis-free survival (p=0.01).

Conclusion

Sinonasal adenocarcinomas are heterogeneous tumors, essentially with local recurrence and a poor functional and vital prognosis. Multidisciplinary evaluation of these patients is mandatory, as radiotherapy plays an important role in the treatment of sinonasal cancer, especially in an adjuvant setting after surgical resection. Our retrospective study demonstrated that R0 resectability is often difficult to ensure and therefore adjuvant treatment is important. The total dose regimen of 60 Gy in 30 fractions is the most commonly used. In our sample, imaging-proven intracranial invasion and histological venous invasion are associated with a worse prognosis.

262

Risk of Depression in tongue cancer patients as Per Hospital Anxiety and Depression Scale

imane lahlali[1], agdi boutaina[1], amine lachgar[2], hanan elkacemi[1], tayeb kebdani[1], khalid hassouni[1]

[1]ino, faculty of medecine, RABAT, Morocco. [2]RABAT, radiotherapy, RABAT, Morocco

Topic

Quality of life and outcomes

Keywords

Depression, Tongue cancer

Purpose/Objective

tongue cancer patients are at risk of depression during treatment yet there are very few tools to highlight patients at risk. We aimed to use a validated scale to identify risk factors associated with post treatment depression in oral cancer patients.

Material/Methods

We conducted a cross sectional study from January 2022 to September 2023 during post-therapeutic monitoring in the radiotherapy department of the rabat national oncology institute. Tongue cancer patients filled out Hospital Anxiety and Depression Scale questionnaire post RCC. Factors associated with risk of depression were analysed

Results

56 patients participated in the study, 64.7% of them being males. Females had a significantly higher mean depression score of 14.20 compared to males score of 11.96. Females and patients with buccal tumors were associated with a higher risk of post treatment depression.

Conclusion

Tongue cancer patients, especially females, need special attention in regard to their psychological well-being post treatment to optimize patient compliance, improve patient care and quality of life.