10TH EUROPEAN CONGRESS ON HEAD & NECK ONCOLOGY

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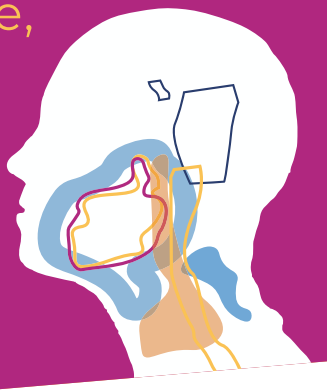

ABSTRACT BOOK

ORAL COMMUNICATIONS

POSTERS

PO309 Therapy with Cetuximab in Laryngeal Carcinoma: May HER1 Be Useful in the Bioselection of Patients?

PO311 Radiosurgery in the treatment of oligometastatic disease from head and neck cancer. Is there a role?

PO313 Nasopharynx carcinoma: predictive factors of survival outcomes – RWD real world data

PO314 Accuracy of fine-needle aspiration and core needle biopsy in the diagnosis of salivary gland tumors

PO315 Induction chemotherapy in oral cavity cancer: the experience of a Cancer Reference Center

PO316 Multiple Paragangliomas of the Head and Neck: A Systematic Review

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PO319 Surgical treatment of head and neck paragangliomas: 15 years experience of a Cancer Reference Center

PO320 The treatment of the patients with oropharyngeal cancer with the use of Da Vinci Xi system.

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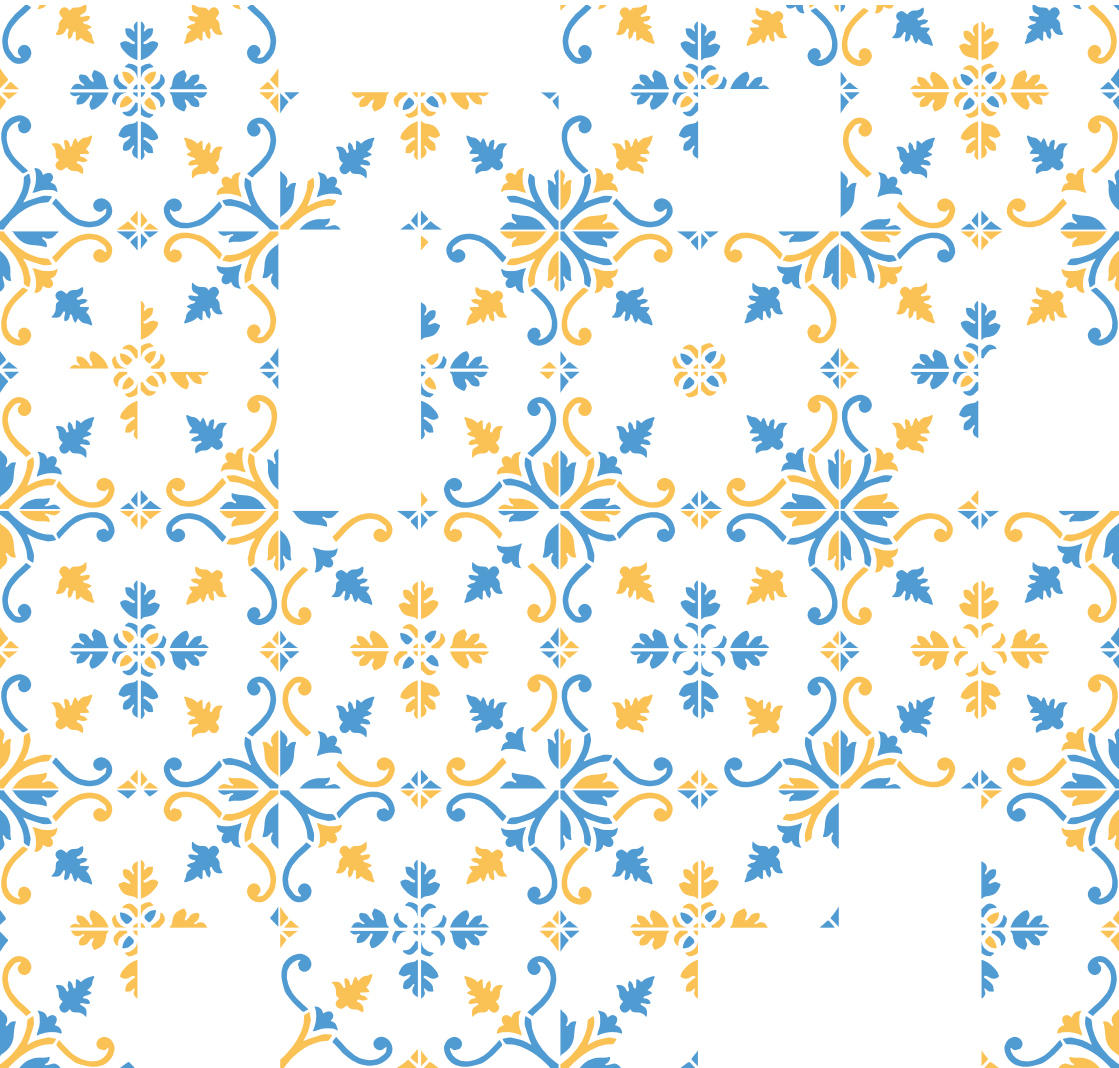
EHNS
European Head & Neck Society

ORAL COMMUNICATIONS



OC-008 | The development of a decision aid for operable oropharyngeal carcinoma, a mixed methods study

Anne Nadine Heirman [1]; Lisette Van Der Molen [1]; Richard Dirven [1]; Gyorgi b. Halmos [2]; Michiel W.M. Van Den Brekel [1]

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Keywords

Decision aid, oropharyngeal carcinoma, shared decision making

Objective

The incidence of oropharyngeal squamous cell cancer (OPSCC) is rising due to human papillomavirus (HPV). The patient population is becoming younger and have an expected long-term survival. So far there is no significant difference found in survival and oncological outcomes among primary transoral (robotic) surgery and radiotherapy. Prospective results on functional outcomes will emerge in the coming years. This leaves patients with the difficulty of choosing between treatments with similar oncological and survival outcomes, but with uncertainty in long-term functional outcomes. With this study, we wanted to identify the wants and needs of patients and caregivers to develop a comprehensible patient decision aid (PDA).

Methods

The development of this PDA aid is based on the quality criteria as set out by the International Patient Decision Aid Standards (IPDAS) collaboration. We followed the three phases in the development process. In phase 1, relevant literature was reviewed and compared to currently used counseling papers. We held semi-structured in-depth interviews with ten post-treatment patients and ten doctors (head and neck surgeons and radiotherapists) from four head and neck centers in the Netherlands. Audio-re-

corded interviews were transcribed and analyzed. With these results, the first draft of the PDA was developed. Phase 2 beholds testing the first draft for comprehensibility and usability in the same group of patients and doctors. Testing for feasibility, phase 3, has been done in twenty patients, the patient society board, communication specialists and doctors. After this phase, the final version of the PDA was developed.

Results

All doctors and patients agreed a PDA was needed. Phase 1 showed that 50% of patients felt well-informed after standard care and 35% missed information about treatment possibilities. Side effects and functional outcomes were rated as most important for decision-making. With this information, the first version was developed. Doctors and patients stated (phase 2) that they were satisfied with the comprehensibility and usability, but there was too much text. The PDA underwent text reduction revisions and got more graphics. After revisions, all doctors found the PDA feasible and would contribute to regular counseling. Patients were satisfied with the results and wished they would have seen it before their treatment.

Conclusion

Decision-making for OPSCC should focus on differences in side--effects and functional outcomes. Patients and doctors found the PDA to be of great value. Future research will explore the benefits of the PDA in clinical practice.

OC-015 | Diagnostic test accuracy of sentinel lymph node biopsy in larynx & pharynx cancers: a meta-analysis

Van Den Bosch [1]; Czerwinski [1]; Govers [1]; Takes [1]; de Bree [2]; Al-Mamgani [3]; Hannink [1]; Kaanders [1]

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Purpose/Objective

Sentinel lymph node biopsy (SLNB) is not performed routinely in patients with larynx and pharynx squamous cell carcinoma (SCC) that are primarily treated with (chemo)radiotherapy. It is conceivable that this diagnostic procedure can reduce the need for elective neck irradiation, avoiding unnecessary treatment-associated morbidity. Before such strategy can be implemented in clinical trials, data on diagnostic test accuracy is mandatory. Therefore, a systematic review and meta-analysis was performed to determine the diagnostic test accuracy of SLNB for the detection of cervical lymph node metastases in patients with oropharyngeal, laryngeal or hypopharyngeal SCC.

Material/Methods

A literature search was performed in MEDLINE, EMBASE and Web of Science (from inception to March 8, 2022) to identify relevant studies. Included were clinical studies evaluating diagnostic test accuracy of SLNB with elective neck dissection or follow-up without treatment of the neck as reference standard in patients with oropharyngeal, laryngeal or hypopharyngeal SCC. Data were extracted independently by two reviewers. Authors were contacted to retrieve missing data. Risk for bias and applicability of included studies was evaluated using the QUADAS-2 tool. A bivariate generalized linear mixed model approach was used for the

meta-analysis. Subgroup analysis was performed for the tumor sites oropharynx and larynx/hypopharynx.

Results

The search yielded 11,687 records. After deduplication and abstract screening, 112 full-text articles were assessed for eligibility. All in- and exclusion criteria were met in 19 studies evaluating 377 cases in total. The pooled estimates of sensitivity and NPV of SLNB were 0.93 (95% CI:0.86-0.96) and 0.97 (95% CI:0.94-0.98), respectively. Subgroup analysis on tumor site (oropharynx and larynx/hypopharynx) demonstrated no relevant differences in diagnostic test accuracy (Figure 1). The pooled SLN detection rate was 0.98 (95% CI:0.94-1.0) with mean 2.6 SLNs per patient. The pooled prevalence of contralateral SLNs was 0.26 (95% CI:0.15-0.38) and clinically occult nodal metastases were detected in 0.29 (95% CI:0.22-0.37) of the patients. Tumor site specific results of SLNB and the anatomical distribution of SLNs are shown in Table 1.

Conclusion

The excellent diagnostic test accuracy of SLNB justifies a place in the diagnostic workup of patients with larynx and pharynx SCC. Currently, a multicenter randomized controlled trial is in preparation, evaluating elective neck irradiation guided by SLNB in patients receiving (chemo)radiotherapy for SCC of the oropharynx, larynx or hypopharynx with a clinically negative neck (the PRIMO trial, ClinicalTrials.gov Identifier: NCT05333523). The aim is to investigate oncologic safety and benefits on treatment related morbidity and quality of life.

Figure 1 - Pooled estimates of sensitivity and NPV of all studies, subgroups and sensitivity analysis

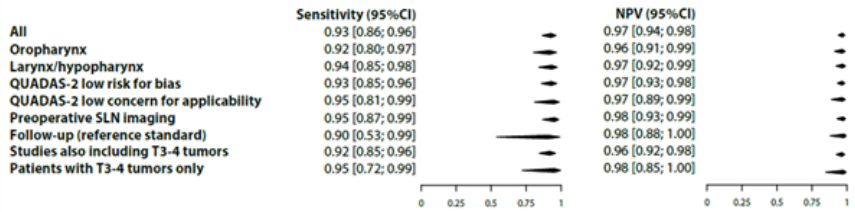


Table 1 - Tumor site specific results of sentinel lymph node biopsy

	Oropharynx	Larynx and hypopharynx	p-value
No. of patients	**162** (reported in 12 studies)	**215** (reported in 10 studies)	NA
Pooled detection rate of SLNs	**1.0** (95% CI:0.96-1.0)	**0.96** (95% CI:0.87-1.0)	0.37
Mean number of SLNs per patient	**2.2**	**2.7**	NA
Pooled prevalence of contralateral SLN	**0.16** (95% CI:0.06-0.29)	**0.35** (95% CI:0.19-0.52)	0.09
Anatomical neck levels of SLN	**Level I** in **5%** **Level II** in **69%** **Level III** in **22%** **Level IV** in **2%** **Level V** in **1%** **Level VI** in **1%**	**Level I** in **1%** **Level II** in **48%** **Level III** in **41%** **Level IV** in **7%** **Level V** in **1%** **Level VI** in **3%**	NA
No. of patients with nodal metastases	**49** of which 45 were detected by SLNB and 4 with END/FU (with negative SLNB)	**64** of which 60 were detected by SLNB and 4 with END/FU (with negative SLNB)	NA
Pooled prevalence of nodal metastases	**0.29** (95% CI:0.18-0.41)	**0.30** (95% CI:0.20-0.41)	0.93

OC-016 | Deep learning NTCP model for late dysphagia based on 3D dose, CT and segmentations

Suzanne P.M. de Vette [(1)]; Hung Chu [(1)]; Hendrike Neh [(1)]; Roel J.H.M. Steenbakkers [(1)]; Peter M.A. Van Ooijen [(1)]; Clifton D.A. Fuller [(2)]; Johannes A. Langendijk [(1)]; Nanna M. Sijtsema [(1)]; Lisanne v. Van Dijk [(1)]

(1) University Medical Centre Groningen (2) MD Anderson Cancer Centre

Keywords

Dysphagia, NTCP modelling, Deep learning

Purpose/Objective

Dysphagia after radiotherapy for head and neck cancer (HNC) has a large impact on patient-reported quality of life. Normal tissue complication probability (NTCP) models that predict the dysphagia risk after radiotherapy can be utilized to guide therapy decisions by estimating the toxicity risk before treatment. These NTCP models are currently based on discrete dose parameters of a distinct set of swallowing-related structures (e.g., the pharyngeal constrictor muscles (PCMs) and the oral cavity). However, dysphagia development is a complicated inter-connected process involving many swallowing muscles and structures. Deep learning (DL) has the potential to improve dysphagia prediction, as it can predict based on the whole 3D dose distribution instead of reducing this to a single dose value. The aim of this study is to improve the prediction of dysphagia at 6 months after radiotherapy with 3D DL models compared to conventional NTCP models.

Material/Methods

1113 HNC patients were included that received primary radiotherapy between 2007 and 2021 at a single centre. The cohort was split in a training (70%), cross-validation (15%), and independent "never-seen-by-the-model" test (15%) set. The endpoint was grade ≥2 physician-rated dysphagia at 6 months after radiotherapy

(CTCAEv4.0). Input for the DL model were 3D planning CTs, dose distributions and swallowing structure segmentations (Brouwer et al., 2015). After hyperparameter tuning, a ResNet Deep Convolutional Neural Network (DCNN) was trained and optimized on a combination of cross-entropy and Area Under the Curve (AUC).

For comparison with the DL model, the performance of the recently published dysphagia NTCP model, which was trained on a comprehensive study cohort, was determined in our current dataset. Furthermore, attention maps that highlight the areas that the DL model focuses on per individual patient were visually evaluated.

Results

Hyperparameter tuning showed that a combination of the AdaBelief optimizer and a batch size of 8 resulted in the highest training and validation AUC (Table 1). The final DL NTCP model showed excellent performance in the independent test set (AUC = 0.86 (95% Confidence Interval [0.80–0.93])). This performance was improved compared to the conventional NTCP model (AUC = 0.80 [0.72-0.87]), suggesting that 3D information enhanced dysphagia prediction. The attention maps revealed that the regions that have previously been associated with dysphagia development (e.g. the oral cavity and PCMs) were highlighted by the DL model (Figure 1), yet additionally the DL model focused on the parotid glands, submandibular glands, base-of-tongue and the larynx area.

Conclusion

Combining 3D information of the dose distribution, CT and swallowing-related segmentations in a DL model showed an improved prediction of late dysphagia compared to conventional NTCP models based on discrete dose parameters. Currently these models are in the process of being externally validated to evaluate their generalizability.

	Conventional NTCP model	Deep Learning model
Input	Baseline toxicity Tumour location Oral cavity mean dose PCMs mean dose	3D dose distribution 3D planning CT 3D segmentations of swallowing structures
AUC (95% confidence interval)		
Training	0.82 (0.79 – 0.85)	0.87 (0.85 – 0.90)
Validation	0.81 (0.78 – 0.84)	0.80 (0.77 – 0.83)
Test	0.80 (0.72 – 0.87)	0.86 (0.80 – 0.93)

Table 1: Comparison of input between the conventional Normal Tissue Complication Probability (NTCP) model and the DL model, as well as the AUC on the training, validation and testing set in both models. PCMs = pharyngeal constrictor muscles.

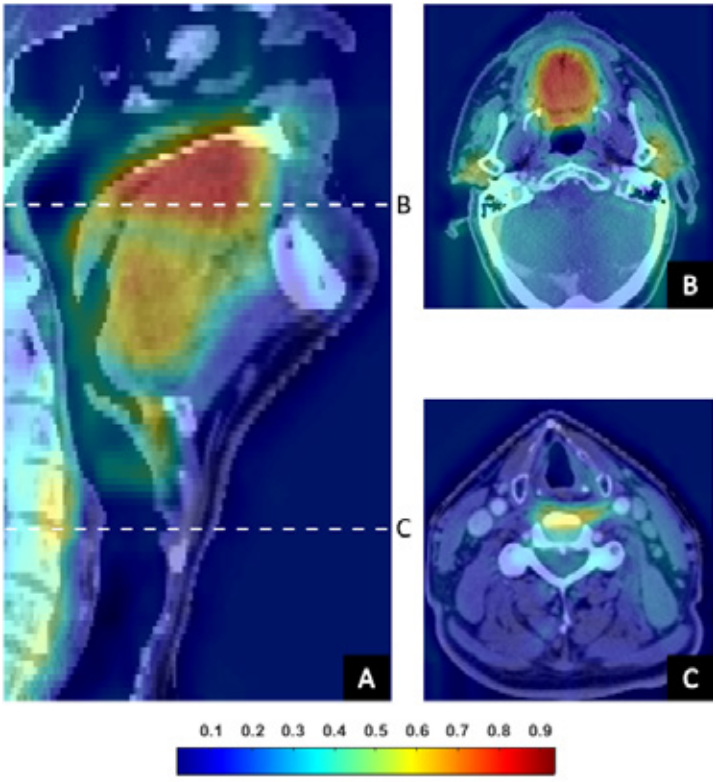


Figure 1. CT and overlay of attention map for 1 patient. A) Saggital view. B) Transversal view at level B in Figure A. C) Transversal view at level C in Figure A.

OC-022 | IMPACT OF ARTIFICIAL INTELLIGENCE IN HEAD AND NECK CANCER DIAGNOSIS

Sara Bassani [(1)]; Santonicco Nicola [(1)]; Eccher Albino [(1)]; Pantanowitz Liron [(2)]; Girolami Ilaria [(1)]; Molteni Gabriele [(1)]

(1) University of Verona (2) University of Michigan

Keywords

Artificial intelligence, head and neck cancer, pathology.

Introduction

Artificial intelligence (AI) is currently being used to augment histopathological diagnostics in pathology. This systematic review aims to evaluate the evolution of these AI-based diagnostic techniques for diagnosing head and neck neoplasms.

Materials and Methods

Articles regarding the use of AI for head and neck pathology published from 1982 until March 2022 were evaluated based on a search strategy determined by a multidisciplinary team of pathologists and otolaryngologists. Data from eligible articles were summarized according to author, year of publication, country, study population, tumor details, study results and limitations.

Results

Thirteen articles were included according to inclusion criteria. The selected studies were published between 2012 and March 1, 2022. Most of these studies concern the diagnosis of oral cancer; in particular, 6 are related to the oral cavity, 2 to the larynx, 1 to the salivary glands and 4 to head and neck squamous cell carcinoma not otherwise specified (NOS). As for the type of diagnostics considered, 12 concerned histopathology and 1 cytology.

Conclusions

Starting from the pathological examination, artificial intelligence tools are an excellent solution for implementing diagnosis capability. Nevertheless, today the unavailability of large training datasets is a main issue that needs to be overcome to realize the true potential.

OC-028 | Effects of popliteal nerve blocks on postoperative pain after fibular free flap reconstruction

Amanda Gemmiti [1]; *Jesse Ryan, md* [1]; *Nadia Debick, MPH* [1]; *Jason Audlin, md* [1]; *Heidi Proper, bs* [1]

(1) SUNY Upstate Medical University

Keywords

Fibula free flaps, head and neck cancer, pain management, peripheral nerve block, postoperative rehabilitation

Objective

To determine if performing popliteal nerve blocks pre-operatively in patients undergoing fibula free flap surgery for head and neck cancer reconstruction decreases narcotic usage and subjective pain scores and improves mobility in the acute post-operative time period when compared to alternative pain control regimens.

Material/Methods

A retrospective review of the medical records of patients who underwent fibula free flap reconstruction for head and neck malignancy at SUNY Upstate Medical University during the time period from 2015 - 2022 was performed. Collected data consisted of patient demographics and clinical characteristics, postoperative pain management modalities, reported pain scores, postoperative narcotic usage, length of hospital stay, and days until out of bed without personal assist.

Results

A total of 40 patients were included in the study. The average reported pain score was reduced in the nerve block group compared to the control group (1.7 vs 4.0, p-value = .003). Similarly, the average maximum reported pain score was also lower in patients

who received a nerve block (3.4 vs 6.9, p-value = .002). None of the patients that received popliteal nerve blocks required pain control with parenteral narcotics postoperatively, whereas 82.9% of patients without a nerve block did. Patients who received a popliteal nerve block consumed an average of 103.5 MME while those who did not receive a block consumed an average of 523.0 MME. No statistically significant difference was found between the groups regarding time from surgery until transfer without personal assist or length of hospital stay.

Conclusion

Popliteal nerve blocks can reduce postoperative pain and narcotic use in patients undergoing fibular free flap reconstruction for head and neck cancer.

OC-033 | Adherence to prophylactic swallowing exercises during head neck radiotherapy – the PRESTO-trial

Margot Baudelet *[1]; Leen Van Den Steen [2]; Caroline Vandenbruaene [3]; Ann Goeleven [4]; Sandra Nuyts [4]; Daan Nevens [5]; Fréderic Duprez [6]; Gwen Van Nuffelen [2]*

(1) University of Ghent (2) University Hospital Antwerp (3) General Hospital AZ Sint-Jan Brugge (4) University Hospital Leuven (5) Iridium Network Antwerp (6) University Hospital Ghent

Purpose

Prophylactic swallowing exercises (PSE) during head-and-neck cancer (HNC) radiotherapy (RT) have a positive effect on swallowing function. However, moderate to low adherence rates during the burdensome therapy period are undermining these beneficial effects. Hence, the first goal of this prospective multicenter randomized controlled trial (RCT) was to investigate the effect of service-delivery mode (SDM), the way the exercises are offered to patients, on actual patients' adherence. The second goal was to assess the effect of SDM and overall adherence (OA) – independent of SDM – on swallowing function.

Materials/Methods

A total of 148 HNC patients treated with radiotherapy were randomly assigned to a 4 weeks PSE intervention, either diary-supported (paper group; n=49), app-supported (app group; n=49) or speech-language pathologist (SLP)-supported (therapist group; n=50). All participants practiced 5 days/week, daily alternating tongue strengthening exercises (120 repetitions[reps]/session) with chin tuck against resistance exercises (150 reps/session). To investigate the impact of SDM on adherence, the percentage of completed reps per week (%reps) was used. OA was calculated based on the mean percentage of completed exercises over the 4 PSE weeks. Patients were divided into OA levels: the OA75+

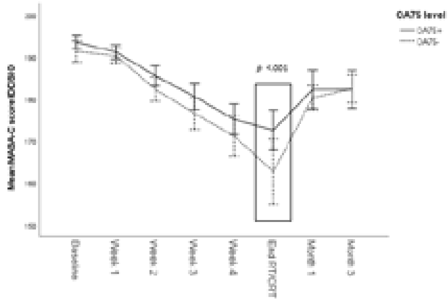
and OA75- group performed respectively ≥75% and <75% of the prescribed exercises. Swallowing function based on MASA-C was compared between the SDM's and OA level groups during and up to three months after RT. Statistical analysis was performed by means of SPSSv27, using Linear Mixed-effects Models (LMM) with post-hoc pairwise testing and Bonferroni-Holm correction. The statistical significance level was set at .05.

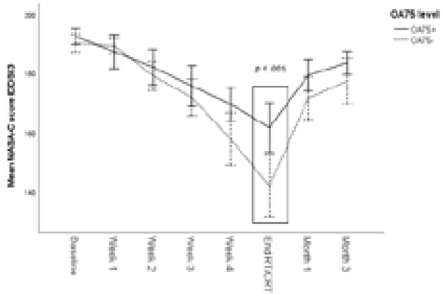
Results

LMM showed significant effects of SDM on patients' adherence ($p < .001$). Moreover, significant time and SDM by time interaction ($p < .001$) were observed: adherence rates decreased in all three SDM's during the 4 training weeks ($p < .001$). The therapist group achieved significantly higher adherence rates compared to the other SDM's across all weeks (fig. 1). Next, LMM showed no significant differences of SDM on swallowing function. However, significant OA effects were found by the end of RT: the OA75+ group showed significantly better swallowing function compared to OA75- (Fig. 2).

Conclusion

The results of this RCT show that PSE adherence decreases in all SDM's during the first 4 radiotherapy weeks, with significantly higher adherence rates in the therapist group. Although SDM had no impact on swallowing function, significant effects were found with respect to patients' OA. Patients practicing more than 75% of the prescribed exercises showed significant better results than patients practicing less. It can be concluded that increasing the face-to-face contact with an SLP can improve adherence rates, which is essential since performing a high level of exercise repetitions is needed to benefit from PSE.


OA75 level
Baseline
Week 1
Week 2
Week 3
Week 4
End RT/CRT
Month 1
Month 3


OA75 level
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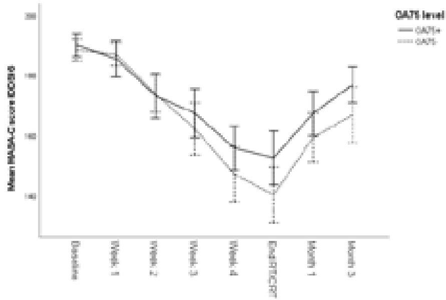
OA75 level
Baseline
Week 1
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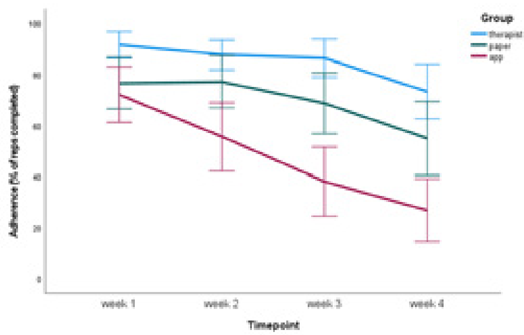
Week 4
End RT/CRT
Month 1
Month 3


Group
therapist
paper
app
week 1
week 2
week 3
week 4
Timepoint

C-038 | HNC-PREDICTOR model to select head and neck patients for personalized treatment

Dr. Lisanne v Van Dijk [1]; Abdallah s r Mohamed [2]; Sara Ahmed [2]; Kareem Wahid [2]; Nafiul Nipu [3]; g. Elisabeta Marai [3]; Nanna m. Sijtsema [1]; Brandon Gunn [2]; Adam s. Garden [2]; Amy Moreno [2]; Andrew j. Hope [4]; Johannes a. Langendijk [1]; Clifton d. Fuller [5]

(1) University Medical Centre Groningen (2) MD Anderson Cancer Center (3) The University of Illinois Chicago (4) Princess Margaret Cancer Centre (5) Clifton D. Fuller

Purpose

Current radiation dose de- or escalation trials for head and neck cancer (HNC) patients generally use tumor staging (including HPV status) as patient eligibility criteria. The effectiveness of personalized therapy strategies could be improved with model-based selection of low, intermediate and high-risk patients. The aim was to develop a robust international survival risk-stratification model based on more than 4500 HNC patients. Additionally, an interactive web-based risk prediction tool was pursued to make the models direct clinically-actionable for clinicians.

Material & Methods

Squamous cell carcinomas HNC patients were included that were treated with primary (chemo)radiation. The patients were treated at MDACC, UMCG and PMH, and cohorts were split into a training (n=2241), independent test (n=786), and external validation cohort 1 (n=1087) and cohort 2 (n=497). Data imputation was applied in the training cohort; all other data was complete.

A survival prediction model with clinical variables was trained and validated on the full large-scale data. An *optional radiomics component* was tested for further prediction improvement in a subcohort. Subsequently, models were integrated in a web-based interface.

Training of the Cox regression models was performed with bootstrapped forward selection. The clinical models were validated in the independent test and 2 validation cohorts. Subsequently, patients were stratified into high, intermediate and low risk overall survival probability based on the predicted 2-year mortality risk; with a *priori* thresholds of >25% for high risk and <5% for low risk. The additional radiomics component was developed in imaging sub cohorts (Table). The selected radiomics predictors were added to the linear predictor from the final clinical model.

Results

The median follow-up time was 4.3 year [IQR: 2.1-6.7]. In the multivariable analyses *Performance score*, *AJCC*^{8th} stage, *pack years*, and Age were selected for the prediction of overall survival (NB: *AJCC*^{8th} *stage* is based on *T* and *N stage*, *tumor site* and *HPV status*). Model performance was stable over different cohorts with c-indices ranging from 0.72-0.76 (Table). The prediction model was highly discriminative for stratifying high, intermediate and low risk patients (Figure); the cumulative 5-year overall survival ranged from 92-98% for the low risk group and from 17-46% for the high risk group. The clinical prediction model outperformed clinical standard-of-care *AJCC*^{8th} *stage prognosis (Table)*. This model (and for disease control) are integrated in a clinic-ready interactive web-interface: https://uic-evl.github.io/hnc-predictor/

In smaller imaging cohorts, the addition of selected radiomics features to the clinical model's linear predictor further improved the performance in training and validation cohort 1 (Table).

Conclusion

This international multi-institutional dataset allowed for the development and validation of a robust overall survival risk-stratification model with exceptional distinction capacity to select patients. The web-based decision support tool can be used to select for intensified versus de-intensified treatment strategies.

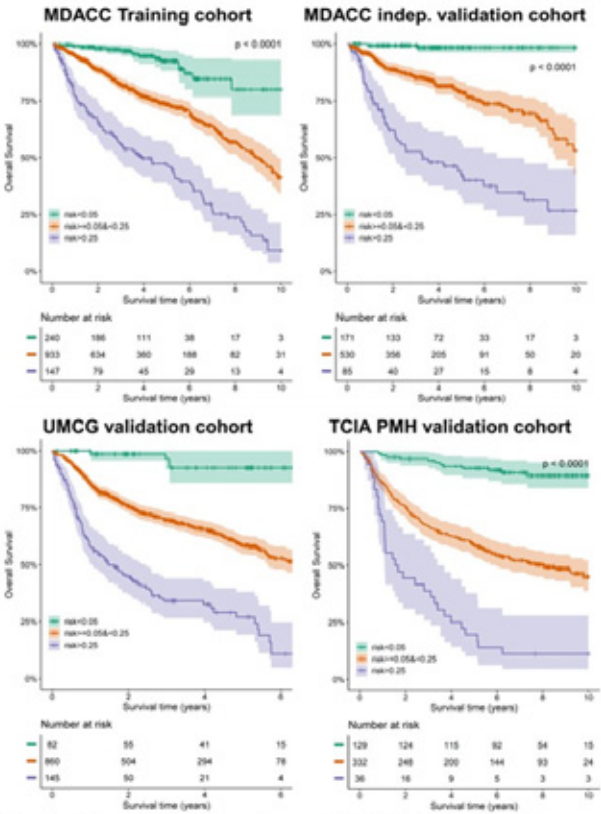


Figure. Survival curves for low risk (green; 2 year mortality risk<5%), intermediate risk (orange; risk≥5 & <25%), and high risk (blue; ≥25%) in training, and 3 validation cohorts

Table. C-indices [95%CI] of clinical models and clinical model + radiomics in the training independent validation, and 2 external validation cohorts.

Clinical models	**Training** *(N=2241)*	**Independ. test** *(N=786)*	**External val. 1** *(N=1087)*	**External val.1** *(N=497)*
Ref Model: • *AJCC^{8th} stage*	0.65 [0.60-0.70]	0.72 [0.64-0.80]	0.66 [0.62-0.70]	0.69 [0.62-0.76]
Clinical Model: • Performance score • *AJCC^{8th} stage* • Pack years • Age	0.72 [0.66-0.78]	0.76 [0.68-0.83]	0.73 [0.68-0.78]	0.75 [0.68-0.81]
	(N=315)	-	*(N=229)*	*(N=300)*
Clin + radiomics Model: • Linear predictor clinical model • Minor axis length	0.75 [0.65-0.85]	-	0.74 [0.64-0.83]	0.73 [0.62-0.83]

OC-039 | Deep learning-based xerostomia prediction using 3D radiation dose and imaging information

Hung Chu [1]; Suzanne P.M. de Vette [1]; Hendrike Neh [1]; Nanna m. Sijtsema [1]; Roel J.H.M. Steenbakkers [1]; Clifton d. Fuller [2]; Johannes a. Langendijk [1]; Peter M.A. Van Ooijen [1]; Lisanne v. Van Dijk [1]

(1) University Medical Centre Groningen (2) MD Anderson Cancer Center

Keywords

Xerostomia, Deep learning, NTCP

Purpose/Objective

Normal tissue complication probability (NTCP) models aim to predict radiation-induced toxicities. Conventional NTCP models are typically based on limited discrete input features. Xerostomia is one of the most common radiation-induced toxicities for head and neck cancer (HNC) patients, which can have a big impact on the quality of life. Current NTCP xerostomia prediction is based on salivary glands mean dose and baseline complaints, thereby reducing the radiation dose admitted to these organs-at-risk (OAR) to single values. Deep learning (DL) models have the potential to improve xerostomia prediction by utilizing full 3-dimensional (3D) dose distribution and imaging information, rather than using 1D dose representations. The aim was to develop a DL-based NTCP model to predict xerostomia 12 months after HNC radiotherapy and compare the prediction performance to a conventional NTCP model.

Material/Methods

The cohort contained 898 HNC patients that were treated with radiotherapy between 2007 and 2021, and was split into a training (70%), internal validation (15%) and test (15%) set. The endpoint was moderate-to-severe xerostomia after 12 month of radiotherapy. DL models input were dose distributions, computed tomography (CT) scans, OARs contours and baseline xerostomia level (Figure 1). The

following model architectures were considered: EfficientNet-v2, a residual neural network (ResNet) and a deep convolutional neural network (DCNN). The models were optimized individually by hyper-parameter tuning. Model performance was evaluated in terms of area under the curve (AUC) criteria in the validation and test cohort. The DL model prediction performances were compared to that of the recently published xerostomia NTCP model by Van den Bosch et. al (2019), which includes salivary glands mean dose and baseline xerostomia level. Attention maps were constructed to visualize areas of the input imaging where the DL models focused on when doing predictions.

Results

Each DL model achieved higher validation (AUC = 0.79 – 0.82) and test (AUC = 0.78 – 0.79) performance than the conventional NTCP model (AUC-validation = 0.75, 95% CI [0.67 – 0.83]; AUC-test = 0.75 [0.67 – 0.84]). This confirms the benefit of utilizing 3D information for predicting late xerostomia. ResNet achieved best performance with validation AUC = 0.82 ([0.73 – 0.89]) and test AUC = 0.79 [0.70 – 0.87]. Best internal validation performance was achieved by using AdaBound optimizer, learning rate of 0.0001 and batch size of 8. Moreover, from attention maps we observed that ResNet focused on salivary glands and oral cavity when making predictions (Figure 2).

Conclusion

DL models using 3D dose distribution, CT, OAR segmentations and a clinical parameter showed to predict late xerostomia well, and outperformed the conventional logistic regression-based NTCP model. With this, DL based approach using 3D dose and imaging shows potential to improve clinical decision-making.

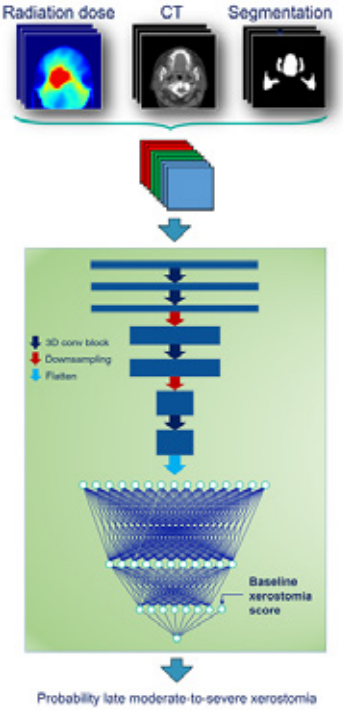
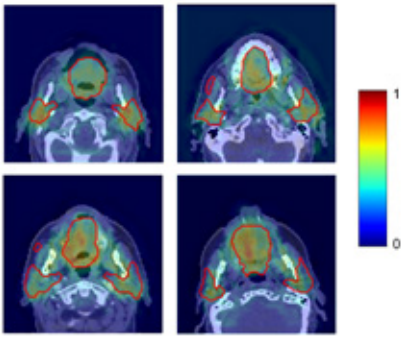


Figure 1: Schematic overview of the model architectures. Inputs 3D dose distribution, CT scans and contours of OARs were stacked channel-wise. The baseline xerostomia score was added at the final fully-connected layer. Output is the NTCP for moderate-to-severe xerostomia after 12 month of radiotherapy.

Figure 2: Attention maps from ResNet (AUC_{val} = 0.82, AUC_{test} = 0.79) overlayed on CT for four patients.



The parotid glands and oral cavity are contoured in red. The attention maps show high attention for salivary glands and oral cavity. The attention for submandibular glands is outside this field of view.

OC-046 | Preliminary results of mutational analysis in tumor tissue and liquid biopsy in LAHNSCC

Alex Corbera [(1)]; *Sergi Clavé* [(1)]; *Rafael Bach* [(1)]; *Anna Sumarroca* [(1)]; *Ana Isabel Alvarez Macha* [(1)]; *Jacinto Garcia* [(1)]; *Clara Montagut* [(1)]; *Beatriz Bellosillo* [(1)]; *Marta Guix* [(1)]

(1) Hospital del Mar

Objectives

Treatment of locally advanced head and neck squamous cell carcinoma (LAHNSCC) is often not curative and relapses are frequent. Molecular testing on tumor cell-free DNA (liquid biopsy, LB) is a non-invasive tool that allows the detection of biomarkers from tumors in biological fluids, such as blood. We hypothesized that LB would be useful to detect residual tumor or relapses in addition to physical examination and imaging studies, to help guide clinical decisions in LAHNSCC after treatment with curative intent. The first step in our project was to explore the correlation of mutational findings in tumor tissue and LB in patients with LAHNSCC.

Methods

From September to November 2021 we included patients with LAHNSCC candidates for radical treatment. Demographic and clinical data were collected from medical records. We performed NGS from the initial diagnostic biopsy (using the Oncomine Solid Tumor DNA) and collected a plasma sample for LB testing (using the Oncomine Pan-Cancer Cell-Free Assay) before treatment initiation (baseline).

Results

The results of the first 6 patients included are summarized in the Table 1. As reported in the literature, *TP53* mutations were

the most frequent genomic alteration. In 5 out of 6 patients, the same mutations were detected in blood and tissue. In one case, mutations were detected in LB but not in tumor tissue (Pt 3; *TP53* mutation), probably due to tumor heterogeneity. Finally, a good correlation was also found for HPV detection, as HPV16 was detected in the LB samples from the 3 patients with oropharynx tumors that were HPV +.

Conclusion

Our preliminary results show good correlation of gene mutation and HPV detection between tumor tissue and baseline LB at initial diagnosis. We will continue patient recruitment and start the analysis of sequential LB after tumor treatment and during follow-up.

Pt #	Tumor localization	TNM	Mutations Tissue	Mutations LB
1	Oropharynx HPV+	T3N2	KRAS p.(Gly12Val) GNAS p.(Arg201Leu) HPV 16	KRAS p.(Gly12Val) EGFR p.(Ser484Phe) FGFR3 p.(Ser249Cys) HPV 16
2	Oropharynx HPV+	T1N2	HPV 16	HPV 16
3	Oropharynx HPV-	T4aN0	None detected	TP53 p.(Trp91Ter) TP53 p.(Arg248Trp)
4	Oropharynx HPV+	T4N0	PIK3CA p.(Glu545Lys) ALK p.(Glu1197Gln) HPV 16	PIK3CA p.(Glu545Lys) ALK p.(Glu1197Gln) FGFR3 p.(Ser249Cys) HPV 16
5	Larynx	T4N1	TP53 p.(Cys176Ser)	TP53 p.(Cys176Ser) ERBB4 p.(Ser302Arg) HPV16 (+)

OC-050 | Evaluating the Implementation of Enhanced Recovery after Oropharyngeal Transoral Robotic Surgery

Shivun Khosla [1]; *Stephen Derbyshire* [1]; *Chris Jones* [1]; *David Walker* [1]

(1) Department of Head and Neck Surgery, Royal Surrey County Hospital, Guildford

Keywords

Transoral Robotic Surgery, Enhanced Recovery After Surgery

Purpose/Objective

To evaluate the impact and patient related outcomes from local implementation of a standardised enhanced recovery pathway for patients undergoing transoral robotic oropharyngeal surgery (TORS) for head and neck cancer.

Material/Methods

A cohort of 47 consecutive patients undergoing diagnostic or therapeutic TORS for oropharyngeal carcinoma between November 2019 – February 2022 were collected prospectively. Retrospective interrogation of medical charts and standardised patient questionnaires were used to determine post operative analgesic requirement and cessation, time to discharge, time to normal diet, surgical complications and surgical outcomes.

Results

Average patient age was 62.9 years with 27 males and 20 females. Average surgical duration was 155.8 minutes with 42 primary resections, 2 salvage resections and 3 diagnostic procedures. 32 patients had a concomitant selective neck dissection. All patients received the standardised post-operative multimodal analgesia regimen of pregabalin, codeine phosphate and paracetamol. Average time to analgesia cessation was 12.3 days and average

time to normal diet was 5 days. 70% of patients were discharged within 48 hours of surgery. 2 patients required a return to theatre to manage acute post operative complications.

Conclusion

TORS surgery can have significant short term morbidity in the peri-operative period especially in relation to feeding and pain. Our use of a standardised ERAS pathway facilitated early return to normal diet and activities of daily living, reducing acute post-operative complications and allowed patients to begin adjuvant oncological treatment in a timely fashion. As more radical TORS procedures become adopted, including salvage surgery, guidelines for ERAS in TORS patients will become essential to facilitate good patient surgical and oncological outcomes similar to that for patients undergoing head and neck surgery with microvascular reconstruction. We hope our local pathway can be used to aid development of such a guideline.

OC-051 | Clinical predictors of immune-related events in head & neck cancer patients receiving immunotherapy

Majd Issa [1]; Brett Klamer [1]; Priyanka Bhateja [1]; Fahad Rind [1]; Mohammad Bilal Alsavaf [1]; Khaled Dibs [1]; Xueliang Pan [1]; Matthew Old [1]; Esmerina Tili [1]; Arnab Chakravarti [1]; John c Grecula [1]; Sachin r Jhawar[1]; Darrion l Mitchell[1]; Sujith Baliga[1]; Ricardo l Carrau [1]; James w Rocco [1]; Dukagjin m Blakaj [1]; Marcelo r Bonomi [1]

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Objective

Immune checkpoint inhibitors (ICI) are standard of care in the treatment of recurrent-metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). The recognition of unique immune-related adverse events (irAE) related to ICI, promote the need to identify potential risk factors and biomarkers that may assist in clinical decision making. We report a single institution retrospective analysis of pre-treatment characteristics associated with development of irAE in patients (pts) with R/M HNSCC, while assessing the correlation between the development of irAE and survival outcomes.

Methods

Between January 15th 2016 and April 16th 2020, pts with R/M HNSCC received ICI in the first line setting and beyond. Data on P-16 tumor status, hemoglobin, albumin, LDH, absolute neutrophil count (neu), absolute lymphocyte count (lymph), platelet count (plt), neutrophil to lymphocyte ratio (NLR), and platelet to lymphocyte ratio (PLR) were recorded at the time of starting ICI. We captured the time elapsed between finishing radiation (RT) to the original tumor site and starting ICI, measured in months. IrAE were captured through retrospective chart review and graded using the CTCAE v5.0. Progression free survival (PFS) was de-

fined as the time from ICI initiation and disease progression or death, measured in months. Overall survival (OS) was defined as the time from ICI initiation and death, measured in months. Descriptive statistics were used to explore study variables.

Results

177 pts were analyzed, sex: male 140 (79%), female 37 (21%). Median age 61 (IQR: 55-68). Tumor site: oropharynx 81 (46%), oral cavity 43 (24%), larynx 24 (14%), other 29 (16%). P-16 tumor status: Negative 111 (63%), positive 66 (37%). ICI: pembrolizumab 92 (52%), nivolumab 85 (48%). Hemoglobin: normal/low 87/90 (49%/51%), albumin: normal/low 136/41 (77%/23%), LDH: normal/high 109/68 (62%/38%). Median neu: 4.5 (IQR: 3.4, 6.3), median lymph: 0.66 (IQR: 0.47, 1.05), median plt: 228 (IQR: 187, 296), median NLR: 6 (IQR: 4, 11), median PLR: 321 (IQR: 209, 524). Median time between completing RT and ICI: 11 (IQR: 6, 23). Median PFS 4 (IQR: 2, 12), median OS: 12 (IQR: 3, 25). ICI toxicity: Yes 133 (75%), no 44 (25%). Most common toxicities: Fatigue 109 pts (62%), dermatitis 35 pts (20%), and diarrhea 27 pts (15%). Toxicities grade 3 or higher: 38 pts (22%). The variables associated with irAE were: lower neu (4.2 [IQR: 3.4, 5.8] vs. 5.2 [IQR: 4, 7.7]; p=0.012), lower NLR (6 [IQR: 4, 10] vs. 9 [IQR: 5, 15]; p=0.013), longer interval between stopping RT and starting ICI: (11 [IQR: 7, 26) vs. 8 [IQR: 4, 15]; p=0.009). The development of irAE was associated with longer PFS (5 [IQR: 2, 15] vs. 2 [IQR: 1, 4]; p <0.001), and longer OS (16 [IQR: 7, 29] vs. 3 [IQR: 1, 8]; p <0.001).

Conclusion

The pre-treatment characteristics associated with higher incidence of irAE were lower neutrophil count, lower NLR, and longer interval between stopping RT and starting ICI. The development of irAE was associated with longer PFS and OS.

OC-052 | Potential benefit of proton arc therapy over VMAT and IMPT for nasopharyngeal cancer patients

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(1) University Medical Center Groningen

Purpose

Nasopharyngeal cancer (NPC) is a challenging indication due to critical structures in proximity of the target, including the brainstem and optical nerves. Strict dose constraints for these structures are used to reduce the risk of serious treatment side-effects. In proton arc therapy (PAT) an increased number of irradiation directions is employed, adding degrees of freedom to plan optimization, resulting in a potential to reduce dose in healthy tissues compared to intensity modulated proton therapy (IMPT) and volumetric modulated arc therapy (VMAT). We investigated the potential impact of PAT on the most common acute and late radiation induced toxicities for NPC patients.

Methods

Clinical 6 MV dual arc VMAT- and IMPT plans of a cohort of 10 most recent NPC patients treated with IMPT at our institute were used for a treatment plan comparison study. Robust optimized PAT plans employing 30 gantry angles and 360 energy layers were produced using an energy layer reduction algorithm in RayStation. Similar dose constraints for critical structures and target coverage were imposed on VMAT, IMPT and PAT treatment planning. The difference in integral dose in the body including CTV and mean dose (D_{mean}) in structures predictive for toxicities were evaluated. The impact on normal tissue complication probability (NTCP) for the 22 most common radiation induced toxicities for head and neck patients was studied at acute (week 6 of treat-

ment) and late (6 months after the end of treatment) timepoints, using a comprehensive individual toxicity risk (CITOR) profile published in 2021. The NTCP reduction in the PAT plans relative to the value for IMPT was calculated as: *Relative NTCP reduction (Rel. red.) = (NTCPIMPT -NTCPPAT)/NTCPIMPT × 100%*

Results

A transverse slice of the dose distribution of a VMAT, PAT and IMPT plan at the level of the nasopharynx for an example patient can be seen in figure 1. In the PAT plans integral dose reduced by on average 56 % and 18 % compared with the VMAT and IMPT plans respectively. Compared with the IMPT plans, D_{mean} was reduced in the PAT plans by 7.0 Gy, 4.8 Gy and 4.1 Gy in the Brainstem, Pharyngeal constructor muscles and submandibular glands, respectively. All average NTCP's in the CITOR-profile at acute and late timepoints of 10 NPC patients reduced in the PAT plans and can be found in table 1. The relative NTCP reduction in the PAT plans was on average 11 ± 8 % and 14 ± 11 % for all acute and late toxicities, respectively.

Conclusion

Compared to IMPT and VMAT, PAT shows potential to reduce healthy tissue dose, and lower toxicity risks in NPC patients for a broad range of toxicities associated with head and neck radiation treatment at acute and late timepoints.

Table [1]: The average normal tissue complication probability (NTCP) at the acute and late timepoint for volumetric modulated arc therapy (VMAT) intensity modulated proton therapy (IMPT) and proton arc therapy (PAT) and plans for 10 nasopharyngeal cancer patients. NTCP's are given for the 6 toxicity domains: 1 Swallowing, 2 Salivary, 3 Mucosal, 4 Speech, 5 Pain, 6 General. The relative reduction in NTCP in the PAT plans with respect to the NTCP for IMPT is shown in the last column for both timpoints.

	Average CITOR NTCP-profile for 10 NPC patients	Acute (week 6)				Late (month 6)			
		VMAT	IMPT	PAT	Rel. red.	VMAT	IMPT	PAT	Rel. red.
1	Physician-rated grade 2-4 dysphagia	83%	76%	74%	3%	12%	6%	4%	27%
	Physician-rated grade 3-4 dysphagia	68%	60%	58%	6%	2%	0,5%	0,3%	48%
	Physician-rated grade 2-4 aspiration	23%	17%	16%	7%	12%	10%	9%	8%
	Patient-reported moderate-severe aspiration	20%	20%	20%	0%	7%	5%	4%	17%
2	Patient-reported moderate-severe xerostomia	47%	34%	31%	10%	39%	31%	27%	12%
	Patient-reported severe xerostomia	16%	10%	9%	12%	9%	7%	6%	16%
	Physician-rated grade 2-4 xerostomia	51%	30%	26%	13%	39%	25%	20%	24%
	Patient-reported moderate-severe sticky saliva	52%	44%	41%	7%	30%	25%	23%	8%
	Patient-reported severe sticky saliva	19%	16%	14%	11%	9%	8%	7%	10%
	Physician-rated grade 2-4 sticky saliva	59%	34%	30%	14%	9%	6%	5%	14%
	Patient-reported moderate-severe loss of taste	59%	41%	35%	17%	24%	16%	14%	14%
	Physician-rated grade 2-4 loss of taste	50%	30%	24%	22%	23%	18%	16%	13%
3	Physician-rated grade 2-4 mucositis	21%	16%	14%	9%				
	Physician-rated grade 3-4 mucositis	5%	1%	1%	24%				
4	Patient-reported moderate-severe hoarseness	11%	8%	6%	23%	3%	2%	1%	23%
	Patient-reported moderate-severe speech problems	20%	16%	15%	5%	9%	7%	7%	4%
5	Patient-reported moderate-severe oral pain	30%	17%	16%	5%	12%	8%	8%	3%
	Patient-reported moderate-severe throat pain	58%	58%	58%	0%	9%	7%	7%	6%
	Patient-reported moderate-severe jaw pain	10%	10%	10%	0%	7%	4%	4%	5%
6	Physician-rated grade 2-4 weight loss	3%	2%	2%	25%	21%	13%	10%	23%
	Patient-reported moderate-severe nausea and vomiting					8%	5%	5%	11%
	Patient-reported moderate-severe fatigue					35%	30%	29%	5%
	Average	35%	27%	25%	**11%**	16%	12%	10%	**14%**

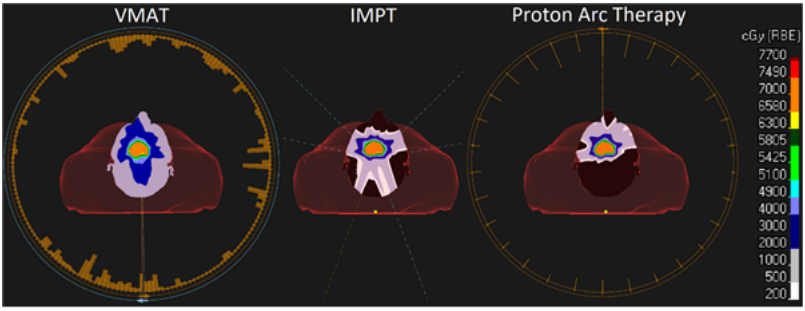


Figure [1]: Visualization of a volumetric mudulated arc therapy (VMAT), intensity modulated proton therapy (IMPT) and proton arc therapy plan beam setup. The dose distribution is shown at a transverse slice at the level of the nasopharynx.

OC-054 | Salvage laryngectomy for SCC of the larynx and hypopharynx: validated nomograms predicting outcomes

Jeroen Meulemans [(1)]; *Alexander Van Boven* [(1)]; *Jens Debacker* [(2)]; *Annouschka Laenen* [(3)]; *Pierre Delaere* [(1)]; *Charlotte Vanlierde* [(1)]; *Wouter Huvenne* [(2)]; *Vincent Vander Poorten* [(1)]

(1) University Hospitals Leuven (2) University of Ghent (3) 5 Interuniversity Institute for Biostatistics and statistical Bioinformatics

Kewords

Nomogram, salvage surgery, laryngeal cancer

Purpose

Salvage total laryngectomy (STL) is often the preferred treatment for patients with residual, recurrent and second primary squamous cell carcinoma (SCC) of the larynx and hypopharynx after initial (chemo)radiation. Previously, we identified multiple solid prognosticators for oncological outcomes after STL, which could allow for postoperative risk stratification.In this study we aimed to design and validate nomograms, potentially allowing for a more individualized estimate of the expected oncological outcome.

Figure 1: nomogram predicting DSS using postoperative variable

Methods

We used a dataset of 290 patients who underwent STL in University Hospitals Leuven (Belgium) between 2002 and 2022. Kaplan Meier estimates were used for estimating overall survival (OS) and disease-free survival (DFS). The cumulative incidence function was used for estimating disease-specific survival (DSS). Cox proportional hazard models were used for the analysis of prognostic factors on oncological outcomes. A forward stepwise model selection procedure was used for the construction of multivariable

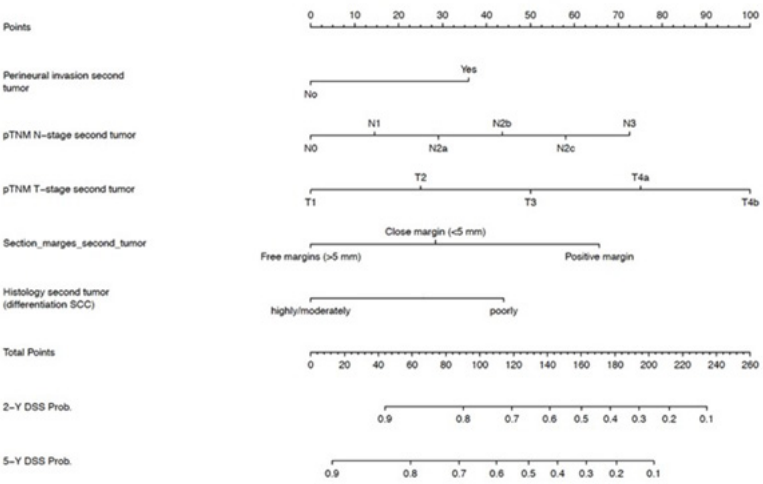
models, adopting a 5% significance level for entering or leaving of variables. Harrel's C-index was used to quantify the discriminative value of the multivariable models. Nomograms predicting 2- and 5-year OS, DFS and DSS were developed, either using variables which are identified pre-operatively (e.g. clinical tumor stage, tumor location, etc) or postoperatively (e.g. presence of perineural invasion, pT, etc). The nomograms were externally validated on a dataset of 109 patients who underwent STL in Ghent University Hospitals Ghent. Validation was performed using discrimination and calibration, evaluated by calibration plots.

Results

The nomograms based on postoperative variables performed better than the nomograms based on pre-operative variables, for all outcomes (OS: c = 0.68 vs 0.64; DFS: c=0.70 vs 0.64; DSS: c= 0.74 vs 0.64). The nomogram predicting DSS based on postoperative variables performed best (*cfr Figure 1*). C index for this nomogram on external validation was 0.65. As an example: for a patient with a pT4aN3b moderately differentiated supraglottic cancer treated with STL, free section margins and absence of perineural invasion, the designed and validated nomogram estimates a 2-year DSS probability of 56.7%.

Conclusions

The presented prognostic nomograms for predicting oncological outcomes in patients who underwent STL are user-friendly, visual tools which allow for a reliable prognostic assessment and result in a more individualized estimate of the expected outcomes, which can guide a patient-tailored adjuvant treatment (eg re-irradiation or immunotherapy). Postoperatively available variables, related to anatomopathologic features, boost nomogram accuracy. Further external validation on bigger datasets from multiple centers is warranted.


Points
0 10 20 30 40 50 60 70 80 90 100
Perineural invasion second tumor
Yes
No
pTNM N–stage second tumor
N1 N2b N3
N0 N2a N2c
pTNM T–stage second tumor
T2 T4a
T1 T3 T4b
Section_marges_second_tumor
Close margin (<5 mm)
Free margins (>5 mm) Positive margin
Histology second tumor (differentiation SCC)
highly/moderately poorly
Total Points
0 20 40 60 80 100 120 140 160 180 200 220 240 260
2–Y DSS Prob.
0.9 0.8 0.7 0.6 0.5 0.4 0.3 0.2 0.1
5–Y DSS Prob.
0.9 0.8 0.7 0.6 0.5 0.4 0.3 0.2 0.1

OC-064 | Oligometastasis has better quality of life than polymetastasis in patients with head and neck cancer

Diako Berzenji [(1)]; *Maarten Dorr* [(1)]; *Marinella Offerman* [(1)]; *Robert Jan Baatenburg de Jong* [(1)]; *Jose Hardillo* [(1)]

(1) Erasmus MC Rotterdam

Keywords

Polymetastasis, Distant metastasis, Oligometastasis

Purpose/Objective

There is increasing evidence that distant metastasis (DM) in head and neck squamous cell carcinoma is a spectrum of disease. Previous studies have shown that oligometastasis has favorable survival compared to polymetastasis. However, the quality of life (QoL) of patients with oligometastasis, as opposed to polymetastasis, is unknown. We hypothesized that the QoL of patients with OM is better than those with a polymetastatic pattern.

Material/Methods

Retrospective cohort study in which patients with DM were stratified into three groups: oligometastasis (OM) (maximum of 3 metastatic foci in ≤2 anatomic sites), explosive metastasis (EM) (≥4 metastatic foci at one anatomic site) and explosive-disseminating metastasis (EDM) (spread to ≥3 anatomic sites). QoL was assessed using the EORTC QLQ-C15-PAL questionnaire every two months post diagnosis of DM.

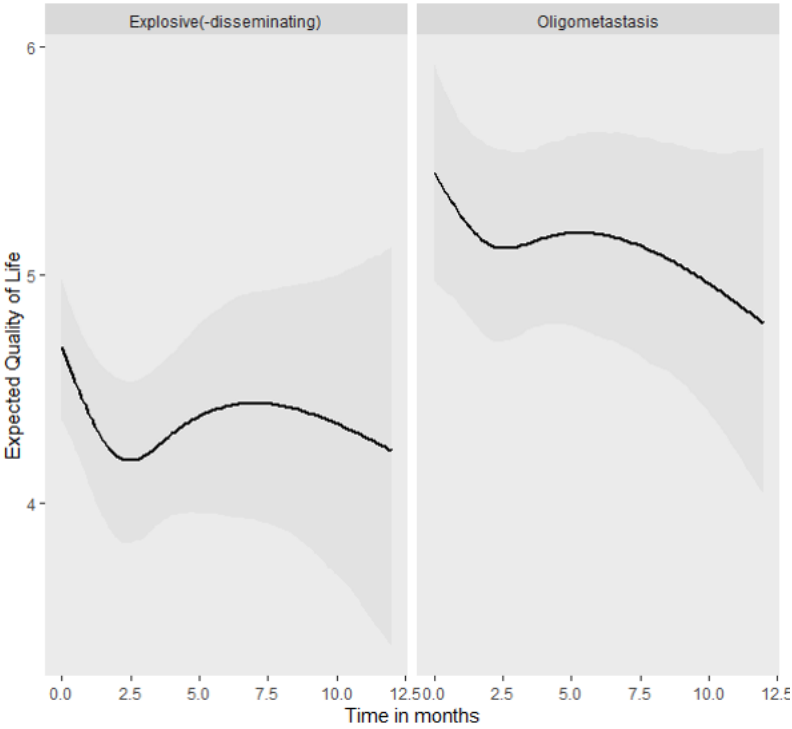
Results

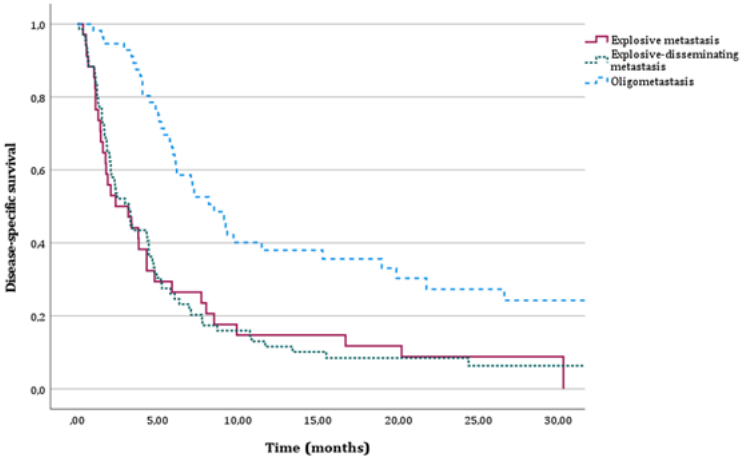
Between January 1, 2016 and December 31, 2021, a total of 161 patients with DM were identified with in total 397 QoL measurements. In this group, 57 (35.4%) patients had OM, 35 (21.7%) patients had EM and 69 (42.9%) patients had EDM. The median post-DM

survival was 8.5 months in the OM group and 3.2 months in both the EM and EDM groups (p<.001). Corrected for treatment and time, linear mixed-model analyses showed a significantly better post-diagnosis overall QoL in the OM group in comparison to the non-OM group at diagnosis and during the whole course of the follow-up (+0.75 out of 7, p<.05). In addition, patients with OM performed better in the subdomains of “physical functioning”, “fatigue” and “pain” both at diagnosis and during the remainder of the follow-up.

Conclusion

Better QoL is observed in the OM group as opposed to the non-OM groups. Results from this study allow for interventions aimed at improving the QoL of the more vulnerable polymetastatic group. In addition, this study solidifies the position of OM as a separate entity within the distant metastatic spectrum of disease.


Explosive(-disseminating)
Oligometastasis
Expected Quality of Life
6
5
4
0.0
2.5
5.0
7.5
10.0
12.5
Time in months


Disease-specific survival
1.0
0.8
0.6
0.4
0.2
0.0
.00
5.00
10.00
15.00
20.00
25.00
30.00
Time (months)
Explosive metastasis
Explosive-disseminating metastasis
Oligometastasis

OC-068 | Intraoperative assessment of resection margins by Raman spectroscopy to guide oral cancer surgery

Yassine Aaboubout [1]; Maria r. Nunes Soares [1]; Tom c. Bakker Schut [1]; Elisa m. Barroso [1]; Martin Van Der Wolf [2]; Elena Sokolova [2]; Viacheslav Artyushenko [3]; Alexey Bocharnikov [3]; C.G.F. Van Lanschot [1]; Lars Ottevanger [1]; Hetty Mast [1]; Ivo Ten Hove [1]; Brend p. Jonker [1]; Stijn Keereweer [1]; Dominiek a. Monserez [1]; Aniel Sewnaik [1]; Jose a. Hardillo [1]; Rob j. Baatenburg de Jong [1]; Senada Koljenovic [4]; Gerwin j. Puppels [1]

(1) Erasmus MC Rotterdam (2) RiverD (3) art photonics GmbH (4) University Hospital Antwerp (UZA)

Keywords

Intraoperative assessment, resection margins, Raman spectroscopy

Objective/Objective

The goal of oral cavity squamous cell carcinoma (OCSCC) surgery is complete tumor resection. However, adequate resection margins are achieved in only 15-26% due to the lack of information on the resection margins during surgery. Therefore, we developed and validated an technology for intraoperative assessment of tumor resection margins, based on Raman spectroscopy in patients with OCSCC.

Material/Methods

Patients with OCSCC who underwent surgical treatment from May 2019 until September 2021 were included. The measurements were performed on fresh resection specimens by the Raman spectroscopic device with a disposable fiber-optic needle probe. First, a tissue classification model was created and tested based on measurements that were histologically classified as healthy tissue or tumor. This model resulted in probability profiles. These profiles were used to develop a margin length prediction model, which was tested on an independent data set.

Results

The tissue classification model was based on a data set of 1347 tumor spectra and 1784 healthy tissue spectra (from 25 patients). The discriminative power was 0.93 (AUC), accuracy was 0.89, sensitivity was 0.87, and specificity was 0.91. This model was tested on an independent data set of 426 tumor spectra and 1240 healthy tissue spectra (from 15 patients). The discriminative power was 0.92 (AUC), accuracy was 0.90, sensitivity was 0.85, and specificity was 0.92.

Next, a margin length prediction model was developed on 217 probability profiles (from 14 patients). The mean difference between margin length prediction by the device and histology was -0.15 mm. This model was tested on an independent data set of 211 probability profiles (from 17 patients). The mean difference between margin length prediction by the device and histopathology was -0.17 mm.

Conclusion

The results of this technical validation of the Raman spectroscopic device show that it enables an accurate assessment of the resection margins. This brings the technology only one step away from the patient. Currently, we are preparing (pre)clinical, multi-center validation studies.

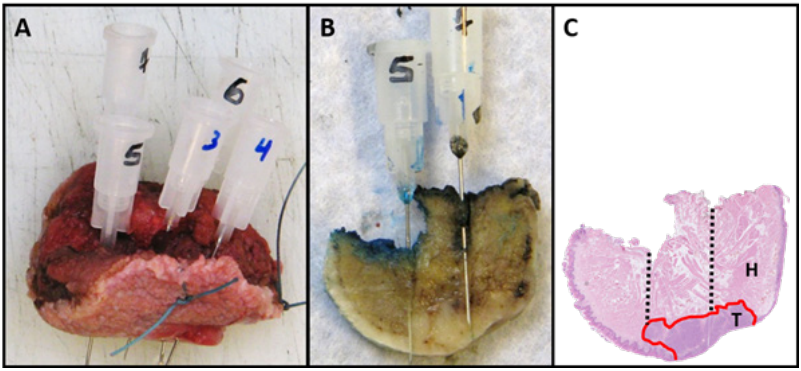
FIGURE 1. Illustration of intraoperative assessment on fresh resection specimen and final pathology for histological annotation of measurements.

1.

A. *Intact fresh resection specimen with numbered needles demarcating the position of measurements.*

B. *Final pathology: formalin-fixed section of the measured area.*

C. *Annotation of measurements: H&E-slide showing the measurement location, enabling the determination of the margin length. Red line: tumor border. H: healthy tissue, T: tumor.*


A
B
C
H
T

OC-069 | The benefits of oncologic care optimization in a regional referral network for head and neck cancer

Henrieke Schutte [1]; n. Labbé [1]; G.B. Van Den Broek [1]; j. Honings [1]; H.A.M. Marres [1]; W.L.J. Weijs [1]; S.C.A. Steens [1]; A.I.J. Arens [1]; A.C.H. Van Engen - Van Grunsven [1]; C.M.L Driessen [1]; j. H.A.M. Kaanders [1]; R.P. Takes [1]; F.J.A. Van Den Hoogen [1]

(1) Radboudumc, Nijmegen, The Netherlands

Keywords

Head and neck cancer. Time-to-treatment. Network. Optimized oncological work-up. Oncologic care.

Objectives

Patients with head and neck cancer (HNC) benefit from early treatment initiation. Previously we implemented a fast-track multidisciplinary integrated care program to reduce time to treatment in our head and neck oncological center. This included initial joint consultation involving all healthcare disciplines relevant for HNC, the use of time slots for imaging with an optimized order of imaging, and a shift from endoscopy in general anesthesia to office-based procedures. To further improve HNC care and shorten time-to-treatment interval, we extended the HNC care path optimization to our referral network and agreed with all regional clinics to immediately refer patients based only on clinical suspicion of HNC and refrain from any diagnostic procedure.

Methods

We compared all patients with suspected primary HNC diagnosed in 2008 and 2016, before and after the agreement respectively. All patients were treated with curative intent in the Radboud University Medical Center Nijmegen.

Results

Five hundred and fifty-nine patients with suspected HNC were eligible for inclusion. Twohunderd sixty-six patients were included in 2008 and 293 patients were included in 2016. The agreement in our referral network did not led to an increase in referral of patients with benign lesions. Time from the initial consultation of the referring medical specialist to referral to our HNOC was significantly reduced from a median 16 to 11 days (p=0.002). Overall this resulted in a significant reduction of the time from the initial consultation of the referring medical specialist to the start of treatment in a HNOC, from 56 days in 2008 to 38 days in 2016 ($p < 0.001$) including the optimized workup in our HNOC. In addition, rigid laryngopharyngoscopies under general anesthesia were reduced by approximately 50% ($p < 0.001$).

Conclusions

Efficiently organizing HNC care in a network led to earlier treatment and reduced the number of diagnostic procedures performed under general anesthesia with its associated risks and costs. This study demonstrates the benefits of oncologic care optimization in a network.

OC-074 | The predictive value of depth of invasion of oral cavity carcinoma for cervical nodal metastasis

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Keywords

Tongue carcinoma, floor of mouth carcinoma, depth of invasion, elective neck dissection, treatment threshold

Purpose/Objective

The depth of invasion (DOI) is considered an independent risk factor for occult regional lymph node metastasis (RLNMs) in oral squamous cell carcinoma (OSCC). It is used post-operatively to decide whether or not to perform an elective neck dissection (END) in case of a clinically negative neck for early stage carcinoma (pT1/pT2). The current international consensus it that an END should be performed if the risk of occult RLNMs is > 20%. However, there is much debate on the optimal cut-off value of the DOI for performing an END. The aim of this study was to determine the optimal threshold in a single center retrospective OSCC cohort, and investigate whether optimal cut-off values differ per subsite. Furthermore, it was investigated whether DOI alone is sufficient for the clinical decision to perform an END, or whether it should be corrected for other histopathological characteristics.

Material/Methods

A retrospective cohort study was conducted. Surgically treated patients with primary tongue, floor of mouth (FOM) or buccal mucosa carcinoma (pT1 or pT2) and clinically negative lymph nodes (cN0) were included between January 2006 and December 2018. The DOI was measured following the recommendation from the 8th edition of the AJCC. A univariate logistic regression was per-

formed to assess the contribution of DOI to the odds of occult neck metastasis and to determine the optimal cut-off value for DOI in predicting the possibility of neck metastasis. A multivariate logistic regression was performed to assess the combined effect of DOI and perineural invasion on neck metastasis.

Results

A total of 245 patients were included whereof 146 patients with carcinoma of the tongue, 83 FOM and 16 patients buccal mucosa. The optimal DOI cut-off value with 20% probability on lymph node metastasis for the total cohort was 5.5 mm, for the tongue 5.1 mm and for the FOM 5.8 mm. Perineural invasion is significantly associated with the presence of RLNMs (OR 2.8). Correcting for both DOI and perineural invasion lowers the DOI threshold from 6 mm to 2 mm.

Conclusion

DOI has a significant predictive value for neck metastasis and an END should be performed when the DOI is >5.1 for tongue carcinomas and >5.8 for FOM carcinomas. [JH1] Perineural invasion should be considered in the decision whether to perform an END. The optimal DOI cut-off value with 20% probability on lymph node metastasis lies between 5.1 and 5.8 mm depending on the subsite, indicating that performing END at DOI 4 mm is adequate standard operating procedure. These results indicate that possibly a general threshold for DOI is suboptimal in modern patient care, and multivariable models incorporating other histopathological factors should be developed to improve shared decision making.

OC-080 | The association between Multidimensional Prognostic Index and mortality in patients with HNC

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Keywords

Comprehensive Geriatric Assessment; Mortality, Head and Neck Cancer, Multidimensional Prognostic Index, Elderly, Complications

Purpose

Head and Neck Cancer (HNC) is especially present in older adults with comorbidity burden, with high risk of frailty. The Multiple Prognostic Index (MPI) reflects the degree of frailty and was developed to predict one-year mortality risk outcomes. The aim of this study is to investigate whether the MPI is associated with mortality in HNC patients. Secondary we will evaluate whether a higher MPI is associated with a higher grade of complications.

Methods

From December 2019 to June 2021, an observational cohort study enrolled patients with HNC aged ≥70 years, and patients <70 years with a G8 score ≤14, who all received a comprehensive geriatric assessment (CGA). The MPI score was calculated based on the CGA. Complications were graded, using the 5 grades by Clavien-Dindo. Survival analyses were performed using Kaplan Meier curves, whereas the association between MPI and mortality was evaluated using univariable and multivariable Cox regression. The association between the MPI and complications was evaluated using a logistic regression.

Results

A total of 423 patients were included with a median age of 76 [72-81] years and 68.6% were men. During a mean follow-up time

of 595 days (95% CI 567-623), 115 (29%) patients died. In univariable analysis determinants associated with mortality were: BMI, tumor stage, tumor location, MPI score, gait speed, handgrip strength and use of a walking aid. In the multivariable analysis a higher MPI score was significantly associated with higher mortality risk (HR 7.96, [95% CI 2.44-26.0], p=0.001). Of the MPI subdomains, the risk of malnutrition was significantly associated with mortality, whereas the other individual subdomains were not. Next, the multivariable model was repeated in patients with curative treatment intention only, in which a higher MPI score was significantly associated with a higher mortality risk (HR 5.01, [95% CI 1.11-22.7] p=0.04). 35 of the patients (17,3%) had a post-operative complication. The MPI was not statistically significant associated with mortality (HR 1.080, [95% CI 0.446-2.614], p=0.086).

Conclusion

A higher MPI score is associated with higher mortality risk in HNC patients who received treatment with curative intention. The MPI is not associated with a higher risk of post-operative complications.

OC-087 | Prognostic Implication of p16 and HPV discordance in oropharyngeal cancer: the EPIC-OP study

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Purpose/Objective

p16^{INK4a} (p16) immunohistochemistry (IHC) is the most widely-used biomarker assay for inferring HPV causation in oropharynge-

al cancer (OPC) in clinical and trial settings. However, discordance exists between p16 and HPV DNA/RNA status in a subset of OPC. This international multicenter study aims to clearly quantify the extent of discordance, and its prognostic implication.

Methods

An international consortium comprising 13 cohorts of OPC patients from 9 countries with data on p16 IHC, HPV (DNA/RNA), and clinical information was established. A centralised individual patient data reanalysis was performed. Multivariable analysis models were used to calculate adjusted hazard ratio (aHR) of different p16 and HPV testing methods for overall survival (OS), adjusted for confounding factors. Additional analyses in different geographical regions were performed.

Results

In total 7654 OPC cases were included. The percentages of p16-/HPV-, p16-/HPV+, p16+/HPV-, and p16+/HPV+ were 46.5%, 3.8%, 5.4%, and 44.3%, respectively. Among 3805 p16+ cases, 415 (10.9%) were HPV-. This proportion differed significantly by geographic region ($p<0.001$) and was highest in the areas with lowest HPV-attributable fractions (HPV-AF). The proportion of p16+/HPV- was higher in subsites outside the tonsil/base-of-tongue (26.2% vs 6.0%, $p<0.001$). Compared to p16+/HPV+ tumours, p16-/HPV- tumours showed the worst prognosis for 5-year OS (aHR 3.93 (95%CI 3.50,4.43)); while discordant OPC cases showed intermediate prognosis [p16-/HPV+ aHR 2.76 (95%CI 2.22,3.45); p16+/HPV- aHR 2.61 (95%CI 2.16,3.17)]. This was similar across all European sub-regions.

Conclusions

Discordant positive (p16-/HPV+ and p16+/HPV-) OPC patients demonstrate significantly worse prognosis than p16+/HPV+ (double positive) OPC, and significantly better prognosis than p16-/HPV- OPC. Along with routine p16 IHC testing, HPV testing for

all patients, or at least following a positive p16 test, is strongly recommended where HPV status determines eligibility for clinical trials, treatment decision-making and counselling on prognosis in a clinical setting.

OC-089 | Incidental thyroid carcinoma. What have we learned?

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(1) Outro

Purpose/Objective

Incidental thyroid carcinoma (ITC) is known as the unexpected pathological finding of malignancy, in patients undergoing thyroid surgery for a preoperatively considered benign disease. The aim of this study is to describe a cohort with ITC and to identify the main risk factors for malignancy in patients with goiter.

Material/Methods

Retrospective cohort study, of patients with goiter and Bethesda II cytology nodules, that were taken to any type of thyroidectomy from january 2017, to december 2020, at the National Universitary Hospital of Colombia, in Bogotá, Colombia. Demographic and ecographic variables were studied with descriptive statistics, bivariate and multivariate analysis, with ITC as the main outcome.

Results

In the 4 years period, 1889 patients were operated for thyroid pathology of which 299 had Bethesda II cytology and met the inclusion criteria for the study. The mean age in the ITC group was 48.42 years (+/-14.30) and 50.16 (+/-13.97) for the benign disease group. The most frequent type of operated goiter was multinodular in 148 patients (49,49%) and 138 (46,15%) had uninodular goiter. The 44.1% were treated with total thyroidectomy, and the rest were managed with partial thyroidectomy. ITC was diagnosed in 38 patients (12.7%). The most frequent malignant histology was papillary carcinoma (83,7%), with the classic variant as the most frequent (43,2%) and with micropapillary thyroid carcinoma

in 60.52% of the cases. One medullary carcinoma (2,7%) and one primary thyroid lymphoma (2,7%) were documented. In the bivariate and multivariate statistical analysis, uninodular goiter was found to be a protective factor for presenting malignant thyroid pathology (p=0,023; OR:0.406(CI:0.273-0.604). None of the variables studied were found to increase the risk of ITC.

Conclusion

ITC is not an infrequent entity in patients with goiter, even if they have benign cytology. Most of the ITC patients have micropapillary thyroid carcinomas but there is an important incidence rate of aggressive histologies such as lymphomas or medullary carcinomas. Uninodular goiter is a protective factor for ITC. Other studies with a larger sample size are necessary to confirm these findings.

OC-090 | Early mortality among Curative Head and Neck cancer patients, who and why?

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Keywords

Early mortality, Head and neck cancer

Purpose/Objective

Patients with Head and Neck cancer (HNC) and a curative treatment intent at multidisciplinary tumor board still die within six months in 4.5% of the cases. To our knowledge little has been written about this group. The aim of this study was to identify risk factors for early death among patients with curative treatment, and to analyze if the risk of early death has decreased over recent years.

Material/Methods

This real-world, population-based, nationwide study from the Swedish Head and Neck Cancer Register (SweHNCR) included data from 2008-2020 and 16.786 patients with curative treatment.

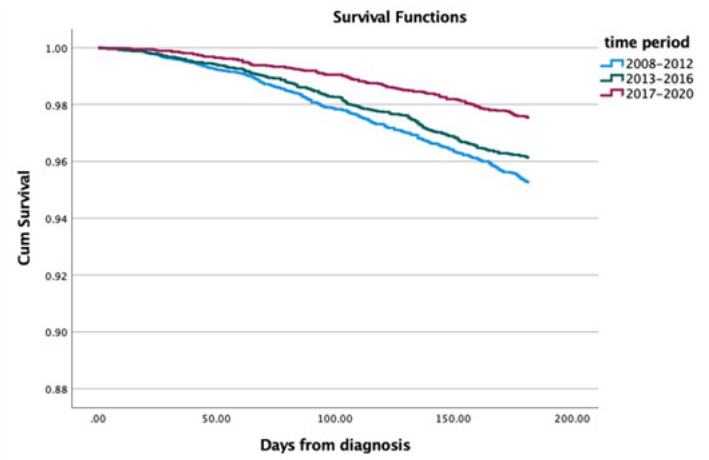
Results

Between 2008 to 2020 618 (3.7%) of a total of 16786 patients died within six months despite having a curative intended treatment. The risk factors for death within six months has been divided into tumor- and patient related factors. Age, high WHO class, hypopharyngeal cancer, and high T stage were independent factors for early death. For every year older the patients became, the risk of early death increased by 4.7% ($p<0.001$). The relative risk of death was 2.40 times higher (140%) for patients with WHO score 1 compared with WHO score 0. A primary tumor in the hypopharynx had the highest risk of early death among all sites and correlated

with a 62% increased risk over the oropharynx (p=0.002). Patients with T3 or T4 disease had a 2.9 times greater risk of early death than those with T1 or T2 tumors (p<0.001). Unexpectedly, we found that females had a risk reduction for early death of 20% compared to males. Between 2008-2012 the six months mortality was 4.7% compared to 3.9% and 2.5% for the years 2013-2016 and 2017-2020 respectively (p<0.001).

Conclusion

This real-world, nationwide, register-based study including 16.786 patients with HNC, and curative treatment intent, shows that the risk of early death has decreased significantly since 2008. High age, male sex, high WHO function class, and a tumor in hypopharynx with a high stage were independent risk factors for death within in six months after diagnosis.



OC-093 | Net treatment benefit of avasopasem manganese for severe oral mucositis from the ROMAN trial

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Keywords

Avasopasem, IMRT, severe oral mucositis

Purpose/Objective

Oral mucositis is a common and debilitating side effect of concurrent cisplatin and intensity-modulated radiation therapy (IMRT) in patients with head and neck squamous cell carcinoma (HNSCC). Recent randomized phase 3 data from the ROMAN trial (NCT03689712) showed that the investigational dismutase mimetic avasopasem manganese (AVA) statistically significantly decreased the incidence and duration of severe oral mucositis (SOM, WHO grade 3-4), with a nominal decrease in severity (WHO grade 4) and delay in onset of SOM (Anderson, ASCO 2022). We sought to determine the net treatment benefit (NTB) of AVA versus placebo using the generalized pairwise comparisons (GPC) method.

Material/Methods

GPC is a statistical method that permits the simultaneous analysis of several prioritized outcome measures. The core idea relies on the comparison of all pairs of patients that can be constructed with one patient from the AVA group and one patient from the placebo group. For each pair, the prioritized outcome measures serve to define which of the two patients composing the pair has a better outcome. The results of all the comparisons are then aggregated in a summary measure that estimates the NTB. The NTB is the net probability that a random patient from the AVA

group would have a better outcome than a random patient from the placebo group. Clinically relevant outcomes from ROMAN were prioritized as follows: 1) incidence of WHO grade 4 SOM, 2) incidence of SOM (WHO grade 3 or 4), 3) number of days of SOM through IMRT, 4) time to onset of SOM. For the latter two outcomes, a minimal difference of 7 days was defined as the threshold of clinical relevance, i.e., the difference under which observed differences are not sufficiently large to determine which patient had a better outcome. Analyses were stratified for cisplatin schedule (weekly vs Q3 week) and treatment setting (post-operative vs definitive treatment).

Results

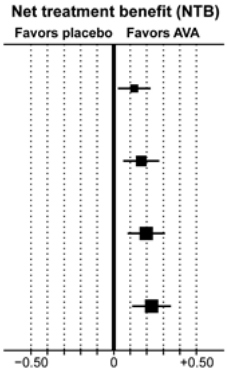
Data from this post-hoc analysis of 407 patients (AVA = 241, Placebo = 166) resulted in 13,969 pairwise comparisons. AVA showed a statistically significant benefit in all prioritized outcomes (Figure 1); when considering a random patient who received AVA and a random patient who received placebo, there is a 56.2% probability that the patient who received AVA would have a better outcome, vs a 33.1% probability for the opposite situation. The difference between these probabilities is a NTB of 23.1% (P=0.00019), translating to a number needed to treat (NNT) of 4.33 patients (= 1/23.1%). All sensitivity analyses were statistically significant and consistent with the primary GPC analysis, providing evidence of the robustness of the analysis and its conclusions.

Conclusion

This post-hoc GPC analysis shows compelling evidence of clinical benefit to HNSCC patients who received AVA as compared to those who received placebo on the ROMAN trial. Submission to the US Food and Drug Administration is in progress.

Figure 1. Forest Plot of NTBs (95% CI)

Outcomes	Wins (%)	Losses (%)	Ties (%)	NTB (95% CI)	*P* value
WHO grade 4 SOM	3855 (0.276)	2095 (0.150)	8019 (0.574)	NTB = 0.126 (0.029, 0.222)	*P* = 0.011
Any SOM (WHO grade 3 or 4)	5839 (0.418)	3492 (0.250)	4638 (0.332)	NTB = 0.168 (0.053, 0.282)	*P* = 0.004
Number of days SOM (WHO grade 3 or 4) at least 7 days later	7166 (0.513)	4372 (0.313)	2431 (0.174)	NTB = 0.200 (0.083, 0.316)	*P* = 0.00081
Time to onset SOM (WHO grade 3 or 4) at least 7 days later	7851 (0.562)	4623 (0.331)	1495 (0.107)	NTB = 0.231 (0.110, 0.351)	*P* = 0.00019



OC-099 | Early swallow outcomes following dysphagia-optimised radiotherapy for head and neck cancer

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Keywords

Dysphagia-optimised radiotherapy, swallowing

Purpose

Radiation-associated dysphagia following primary radiotherapy (RT) has a significant impact on quality of life. Reducing RT dose to dysphagia/aspiration-related structures with dysphagia-optimised intensity-modulated RT (DO-IMRT) is associated with an improvement in patient-reported swallow outcomes and a trend for better post--treatment swallow performance. DO-IMRT was implemented as standard of care at our UK centre in October 2021, with the volumes of pharyngeal constrictor muscles, oral cavity and larynx lying outside the planning target volume set an optimal mean dose constraint of ≤50 Gy, ≤40 Gy and ≤30 Gy respectively. We report early swallow outcomes up to six months post-treatment for an initial mixed cohort.

Methods

All patients treated with primary curative DO-IMRT from October 2021 to January 2022 were included. Functional swallow measures (Performance Status Scale Head & Neck (PSS-HN), 100ml Water Swallow Test swallow volume and capacity) and rates of enteral feeding were prospectively collected at baseline and at six weeks, three months and six months post-treatment, either face to face or during virtual consultation. PSS-HN was dichotomised to indicate good (>50) or impaired (≤50) function. Descriptive statistics were used to report results.

Results

Twenty four patients were included (Table 1). By six months post--treatment two patients (8%) had died and one (4%) who required tracheostomy and enteral feeding pre-treatment had undergone salvage functional total laryngectomy and remained gastrostomy-dependent. Outcome measures are summarised in Table 2; there were some missing data, typically due to limitations of virtual consultations. There was a deterioration in function on all measures from baseline to six weeks post-treatment, and subsequent gradual improvement. By six months post-treatment, the proportion of patients with good swallow function (PSS-HN Normalcy of Diet score >50) was similar to baseline (77% vs 79%), and most (76%) had returned to public eating (PSS-HN Eating in Public score >50). Eight patients (35%) commenced enteral feeding during or post-treatment; all had returned to full oral intake by six months. Swallow volume and capacity remained below baseline levels by six months post-treatment.

Conclusion

Most patients treated with DO-IMRT in this first mixed cohort returned to good swallow performance by six months post-treatment. Further longitudinal data is being collected on a larger cohort to determine long term swallow outcomes.

Table 1. Patient characteristics

	n	(%)
Age		
Mean (years)	64.5	
Range	54 - 79	
Sex		
Female	5	(21)
Male	19	(79)
Smoking status		
Current	4	(17)
Previous	14	(58)
Never	6	(25)
Tumour site		
Nasopharynx	0	(0)
Oropharynx	19	(79)
Larynx	2	(8)
Hypopharynx	2	(8)
Other	1	(4)
T stage		
T1	0	(0)
T2	6	(25)
T3	5	(21)
T4	13	(54)
N stage		
N0	10	(42)
N1	3	(13)
N2a	1	(4)
N2b	6	(25)
N2c	2	(8)
N3	2	(8)
TNM stage (AJCC 7th Edition)		
II	3	(14)
III	3	(14)
IV	16	(73)
Treatment plan		
Induction + CRT	3	(13)
CRT	13	(54)
RT	8	(33)
Neck radiation		
Unilateral	0	(0)
Bilateral	24	(100)

Table 2. Outcome measures over time.

	Baseline	6 weeks	3 months	6 months
PSS Normalcy of Diet score >50*	79% [24]	35% [23]	38% [24]	77% [22]
PSS Eating in Public score >50*	100% [19]	55% [20]	48% [21]	76% [21]
Enteral feeding*	4% [24]	33% [24]	17% [24]	5% [22]
Swallow volume (ml/swallow)**	19.7 (11.1) [11]	13.3 (7.4) [16]	14.4 (11.0) [16]	17.1 (7.6) [17]
Swallow capacity (ml/second)**	15.4 (7.9) [11]	7.6 (5.8) [16]	9.6 (6.9) [16]	11.1 (6.1) [17]

*Percentage [N]
**Mean (standard deviation) [N]

OC-103 | DEPTH OF INVASION AS A PROGNOSTIC FACTOR OF LARYNX CANCER

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Keywords

Depth of invasion, laryngeal carcinoma, prognosis

Purpose/Objective

In literature review, the degree of invasion in depth is associated with biological aggressiveness of the tumor. The aim of this study is to analyses the impact on prognosis of the deep invasion by laryngeal cancer.

Materials and Methods

We studied the depth invasion of the tumors of 85 patients, dividing them into two groups based on whether the invasion was greater or less than 5 mm. We performed a statistical study of the in-depth invasion in relation to the presence of cervical lymph node metastases and/or tumor recurrence.

Results

Of the 85 patients, 25 were supraglottic tumors, 33 glottic, 17 transglottic and 10 pyriform sinuses. Of 85 patients, 28 patients presented lymph node metastases. Median depth invasion in our series was 11 mm (2-24 mm). If the depth of invasion was > 5 mm, the frequency of cervical metastases was eight times higher. Only 3 tumors with invasion of less than 5 mm presented cervical metastases. Of the 14 patients who presented recurrence, 11 also presented invasion greater than 5 mm.

Conclusion

Tumor invasion of more than 5 mm was associated in our series with a higher risk of cervical metastasis and tumor recurrence.

OC-110 | Clinical and genomic determinants of the efficacy of immune checkpoint blockade therapy in HNSCC

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(1) Memorial Sloan Kettering Cancer Center (2) Illumina Inc. (3) NKI-AvL, Amsterdam (4) Icahn School of Medicine at Mount Sinai (5) Lerner Research Institute Cleveland Clinic

Objective

While immune checkpoint blockade (ICB) drugs are effective in ~20% of patients with recurrent and/or metastatic (R/M) head and neck squamous cell carcinoma (HNSCC), the remaining 80% experience limited clinical benefit and are exposed to potential adverse effects at financial costs to healthcare systems. The clinically approved biomarker of tumor mutational burden (TMB) has modest predictive value in HNSCC. We aimed to investigate potential clinical and genomic biomarkers predicting a favorable outcome after ICB with greater accuracy.

Methods

Whole-exome sequencing (WES; median coverage 776x) was performed on tumors obtained from 133 R/M HNSCC patients (64 virus-negative [V–] and 69 virus-positive [V+]) who were treated with ICB. Clinical endpoints including objective response, progression-free survival (PFS), and overall survival (OS) were collected from the medical record. Hierarchical clustering based on genomic features and viral status was used to distinguish molecular subtypes of HNSCC. Random forest modeling and recursive partitioning analysis were used to develop two models predicting

PFS using clinical and genomic features. Two independent datasets of ICB-treated HNSCC patients were used for validation.

Results

The overall objective response rate (ORR), 1-year PFS, and 1-year OS were 24%, 20%, and 49%, respectively. V– tumors had a lower ORR *(19% vs. 29%, P = 0.22)*, 1-year PFS *(13% vs. 26%, P = 0.07)*, and 1-year OS *(36% vs. 61%, P = 0.002)* than V+ HNSCC. V– HNSCC was characterized by a higher TMB (median 3.7 vs. 2.3 muts/Mbp, *P* = 0.006) and a stronger smoking signature (median contribution 0.29 vs. 0.16, P = 3.6·10–6) compared to V+ tumors. Hierarchical clustering based on 13 genomic features and viral status revealed 6 molecular subtypes that displayed divergent ORR (7–48%), PFS (median 1.7–9.1 months), and OS (median 6.5–34.8 months) after ICB. The prognostic relevance of these subtypes was validated in an independent cohort. Compared to TMB alone, a random forest classifier including 14 features (clinical, laboratory, and genomic) predicted 6-month PFS, 1-year OS, and response with greater accuracy, which was validated in an independent cohort. Finally, recursive partitioning analysis yielded a simple classifier comprised of 3 features that identified patients at high-, intermediate-, and low-risk of death after ICB therapy.

Conclusions

The findings from this large cohort of R/M HNSCC patients shed light on the immunogenomic characteristics driving differential response to ICB and identify and validate a clinical-genomic classifier that outperforms TMB.

OC-112 | Tumor-Intrinsic Nuclear ß-Catenin associates with low CD8+ TILs and a poorer prognosis in HNSCCs

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Purpose/Objective

Activation of WNT/ß-catenin signaling has been associated with a non-T-cell-inflamed tumor microenvironment (TME) in several cancers. The aim of this work was to investigate the relationship between ß-catenin signaling and TME inflammation in head and neck squamous cell carcinomas (HNSCCs).

Material/Methods

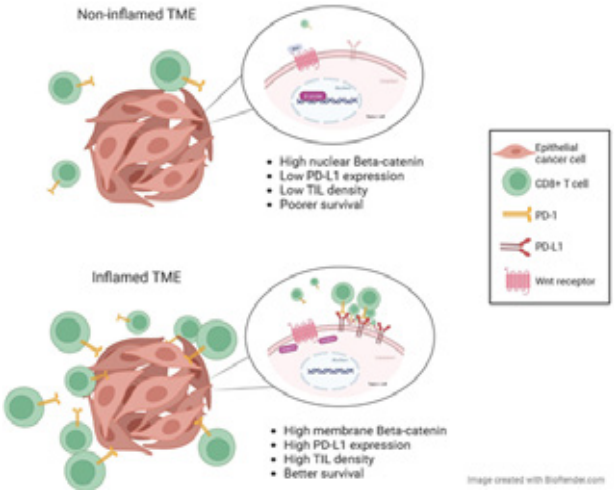
Membrane and nuclear ß-catenin expression, PD-L1 expression, and CD8+ tumor-infiltrating lymphocyte (TIL) density were jointly evaluated by immunohistochemistry in a series of 372 HPV-negative HNSCCs.

Results

Membrane ß-catenin levels decreased in carcinomas compared to the normal epithelium. Positive nuclear ß-catenin was detected in 50 tumors (14.3%) and was significantly associated with a low CD8+ TIL density (168 cells/mm2 versus 293 cells/mm2 in nuclear-ß-catenin-negative cases; p = 0.01) and a tendency for a lower expression of PD-L1, resulting in association with a noninflamed TME (i.e., type II, immunological ignorance). Multivariate Cox analysis further demonstrated that low infiltration by CD8+ TILs (HR = 1.6, 95% CI = 1.19–2.14, p = 0.002) and nuclear ß-catenin expression (HR = 1.47, 95% CI = 1.01–2.16, p = 0.04) were both independently associated with a poorer disease-specific survival.

Conclusion

Tumor-intrinsic nuclear ß-catenin activation is associated with a non-inflamed TME phenotype and a poorer prognosis, thereby suggesting a possible implication as an immune exclusion mechanism for a subset of HNSCC patients.



OC-117 | Federated learning- OS modeling of larynx cancer without patient-sensitive data leaving the hospital

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(1) Odense University Hospital (2) The Christie NHS Foundation Trust, Manchester (3) Ingham Institute for Applied Medical Research (4) Aarhus University Hospital (5) Institute of Medical Physics, School of Physics, University of Sydney

Introduction

Federated learning has the potential to perform analysis on decentralised data, where patient-sensitive data stay in the local hospitals; however, there are some obstacles to survival analyses as there is a risk of data leakage.

This study demonstrates how to perform a stratified Cox regression survival analysis specifically designed to avoid data leakage using federated learning on larynx cancer patients from centres in three different countries.

Methods

Data were obtained from 1821 larynx cancer patients treated with radiotherapy in three centres. Tumour volume was available for all 786 of the included patients.

Parameter selection among eleven clinical and radiotherapy parameters were performed using best subset selection and cross-validation through the federated learning system, AusCAT.

After parameter selection, b regression coefficients were estimated using bootstrap. Calibration plots were generated at 2, and 5-year survival and inner and outer risk groups' Kaplan-Meier curves were compared to the Cox model prediction (fig 2).

Results

The best performing Cox model included log(GTV), performance status, age, smoking, haemoglobin and N-classification; however, the simplest model with similar statistical prediction power included log(GTV) and performance status only. The Harrell C-indices for the simplest model were for Odense, Christie and Liverpool 0.75[0.71–0.78], 0.65[0.59–0.71], and 0.69[0.59–0.77], respectively. The values are slightly higher for the full model with C-index 0.77[0.74–0.80], 0.67[0.62–0.73], and 0.71[0.61–0.80], respectively. Smoking during treatment has the same hazard as a ten-years older nonsmoking patient (Fig 1).

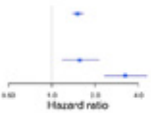
The calibration plots for the three centres with the observed survival are shown in six patient groups at two and five years. Due to censoring, the observed values are measured as the Kaplan-Meier estimate within each of the six groups at the given time point. The reduced model is shown in dark colours, and the full model in light colours. The error bars indicate the 95% confidence interval. Figure 2 bottom: The Kaplan-Meier estimator and Cox model prediction for each risk group of the three centres. The result of the reduced model is presented on the top row, while similar values for the full model are shown on the lower row. The shaded colour indicates the 95% confidence interval of the Kaplan-Meier estimate.

Conclusion

Without any patient-specific data leaving the hospitals, a stratified Cox regression model based on data from centres in three countries was developed without data leakage risks. The overall survival model is primarily driven by tumour volume and performance status.

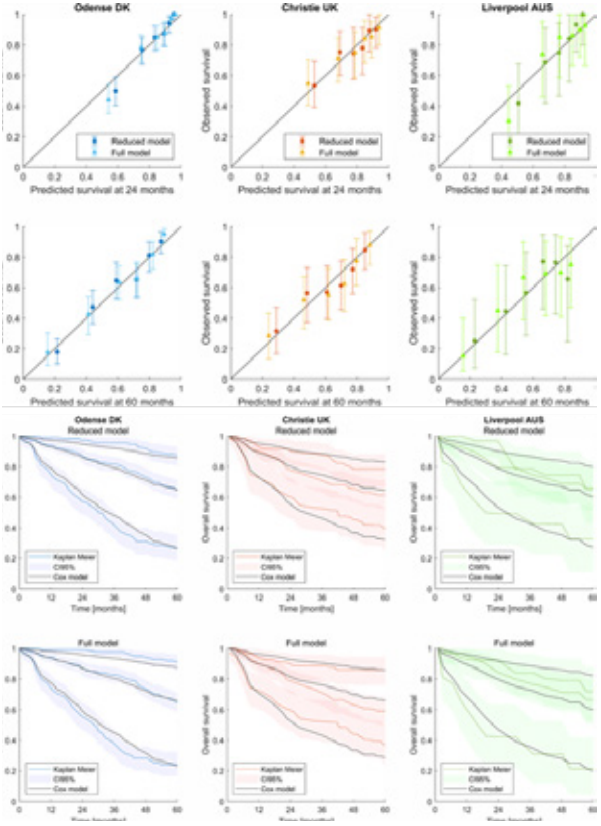
Multivariable Cox analysis OS hazard ratio reduced model

Parameter	Patients	HR	CI95%
log(GTV/1cm3)	786	1.51	[1.39−1.64]
Performance status 0	303	Ref	
Performance status 1	231	1.56	[1.18−2.12]
Performance status 2+	121	3.22	[2.33−4.69]



Multivariable Cox analysis OS hazard ratio full model

Parameter	Patients	HR	CI95%
log(GTV/1cm3)	786	1.48	[1.33−1.63]
Performance status 0	303	Ref	
Performance status 1	231	1.29	[0.98−1.83]
Performance status 2+	121	2.44	[1.73−3.52]
Age at start RT [per 10 years]	786	1.41	[1.24−1.62]
Former or never smoker	368	Ref	
Current smoker	362	1.43	[1.10−1.84]
Haemoglobin [mmol/L]	758	0.83	[0.71−0.96]
N0	431	Ref	
N+	310	1.35	[0.996−1.8]



OC-128 | Impact of osmf on nodal metastases in gingivobuccal-complex carcinoma of oral cavity

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Purpose/Objectives

Oral cavity squamous cell carcinoma (OCSCC) is most common head neck malignancies in Indian population, gingivo-buccal complex(GBC) being the most common subsite. Oral submucous fibrosis (OSMF) is oral potential malignant disorder (OPMD)associated with use of areca nut, particularly in Indian population. Nodal metastasis is an important prognostic factor determining overall survival in oral cavity cancer. Prior evidence states that OCSCC when associated with OSMF has a different behavior in terms of nodal metastasis. This prospective study aims at reporting the impact of OSMF on occult and overt lymph nodal metastasis in gingiva--buccal complex carcinoma (GBCC) of oral cavity.

Materials/Methods

Patients with biopsy proven GBCC (T1-T4) willing to participate in this study were prospectively recruited ,after an informed and written consent. The duration of study was from June 2020 to June 2022. A comprehensive workup of every patient was done which included a detailed inquiry about addictions and a clinical examination. Patients were subjected to a cross sectional imaging of head and neck with “puffed cheek” after injection of intravenous contrast material and images obtained in axial, coronal and sagittal plane. Multiplanar reconstruction (MPR) was done to obtain coronal and sagittal planes. Patients were assigned a TNM staging. Subsequently patients underwent appropriate surgery in accordance to the TNM staging and surgical specimens (pri-

mary tumor and nek dissection) were subjected to histopathological analysis by a dedicated head neck pathologist.

Results

137 patients with GBCC with or without OSMF were enrolled in this study. Patients with GBCC were segregated into three cohorts: GBCC without OSMF(n=98/137; 71%), GBCC with clinical OSMF (n=29/137;15.3%) & GBCC with histological OSMF (n=10/137;7.2%). In GBCC without OSMF (clinical/histological), clinico-radiological evaluation showed cN0 and cN+ in 77.5% (n=76/98) and 22.5% (n=22/98) respectively. On final pathological examination, pN0 and pN+ was seen in 70.4% (n=69/98) and 29.5% (n=29/98) respectively. In GBCC with OSMF (clinical+ histological), clinico-radiological evaluation showed cN0 and cN+ in 53.8% (n=21/39) and 46.6% (n=18/39) respectively. On final pathological examination, pN0 and pN+ was seen in 46.1% (n=18/39) and 53.8% (n=21/39) respectively.With respect to ENE, 50 % population in the cohort of GBCC without OSMF and 40% in the cohort of GBCC with OSMF (clinical/histological) showed ENE . We analyzed all known factors (age, sex, OSMF, clinical and pathologic tumor stage, depth of invasion, grade of differentiation, clinical nodal involvement, LVI, PNI) influencing nodal metastatic involvement in 137 patients. Multivariate cox regression analysis found age>45 yrs., clinico-radiological T stage, presence of skin involvement and depth of invasion (>10 mm) as significant predictor of metastatic nodal involvement in GBCC ($p<0.05$).

Conclusion

Presence or absence of OSMF did not impact nodal metastasis in GBCC. Nodal metastasis in GBCC is influenced by advanced clinico-radiological T stage (T3,T4) with significant depth of invasion (>10mm). Overall incidence of occult and overt nodal metastasis in GBCC in entire cohort was 20.4% (n=28/137) and 79.5% (n=109/137) respectively.

OC-140 | The effect of individualized prognostic counselling on the decision-making process

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Key-words

Head and Neck cancer, Prognostic model, Shared Decision Making, Decisional conflict, Patient-centered care

Objective

Treatment for head and neck squamous cell carcinoma is associated with high morbidity and sometimes compromising vital functions. Therefore, accurate counselling for treatment options, survival rates and quality of life is important. To support prognostication and decision-making in head and neck cancer, an individualized prognostic model named OncologIQ has been developed. This model estimates the 1- to 10-year overall survival (OS) chances of patients with primary HNC, based on the average treatment effect (figure 1). Apart from tumor data, it includes other patient-specific factors, such as age, comorbidity, performance status, and socioeconomic status. The aim of this study is to evaluate the effect of individualized prognostic counseling with OncologIQ on the decision-making process.

Materials and Methods

A prospective clinical trial with sequential cohorts was performed. Newly diagnosed patients, eligible for curative treatment of a primary squamous cell carcinoma were included. Patients within the first cohort (N=200) received standard counseling from their treating physician. Patients within the second cohort (N=200) received additional individualized prognostic counselling, calculated and visualized by OncologIQ. Main study parameters were: decisional conflict

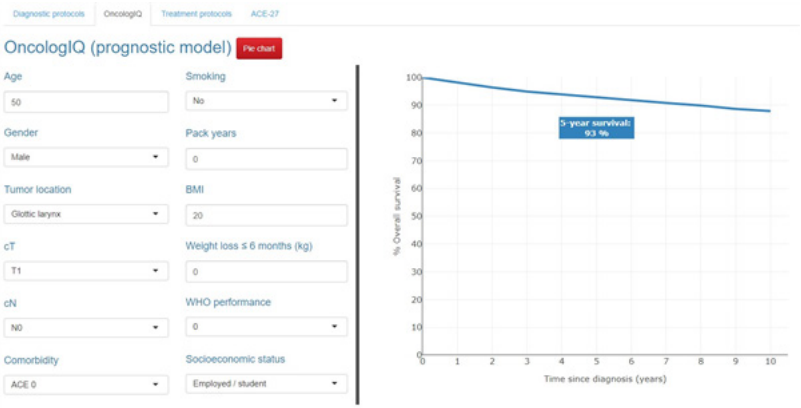
and shared decision making at baseline, choice of treatment, decisional regret at 6 months, and quality of life after 6 and 12 months.

Results

At baseline, mean age was 66.1 (SD 8.8). No significant demographical and clinical differences between both cohorts were found. The median decisional conflict score after individual counseling was significant lower in cohort II compared to cohort I (23.4 vs. 14.1, P<0.001). Lower decisional conflict on all subscales (informed, values clarity, support, uncertainty and effective decision making) were found in cohort II. In cohort I, 38.2% of the patients felt they had made a shared decision, while 19.7% felt they had made the decision themselves after considering the doctor's opinion. In Cohort II, 38.5% felt it was an shared decision, while 23.0% felt they made the decision themselves. No differences in treatment decisions after individual counseling were found. Decisional conflict was significantly lower in cohort II compared to cohort I (13.3 vs. 19.6, p<0.04). Data on quality of life after individualized prognostic counseling is currently analyzed and expected in december 2022.

Conclusion

The prognostic model OncologIQ improves the decision-making process by lowering decisional conflict and decisional regret. After individual counseling with OncologIQ, patients were able to make treatment decisions more autonomously while considering the doctor's opinion.


Diagnostic protocols
OncologIQ
Treatment protocols
ACE-27
OncologIQ (prognostic model)
Pie chart
Age
50
Smoking
No
Gender
Male
Pack years
0
Tumor location
Glottic larynx
BMI
20
cT
T1
Weight loss ≤ 6 months (kg)
0
cN
N0
WHO performance
0
Comorbidity
ACE 0
Socioeconomic status
Employed / student
5-year survival:
93 %
% Overall survival
Time since diagnosis (years)

OC-141 | Exercise prehabilitation in head & neck cancer patients: Preliminary results of the FIT4TREAT trial

Catarina Garcia [1]; Inês Leão [2]; Diogo Pinto [1]; Nuno Dias Rato [1]; Ana Campolargo [2]; Isabel Dias [2]; Ana Raquel Monteiro [2]; Adriana Monteiro Soares [2]; Raquel Basto [2]; Eduardo Vilela [2]; Madalena Teixeira [2]; Edite Coimbra [2]; Pedro Oliveira [2]; Anabela Amarelo [2]; Andreia Capela [2]; Sofia Viamonte [2]; Horácio Costa [2]; Ana Joaquim [2]; Fernando Ribeiro [3]; Alberto Alves [1]

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Keywords

Exercise, Prehabilitation, Physical Fitness

Purpose/Objective

Head and neck cancer (HNC) patients submitted to radical chemoradiotherapy (CRT) experience substantial treatment--related toxicities that negatively impact physical fitness and quality of life (QoL). Poorer initial physical health has been associated with a higher risk of treatment-related complications and worse post-treatment health outcomes in cancer survivors. Therefore, the main aim of this preliminary work was to analyze the impact of an exercise prehabilitation program on the functional capacity of HNC patients.

Mateiral/Methods

In this randomized-control trial (NCT05418842), the total planned enrollment is 46 patients. From May 2021 to November 2022, 23 HNC patients (stages III-IVB) proposed for radical CRT were randomly allocated to an exercise prehabilitation group (EP, n=12) or usual care (UC, n=11). Of these, 1 patient dropped out of the program and 2 patients changed their treatment plan in the EP

group, and 1 patient in the UC group was unable to attend the follow-up assessments. The EP group participated in a prehabilitation program that consisted of a combined aerobic and resistance training program (60 minutes), 3 sessions/week, from the time of randomization to the beginning of radiotherapy (pre-treatment phase). Aerobic capacity (6-minute walk test, 6MWT), isometric handgrip muscle strength (using a dynamometer), and lower limb functional capacity (30 seconds chair sit-to-stand test, STS) were assessed at diagnosis (baseline, M0), 1-3 days before starting radiation therapy (M1) and 4 weeks after radiation therapy cessation (M2). Here, we present the preliminary results of the pre-treatment phase (M0 to M1).

Results

Participants had a median age of 60 years (IQR, 54-70), and 94.7% were men. Baseline characteristics and treatment variables were similar between groups. The median length of the pre-treatment phase in the UC group was 30 days (IQR, 23-33 days, p=0.803) whereas the median length of the EP program was 28 days (IQR, 26-44 days). Patients adhered on average to 69.7±32.0% of the exercise sessions. No differences between groups were observed in any variable at baseline (M0, table 1). The 30 seconds STS performance improved with the EP program (14.2±2.0 to 19.0±4.8 repetitions, p=0.025), and remained unchanged in the UC group (15.1±4.3 to 15.5±4.4 repetitions, p=0.653). No differences between groups were observed for the change in the 6MWT (p=0.396) or the handgrip muscle strength (dominant hand: p=0.408; non-dominant hand, p=0.462). Moreover, no serious adverse events related to exercise were reported in the EP group.

Conclusion

These preliminary results suggest that an EP program can improve lower limb functionality in HNC patients proposed for CRT.

These findings may be important given the vulnerability associated with HNC patients at the time of diagnosis. Therefore, the optimization of physical fitness before CRT may mitigate the expected physical decline during treatment.

Table 1. Changes in physical function parameters

	UC (n=10)			**EP** (n=9)			**p-value**
	M0	**M1**	**ΔM1–M0**	**M0**	**M1**	**ΔM1–M0**	**(ΔUC vs ΔEP)**
30 Seconds STS Test (repetitions)	15.1±4.3	15.5±4.4	0.4±2.7	14.2±2.0	19.0±4.8	4.8±5.2	0.032
6MWT (meters)	531.2±101.1	524.7±82.3	-6.5±41.0	511.3±64.3	520.3±71.4	9±36.1	0.396
Isometric handgrip muscle strength (kgf)							
Dominant Hand	40.1±6.8	40.4±6.6	0.3±2.3	40.0±6.3	39.4±5.7	-0.6±2.3	0.408
Non-Dominant Hand	35.9±6.0	36.5±6.2	0.5±1.4	37.9±6.6	37.7±7.1	-0.2±2.8	0.462

6MWT, Six-minute walk test; EP, Exercise prehabilitation; STS, Sit to stand; UC, Usual care.

OC-146 | The immunosuppressive role of CD73 in head and neck cancer patients treated with immunotherapy

Alessio Cirillo [1]; Bruna Cerbelli [1]; Raffaella Carletti [1]; Antonella Chiavassa [1]; Fabio Ciurluini [1]; Valentino Valentini [1]; Marco De Vincentiis [1]; Francesca De Felice [1]; Carlo Della Rocca [1]; Enrico Cortesi[1]; Daniele Santini [1]; Giulia D'amati [1]; Alessandro Corsi [1]; Daniela Messineo [1]; Umberto Romeo [1]; Antonella Polimeni [1]; Paolo Marchetti[2]; Cira Di Gioia [1]; Andrea Botticelli [1]

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Keywords

Head and neck cancer; immunotherapy; CD73.

Purpose/Objective

Immunotherapy has revolutionized the landscape of systemic treatment of recurrent or metastatic head and neck squamous cell carcinoma (R/M HNSCC). However, only 20% of patients really benefit from this treatment. Indeed the HNSCC microenvironment is distinctly immunosuppressive due to the high concentration of several biomarkers such as ectoenzyme 5'-ecto-nucleotidase (CD73). The aim of our study is to investigate if the expression of CD73 on neoplastic cells could affect the therapeutic efficacy of anti-programmed cell death 1 (anti-PD-1) therapy in R/M HNSCC.

Material/Methods

Data from 50 patients with combined positive score (CPS) positive R/M HNSCC receiving first line immunotherapy or immunotherapy in association with chemotherapy, from February 2021 to July 2022 were prospectively reviewed. CD73 expression on neoplastic cells of 32 core biopsies and 18 surgical samples was evaluated. The study samples were divided in two subgroups: "low-CD73" (L-CD73) and "high CD73" (H-CD73), respectively with CD73 ex-

pression levels below or equal and above the median value. We evaluated the associations between Early progression (EP), defines as progression occurred within 3 months, progression-free survival (PFS), overall survival (OS), objective response rate (ORR) and the expression of CD73 on neoplastic cells.

Results

Thirty-seven patients were male (74 %), 13 female (26 %) and median age was 67,52 years (range 38-87). Pre-treatment ECOG PS was 0 in 10 patients (20%), 1 in 24 patients (48%) and 2 in 16 patients (32%). Smoking habits and previous alcohol abuse were reported in 38 (76 %) and 33 (66 %) of patients, respectively. The primary tumour site was the oral cavity in 30 patients (60 %), the larynx in 16 patients (32 %), hypopharynx in 4 patients (8%). Thirty patients (60%) received pembrolizumab in monotherapy while 20 (40%) patients received the association of immunotherapy with chemotherapy. Twenty-six cases (52%) were "Low--CD73" while 24 patients (48%) were in the "High-CD73" group. EP was recorded in 26 patients (52%). We observed a significant association between the expression of CD73 on neoplastic cells and EP. In particular, 16 (66,6%) out of 24 patients with H-CD73 had early progression of disease (p=0.043). On the other hand, 16/26 patients (61,5%) with L-CD73 did not experience disease progression disease within three months. Both in univariate and multivariate analysis ($p = 0.049$; $p = 0.033$ respectively) only the expression of CD73 on neoplastic cells was correlated with the evidence of EP disease.

Conclusion

Our findings suggest that higher expression levels of CD73 could predict resistance to immunotherapy in patients with CPS positive R/M HNSCC. The addition of this biomarker to the routine evaluation of CPS could help to select the patients primary resistant to anti-PD-1 immunotherapy.

OC-152 | Circulating CD137+ T cells correlate with response to immunotherapy in head and neck cancer patients

Alessio Cirillo [1]; Bruna Cerbelli [1]; Antonella Chiavassa [1]; Fabio Ciurluini [1]; Valentino Valentini [1]; Marco De Vincentiis [1]; Francesca De Felice [1]; Carlo Della Rocca [1]; Enrico Cortesi [1]; Daniele Santini [1]; Giulia D'amati [1]; Alessandro Corsi [1]; Umberto Romeo [1]; Antonella Polimeni [1]; Cira Di Gioia [1]; Lidia Strigari [2]; Ilaria Grazia Zizzari [1]; Aurelia Rughetti [1]; Marianna Nuti [1]; Paolo Marchetti [3]; Chiara Napoletano [1]; Andrea Botticelli [1]

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Keywords

Head and neck cancer; immunotherapy; CD137.

Purpose/Objective

Immune checkpoint inhibitors (ICIs) have been approved as the first-line of treatment for recurrent or metastatic (R/M HNSCC). In clinical practice, only a minority of patients with R/M HNSCC derive benefit from immunotherapy and it is urgently needed to identify novel biomarkers to optimize treatment strategies. CD137 T cells were identified as tumor specific T cells. Their presence in tumor microenvironment correlated with the response to immunotherapy. The purpose of our study is to investigate if high levels of circulating CD137 T cells are associated with response to ICI and patients' survival.

Material/Methods

Data from 40 patients with combined positive score (CPS) positive R/M HNSCC receiving immunotherapy or immunotherapy in association with chemotherapy as first line treatment, from March 2021 to April 2022 were prospectively reviewed. PBMCs of cancer patients were isolated before the beginning of immu-

notherapy treatment and T cells (CD3+) were analysed for the expression of CD137 markers by cytofluorimetry. The percentage of CD3+CD137+ cells was correlated with clinical response rate after six months of therapy, progression-free survival (PFS) and overall survival (OS) defined as the interval between the beginning of immunotherapy to death for any case.

Results

Thirty-one patients were male (78%), 9 female (22 %) and median age was 71 years. Baseline ECOG PS, evaluated before the start of treatment, was 0, 1, and 2 in 16 (40%), 16 (40 %) and 8 (20%) patients, respectively. The primary tumor site was the oral cavity in 24 patients (60 %), the larynx in 8 patients (20 %), oropharynx 4 (10 %), salivary glands 3 (8%) and nasopharynx 1 (2%). The status of current smoker as well as habits alcohol were reported in 12 (30 %) and 17 (42 %) of patients, respectively. Thirty (75 %) patients received pembrolizumab alone, 8 (20%) patients received pembrolizumab in association with chemotherapy (carboplatin or cisplatin and 5-fluorouracil) and finally 2 (5 %) patients received nivolumab single agent.

The analysis of the expression of CD137 on T cells revealed that patients that respond to anti-PD1 treatment showed significantly high levels of CD3+CD137+ cells compared to non-responder (R vs. NR: 1.8%+0.24% vs. 1.1%+0.5%; p=0.03). Moreover, patients with a percentage of CD3+CD137+ >1.65% had a prolonged OS (HR:2.34 95% CI:1.02-5.42; p=0.04) and PFS (HR:2.26 95% CI:1.07-6.54; p=0.03). The multivariate analysis showed that a high level of CD3+CD137+ cells was an independent prognostic factor of PFS (HR:0.3 95% CI:0.11-0.8; p=0.001) and OS (HR:0.3 95% CI:0.11-0.79; p=0.01).

Conclusion

Our results suggest that in R/M HNSCC patients the levels of circulating CD137+T cells could predict the response to immunotherapy and could be used as biomarkers for successful anti-cancer immunotherapy.

OC-166 | Superficial Circumflex Iliac Artery Perforator Flap: ideal choice in head and neck reconstruction?

Roland Giger *(1); Cedric Zubler (2); Adriaan O. Grobbelaar (2); Mihai A. Constantinescu (2); Radu Olariu (2)*

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Key words

SCIP flap, head and neck, reconstruction

Purpose/Objective

A thin skin flap is often desirable in order to achieve a satisfactory and aesthetic result in head and neck reconstruction after ablative tumor surgery. Superficial circumflex iliac artery perforator (SCIP) flaps have been used for this purpose and its minimal donor-site morbidity mainly in the Asian population but have yet to gain acceptance in the Western world due to lack of thorough anatomical studies quantifying the vascular pedicle and surface area of the flap. The authors present their experience within an anatomical study and with simple and chimeric SCIP flap reconstructions for complex defects in different head and neck localisations.

Material/Method

We performed an anatomical study on 21 Thiel-fixated cadavers and used the knowledge gained in a series of 39 head and neck reconstructions undergoing ablative surgery since 2018.

Results

A total of 21 flaps were harvested and analyzed on the cadavers. The deep and superficial branch (present in each specimen) provided each more than 3 perforators (3.4 vs 3.6, p=0.61). The length

of the pedicle was significantly increased in the deep branch (9.1 cm vs 6.6 cm superficial branch, p <0.01) as was the perfused area (202 cm^2 vs. 112 cm^2 p<0.01). The deep branch offers a significantly thinner flap on the deep plane (8.6 vs. 9.7 mm, p <0.01) and on the superficial plane (5.6 vs 6.1 mm, p <0.05), however the superficial plane offers a significantly reduced variability in thickness.

Thirty-nine clinical cases were reconstructed by means of a SCIP flap (37 adipocutaneous, 2 osteocutaneous). In 25 flaps, the mean length and width of the flaps were 14.9 and 7.2 cm, respectively and the pedicle was in average 7.2 cm long. The SCIP flap was used in 34 patients for oral cavity defects, in four patients for skin--soft tissue-bone defect and in one patient for the reconstruction of the hypopharyngeal wall. There were two total flap losses (5%), and it was replaced for each patient with an anterior lateral thigh flap. One flap was revised for venous thrombosis with flap salvage and another showed minimal partial necrosis, which could be managed by local debridement. Two flap dehiscences had to be re-sutured in general anesthesia. Three patients showed donor--site complications (7.6%): one hematoma undergoing revision surgery and two seromas conservatively treated. Good functional and aesthetic results could be obtained in all patients.

Conclusion

Our anatomical studies indicate that the deep branch based SCIP flap cutaneous territory is reliable and easy to raise. The case series demonstrated the versatility of the SCIP flap for head and neck reconstructions. It provides a safe and ideal alternative to the radial forearm or anterior lateral thigh flap if a thin pliable simple or chimeric flap is required, without major donor-site complications.

OC-167 | Fusobacterium nucleatum potentiates head and neck squamous cell carcinoma (HN-SCC) treatment

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Purpose/Objectives

Published research suggests a role for upper aerodigestive tract (UAT) microbiota in HN-SCC development, via possible immune evasion but its impact on treatment efficacy is under-researched. Using clinical data, we investigated the role of UAT microbiota in HN-SCC prognosis and then validated results using a 2D co-culture model.

Material/Methods

Microbiome data from HN-SCC patients was obtained from the cancer microbiome atlas database (TCMA). Bacteria where relative abundance >0 in ≥1 patient were included. Metadata, including curated survival data, were obtained from TCMA and the cancer genome atlas databases. Only patients where microbiome and survival outcomes were available were retained (n=155). Linear regression, Cox proportional hazards regression, and Kaplan Meier models were used to identify bacteria associating with overall (OS) and disease-specific survival (DSS). For survival analyses, patient groups were divided as bacteria detectable vs undetectable (relative abundance = 0), or relative abundance above vs below cohort median. A 2D co-culture model consisting of human buccal SCC (TR146), +/- NK cells (KHYG-1), +/- *Fusobacterium nucleatum* (*Fnuc*; Fn23 and Fn237 strains) was developed. Multiplicity of Infection (MOI) ratios ranging 0.5-5 were used for *Fnuc*. Single infection with *Fnuc* on day 0 or daily infection were compared. HN-SCC viability was assessed with an ATP-based assay and con-

firmed with the annexin V/propidium iodide (flow cytometry) assay at D5. Significance was assessed with ANOVA.

Results

Stepwise regression modelling identified relative abundances of *Tannerella, Pyramidobacter, Fusobacterium, Eggerthia, Campylobacter, Filifactor, Peptostreptococcus* and *Alloprevetolla* to be predictive of OS time. These bacterial genera were retained for Cox proportional hazards regression where only *Fusobacterium* (HR=0.36, 95% CI 0.19-0.65; p<0.001) and *Tannerella* (0.40, 0.17-0.90; p=0.03) were predictive of OS. Multiple linear regression showed no interactions between *Tannerella* and *Fusobacterium* and only *Fusobacterium* was significant (p<0.05). Kaplan-Meier analysis confirmed that *Fusobacterium* detectability was associated with better OS and DSS. *Fusobacterium* was more abundant in tumours compared to normal tissue (p=0.002). At species level, *Fusobacterium nucleatum* detectability (p<0.001) or relative abundance above/below the cohort median (p=0.03) was associated with superior survival.

With co-culture, there was a significant reduction in HN-SCC D5 viability on addition of *Fnuc* (p<0.001). HN-SCC killing rose with MOI and daily compared to single infection. There was a significant reduction in HN-SCC viability in HN-SCC/NK/Fnuc co-culture compared with HN-SCC alone or HN-SCC/NK co-culture (p<0.05).

Conclusion

Unlike within colorectal cancer, *Fnuc* may favour reduced HN-SCC cell viability and improved survival outcomes. Ongoing research will further validate results and elucidate mechanisms.

OC-171 | Neck lymph node metastasis in oral maxillary squamous carcinoma - a retrospective analysis

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Keywords

Oral maxillary carcinoma, Squamous cell carcinoma, Cervical metastasis

Purpose/Objective

Management of oral squamous cell carcinoma (SCC) involving the upper alveolar regions and hard palate, presenting with cN0 neck remains controversial due to lack of studies and comparatively lower metastatic rate compared to other oral cavity subsites. Traditionally, management of the neck has been conservative, with close surveillance.

However, emerging evidence suggests that the risk of metastasis to cervical lymph nodes is similar to other subsites of the oral cavity, as well as there may be an indication for prophylactic neck dissection, because in certain maxillary oral SCC scenarios, the risk threshold for occult neck metastasis is greater than 20% as determined by Weiss et al.

The present study aims to analyse the risk of cervical lymph node metastases from oral tumors of the maxilla and hard palate in a Portuguese population, treated at a reference centre for head and neck cancer, and whether there are implications for neck management.

Material/Method

Records from a tertiary referral centre for head and neck cancer between 2017 and 2020 were retrospectively evaluated. Pa-

tients diagnosed with oral SCC of the maxilla and hard palate were selected and information was collected on the population's characteristics and risk factors, staging, treatment modality and follow-up. A review of the current literature was carried out to compare with the results obtained.

Results

Thirty-six patients were included in the present study. Male to female ratio was 1:1, median age was 71 years, two-thirds had oral SCC of the maxilla and one-third of the hard palate. Eighteen patients were cN0 at clinical presentation, and the most frequent treatment modality was surgical resection and adjuvant radiotherapy. The presence of long-term regional recurrence in these patients was below the limit determined by Weiss et al for indication of prophylactic neck dissection.

Conclusion

The present study does not support the indication of prophylactic neck dissection in patients with cN0 maxillary oral SCC. The contribution and source of bias of other treatment modalities - namely radiotherapy and chemotherapy - must be evaluated, as well as further studies on this subject, in order to further assess the implications for the management of cervical ganglia in these patients.

OC-173 | Nivolumab in patients with head and neck cancer. Results of Polish multicenter observational study

Katarzyna Drosik-Rutowicz [1]; Dorota Kiprian [2]; Izabella Debicka [3]; Ewa Sierko [4]; Joanna Kazmierczak [5]; Ewa Chmielowska [6]; Agnieszka Karpinska [7]; Renata Pacholczak-Madej [8]; Dominika Les [1]; Agnieszka Pietruszka [1]; Krzysztof Skladowski [1]; Tomasz Rutkowski [1]

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Purpose/Objective

Patients with head and neck squamous cell carcinoma (HNSCC) who progressed after primary radical treatment due to recurrence or metastatic disease (R/M HHSCC) have poor prognosis and limited treatment options. If salvage surgery or radiotherapy is not applicable platinum-based chemotherapy (CHT) should be used. For these who progressed Nivolumab could be used on the basis of the results of Phase-III clinical trial, CheckMate 141, and since 2019 this option is also available for Polish patients. Real-data of clinical use of Nivolumab in Polish patients with R/M HNSCC has been presented.

Material/Method and methods

There were 256 patients form 8 Polish Oncological Centers treated with Nivolumab due to R/M HNSCC between 09/2019 and 09/2022. There were 199 (78%) males and 57 (22%) females in the median age of 62 years. Nivolumab was given in the dose of 240 mg each 14 days. Patient characteristics is shown in Table 1. Ove-

rall survival (OS) was calculated as a time from beginning of Nivolumab to the death or last patient control. Overall survival after Nivolumab (OSpostNivo) was calculated as time since Nivolumab discontinuation to the death or last patient control. Number of Nivolumab infusion, OS and OSpostNivo was calculated in subgroups of patients according to several clinical factors.

Results

Median number of Nivolumab infusions was 7 (range: 1 – 71). Median OS was 6,3 months (range: 0-35). Median OSpostNivo was 2 months (range: 0-27). Patients with nasopharyngeal cancer had significantly longer OS and OSpostNivo comparing to other sites of primary tumor (p=0,006). Reason of Nivolumab discontinuation significantly influenced the length of therapy. Tolerance of Nivolumab was good in 85% of patients. Detailed results are presented in Table 1.

Conclusion

In the population of Polish patients with R/M HNSCC Nivolumab is well tolerated and gives the benefit of about 6 months of OS.

	Number of patients	Nivolumab infusions (median)	OS months (median)	OSpostNivo months (median)
smoking history				
yes	144 (56%)	6	5,8	2
no	66 (26%)	7	7,0	2
nd	46 (18%)	-	-	-
site of primary tumor				
oral cavity	75 (29%)	6	5,5	1,6
oropharynx	76 (30%)	7	7	1,8
hypopharynx	30 (11%)	6	6	2,5
larynx	54 (22%)	7	7,5	2,5
nasopharynx	7 (3%)	25*	24,5*	4,3*
other	13 (5%)	8	6,2	3,2
platinum sensitivity status^				
refractory	50 (17,5%)	7	5,4	1
sensitivity	184 (58%)	7	6,4	2*
nd	22 (24,5%)	-	-	-
reason of Nivolumab initiation				
progression	52 (20%)	6	6,5	2,8
recurrence	98 (38%)	7	6,0	1,7
metastatic disease	55 (22%)	2	7,5	1,9
more than one reason	39 (15%)	7	5,6	2,0
nd	12 (5%)	-	-	-
reason of Nivolumab discontinuation				
continuation	26 (10%)	21	12,8	-
progression of disease	146 (57%)	7	7,9*	3,4*
death	41 (16%)	5*	3,5*	0,8*
lost from observation	14 (5,5%)	1*	0,8*	0,5*
side effects	6 (2%)	15*	14,6*	9,2*
deterioration of general condition	10 (4%)	3*	4,1*	1,3*
withdrawal of consent	2 (0,5%)	22*	19,3*	6,0*
tolerance				
good	218 (85%)	7	6,0	2,0
1-2 CTCAE	16 (6%)	8	9,6	3,1
3-4 CTCAE	7 (3%)	3	9.8	3,4
nd	15 (6%)			
All patients	256	7	6,3	2,0

Table 1. *Significant difference (p<0,05), ^Platinum refractory status included patients with progression during or within 6 months after platinum-based CHT, platinum sensitivity status included patients with progression 6 months or more after platinum-based CHT

OC-175 | Voice prosthesis post-laryngectomy: 5 years data of the Portuguese Institute of Oncology Lisbon

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Key words

Laryngectomy; Tracheoesophageal puncture; vocal prothesis

Objective

Voice rehabilitation has been an integral aspect of treatment after total laryngectomy from the very beginning and since the introduction of tracheoesophageal puncture (TEP), the voice prothesis has become its gold standard. The propose of the study is to present the experience of the institution and to analyze the different variables that have influenced the success of speech rehabilitation.

Material and Methods

Age, type of tumor, surgical or prosthesis complications, use of prior or post radiation therapy, type of puncture, first prosthesis replacement, number of replacements per year and causes for prosthetic success or failure were analyzed. We also briefly review the relevant literature about voice rehabilitation with TEP.

Results

Voice prosthesis was inserted in 108 patients in the ENT Department, Portuguese Institute of Oncology Lisbon during the 5 years from January 2016 until December 2020. Follow-up duration data was 2 years minimum. A cricopharyngeal myotomy was performed in all patients. The prosthesis was inserted secondary at only 4 patients. Voice rehabilitation was initiated 10th day after pri-

mary insertion. The rehabilitation was successful in around 80% of our patients. Prosthetic replacement is generally performed because of a prosthetic or fistula related disease. Early complication rate was around 5% and around 10% of patients had late fistula closure. The main cause for prothesis replacement was prosthetic leakage. Prior or post radiation did not affect overall rehabilitation success.

Conclusion

Details such as the tonicity and thickness variations of the pharyngoesophageal segment, according to the valve size are very important during the voice rehabilitation with voice prothesis follow up. Leakage and granuloma continue to remain a constant prothesis failure and poor motivation to speech therapy remains a voice failure. This data had demonstrated the experience of this single institute and how can a therapeutic protocol can benefit and maximize the success rate of tracheoesophageal voice.

OC-176 | Evolution of neutrophil-to-lymphocyte during treatment ratio predicts response to nivolumab

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Introduction

Nivolumab is approved for platinum-resistant recurrent/metastatic head and neck squamous cell carcinoma (HNSCC). The neutrophil/lymphocyte ratio (NLR) has already been validated as a prognostic factor in several diseases. Previous studies describe NLR variation as a response predictor in patients under nivolumab in cancers other than HNSCC.

Objectives

We aimed to evaluate the ratio between the NLR at 6 weeks post-treatment (NLR6w) and the pre-treatment value (NLRpt) as a response predictor in patients under nivolumab for HNSCC.

Material and Methods

We performed a retrospective analysis of all patients with non-resectable/metastatic HNSCC followed at our Medical Oncology department between January 1st of 2018 and January 1st of 2022. Survival analysis was done using the Kaplan-Meier method and Cox regression. We determined the optimum cutoff value for the NLR6w/NLRpt ratio through analysis of the ROC curve.

Results

We identified 21 patients, 91% male, with a median age of 63 years old (min 47, max 73). In 81% initial ECOG performance status (PS)

was 0 or 1. Regarding tumor location, 52% (n=11) of tumors were located in the larynx and 29% (n=6) were located in the oral cavity. Forty-eight percent (n=10) of patients stage IVA disease at diagnosis and 91% had undergone previous definitive treatment: 48% (n=10) surgery followed by adjuvant chemoradiation (ChT/RT), 19% (n=4) definitive ChT/RT, 10% (n=2) surgery followed by adjuvant radiotherapy (RT) and 10% (n=2) induction chemotherapy followed by ChT/RT. Of the 19 patients, 24% (n=5) had disease persistence, 33% (n=7) had local relapse and 62% (n=13) had distant relapse. Nivolumab was used in the palliative setting as 1st line in 57% of patients (n=12) and 2nd line in 29% of patients (n=6). All patients had previously been treated with platinum as definitive and/or palliative treatment. Seventy-one percent of patients (n=15) discontinued treatment due to disease progression. Median follow-up since diagnosis of recurrent/metastatic disease was 6.7 months. We obtained an optimal cutoff for the NLR6w/NLRpt of 1.51. When stratifying according to this value, median progression-free survival (PFS) for the group with NLR6w/NLRpt < 1.51 was 3.5 months, significantly better than the PFS of 2.0 months for the group with NLR6w/NLRpt ≥ 1.51 (HR 0.195; IC 95% 0.049-0.771, p < 0.011).

Conclusion

A lower NLR6w/NLRpt ratio was significantly associated with longer PFS in patients treated with nivolumab. This is a small retrospective study, and a replication on a larger sample is necessary to validate this ratio as a treatment response predictor in this disease.

OC-180 | Serum proteomics in head and neck cancer - peripheral blood immune response to treatment

Thorsteinn Astradsson [1]; Felix Sellberg [2]; Ylva Tiblom Ehrsson [1]; Karl Sandström [1]; Göran Laurell [1]

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Objective

In this prospective real-world study, the aim was to evaluate the expression of inflammatory proteins in serum collected from head and neck cancer patients before and after treatment and to assess potential differences in expression of inflammatory proteins associated with treatment modalities.

Materials and Methods

The study cohort consisted of 180 patients with head and neck cancer. The most common histopathological type was squamous cell carcinoma and 74% of the patients had either oral or oropharyngeal cancer. Blood was drawn at four time-points and the expression of 83 different inflammatory proteins was assessed through proteomic technique on each occasion (Multiplex immunoassay analysis, Olink Proteomics, Uppsala, Sweden). The patients were divided into 4 treatment groups: Surgery only, radiotherapy with or without surgery, chemoradiotherapy (cisplatin) with or without surgery, and radiotherapy with targeted therapy (cetuximab) with or without surgery.

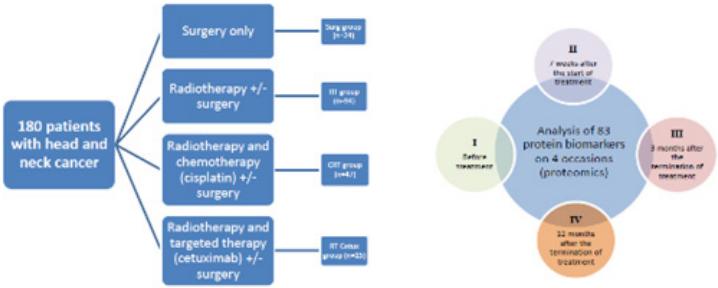
Results

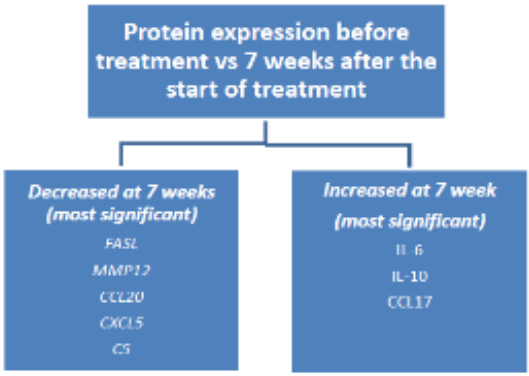
For the overall cohort, the expression levels of 15 proteins changed significantly between the sample taken before treatment and the sample taken 7 weeks after the start of treatment which coincided with the termination of radiotherapy for a large proportion of the patients. At 7 weeks after the start of treatment, 13

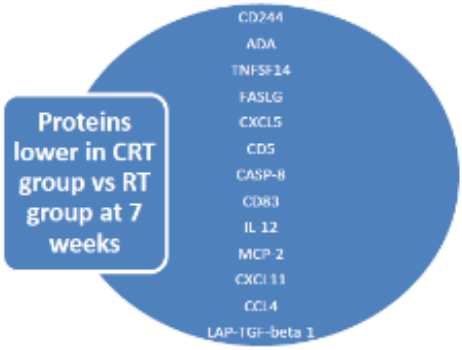
proteins showed lower expression levels in the chemoradiotherapy group compared to the radiotherapy group. The majority of the proteins had returned to their pretreatment expression levels after 12 months.

Conclusion

A significant relation between the expression of a number of inflammatory proteins and treatment modality was seen. When compared to patients undergoing radiotherapy only, patients undergoing chemoradiotherapy with concomitant cisplatin showed lower expression of 13 inflammatory proteins at 7 weeks after the start of treatment. The results draw attention to a number of inflammatory proteins that provide insight into the immuno-modulatory effects of cisplatin in head and neck cancer. The results of this study could pave the way for further clinical studies on cisplatin therapeutic effects.




Protein expression before treatment vs 7 weeks after the start of treatment
Decreased at 7 weeks (most significant)
FASL
MMP12
CCL20
CXCL5
C5
Increased at 7 week (most significant)
IL-6
IL-10
CCL17


Proteins lower in CRT group vs RT group at 7 weeks
CD244
ADA
TNFSF14
FASLG
CXCL5
CD5
CASP-8
CD83
IL-12
MCP-2
CXCL11
CCL4
LAP-TGF-beta-1

OC-181 | Prognostic nutritional index as a prognostic factor for locally advanced head and neck cancer

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Keywords

Head and neck cancer, induction chemotherapy, prognostic nutritional index.

Purpose

Induction chemotherapy with docetaxel, cisplatin and 5-fluorouracil (TPF) has a high response rate but a significant risk of toxicity and morbidity. Nutritional and inflammatory status have been shown to be predictors of toxicity and survival for several solid tumors. The purpose of the study was to investigate the impact of nutritional and inflammatory status on the prognosis of patients with locally advanced head and neck cancer treated with TPF induction chemotherapy.

Methods

Retrospective analysis of patients with head and neck cancer treated with induction chemotherapy with TPF, between 01/2008 and 05/2022. The prognostic nutritional index (PNI) was calculated according to Onodera's formula (PNI = serum albumin g/L + 5 x lymphocytes absolute number/L) and the low/high PNI was defined according to the median value. Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) were also calculated according to the median value. Survival analysis was performed using the Kaplan-Meier method and prognostic factors assessed by univariate analysis and by the Cox regression model.

Results

A total of 68 patients were included, with a median age of 53 years old (41-71). At diagnosis, the median body mass index (BMI) was 21,9 kg/m2 and 16 patients had a weight loss of 10% or more in the past 6 months. PNI ≤ 50.4 was observed in 34 patients. The median progression free survival (mPFS) and overall survival (mOS) was 12 and 19 months, respectively. Radiologic complete response was observed in 29% of patients, 60% had a partial response and 11% of patients did not respond to treatment. In the multivariate analysis, low PNI was significantly associated with worse progression free survival (mPFS 10 vs 28 months, p=0,000) and overall survival (mOS 14 vs 33 months, p=0.023). Patients with high NLR (mOS 19 vs 14 months, p=0.143) and >10% weight loss (mOS 12 vs 29 months, p=0.071) also demonstrate a trend towards worse overall survival outcomes.

Conclusion

According to our data, low PNI was associated with worse survival outcomes. These data corroborate that malnutrition and the pro-inflammatory status appear as prognostic factors predictive of survival in patients with locally advanced head and neck cancer treated with induction chemotherapy with TPF. For these patients, regular nutritional counseling is essential. However, further research and prospective randomized trials are needed to validate these results.

OC-182 | Transcriptomic response of oral squamous cell carcinoma to metformin treatment - a prospective study

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Purpose/Objective

Metformin was first approved in 1958 for type 2 diabetes and has remained at the frontline of treatment ever since. Despite its enduring success, 75 years later, its mechanisms of action are still not fully understood. In recent years, it has once again captured the spotlight for its potentially beneficial effects in cancer treatment suggested by cell lines, mouse models and clinical data. One hypothesis is that metformin improves tumor hypoxia, rendering it a potential radiosensitizer. The purpose of this study was to investigate if administration of metformin to patients with oral squamous cell carcinoma (OSCC) leads to measurable change in the transcriptome, with emphasis on the hypoxia-inducible factor 1 alpha (HIF1A) regulatory pathway.

Materials/Methods

For this prospective window-of-opportunity study, we collected tumor tissue samples of OSCC patients during diagnostic panendoscopy and again at the date of tumor resection. Patients

received metformin 850 mg BID for 10 to 14 days in between interventions. To avoid bias caused by oxygen depletion after interruption of blood supply, samples were snap-frozen within <30 seconds after resection and processed via a specifically developed pipeline allowing all steps until RNA extraction to be executed without thawing. Additional biopsies of healthy oral mucosa were obtained from five patients before and after metformin treatment. Pooled cDNA libraries were sequenced on a S4 Flow Cell on Illumina NovaSeq6000 with a length of 2 x 150 base pairs in paired-end format to a minimum of 50 million reads/sample. Differential expression analysis was performed in R software based on DESeq2 3.15 package.

Results

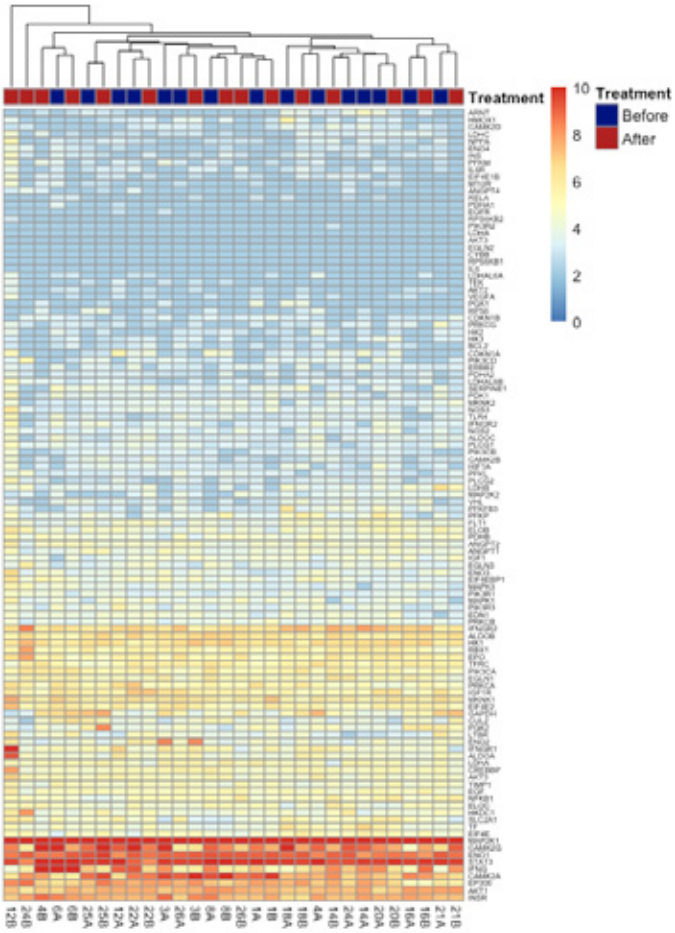
Twenty-six non-diabetic patients were recruited. Nine patients were excluded because of a switch to non-surgical treatment (n=1), discontinuation of metformin due to side effects or dysphagia caused by tumor (n=4), and low tumor content in one or both of the two biopsies (n=4). Two patients were removed after sequencing because of failed quality checks. Of the 15 patients retained for analysis, mean duration of metformin intake was 12.1 days (range: 10-14). Compliance with planned metformin intake was 98% (range: 86-100%). There were no significantly differentially expressed single genes after metformin therapy. Pathway analysis did not show significant alterations in the HIF1A pathway (Figure 1), nor an inhibition of the mTOR signaling pathway, or any other known cancer pathway.

Conclusion

This is the first clinical study to holistically examine the transcriptome of OSCC before and after the administration of metformin. After 10 to 14 days of metformin in a clinically common dose, we neither found evidence of a significant alteration of the main hypoxia-associated pathway, nor in other common cancer pa-

thways. Notwithstanding the fact that the impact of metformin on gene expression may be dose and time dependent, our study does not support the hypothesis that metformin improves tumor hypoxia.

Figure 1: Heatmap showing unsupervised clustering of 30 samples from 15 patients with oral squamous cell carcinoma, with one sample taken before and one after metformin treatment, based on the expression level of genes associated with the HIF1A pathway. Samples before and after administration of treatment do not cluster separately.



OC-185 | Lingual group of Lymph nodes in carcinoma tongue: Prevalence and Significance

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Keywords

Tongue cancer, Lingual Lymph node, Compartmental surgery

Purpose/Objective

The lymphatic drainage from the tongue passes through the floor of the mouth before moving up to the upper neck. The lingual lymph nodes that emerge between the lingual structure and the cervical regional lymph nodes have received little attention. In particular, the metastasis of oral tongue carcinoma to the lingual lymph nodes is the subject of increasing scientific research.

Aim

To evaluate the prevalence of pre-cervical lingual lymph nodes in the tongue and to evaluate the prevalence of metastasis to these nodes in patients with tongue cancer.

Material/Methods

Our department included a prospective study of consecutive patients undergoing compartmental tongue resection and subtotal glossectomy for primary tongue cancer (T2-T4a) from June 2020 to August 2022. T1 and T4b tongue cancer, unresectable advanced tongue cancer, and tumors with distant metastases were excluded from the study. Neck dissections were performed based on lymph node status. The glossectomy specimen was examined histologically for lingual lymph nodes.

Results

A total of 64 patients were included, 37 had compartmental glossectomy, and 27 had subtotal glossectomy. Nine (14%) patients were noted to have lingual lymph nodes, Six in the lateral group and three in the medial group. Three (4.7%) of the nine patients had lingual lymph node metastases, which were noted in the 2/3 medial group and 1/6 in the lateral group. None of these three patients had clinical or pathological evidence of metastasis in the ipsilateral cervical nodes, and only one had contralateral occult metastasis in the level 1b node. The Three patients with lingual node metastasis had T stages varying from T2, T3, and T4a.

Conclusion

3/64 (4.7%) patients with tongue cancer develop metastases in the pre-cervical lingual lymph nodes. These may not manifest with cervical lymph node metastases. Discontinuous wide local resection with neck dissection is likely to miss tumor residues in these sites and be a nidus for local recurrence. Data presented forms one of the rationales for considering compartment tongue resection to improve oncological control of tongue cancers.

OC-187 | The role of RNA methylation in HNSCC pathogenesis: in search of clinical and biological meaning

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Keywords

Head and Neck Squamous Cell Carcinoma; RNA methylation

Background/Aim of the study

High genetic and histologic diversity of head and neck cancer, its molecular pathogenesis, tumor formation and progression are complex processes, including disorders driven not only by the accumulation of genetic alterations but also changes in the epigenetic landscape. The epigenetic variations in HNSCC include DNA methylation, histone modifications, non-coding RNA activity and poorly described RNA methylation. RNA methylation of adenosine has been considered the most prevalent, dynamic and conserved internal transcription modification among more than 100 different chemical RNA modifications. RNA methylation-related effects are the result of the cooperation of multiprotein complexes known as “writers”, “erasers”, and “readers”. Since, most epigenetic alterations promote cancer formation and progression by controlling the expression machinery, they can be used as biomarkers for the clinical detection and surveillance of cancer and will reveal new therapeutic opportunities for cancer patients.

Aim

Here, 1) we have focused on signs of RNA methylation in HNSCC patients, and cell lines and 2) we determined the methyltransferase 3 (METTL3) knock-out impact on HNSCC cells development *in vitro*.

Method

Head and neck squamous cell carcinoma tissues and paired--matched histopathologically unchanged tissues were collected from 45 patients. The FaDu, Detroit 562, A-253, SCC-15 and PCS-200-014 cell lines were obtained from the American Type Culture Collection and correspond with different tumor locations: hypopharynx, pharynx, salivary gland, tongue, and primary gingival keratinocytes, respectively. LC-ESI-MS/MS (liquid chromatography-electrospray ionization tandem mass spectrometric) analysis of nucleosides was used to determine the percentage ratio of m6A to A in total RNA samples. Real Time Quantitative Polymerase Chain Reaction (RT-qPCR) and Western Blot were used to quantify gene expression levels. The lentiviral CRISPR-Cas9 system was used for target cell transduction. *In vitro* functional studies of the cell cycle, apoptosis, steaminess, and chemo- and radiotherapy response effects were analyzed with flow cytometry.

Results

We have determined the differences in mRNA level of selected RNA methylation machinery genes in HNSCC patients' cancerous tissues compared to histopathological unchanged tissues. We have correlated these results with patients' clinical data and suggest probable essential factors in HNSCC tumorigenesis. Moreover, we found that METTL3 silencing slowed down divisions and induced apoptosis of cancer cells, supporting cell arrest in the G2 phase, increased apoptosis activity in response to cisplatin treatment, and increased the stemness markers expression.

Conclusion

The RNA methylation process may significantly impact HNSCC progression. The future perspectives of the study encompass high--throughput analysis and estimation of RNA methylation targets.

OC-188 | Modeling the tumor microenvironment in Head and Neck Squamous Cell Carcinoma organoids

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Keywords

Preclinical models; 3D culture; air-liquid interface patient derived organoids (ALI-PDO)

Purpose/Objective

Patient-derived organoids (PDOs) are generated using 3D cell culture methods, which maintain the self-organizing capacities of tumor cells and preserve the histopathological features of the parental tumors. These features makes these preclinical models an ideal tool to perform drug screenings and develop personalized treatments. Nonetheless, with the majority of the current protocols cell-type complexity is lost during serial passages ex vivo, resulting in PDO cultures that lack the native tumor microenvironment. Recently, an air-liquid interface (ALI) culture technique for clinical tumor samples has been described (PMID: 30550791) which allows to generate PDOs that maintain the cellular heterogeneity (tumor cells, stromal and immune cells) that constitutes the cancer ecosystem, making ALI-PDOs an optimal tool to mimic, at least in part, what transpires in vivo. In this study, we aim to adopt the ALI culture protocol for generating PDOs that model the tumor immune microenvironment of head and neck cancer. Here, we report first results from the ongoing protocol optimization.

Material/Methods

ALI-PDOs are generated through the culture of tumor fragments placed in a culture well insert that contains two different layers

of matrix. The top layer (cellular layer) contains the tumor fragments embedded in a matrix and is exposed to the air, whereas the bottom layer (acellular layer) is composed of matrix and is in contact with the medium. We optimized the mechanical processing of the clinical specimen, and tested various antibiotics to eliminate possible contaminations, an inherent risk associated with oral cavity carcinomas.

Results

Then we tested different matrix and medium compositions to understand their influence in the cellular composition of ALI-PDOs. Preliminary results indicate that there are no differences by the type of matrix (Cell Matrix I-A vs. Rat Tail Collagen I), or the time of the first culture passage with respect to the number or size of ALI-PDOs (median of 39µm vs. 43µm in passage 1). Considering the models established so far (n=6), we can conclude that the success rate of ALI-PDOs formation is dependent on the tumor model rather than the matrix composition. We further established the protocols for ALI-PDOs collection and cryosectioning, allowing their comprehensive histomorphological and multiparametric immunofluorescence analysis. The ongoing basal characterization includes the assessment of proliferation (Ki67) and their cellular composition using markers for epithelial/tumor cells (EpCAM and CK5/6), fibroblasts (vimentin) and immune cells (CD45, CD3, CD19, CD68).

Conclusion

Our preliminary results suggest the applicability of the ALI protocol for head and neck cancer. Nonetheless, it remains necessary to understand the cell heterogeneity of these formed organoids.

OC-195 | The causes of death in patients with head and neck cancer in the Netherlands

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Keywords

Euthanasia, cause of death, head and neck cancer

Purpose/Objective

Head and neck cancer (HNC) accounts for nearly 3% of new cancer diagnoses in the Netherlands and despite improvements in treatment, recurrence rates in HNC patients are still high. Amongst others, this is a reason that survival rates in HNC patients remain relatively poor. To provide optimal care, especially in the palliative phase, a deeper insight into the different causes and ways of death in HNC patients is desired. However, current literature on the exact cause and way of death, including euthanasia and suicide, in HNC patients is limited. Therefore, the aim of this study is two-fold. First, we want to give insight in the association between the way of death and the underlying cause of death or socioeconomic status. Second,we want to provide an overview on the different causes of death among HNC patients in the Netherlands.

Material/Method

A retrospective consecutive cohort study of HNC patients treated in the Erasmus MC was conducted. All patients diagnosed between January 1st 2006 and December 31st 2013 were included from the Rotterdam Oncological Documentation database. Follow-up time of patients was specified as the date of diagnosis until death or until December 31st 2019, whichever came first.

Results

In total, 2180 patients were included, of which 1291 (59.2%) patients died during follow up. The main cause of death was HNC with 557 cases (43.1%). The most common competing cause of death was other malignancies with 344 cases (26.6%), followed by cardiovascular disease (9.5%). In this cohort only 6 patients (0.5%) died of suicide. In total 240 patients (18.6%) received palliative sedation and 70 patients (5.4%) euthanasia. Patients with HNC as the registered underlying cause of death received significantly more palliative sedation and euthanasia than patients with other listed causes of death. Furthermore, in the group of patients with a low income there was less palliative sedation and euthanasia in comparison to patients with a high income (14.8% and 3.0% vs. 23.0% and 8.3%). In the group of employed patients there was a significant higher proportion receiving palliative sedation in comparison to the proportion in the group of retired patients (23.8% vs 15.5%).

Conclusion

This study provided a unique insight into palliative sedation and euthanasia in a large cohort of head and neck cancer patients. We showed that these ways of death were more common in patients with HNC as the underlying cause of death, compared to patients with other underlying listed causes of death. Also, patients with a higher socioeconomic status more frequently opted for palliative sedation and euthanasia. Lastly, we demonstrated that more than half of the HNC patients died from competing causes. These insights can help healthcare professionals to identify opportunities to optimize care, especially for patients in the palliative phase.

OC-198 | IMPACT OF LYMPH NODE RATIO AND NUMBER OF LYMPH NODE METASTASES IN LARYNGEAL SQUAMOUS CELL CARCINOMA

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Keywords

Larynx, prognosis, lymph node metastasis

Introduction

Squamous cell carcinomas account for 95% of malignant laryngeal tumors. The presence of lymph node metastases is a highly significant negative prognostic factor in patients with laryngeal carcinoma. Recently, attention has been paid to the concept of lymph node ratio (LNR) or lymph node density (LND), which is the ratio of the number of metastatic lymph nodes to the total number of lymph nodes removed during surgical treatment. This study aimed to assess the impact of LNR and absolute number of metastatic lymph nodes on mortality and recurrence rates in patients with laryngeal squamous cell carcinoma.

Materials and Methods

This retrospective multicenter international study involved 24 Otorhinolaryngology-Head and Neck Surgery (OHNS) divisions. The absolute number of metastatic lymph nodes and the LNR in histological specimens were calculated. Overall survival (OS), disease-specific survival (DSS), and disease-free survival (DFS) were evaluated as the main outcomes.

Results

Overall, 2507 patients (mean age 67.5 years, range: 23-94 years), of whom 2224 (89%) were men, met the inclusion criteria. An incre-

ased number of metastatic lymph nodes and increased LNR correlated with poorer DSS and DFS; both outcomes continuously increased without a plateau. The cut-offs obtained for LNR were 0.1, 0.2, and 0.4, and the cut-offs for the number of positive lymph nodes were 5, 10, and 20. These cut-off values were subsequently used to obtain different DSS and DFS curves.

Conclusion

This study provides strong evidence and important insights into nodal staging. Our data demonstrate the prognostic value of NPLN and LNR in laryngeal squamous cell carcinoma.

OC-199 | Clinical outcome of lung-only oligometastatic HNSCC patients treated with SBRT: Update results

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Purpose or Objective

Oligometastatic disease in head and neck squamous cell carcinoma (HNSCC) is an atypical scenario. Local ablative treatments are the most adopted strategies although no evidence-based recommendations are currently available. The purpose of our analysis was to update and report on long-term clinical outcomes of a cohort of HNSCC patients treated with stereotactic body radiotherapy (SBRT) for lung-only oligometastatic disease.

Materials and Method

We included patients with 1 to 5 pulmonary lesions. The oligometastatic pattern was defined as “de novo” (suitable for SBRT only) or “oligoprogressive” (after first line of systemic therapy). We evaluated time to progression (TTP) as the time from the last day of SBRT to disease progression or death from any cause. Predictive factors of better clinical outcome and survival analysis were performed by Cox regression and Kaplan Meier methods, respectively.

Results

A cohort of 47 patients and 48 metastases were retrospectively evaluated (Table 1). The median age was 67 years (range 37-86)

and 87% of patients had a ECOG PS 0-1. HPV negative status (77%) and “de novo” oligometastatic pattern (78%) were reported by the majority of patients. After a median follow up of 28 months (range 2-88), median TTP and overall survival (OS) were 18 months (95% CI 4.8 – 31.2) and 62 months (95%CI 10,8 - 113.2), respectively (Figure 1). At univariate analysis, patients aged > 70 years reported a better TTP (p 0.013). No statistically significant correlation was observed in respect with gender (p 0.23), ECOG PS (p 0.34), oligometastatic pattern (p 0.13) and p16/HPV status (p 0.22). Out of 26 histologically proven metastases, we collected only 2 patients reporting concordance between p16/HPV positive status of primary tumor and lung metastases. Overall, 6 patients reported grade (G) 1-2 acute toxicity and no acute G3 adverse events were observed.

Conclusion

In appropriately selected HNSCC patients with lung-only oligometastatic disease, SBRT may improve clinical outcome prolonging time to progression and to systemic treatments. Distant metastases from HPV-related primary HNSCC should be tested for p16/HPV status given the clinical implications of HPV positivity for diagnosis and treatment.

OC-206 | Predictive value of body composition assessment in R/M SCCHN treated with immunotherapy(NCT04721184)

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Keywords

Nutrition, immunotherapy, recurrent/metastatic.

Introduction and Purpose

Patients with recurrent/metastatic (R/M) squamous cell carcinoma of head and neck (SCCHN) have an increased risk of malnutrition. Low skeletal muscle index before immune checkpoints inhibitors (ICI) treatment in R/M SCCHN patients has shown to negatively impact on overall survival (OS) and progression-free-survival (PFS) (1). The "Immuno-Nutri" study (NCT04721184) aims to prospectively evaluate the impact of body composition on the efficacy of immunotherapy in R/M SCCHN patients. Preliminary results of first interim analysis are presented.

Method

Single-institutional, prospective observational study involving R/M SCCHN patients to be treated with antiPD-(L)1-based therapy. Planned accrual= 120 patients. Demographic, clinical and analytical variables are collected. A CT scan at L3 is performed to assess body composition according to skeletal muscle area and total adipose tissue area, both adjusted to patient's height: skeletal muscle index (SMI) and total adipose tissue index (TATI), respectively. Toxicity is recorded using Common Terminology Criteria for Adverse Event v5 and objective response rate (ORR) is evaluated using Recist1.1. Kaplan-Meier was used to estimate PFS and OS. The impact of SMI and TATI in PFS and OS was evaluated with univariant analysis.

Results

41 patients were recruited between January 2021 and September 2022. Table 1 summarizes baseline characteristics and body composition assessment variables. ORR evaluated in 37/41 patients with imaging assessment was 27%: partial response (21.6%), complete response (5.4%), stable disease (48.9%) and progression disease (48.9%). 22 patients (52.4%) had any grade of immune--related toxicity (IRT) and 16 (38%) required oral corticosteroids. 21 (51.2%) patients discontinued therapy due to progression and 4 (9.8%) due to toxicity. With a median follow up of 7 months, median PFS was 2.34 months (IC95% 2.04-4.38) and OS was 11.68 months (IC95% 8.96-NR). In the univariate analysis, higher SMI was associated with better PFS (HR 0.96[IC95% 0.91-1], p=0.049), with no impact observed according to performance status, number of previous lines, type of recurrence, LDH or TATI. Type of recurrence and LDH and type of recurrence had a negative impact on OS in the univariate analysis: HR 3.10 (IC95%[1.07-9.03], p=0.038) and HR 1.01 (IC95%[1-1.01], p=0.021), respectively.

Conclusion

Preliminary results of the first interim analysis showed high pre--treatment SMI could positively impact PFS in patients with R/M SCCHN treated with immunotherapy.

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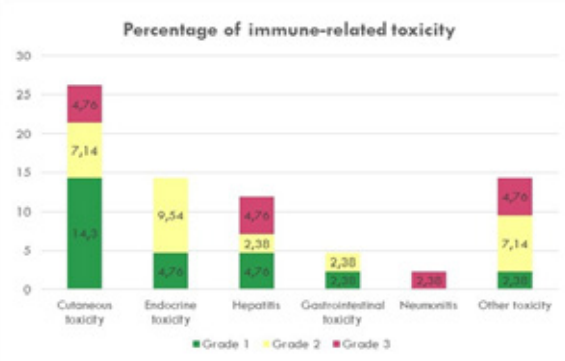
Table 1: Baseline characteristics of cohort.

Variable	N (%)
Age*	62.2[57.8;70.3]
Sex	
Man	31 (75.6%)
Woman	10 (24.4%)
Smoking history	
Ex-smoker	21 (51.2%)
Current smoker	15 (36.6%)
Never smoker	5 (12.2%)
Primary tumour site	
Nasopharynx	1 (2.4%)
Oral cavity	16 (39%)
Oropharynx	8 (19.5%)
Hypopharynx	9 (22%)
Larynx	4 (9.8%)
Other	3 (7.3%)
PDL1 status according to CPS	
Positive	38 (92.7%)
Negative	2 (4.9%)
Unknown	1 (2.4%)
Performance status	
0	3 (7.5%)
1	36 (87.8%)
2	2 (4.7%)
Type of recurrence	
Locoregional	20 (48.8%)
Metastatic	6 (14.6%)
Locoregional and metastatic	15 (36.6%)
Previous systemic treatments for R/M HNCSS	
0	27 (65.9%)
1	13 (31.7%)
2	1 (2.4%)
Kind of received treatment	
Nivolumab	24 (58.5%)
Pembrolizumab	6 (14.6%)
Pembrolizumab + Chemotherapy	4 (9.8%)
Other	7 (17.1%)
BMI (kg/m2)*	23.2 [21-25.7]
SMI (cm2 / m2)*	44.8 [39-5]
TATI (cm2/m2)*	74.2 [45.5-108]
LDH (U/L)*	161 [138-193]
Treatment after immunotherapy	28 (66.7%)
No	16 (57.1%)
Yes	12 (42.9%)

*Continuous variables are shown as median (interquartile range)
BMI: body mass index, SMI: muscle skeletal index, TATI: total adipose index tissue



OC-226 | Incidence of oral cavity cancer in young patients: are we facing a paradigma shift?

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Keywords

Oral cancer; young patients; Covid-19

Purpose/Objective

Oral cancer is a major public health issue, and it seems to be an emerging tendency to affect younger patients, as opposed to the common idea that it is associated with longer exposure periods to risk factors such as tobacco or alcohol, thus affecting predominantly older individuals. Public knowledge about this disease is still poor, which contributes to late-stage diagnosis and higher mortality rates.

Since the beginning of the COVID-19 pandemic, we have been questioning whether there is an increase in the incidence of oral cancer in young people, or if the higher number of cases in our center is strictly due to referral guidelines created during this period. Following this mindset, it is also important to understand what effects the pandemic had on the timing of oral cancer detection, and stage of the disease at that time. The aim of this study is to report the incidence of oral cancer in patients under 40 years old, between 2011 and 2020, in a tertiary oncological center.

Material/Methods

Identification of patients diagnosed with oral cancer in a tertiary oncological center, between 2011 and 2020, and their characte-

rization according to age group (<40 years old or >40 years old). Comparison with the incidence rates of oral cancer in the North Region of Portugal in the previous ten years (2009 – 2019).

Results

Between 2011 and 2020, there was a total of 1777 patients diagnosed with oral cavity cancer, at our institution, with 51 patients aged under 40 years old (Table 1). It was possible to observe that there was a growing tendency of oral cancer diagnosed in younger patients, between 2012 and 2015. This tendency was interrupted by what seems to be an underreporting, between 2016 and 2017, which is in line with what happened in most national cancer records, during the same period. In 2020, the number of cases appears to be exceptional, with 10 cases of oral cancer registered in patients aged < 40 years. (Figure 1)

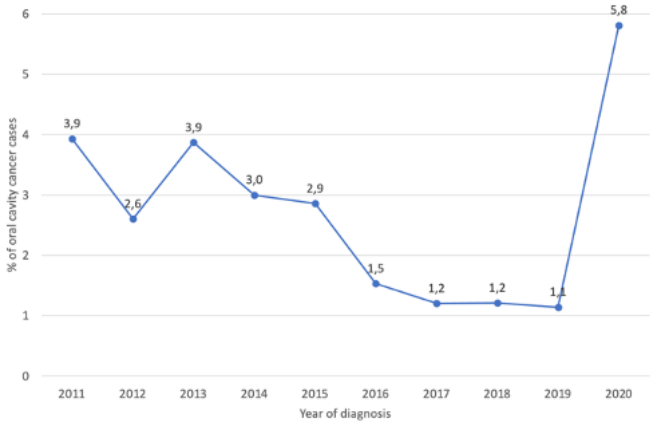
Conclusion

A better understanding of the pathogenesis, progression, and biologic behavior of oral cancer in young patients will contribute to the improvement of specific treatment strategies based on age groups. In what concerns the number of oral cancers in young patients reported in 2020, a longer period is needed to corroborate whether this is a real increase or just a fleeting variation related with mandatory reference to tertiary centers during COVID-19 pandemic.

Table 1. Evolution of oral cavity cancer over 10 years, at a tertiary oncological center

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
<40 years old	7	5	6	6	5	3	3	4	2	10
≥40 years old	171	187	149	194	170	193	164	163	173	162
Total	178	192	155	200	175	196	167	167	175	172

Figure 1. Evolution of oral cavity cancer over 10 years, at a tertiary oncological center (Patients under 40 years old)



OC-236 | The Relationship Between Tumor Purity and Markers of Immune Infiltration in Head and Neck Cancer

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Keywords

Tumor purity, immunotherapy, tumor microenvironment

Purpose/Objective

Immune cell infiltration in the tumor microenvironment (TME) is a predictor of favorable clinical outcome after treatment with immune checkpoint inhibitors (ICI). Data on the TME are often based on RNA sequencing (RNAseq) or quantitative microscopy analyses that are not routinely performed in clinical practice. Tumor purity (TP) represents the fraction of cancer cells in a tumor sample and may be leveraged from more widely available targeted next-generation DNA sequencing (tNGS) data. Low TP suggests a high proportion of other cells in a sample, including immune cells, and may thus offer a surrogate marker for TME immune infiltration. We aim to explore the relationship between TP and markers of tumor immune infiltration in the pan-cancer setting and in HNC specifically. Secondly, we aim to assess the relationship between TP and clinical outcome after ICI treatment in patients with HNC.

Material/Methods

Linear regression was used to correlate tumor purity with nine different RNAseq-based immune infiltration signatures across 21 cancer types using 11,400 samples from The Cancer Genome Atlas (TCGA). Immune infiltration data were obtained from published reports. TP was calculated using the publicly available ESTIMATE

and Absolute algorithms. A separate cohort of 70 HNC patients treated with ICI between 2015 and 2018 with tumor DNA profiling based on the MSKCC IMPACT tNGS panel was identified. In this cohort, TP in was assessed using the FACETS algorithm. A Cox proportional hazards model with TP, tumor mutational burden (TMB), and tumor HPV status as covariates was used to assess the relationship between TP and progression-free survival (PFS) and overall survival (OS) after treatment with ICI.

Results

TP varied across cancer types. Mean TP in HNC was 47 ± 21%. TP was negatively correlated with leukocyte fraction in HNC (R = –0.75, $P < 0.0001$, n = 513) and in the pan-cancer setting (R = –0.71, $P < 0.0001$, n = 9,781). In both settings, TP was weakly negatively associated with interferon gamma and Immune Infiltration Score. In the MSKCC HNC cohort, TP was significantly associated with PFS after ICI treatment in a Cox model that also included TMB and tumor HPV status (HR 6.84, $P = 0.036$). TP was not significantly associated with OS in this cohort (HR 0.90, $P = 0.91$).

Conclusion

TP was negatively correlated to several RNAseq metrics of immune infiltration and circulating immune cells, most notably leukocyte fraction, in both the pan-cancer and HNC TCGA cohorts. TP was significantly and negatively associated with PFS in HNC patients treated with ICI in a model including TMB and HPV status. Upon further validation, TP may offer a surrogate marker for an infiltrated TME with clinical relevance to predicting benefit of ICI treatment in HNC.

OC-242 | Can pre-treatment MR imaging identify hypoxic regions in head and neck squamous cell carcinomas?

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Key words
Hypoxia, MRI

Background

Oxygen Enhanced MRI (OE-MRI) is an imaging technique proposed for studying tumour hypoxia. Changes in longitudinal relaxation times (T_1) following high concentration oxygen can map hypoxic regions of tumours with normoxic areas showing decrease in T_1 times[1]. Combining this with measurements of oxygen induced changes in R_2* rates allows classification of malignant tissue as normoxic, mildly hypoxic, severely hypoxic or vascular steel[2]. Implementation in the head and neck region is of clinical value as hypoxia is a cause of radiotherapy treatment resistance in head and neck squamous cell carcinoma (HNSCC). We report our results of classifying the hypoxic status of malignant tissue in HNSCC using OE-MRI.

Method

5 non-patient volunteers (median age 32 years, range 31 to 60 years) and 19 patients with suspected HNSCC (median age: 57 years, range 36 to 76 years) were scanned on Siemens Sola 1.5T scanners. T_1 mapping was performed over 40 dynamic acquisitions using a 3D spoiled gradient echo sequence (TE/TR: 1.27/10ms, FA=2/18°, matrix: 128, FOV: 200x200mm, 72 x 2.5mm slices) with participants switched from breathing room air to high flow oxygen via a non-rebreather facemask after the 15th acquisition. R_2* mapping was performed on room air and after oxygen using 3D

multi-echo Dixon (TE/TR: 1.10 to 14.28/15.6ms). Images were co-registered and corrected for motion using non-rigid deformation via ANTs (Advanced Normalization Tools).

Volumes of interest (VOI) around biopsy confirmed malignant tissue and benign lymph nodes were delineated using ITK-SNAP software by a clinical oncologist. VOI averaged oxygen induced changes in T_1 times (?T_1) and R_2* rates (?R_2*) were determined and used to classify the oxygenation status of the structure.

Results

14 patients received histological diagnosis of HNSCC. 14 primary tumours (median volume 4.79ml range 0.26ml to 33.70ml), 39 malignant nodal masses (median 3.13ml, 0.26ml to 20.56ml) and 29 benign nodal masses (median 0.51ml, 0.31ml to 4.65ml) were contoured. Data from one volunteer was excluded after failing oxygen delivery quality control check.

The median (range) of ΔT_1 times were -1.9% (-8.0% to 2.2%) for benign nodes, -2.2% (-6.3% to 0.6%) for malignant nodes and -3.0% (-6.3% to 4.3%) for primary tumours with no statistically significant difference between benign and malignant nodes (p=0.5).

11/14 (79%) primary tumours were classified as normoxic with 1 each mild hypoxia, severe hypoxia and vascular steel. For malignant nodes (figure 2), 21/39 (54%) were normoxic, 15/39 (38%) mildly hypoxic, 1 each severely hypoxic, vascular steel and unclassified.

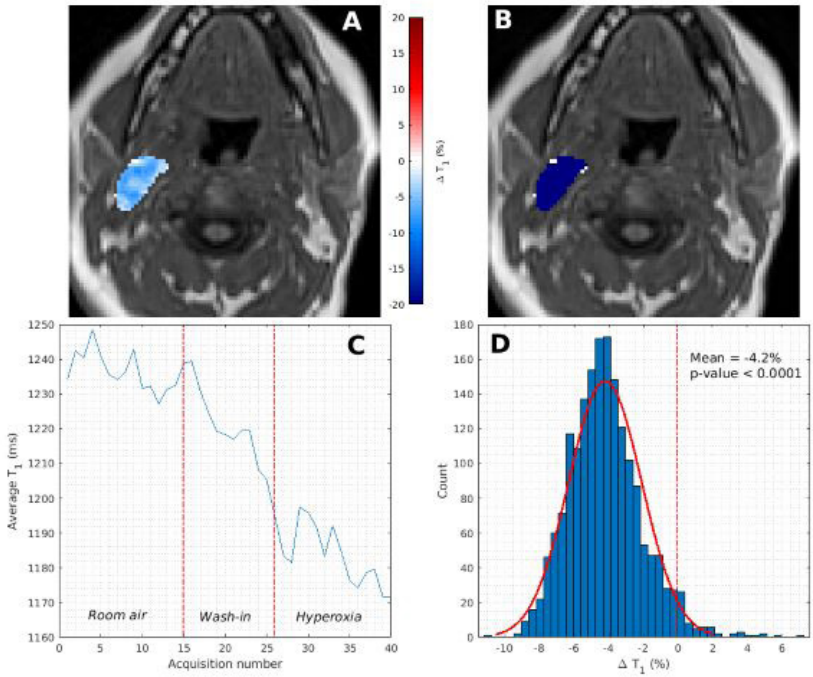
Conclusion

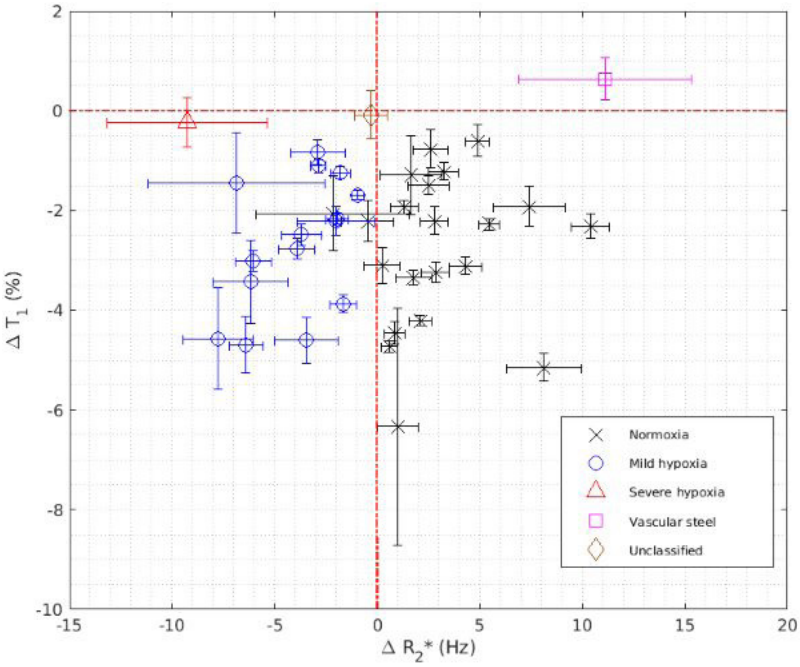
OE-MRI was able to classify HNSCC tumours by hypoxia status. Further work is required to correlation this classifications to outcomes from clinical treatments.

FIGURES

Figure 1: Example normoxic node ΔT_1 map (A) and statistical map (B) with blue indicating statistically significant decrease in T_1 times. Bottom row shows VOI averaged time series of T_1 times (C) and ΔT_1 histogram times for entire VOI.

Figure 2: Scatter plot of malignant nodes based on VOI average ΔT_1 times and DR2 rates (95% CI). Normoxia: significantly decreasing T_1, stable/increasing R_2*; Mild hypoxia: decreasing T_1, decreasing R_2*; Severe hypoxia: stable/increasing T1, decreasing R_2*; Vascular steel: increasing T_1, increasing R_2*.*





ACKNOWLEDGEMENTS

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OC-260 | Evolution of secondary reconstruction of mandible with the aid of cad-cam system

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Keywords

Secondary Reconstruction, Mandible Reconstruction, CAD-CAM System

Purpose

Secondary reconstruction of the mandible has undergone rapid evolution through recent years, thanks to different type of patient and technological advancement. This new class of patients is difficult to treat due to previous reconstructive surgeries, surgical failure and previous adjuvant therapies. However Cad-Cam system simplified surgeon's job especially for pre-operative programming. Several studies have been conducted to evaluate the accuracy of cad-cam method in comparison to traditional surgery, or to evaluate reconstructive results accuracy compared to pre-operative programming. Studies are still lacking on the evolution of secondary reconstruction of the mandible and on the impact that Cad-Cam system had on that procedure.

Material/methods

All the secondary reconstructive surgeries of the mandible performed at A.O.P.R Maxillo-facial surgery unit, have been selected; we performed a comparison between patients that have been treated with traditional method and those treated with Cad-Cam procedure. The comparison has been conducted by measuring the distance between condyle and mandibular angle, mandibular angle and gnathion; healthy side and reconstructed one measurements of the mandibular angle on orthopantomography

after surgery. Patients have been given the University of Washington quality of life Questionnaire (UW-QOL) subjective evaluation test about their health status.

Results

The two cohorts of patients are almost comparable: there were no substantial differences in the measurements, even if the Cad-Cam group had slightly better outcomes. Especially, the major discrimination has been noted in the mandibular angle, in both monolateral and bilateral reconstruction. UW-QOL test has reported an overall result of 88,4% with the difference of 10 units between the traditional group (83,1%) and Cad-Cam group (93,7%).

Conclusion

Patients treated with traditional approach obtained the expected outcome, even if the subjective tests results have a considerable difference. The possibility of an accurate pre-operative planning, a 3D modelling and a preliminary study of future prosthesis rehabilitation, can assist especially less expert surgeons.

OC-264 | Radiotherapy resistance of OCT4-expressing HNSCC can be reversed with cisplatin

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(1) Turku University Hospital, Finland

Keywords

OCT4; radioresistance; cisplatin; HNSCC; TMA;

Purpose

Cisplatin is combined with radiotherapy for advanced head and neck squamous cell carcinoma (HNSCC). While providing a beneficial effect on survival, it also causes side effects and thus is an important target when considering treatment de-escalation.

Currently, there are no biomarkers to predict its patient-selective therapeutic utility. In this study, we examined the role of the stem cell factor OCT4 as a potential biomarker to help clinicians stratify HNSCC patients between radiotherapy and chemoradiotherapy.

Methods

OCT4 immunohistochemical staining of a population-validated tissue microarray (PV-TMA) (n= 166) representative of a standard HNSCC patients was carried out, and 5-year survival was analyzed. The results were validated using *ex vivo* drug sensitivity analysis of HNSCC tumor samples, and further cross-validated in independent oropharyngeal (n=118), nasopharyngeal (n= 170), and vulvar carcinoma (n= 95) clinical datasets. *In vitro,* genetically modified, patient-derived HNSCC cells were used.

Results

OCT4 expression in HNSCC tumors was associated with radioresistance. However, combination therapy with cisplatin was found to overcome this radioresistance in OCT4-expressing HNSCC tumors.

The results were validated by using several independent patient cohorts. Furthermore, CRISPRa-based OCT4 overexpression in the HNSCC cell lineresulted in apoptosis resistance, and cisplatin was found to downregulate OCT4 protein expression *in vitro*. *Ex vivo* drug sensitivity analysis of HNSCC tumors confirmed the association between OCT4 expression and cisplatin sensitivity.

Conclusion

This study introduces OCT4 immunohistochemistry as a simple and costeffective diagnostic approach for clinical practice to identify HNSCC patients who can be treated with radiation therapy alone and on the other hand the patients who has radiotherapy resistant cancer and need cisplatin for radiosensitation.

OC-286 | CLINICAL FACTORS ASSOCIATED WITH BENEFIT TO NIVOLUMAB: REAL-WORLD DATA ANALYSIS

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Keywords

Nivolumab. Real world data. Efficacy/Toxicity

Purpose/Objective

Nivolumab has demonstrated overall survival (OS) improvement in patients (pts) with cisplatin-refractory recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). This real world data study aims to evaluate nivolumab's efficacy and toxicity and to identify clinic and pathological factors associated with greater benefit.

Material/Methods

Retrospective multicenter cohort analysis of R/M HNSCC pts treated with nivolumab at progression to cisplatin-based chemotherapy at 3 centers of the Institut Català d'Oncologia (ICO) between July 2018 and July 2021. Clinical data, PD-L1 status, objective response rate (ORR) and immune related adverse events (irAEs) were collected. OS and progression-free survival (PFS) were estimated using Kaplan-Meier method. A multivariate analysis (MVA) with Cox regression was conducted to identify predictive factors of survival.

Results

A total of 84 pts were included: median age 62 years (38-77); ECOG≤1 88%; disease location: locoregional 42%, distant 19%, both

39%; previous therapy for R/M: none 19%, 1 (64.3%), ≥2 (16.7%). PD-L1 status: positive 63%, negative 29%, unknown 8%. ORR to nivolumab was 18%. 41% presented irAEs (grade ≥3= 4.8%). With a 12 month(m) median follow-up, OS was 9.2m (95%CI 5.4-12.2) and PFS 3.1m (95%CI 2-4.3). ECOG≤1 and irAEs were associated with better OS but not PFS, although a positive trend was observed with irAEs (Table). In MVA adjusted by variables shown in table, ECOG was an independent predictor for OS (HR 0.05, 95% CI 0.-0.37, p=0.003) and PFS (HR 0.12, 95% CI 0.02-0.73, p=0.021). Up to 38% of pts received treatment after nivolumab (taxane +/- cetuximab: 84%; clinical trial: 20%; carboplatin-5FU: 3%), with an ORR of 31% and no OS differences by regimen received (p = 0.285).

Conclusion

In this cohort, nivolumab's efficacy and toxicity were consistent with those reported in the pivotal study and support its use in PD-L1 unselected population in routine clinical practice. Pts with ECOG≤1 and/or who present with irAEs derived greater benefit.

Variables	PFS (CI 95%)	OS (CI 95%)
Loco-regional location vs distance vs both (m)	3.4 (1.6-8.6) vs 4.3 (1.7-20.6) vs 2.5 (1.5-3.4) p=0.174	12.0 (8.3-18.2) vs 12.25 (2.2-21.7) vs 6.5 (2.8-9.2) p=0.310
PDL1 status (positive vs negative) (m)	3.2 (1.9-4.9) vs 3.3 (1.9-6.7) p=0.997	8.3(4.1-13.9) vs 9.3(4.0-13.7) p=0.795
ECOG (≤1 vs 2) (m)	3.3 (2.2-4.8) vs 1.2 (0.1-2.3) p=0.057	9.9 (7.3-13.7) vs 2.0 (0.1-2.8) **p=0.005**
Treatment time with Cetuximab < 6 m vs > 6 m	2.2 (1.6-5.9) vs 3.2 (0.9-5.5) p=0.932	4.3 (2.6-9.9) vs 9.2 (5.4-13.0) p=0.956
Progression to PBT >6 or <6 (m)	8.2 (1.2-NR) vs 2.6 (1.7-3.5) p=0.137	12.1 (1.2-NR) vs 8.4 (5.4-12.2) p=0.390
irAE (yes vs no) (m)	4.9 (2.2-20.6) vs 2.6 (1.6-3.8) p=0.051	13.0 (9.2-24.1) vs 6.5 (2.6-11.1) **p=0.015**
Previous taxane (yes vs no) (m)	1.9 (0.88-NR) vs 3.1 (1.7-4.0) p = 0.112	4.3 (0.19-12.0) vs 8.4 (5.4-12.1) p= 0.43

OC-292 | Impact of margin distance on oral cavity cancer patients' survival

Marc Juarez [(1)]; *Laura Martinez Avila* [(1)]; *Nadia Gomez Serra* [(1)]; *Maria Duch Balust* [(1)]; *Jesus Brenes Castro* [(1)]; *Sandra Llop Serna* [(1)]; *Maria Plana Serrahima* [(1)]; *Marc Oliva* [(1)]; *Isabel Linares Galiana* [(1)]; *Alicia Lozano Borbalas* [(1)]

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Keywords

Oral cavity, margin, adjuvant treatment.

Purpose/Objective

There is a lack of consensus in the precise definition of close margin and its impact on survival in patients (pts) with oral cavity squamous cell carcinoma (OC). A few studies suggested that a distance to the margin below 5 mm might be sufficient to achieve disease control.

The primary objective of this study was to evaluate the effect of different margin distances (1 to 5 mm) on OS, Cancer Specific Survival (CSS) and Local Relapse Free Survival (LFS).

Material/methods

Retrospective cohort analysis of pts with newly diagnosed OC treated with curative-intent surgery plus/minus adjuvant (chemo)radiotherapy in the Head and Neck multidisciplinary Unit of Institut Catala d'Oncologia (ICO) L'Hospitalet between 2011 and 2019. Pts with R1-2 margins and /or non-squamous cell carcinoma histology were excluded.

Cox's regression multivariate analysis (MVA) was used to identify predictors of OS, CSS and LFS, including distance to the margin (categorised from 1 to 5mm). Kaplan Meier method

was used to estimate survival curves. Clinical, pathological, and treatment variables were collected.

Results

A total of 210 patients were included. Patient characteristics are summarised in Table 1. Median OS, CSS and LFS was 61 months (IC 95% 46.2-76.9), 92.1 (IC 95% 82.5-101.7) and 76 (IC 95% 61.5-90.5), respectively.

In the MVA adjusted by age, ECOG and stage, margin distance of 3mm [HR 3.34 (IC 95% 1.6-7.7), p=0.002] and PNI [HR 1.92 (IC 95% 1.1-3.3), p=0.017] were independent prognostic factors of OS. For CSS, 3mm margin was associated with worse outcome [HR 4.13 (IC 95% 1.51-11.28), p=0.006] and a statistical tendency was found in ECE [HR 2.67 (IC 95% 0.9-7.3), p=0.055)]. The 3mm distance was the only factor which trended towards worse LFS [HR 3.2 (IC 95% 0.9-11.0), p=0.066]. Median OS and CSS for ≤3 mm vs >3mm margin groups were 41.3 months (IC 95% 30.4-52.3) vs 76.4 (IC 95% 64.9-87.8, p<0.001) (figure 1), and 66.3 (IC 95% 53.1-79.6) vs 97.2 (IC 95% 85.8-108.6, p=0.01).

Conclusion

In our cohort, a distance to the margin > 3 mm (4-5 mm) did not impact on survival in OC pts. Patients with ≤3 mm have worse OS and CSS. We observed a trend towards worse LFS, which may be due to the effect of adjuvant and/or salvage therapy.

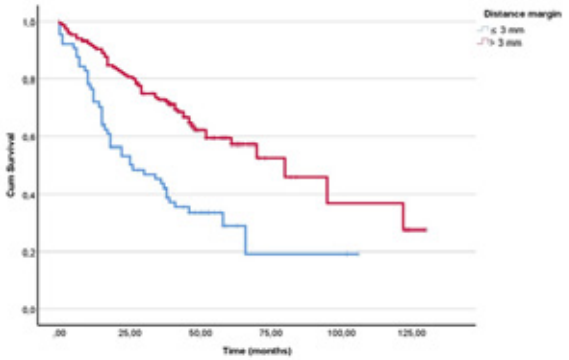

Figure 1. OS of ≤ 3 mm (blue) and >3mm (red) population (p<0.001).

Table 1. Patient characteristics

Characteristic	N (%)
Median age (years) (IQR)	67.9(59-77.2)
PS at diagnosis	
0-1	203(96.6)
≥ 2	7(3.4)
Primary site	
Tongue	80(38.1)
Oral mucosa	61(29)
Lips	24(11.4)
Floor of mouth	20(9.5)
Retromolar trigone	21(10)
Hard palate	4(1.9)
Adjuvant treatment	
RT	64(31.5)
QTRT	13(6.2)
Grade	
1-2	171(81.5)
3	36(17.1)
Non gradable	3(1.4)
PNI	
PNI +	70(33.3)
PNI -	137(65.2)
Non reported	3(1.4)
LVI	42(20)
LVI +	165(78.6)
LVI -	3(1.4)
Non reported	
ECE in lymphadenectomy patients	
ECE +	35(16.7)
ECE -	76(36.2)
Margin distance	
More than 3mm	146(69.5)
Equal or less than 3mm	64(30.5)
Stage grouping	
I-II	93(44.3)
III-IVA	92(43.8)
IVB	25(11.9)

OC-297 | Circulating HPV DNA is linked with disease burden, treatment, and outcomes in a prospective cohort

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(1) University Health Network, Toronto

Purpose/Objective

Rapid clearance of circulating HPV DNA (cHPVDNA) during radiotherapy/chemoradiotherapy (RT/CRT) correlates with favourable outcomes in HPV-positive oropharyngeal cancer (OPC). However, factors that affect and/or confound cHPVDNA clearance kinetics are unclear, limiting clinical utility. We evaluated cHPVDNA kinetics in the largest-to-date prospective cohort of p16-positive (p16+) OPC patients treated with definitive RT or CRT. Our objective was to (1) determine factors that affect cHPVDNA levels and kinetics and (2) estimate recurrence risk from cHPVDNA and clinical factors.

Material/methods

In 262 patients with p16+, stage I-III (TNM-8) OPC treated with curative-intent RT (n=107) or CRT (n=155), blood was drawn at pre-RT, 1-2 times during RT, and 3-months post-RT. HPV16 copies/mL were quantified by a validated multiplex droplet digital PCR assay. Gross tumour volume of primary (GTVp) and lymph nodes (GTVn) were quantified from RT planning contours. cHPVDNA was modelled with a Bayesian generalised linear mixed model (GLMM) that accounts for the RT dose received up to each cHPVDNA measurement and considers GTVp, GTVn, and chemotherapy as patient-level covariates. From the full cHPVDNA timeseries, the GLMM can estimate the RT dose required to clear cHPVDNA (D_{clear}). Using a 1:1 training/

test split, we trained a recurrence-free survival (RFS) model using LASSO Cox regression, choosing lambda with 4-fold cross-validation. Candidate features were D_{clear}, GTVp, GTVn, chemotherapy, and smoking pack-years. Area under the receiver-operator characteristic (AUROC) was computed on the test data. Patterns of failure were studied using a competing-risks Cox model.

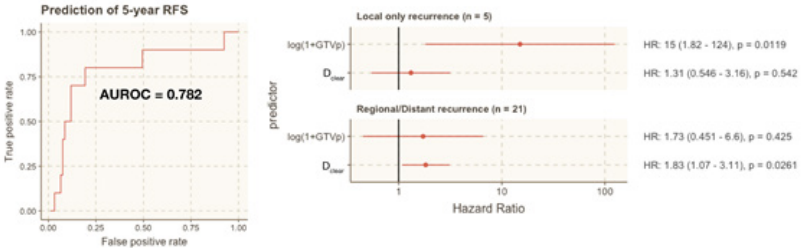
Results

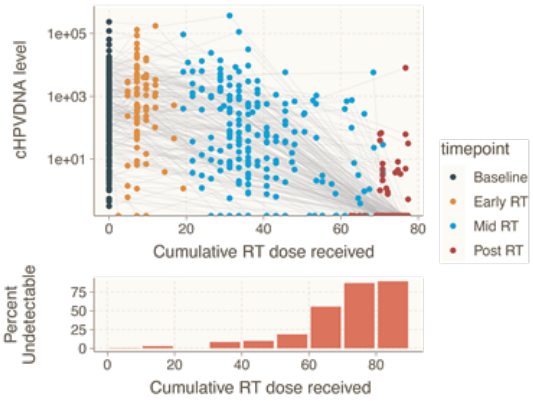
With median follow-up of 52 months, 3-year RFS was 88%. Pre-RT cHPVDNA was detected in 220 (84%) patients and ranged from 0.32 to $2.4x10^5$ copies/mL. Patients with negative baseline cHPVDNA had higher T category (p=0.042) and were more likely to smoke (p=0.025) but had no RFS difference. Marginal effects of the GLMM (Fig 1) show the impact of GTVp, GTVn, and chemotherapy on cHPVDNA levels as a function of RT dose received. Among those with detectable cHPVDNA, higher baseline cHPVDNA was associated with larger GTVp (log odds ratio/LOR: 2.2, 95CI [1.5-3.0]) and GTVn (LOR: 2.03 [1.29-2.73]). Interaction terms with the RT dose showed that cHPVDNA cleared faster during RT in patients with large GTVp (LOR: -0.045 [-0.073– -0.017]) but not large GTVn (LOR: 0.010 [-0.013-0.033]). Concurrent chemotherapy accelerated cHPVDNA clearance (LOR: -0.045 [-0.067– -0.024]). Patients with faster than expected early drop in cHPVDNA were also more likely to clear cHPVDNA after RT/CRT (96% vs 85%, p=0.012). The 193 patients (90.6%) who cleared cHPVDNA had improved RFS (p<0.001, 3-year: 94% vs. 68%). The optimal trained LASSO model of RFS had non-zero coefficients for GTVp and D_{clear}. On the test data, it predicted 5-year RFS with an AUROC of 0.782 (Fig 2). Higher GTVp was associated with local-only failure (hazard ratio 15 [1.82-124], p=0.012) whereas higher D_{clear} was associated with regional/distant failure (1.83 [1.07-3.11], p=0.026).

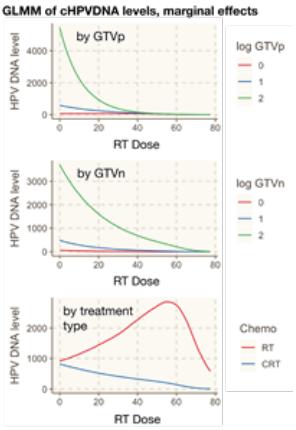
Conclusion

We quantified the impacts of GTVp, GTVn, and chemotherapy on longitudinal cHPVDNA during RT. cHPVDNA kinetics, summari-

sed as D_{clear}, and GTVp accurately estimated 5-year RFS and are associated with different patterns of failure. This approach could guide clinical interpretation of cHPVDNA and inform personalised risk-adapted RT.







OC-310 | Platelet-to-Lymphocyte Ratio Predicts Survival in Head and Neck Cancer Before Radiochemotherapy

Jonas Werner [1]; *Klaus Strobel* [2]; *Dirk Lehnick* [3]; *Gunesh P. Rajan* [1]

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Objective

To conduct a comprehensive investigation of pretherapeutic markers of systemic host immune response and metabolic tumor parameters from FDG-PET/CT and evaluate if they could predict treatment response and survival in head and neck cancer patients prior to primary chemoradiation.

Methods

Pretherapeutic FDG-PET/CT-derived metabolic tumor markers and unspecific inflammatory markers from peripheral blood draw were assessed in a retrospective analysis of a cohort of 110 head & neck squamous cell carcinoma patients undergoing primary chemoradiation. Possible prognosticators were identified using a stepwise multiple Cox regression model. The main outcome measure was survival.

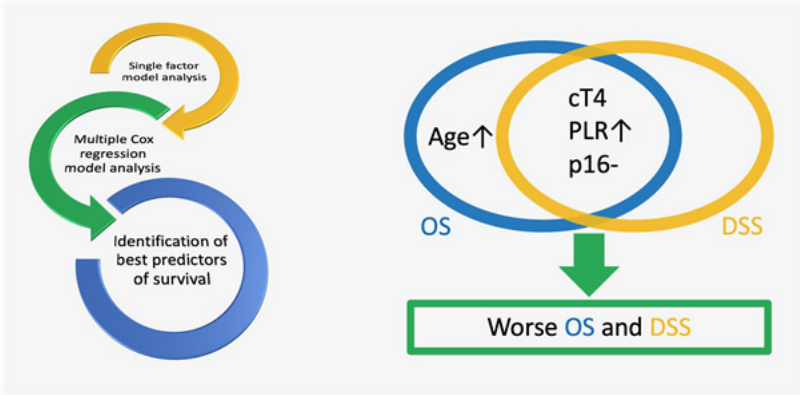
Results

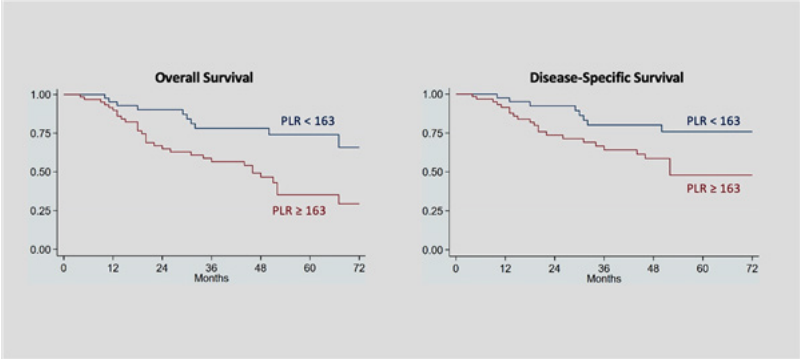
Median follow-up time was 32.5 months (IQR 14–52). Pretherapeutic markers predictive of overall survival were the platelet-to-lymphocyte ratio (PLR) (HR=1.004, 95% CI=1.002-1.007, *P*=0.002), p16-negativity (HR=3.868, 95% CI=1.633-9.161, *P*=0.002), older age (HR=1.059, 95% CI=1.016-1.103, *P*=0.007), and cT4 tumor stage (HR=2.056, 95% CI=1.039-4.069, *P*=0.039). The best prognosticators of disease-specific survical were PLR (HR=1.004, 95%

CI=1.001-1.007, *P*=0.007), p16-negativity (HR=3.054, 95% CI=1.137-8.205, *P*=0.027), and cT4 tumor stage (HR=2.285, 95% CI=1.054-4.950, *P*=0.036). FDG-PET/CT-derived parameters of tumor metabolism did not offer significant additive prognostic value.

Conclusion

PLR is an easily obtainable unspecific inflammatory marker and is predictive of overall and disease-specific survival in head and neck cancer patients before chemoradiation. An algorithm consisting of PLR, T-stage, and p16 status could be used to improve survival prediction in head and neck cancer patients before chemoradiation. Further studies are necessary to provide generalizable algorithms to support treatment decision making.





OC-312 | A predictive model of dosimetric variations in head and neck cancer treatments

Michele Aquilano [1]; Alessia Re [1]; Francesco Catucci [1]; Domenico Piro [1]; Francesca Gruosso [1]; Francesco Preziosi [1]; Andrea D'aviero [1]; Martina Iezzi [1]; Carmela Di Dio [1]; Sebastiano Menna [1]; Flavio Vincenzo Quaranta [1]; Elisa Pilloni [1]; Eleonora Gaia Sanna [1]; Chiara Flore [1]; Simone Scanu [1]; Althea Boschetti [1]; Marco Marras [1]; Nadia Ulgheri [1]; Francesco Floro [1]; Danila Piccari [1]; Vincenzo Valentini [2]; Davide Cusumano [1]; Giancarlo Mattiucci [1]

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Keywords

Artificial Intelligence, predictive model, head and neck cancers, radiotherapy, adaptive radiotherapy

Purpose/Objective

As a new discipline, Adaptive RadioTherapy (ART) requires new indicators to quantify the impact of inter-fraction variations on dose distribution, thus allowing identification of the optimal time to switch towards (online or offline) ART approaches. The aim of this study is the validation of a predictive model able to identify inter treatment fractions where unacceptable dose variations may be present in head and neck squamous cell carcinoma (HNSCC) patients (pts).

Material/methods

A total of 14 pts were treated using an Artificial Intelligence (AI)--based linac, acquiring a daily positioning cone beam computed tomography (CBCT) image without online adaptation. Dose regimens consisted of 70 Gy in 35 fractions or 60 Gy in 30 fractions. For each patient, all CBCT images acquired for patient positioning were rigidly matched to the planning CT (pCT). Daily CBCT images were automatically recontoured and treatment plans were

recalculated on the corresponding synthetic CT. The variation of V95% of Planning Target Volume High Risk (PTV_HR) and max dose of spinal cord, cervical esophagus and constrictors from the original values reported on pCT were collected along with the treatment. Fractions where PTV V95% decreased by 3% and spinal cord Dmax increase of 3% were considered as needed of ART. Radiological parameters were collected on each daily CBCT aligned with pCT to quantify the inter-fraction variability in each RT fraction once compensated for couch shifts. We measured the absolute body variation along antero-posterior (AP) and latero-lateral (LL) directions in the proximity of the plans passing through different vertebrae (C2, C3) and the corresponding discs (C2-C3, C3-C4). The correlation between such parameters and the fractions needed for adaptation was investigated using the Wilcoxon Mann Whitney test and a logistic regression model was created.

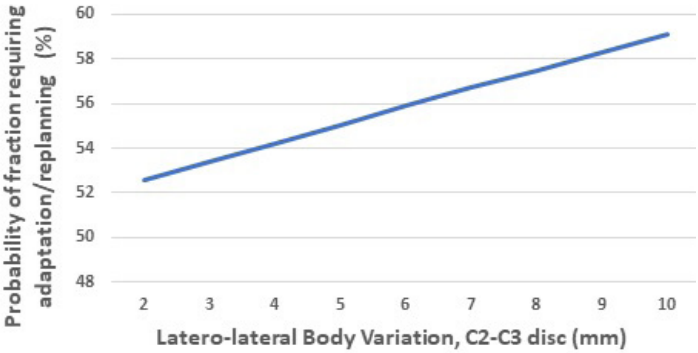
Results

On the basis of the predefined criteria, 212/400 fractions analysed required online adaptation. At the univariate analysis, the most significant parameter was the body variation along the LL direction measured through the C2-C3 disc, able to predict variation of PTV, spinal cord (p=1.7x10-3), cervical esophagus (p=3.44 x10-13) and constrictors (4.78 x10-4). Figure 1 reports the probability of obtaining a fraction requiring online adaptation on the basis of the body variation in LL direction, obtained thanks to the predictive model developed.

Conclusions

A new metric to define the need for replanning was proposed based on body variation measured along the LL direction through the C2-C3 disc: if such value results > 5 mm the treatment fraction has to be considered needed of replanning or ART (85% of probability of not meeting the tolerance criteria). More research is needed to address the gain of the ART in HNSCC.

Figure 1


Probability of fraction requiring adaptation/replanning (%)
60
58
56
54
52
50
48
2
3
4
5
6
7
8
9
10
Latero-lateral Body Variation, C2-C3 disc (mm)

OC-318 | Head and Neck Squamous Cell Carcinoma treated with EXTREME protocol followed by nivolumab

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Keywords

Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma; EXTREME protocol; Immunotherapy

Introduction

The benefit of immunotherapy in patients with Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma (RoMHNSCC) is well established. Previously, 1st line standard of care was platinum/fluoropyrimidine/cetuximab, followed by cetuximab maintenance (EXTREME protocol), leaving immunotherapy for further lines. The current 1st line recommendation is platinum/fluoropyrimidine/pembrolizumab. This work intends to review the impact of immunotherapy use after EXTREME protocol.

Objectives

Retrospective cohort analyses of patients with RoMHNSCC treated in a Portuguese Cancer Centre with EXTREME protocol followed by nivolumab in subsequent lines. The primary aim was to assess efficacy and toxicity.

Results

Thirty-one patients were included, median age of 56.6 years (range 40-74), 96.8% males and ECOG 0-1. The most common tumour location was the hypopharynx (41.9%). Most patients were stage IV at diagnosis (71.0%). Curative intent treatment was performed in 54.8% (28.6% had surgery, 42.8% surgery plus adjuvant RT or

QT/RT and 28.6% radical QT/RT). Regarding these patients, 64.7% relapsed locally and the remaining had distance metastasis. The mDFS was 27.6months.

All patients received 1st line EXTREME protocol. Median ORR was 74.2%, DCR 77.1% and mPFS 8.4months. The median number of palliative treatment lines was 4 (range 2-7). All patients received 2nd line treatment: 61.3% nivolumab, 19.4% paclitaxel, 16.1% carboplatin/paclitaxel and 3.2% methotrexate. Global DCR was 35.5% and mPFS2 11.9months. Twenty-four patients were treated in 3rd line: 37.5% paclitaxel, 29,2% nivolumab, 2 patients included in clinical trials and the remaining with other drugs. Global DCR 41,2%, one patient in nivolumab subgroup had sustained Complete Response (sCR).

Seventeen patients were treated in 4th line, mostly with methotrexate (58.8%) and nivolumab (23.5%). There was progressive disease in 82.3% and one patient had sCR with nivolumab. 16.1% of nivolumab patients, in any line, had G2-3 toxicity (62.5% endocrine and 37.5% skin). The treatment was suspended in one patient due to toxicity. The median follow-up was 22.9months (range 6-60) with a mOS, since the beginning of palliative treatment, of 29.5months. In patients treated with EXTREME protocol followed by nivolumab and paclitaxel, the mOS was 23.3months.

Conclusions

The mOS was significantly higher in our population than in the clinical trials. A favourable disease group of patients may have influenced the present results as most received multiple treatment lines and two patients achieved sCR. Nevertheless, this data substantiates the benefit of immunotherapy in subsequent lines, and validates this option when chemotherapy plus immunotherapy cannot be used in 1stline.

OC-322 | Thyroid gland management in total laryngectomy: is thyroidectomy mandatory?

Cláudia Lopes Rosa [1]; *Mariana Caetano* [1]; *Ana Rita Santos* [1]; *Paulo Pereira* [1]; *Tiago Eça* [1]; *Leonel Luís* [1]

(1) HOSPITAL SANTA MARIA

Keywords

Laryngeal carcinoma, Thyroid invasion, Thyroidectomy

Purpose/Objective

Thyroidectomy for advanced laryngeal squamous cell carcinoma (LSCC) is controversial. This study aimed to evaluate the frequency of thyroid gland (TG) invasion in patients with LSCC and identify predictors of TG invasion.

Material/Methods

Cross-sectional analytical study with retrospective data collection of all the clinical cases of patients submitted to total laryngectomy (TL) for LSCC in a tertiary hospital between January 2012 and October 2022.

Hemithiroidectomy or total thyroidectomy was performed according to subglottic extension or radiological criteria defined by erosion or invasion of the thyroid cartilage. We analyzed the population demography, the preoperative pathological characteristics, the type of surgery performed, and the postoperative histology. We measured the frequency of thyroid gland invasion and clinical and pathological features associated with TG invasion.

Results

89 patients were submitted to TL and 68,5% have been submitted to thyroidectomy. The overall frequency of TG invasion was

11,2%. 80% of the patients with thyroid invasion were staged as T4a and 70% had involvement of the thyroid cartilage and/or extra-laryngeal soft tissues in preoperative CT scan. Of the patients with thyroid invasion, 90% were by contiguous spread and 80% were transglottic tumors. Local recurrence was associated with thyroid invasion (p=0.042).

Conclusion

Invasion of the thyroid gland by laryngeal cancer is uncommon. However, when present, is associated with local recurrence. We can suggest that total thyroidectomy should be done with TL in cases presenting with gross clinical, radiological or intraoperative thyroid gland involvement, transglottic growths with subglottic extension and thyroid cartilage invasion.


EHNS
European Head & Neck Society

POSTERS

PO-002 | incidental thyroid carcinoma as detected on PET-CT scan among breast cancer patients

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Keywords

PETCT, Thyroid malignancy, incidentiloma.

Objective

To study the incidental thyroid malignancy detected by PETCT scans in Ziv-treated breast cancer patients.

Background

Because of the increased use of (18)F-fluorodeoxyglucose positron emission tomography ((18)F-FDG PET) in breast cancer patients, an increasing number of incidentalomas in the thyroid gland have been identified.

Up to 35% of thyroid focal incidentalomas are malignant. Early detection of thyroid cancer allows for less invasive surgical treatment and avoids complicated treatment of advanced thyroid cancer.

Methods

Medical records of 166 breast cancer patients who underwent FDG PET-CT imaging in the nuclear medicine department at ZIV medical center from January 2018 to January 2019 and who were treated in the oncology department at ZIV medical center were reviewed for thyroid incindentiloma, maximal standard uptake value (SUVmax), age, and ethnicity were recorded and compared between patients with thyroid malignant incidentaloma and other breast cancer patients.

Results

Eight patients out of 166 had a focal incidental finding in the thyroid gland. Three patients had significantly higher SUVmax values than the other five. One of these patients had a biopsy that revealed papillary thyroid carcinoma; the SUVmax in this case was 17, and the other two patients were referred for FNA of the incidentaloma. The SUVmax of the remaining five patients is less than 10. Malignant thyroid incidental tumors occurred at a rate of 12.5%.

Conclusion

Thyroid gland incidentalomas with a high focal metabolic rate may be malignant. In these patients, further investigation, including ultrasonography-guided fine needle aspiration, is required.

PO-003 | Is there a correlation between the thyroid nodule's depth and nondiagnostic cytological results?

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(1) Ziv Medical Center, Safed, Israel

Keywords

Fine needle aspiration, thyroid malignancy

Objective

To determine whether thyroid nodule depth in ultrasound-guided fine needle aspiration cytopathology correlates with nondiagnostic outcomes.

Background

Nondiagnostic ultrasound-guided fine needle aspiration cytology is correlated with a number of variables. Few studies, however, have looked at whether there is a connection between the depth of nodules and the percentage of nondiagnostic cytology results. To find out if there is such a correlation, we conducted this study.

Materials and Methods

283 thyroid nodules underwent FNAC between January 2019 and December 2020. According to the Bethesda score, cytological analyses of the nodules were reviewed and classified as nondiagnostic and diagnostic. Clinical information (age, sex, ethnic group) and sonographic characteristics of nodules (such as depth, size, cystic portion, type of calcification and echogenicity) were examined in patient files and ultra sound (US) scans. The shortest distance between the skin and the nodule's most superficial border in the axial plane was used to determine a nodule's depth.

Results

Age, sex, and ethnicity were not significantly different between the nondiagnostic group and the diagnostic group ($p>0.05$). Nodule diameter, cystic portion, calcification and echogenicity were also not associated with the frequency of nondiagnostic results. The depth of nodules ≥ 9 mm was correlated with nondiagnostic US guided FNA cytological results (OR= 2.55, $p=0.018$).

Conclusions

Deep thyroid nodules correlated with nondiagnostic US guided FNA cytological results. Further studies are needed for optimizing the approach to deep thyroid nodules in order to improve the efficacy of FNA in deep thyroid nodules.

PO-010 | Oropharyngeal Cancer in the Elderly: Predictors of Survival in a Single-Center Cohort Study

Tjeerd de Jong [1]; Golzar Asri Aghmuni [1]; Gerda Verduijn [1]; Esther Van Meerten [1]; Emilie Dronkers [1]; Robert Jan Baatenburg de Jong [1]; Jose Hardillo [1]

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Keywords

Oropharyngeal Squamous Cell Carcinoma, Survival, Cisplatin, Cetuximab, Radiotherapy, Elderly Patients

Purpose/Objective

In this study the overall- and disease specific survival of the elderly (≥ 70 years of age) with OPSCC with regard to treatment modality (radiotherapy with concomitant cisplatin (CRT), radiotherapy with concomitant cetuximab (BioRadioTherapy), or radiotherapy alone (RT)) was evaluated.

Material/methods

A retrospective, single-center, observational study was performed. We included 367 patients that were diagnosed with stage III or IV OPSCC, and treated with curative intent at the Erasmus University Medical Center, Rotterdam, between 2006 and 2017.

Results

Of the 367 patients, 64 (17%) were ≥70 years of age. Patients <70 who received CRT had a 5 year overall survival (OS) of 45%, BRT a 5 year OS of 33%, and RT a 5 year OS of 35%. Elderly patients treated with CRT had a 5 year OS of 18%, BRT 33%, RT alone 32%. The survival of both elderly and younger patients with locally advanced OPSCC is significantly associated with tumor stage, WHO performance status, and relative weight loss.

Conclusion

In both younger and elderly patients, overall survival was not better in patients treated with BRT compared to those treated with RT. These results question the role of cetuximab as a substitute for cisplatin as part of CRT

PO-011 | Recurrence and survival outcomes of patients with a submandibular adenoid cystic carcinoma

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(1) Erasmus MC Rotterdam

Keywords

Submandibular gland; adenoid cystic carcinoma; survival; quality of life; local therapy; regional therapy

Purpose/Objective

To evaluate tumor characteristics, quality of life (QoL), disease recurrence and survival of patients with submandibular gland adenoid cystic carcinoma (AdCC)

Material/methods

A single-Twenty five patients diagnosed with a submandibular gland AdCC in the Erasmus Medical Center between January 1995 and 2021 were included. Ten (40%) received local therapy (LT) and 15 (60%) additional therapy of the neck (ATN). Quality of life results were available of 15 patients, and shoulder disability scores of 12 patients. Analyses were performed between October 2021 and February 2022.

Results

Disease recurrence developed in 6 patients (24%). All patients with stage III or IV, 1 of the 11 with stage I (9%) and 1 of the 10 with stage II (10%), treated with ATN, presented with metastasis in the lungs, liver, skeletal system and/or local, 13-232 months after diagnosis of the primary tumor. The disease specific survival (DSS) over 10 years was 86-100% for all therapy groups. The quality of life was 75 ± 16.7, 69.4 ± 29.3 and 85.4 ± 10.7 for patients who received post-operative radiotherapy on the neck, a TND or LT, respectively.

Conclusion

Clinical- and survival outcomes were most favorable in patients who underwent LT for a tumor classified in T1 or T2. Larger tumors seemed to be an important prognostic factor, with a higher risk of metastasis, even after ATN. The QoL in patients who received LT or ATN is similar in patients with and without a medical oncologic history.

PO-013 | Subtotal and near-total glossectomy- Oncological and functional outcome analysis

Smriti Panda [1]; Sandipta Mitra [1]; Vimmi Gautam [1]; Suresh Mani [1]; Chirom Amit Singh [1]; Alok Thakar [1]; Kapil Sikka [1]; Rajeev Kumar [1]; Anup Singh [1]; Aman Sharma [1]; Akash Kumar [1]

(1) All India Institute of Medical Sciences, New Delhi, India

Key-words

Glossectomy, quality of life, survival

Objectives

Locally advanced tongue cancers mandate radical approaches like subtotal (STG) or near-total (NTG) glossectomy.We have undertaken this study to evaluate outcomes following extensive tongue resections from an oncological and functional standpoint.

Methods

Retrospective study was conducted at a tertiary care centre in India on consecutive cases of subtotal or near-total glossectomy from January 2020 to June 2022 for treatment-naïve locally advanced squamous cell carcinoma of the tongue.

Survival analysis and multivariate analysis was performed using Kaplan Meier method and Cox-Proportional Hazards model, respectively.

Quality of life analysis was done using FACT-HN questionnaire. Swallowing analysis was performed using the Penetration-Aspiration Scale and MD Anderson Dysphagia Inventory.

Results

We identified 41 cases (STG: 30,NTG:11) during the above time--period. At the maximum follow-up period of 25 months, overall

survival(OS) and disease-free survival (DFS)of the full cohort was 34.9% and 26.8%, respectively.

Worsening of DFS was noted with incremental increase in depth of invasion(DOI): OS- <10mm:66%, 10 to 15mm: 62% and >15mm: 30% (p-0.30), respectively. On multivariate analysis with OS as the outcome, DOI (HR:8.95), lymphovascular invasion(LVI) (HR:3.89) and pN (HR:7.94) were found to be statistically significant (p-0.05).

With DFS as the outcomes, statistically significant association was noted with DOI (HR: 4.95) and LVI (HR:4.13). The mean (± s.d.) FACT-G and FACT-HN scores were found to be 79.78 (± 17) and 95.913 (± 20) respectively. The median (range) MDADI-GS and PAS scores were 4 (1-5) and 1 (1-6) respectively. Emotional (EWB) and functional well-being (FWB) scores found to be lower in majority of patients assessed.

Conclusion

Extensive tongue resection for locally advanced carcinoma was found to have dismal outcome in terms of survival and local control. Apart from concerns related to swallowing, quality of life analysis also revealed significant deficit in the emotional and functional well-being domains.

PO-014 | A randomized trial of reduced elective neck radiation dose in head & neck cancer: acute toxicity

Hans Kaanders *[1]; Maurice Cox [1]; Patricia Doornaert [2]; Frank Hoebers [3]; Bas Kreike [4]; Marije Vergeer [5]; Ellen Zwijnenburg [1]; Tim Dijkema [1]; Sven Van Den Bosch [1]*

(1) Radboudumc, Nijmegen, The Netherlands (2) UMC Utrecht (3) Maastro Clinic (4) Radiotherapie Groep (5) Amsterdam UMC

Objective

The objective of this randomized trial was to evaluate the safety and clinical benefit of dose de-escalation of elective neck radiotherapy compared to standard elective dose prescription in patients with head and neck cancer. Here we report the acute toxicity findings from this trial.

Methods

The UPGRADE-RT trial is a multicenter, randomized controlled, phase III trial (NCT02442375). In total 300 patients treated with radiotherapy for newly diagnosed stage T2-4N0-2M0 squamous cell carcinoma of the oropharynx, hypopharynx or larynx were randomized in a 2:1 ratio (intervention:control). For all patients a [18]FDG PET-CT scan in radiation treatment position was acquired. In the intervention arm patients were irradiated with a de-escalated dose to the elective neck (43 Gy). In the control arm patients received standard elective dose prescription (50 Gy).

All patients were treated with IMRT or VMAT using an accelerated fractionation schedule, 34 fractions in 5.5 weeks. The primary endpoint was 'normalcy of diet' at 1 year after treatment (clinical benefit). The secondary endpoint was the actuarial rate of recurrence in electively irradiated lymph nodes at 2 years after treatment (safety). Here we present the acute toxicity during treatment until 3 months after start. Radiation induced dermatitis,

mucositis, pharyngeal dysphagia and tube feeding were scored during radiotherapy until complete recovery, according to the common toxicity criteria version 2.0. Acute toxicity was compared between treatment groups using the chi-square test.

Results

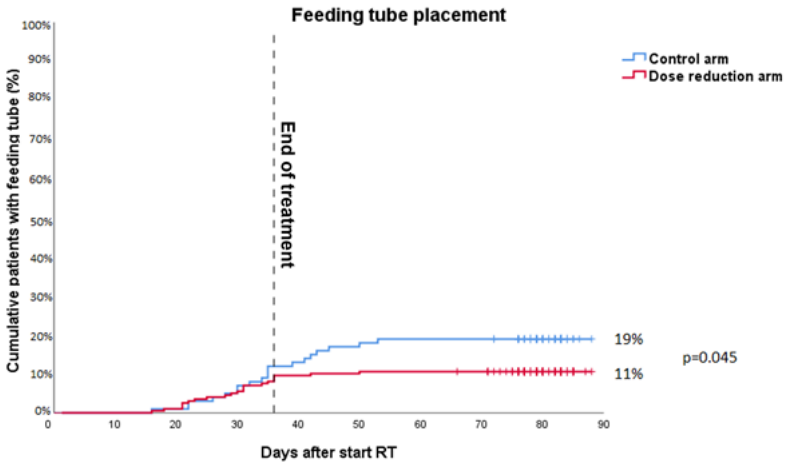
Of the 300, 295 patients were evaluable. 5 patients were excluded for reasons of patient refusal (n=2), prior oncologic surgery of the neck (n=1), concomitant chemotherapy (n=1) or total laryngectomy (n=1). The highest acute toxicity scores during treatment were not statistically significant different between treatment groups. Grade 3 to 4 acute adverse events occurred in 70% of all patients, with mucositis being most frequently reported.

The mean number of grade 3-4 adverse events per patient was similar in the control arm and the dose reduction arm (1.0 and 0.9, respectively, p=0.337). In the dose reduction arm an earlier recovery of grade ≥1 dermatitis (week 9-10; 22% vs. 50%; p=0.042), grade ≥3 mucositis (week 13-14; 0% vs. 17%; p=0.048) and grade ≥2 dysphagia (week 13-14; 11% vs. 35%; p=0.053) was observed. Tube feeding was required in 11% vs. 19% of patients in the dose reduction arm and control arm, respectively (p=0.045; Figure).

The median duration of tube feeding was 36 days (interquartile range (IQR): 23-55) in the dose reduction arm and 34 days (IQR 22-39) in the control arm (p=0.307).

Conclusion

In patients with head and neck cancer de-escalation of the radiation dose to the electively treated neck resulted in a significantly lower rate of patients requiring tube feeding and shorter duration of mucositis and dysphagia.


Feeding tube placement
Cumulative patients with feeding tube (%)
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
End of treatment
Control arm
Dose reduction arm
19%
11%
p=0.045
0
10
20
30
40
50
60
70
80
90
Days after start RT

PO-018 | A site-based study on clinicopathological factors and their influence on recurrence in oral cancers

Jeyashanth Riju j [1]; Amit Jiwan Tirkey [1]; Malavika Babu [2]; Mansi Agarwal [1]; Konduru Vidya [1]; Reshma Kurian [1]

(1) Christian Medical College, Vellore (2) Cardiff university

Keywords

Oral cancer, Tongue cancer, Gingival Neoplasms

Purpose/Objective

Tongue and buccal mucosa being the two major subsites involved by oral squammous cell cancinoma, has varying clinicopathological presentation. Since lifestyles are evolving and staging and management practices are changing, study comparing these anatomically close needs to be updated to better understand the anatomically close subsites. This study is indented to know the current difference in clinicopathological behaviour of these two subsites.

Methodology

This retrospective study included 474 patients which included 232 patients with tongue cancer and 242 patients with buccal alveolar complex cancer. Comparison between the pathological characters including pattern of nodal involvement was studied. Disease free survival(DFS) and factors influencing the DFS were analysed and compared using cox regression analysis.

Result

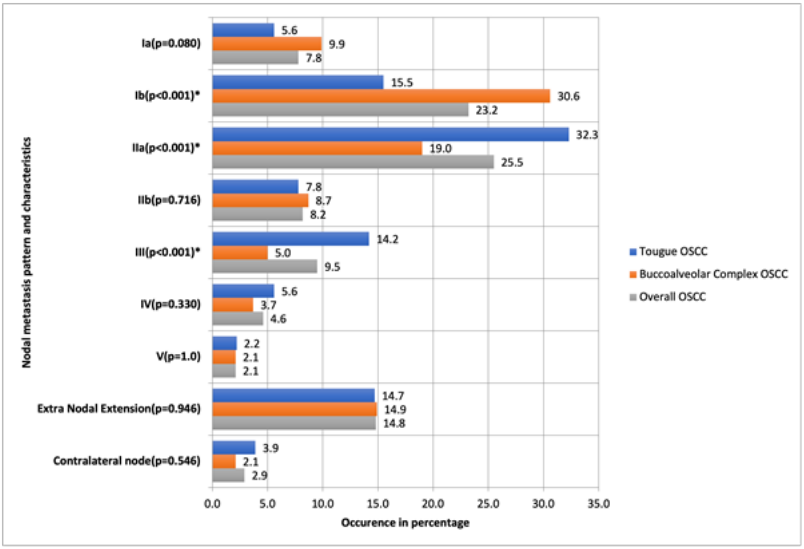
The mean age of the study population was 52.7 years. Female patients accounted for approximately one third of those involved. In the comparison of various substance abuse, among subsites, it was noted that 84% of buccal cancer patients used smokeless

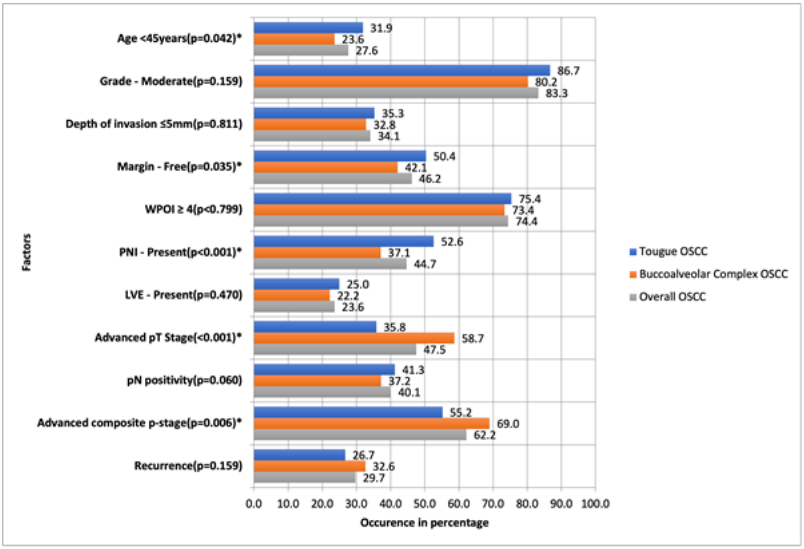
tobacco ($P < 0.001$). On the contrary, 35.8% of patients who developed tongue cancer ($P < 0.001$), did not have any habits. Though significant number of patients in buccal cancer group(58.7%) presented with an advanced tumour stage(p<0.001), involvement of neck nodes was higher(43.1%) in tongue cancer group (p=0.06). Ultimately 69% of buccal cancer and 55.2% of tongue cancers belonged to an advanced composite stage disease(p=0.006).

Tongue cancer differed significantly from buccal cancer in terms of age of presentation, staging and perineural invasion. Among neck nodal involvement tongue cancer commonly involved level IIa(p<0.001) were as buccal cancer involved level Ib(p<0.001). At a median follow-up of 27 months, 141 patient had disease recurrence, tongue cancer commonly recured in neck(p=0.008) and buccal cancer relapsed in primary site(p=0.001). Older patient with BAC cancer had a 70% less risk of recurrence(95%CI, 0.2-0.5; P < 0.0001). Pathological tumor stage in tongue cancer(HR, 14.9; 95%CI, 2.6-84.8; p=0.002) and grade of tumor differentiation in buccal cancer (HR, 9.2; 95%CI, 1.9-43.3; P < 0.005) were the most significant independent factors that influenced tumor recurrence. The overall survival between groups did not vary significantly(p=0.052).

Conclusion

Similar to tumor stage in tongue cancer, nodal stage in buccal cancer acts an independent predictor of DFS. Age plays an important role in recurrence among buccal cancer. The presentation of disease, histologic pattern, pattern of nodal involvement, pattern of relapse and factors influencing relapse are different between the two close anatomical sites implying importance of site based approach in conducting research. Need for adjuvant chemotherapy along with radiotherapy in patient with buccal cancer with node positive neck below level of cricoid cartilage need further exploration.


Nodal metastasis pattern and characteristics
Ia(p=0.080)
5.6
9.9
7.8
Ib(p<0.001)*
15.5
30.6
23.2
IIa(p<0.001)*
32.3
19.0
25.5
IIb(p=0.716)
7.8
8.7
8.2
III(p<0.001)*
14.2
5.0
9.5
IV(p=0.330)
5.6
3.7
4.6
V(p=1.0)
2.2
2.1
2.1
Extra Nodal Extension(p=0.946)
14.7
14.9
14.8
Contralateral node(p=0.546)
3.9
2.1
2.9
0.0 5.0 10.0 15.0 20.0 25.0 30.0 35.0
Occurence in percentage
Tougue OSCC
Buccoalveolar Complex OSCC
Overall OSCC


Factors
Age <45years(p=0.042)*
31.9
23.6
27.6
Grade - Moderate(p=0.159)
86.7
80.2
83.3
Depth of invasion ≤5mm(p=0.811)
35.3
32.8
34.1
Margin - Free(p=0.035)*
50.4
42.1
46.2
WPOI ≥ 4(p<0.799)
75.4
73.4
74.4
PNI - Present(p<0.001)*
52.6
37.1
44.7
LVE - Present(p=0.470)
25.0
22.2
23.6
Advanced pT Stage(<0.001)*
35.8
58.7
47.5
pN positivity(p=0.060)
41.3
37.2
40.1
Advanced composite p-stage(p=0.006)*
55.2
69.0
62.2
Recurrence(p=0.159)
26.7
32.6
29.7
0.0 10.0 20.0 30.0 40.0 50.0 60.0 70.0 80.0 90.0 100.0
Occurence in percentage
Tougue OSCC
Buccoalveolar Complex OSCC
Overall OSCC

PO-019 | Salivary gland tumors- an audit from a tertiary care center in Northern India

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(1) Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

Objective

Salivary gland tumors are uncommon with varied clinical behavior. A single institution audit was carried out to study the natural history, pathology, diagnostic workup and existing management strategies with the aim of optimizing the treatment for improving outcomes.

Materials and methods

Salivary gland tumors as detected on radiology/cytology were included in this audit. Following initial work up, these patients were treated by surgery +/- adjuvant treatment. Demography, treatment intervention and survival outcomes were studied. The analysis was carried out in September 2022 using SPSS 23 software version.

Results

170 (benign 81, (48%) (parotid 76; submandibular gland 5) and malignant 89(52%),(parotid gland - 82, minor salivary gland - 2, s/m gland 5). Malignant gland tumors were treated between Jan 2006 to September 2020, in the departments of Radiotherapy and/or Neuro-otology, SGPGI, Lucknow, India. Median age of presentation was 47 years (47-62y); males predominated (67%); average KPS was 80 and T stage for malignant tumours was (T1-03%, T2-26%, T3-49%, T4-22%) N stage (N0-47%, N1-30%, N2-15%, N3a-1%). 17% patients had features of facial palsy (at baseline 65% and 35% developed due to surgery). 78 Patients underwent surgery of which 52 underwent neck dissection also. Surgical procedures were - superficial parotidectomy- 29 (33%),

total parotidectomy – 35(39%) , excision -07 (08%), radical parotidectomy - 5 (06%), extended radical parotidectomy- 2 (3%). Amongst the histological types seen - mucoepidermoid carcinoma 44 (49%), Adenoid cystic carcinoma 15 (17%), Acinic cell carcinoma 06 (07%), Adenocarcinoma 4 (05%), myoepithelial carcinoma 04 (5%) ,salivary duct carcinoma 04(05%),carcinoma ex-pleomorphic 03(04%), squamous cell carcinoma 02(03%), high grade epithelial malignancy 02 (03%), poorly differentiated carcinoma 01(01%), undifferentiated carcinoma 01(01%),lymphangioma01(01%),mixed malignant tumours 01 (01%),mesenchymal malignant tumours 01 (01%).Amongst the adverse histological features seen – +ve margins 22(25%), LN +ve 32 (36%) Lympho-vascular invasion (LVI) – 16 (18%), extracapsular spread (ECS)-10 (36%), perineural invasion (PNI) - 26 (29%%) cases. Post op RT was given in 52 patients with high risk factors. A post op dose of 60Gy/30# was delivered using 3DCRT/IMRT technique. IMRT technique was preferred in unresectable disease addressed radically and equivalent of 66Gy/30# was delivered. Palliative RT was given to extensive disease patient and the dose was 20Gy/5#. Median follow up of the audit was 44 months. 2yrs OS and DFS for malignant tumors was 85% &84%resp. The presence of factors like margins positivity (p= <0.001 & <0.001), LN positivity (p=<0.001 & <0.001), ECS (p= <0.001 & <0.001), PNI (p=0.004 & 0.007), LVI (p=<0.001 & <0.001) were the significant predictors of DFS and OS on univariate analysis respectively. LVI and ECS emerged as independent prognostic factors for DFS and OS.

Conclusions

Most of the malignant salivary gland tumours arose in parotid gland. Minor salivary gland tumors were grossly under-represented in this audit. There was no uniform policy regarding surgical practice. Radiotherapy practice was relatively streamlined. Features - LN positive, margin positive, LVI, PNI and ECE influenced the DFS and OS adversely.

PO-021 | Intra and postoperative complications in salvage neck dissections: a retrospective study

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(1) University of Verona (2) University of Firenze (3) University of Modena (4) University of Bologna

Keywords

Surgical complications; isolated neck recurrence; salvage neck dissection.

Background and objectives

The current evidence regarding complications after salvage neck dissection (ND) for isolated regional recurrences (IRRs) in head and neck cancers is poor. The aim of this study is to evaluate the incidence and differences in complication rates of salvage ND after primary surgery, radiotherapy, chemoradiotherapy, or combined treatments.

Methods

This was a multicentric retrospective study on 64 patients who underwent salvage ND for IRR in three Italian institutes between 2008 and May 2020.

Results

Complications were detected in 7 of the 34 patients (20.8%) and surgeons described difficult dissection in 20 patients (58.82%). Accidental vascular ligations or nervous injury during surgery were never detected. None of the variables analyzed were statistically significant in predicting the risk of complications, disease-free survival, or overall survival.

Conclusions

IRR represents a rare entity among total relapses. The incidence of complications after salvage ND for IRR is higher than after primary surgery but at an acceptable rate in experienced hands. However, an adequate balance between functional and oncological outcomes is mandatory.

PO-023 | RADIATION-INDUCED MUCOSITIS IS PROGNOSTIC FACTOR OF SURVIVAL FOR HNC PATIENTS

Dorota Ksiezniak-Baran [(1)]; Pawel Polanowski [(1)]; Jolanta Mrochem-Kwarciak [(1)]; Andrzej Wygoda [(1)]; Boleslaw Pilecki [(1)]; Urszula Dworzecka [(1)]; Kinga Debiec [(1)]; Marek Kentnowski [(1)]; Katarzyna Drosik-Rutowicz [(1)]; Natalia Amrogowicz [(1)]; Alexander Cortez [(1)]; Marcela Krzempek [(1)]; Krzysztof Skladowski [(1)]

(1) National Research Institute of Oncology in Gliwice

Purpose/Objective

HN08 PT was the prospective and randomised clinical trial conducted between 2008 and 2015 in the National Research Institute of Oncology in Gliwice, Poland. The purpose of this intended on--inferiority study was to compare accelerated RT alone (ARA) and concurrent chemo-radiotherapy (CCR) for moderate advanced (T2-T4aN0-N2) head and neck squamous-cell cancer patients.

Material/Methods

The group of 101 patients (77 males, 24 females) were enrolled into the study. The mean and the median age was 59 (range: 37-80 years). The primary tumours were localised in oropharynx (47%), larynx (38%) and hypopharynx (15%). In ARA (54 patients) RT was administered 7 times per week as a concomitant boost on Tuesdays and Fridays or continuous weekends-on fractionation (total dose: 66.6-72Gy) over 36-40 days. In CCR (47 patients) conventional fractionation RT (total dose: 66-70Gy) over 45-49 days was delivered simultaneously with maximum 3 courses of cisplatin (100mg/m2). The severity of radiation-induced mucositis was assessed every treatment week with the use of CTCAE scale (version IV).

Results

The median follow-up is 48 months (range: 2-120 months). Comparing CCR to ARA 15% better 5-year OS (51% vs 36%) and 20 mths lon-

ger median OS (p=0.089) was shown. Grade III radiation-induced mucositis was observed in 31 (58%) cases in ARA and in 34 (72%) in CCR, grade II in 13 (28%) and 18 (33%) patients, respectively. In the CCR patients with grade III mucositis 5-year OS was 62%, with grade II - 23% (p=0.021). Corresponded rates in ARA were 37% and 39%, respectively (p=0,37). Multivariate analysis of the risk of death was shown 54% decrease for radiation-induced grade III mucositis in CCR compare to ARA (p=0.004). Statistically significant correlation between the severity of the acute radiation mucosal reaction and the occurrence of HNC distant metastases (p=0.003) and local and/or regional recurrence (p=0.04) was confirmed. The higher the severity of the acute mucositis, the lower the probability of metastasis and loco-regional recurrence of cancer had occurred. For skin toxicity univariate analysis showed significant difference in 5-year OS also in favour of CCR patients (65% vs 25%).

Conclusion

In HNC patients treated by definitive concurrent chemo-radiation the severity of radiation-induced acute mucositis has determined survival prognosis – those who exhibit its higher grade have lower risk of any HNC relapse and, consequently, longer live. This prognosticator is absent in patients treated by radiation therapy alone. It can be speculated that healthy pharynx and larynx mucosa over concurrent chemo-radiation therapy exhibits an individual sensitivity of cisplatin-enhancing radiation damage what reflects an amount of squamous cell cancer cytotoxic effects.

PO-024 | Definitive Radiotherapy outcomes for Oral Cavity cancers

Dr. Najah Mohamed Nizam [(1)]; *Dr. Lauren Sidon* [(1)]; *Dr. Yatman Tsang* [(1)]; *Dr. Ashitha Ashraf* [(1)]; *Dr. Shagun Juneja* [(1)]; *Dr. Catherine Lemon* [(1)]; *Dr. Kevin Chiu* [(1)]

(1) Mount Vernon Cancer Centre, Northwood, London

Keywords

Head and neck , radical radiotherapy, chemotherapy, oral cavity , IMRT

Title

Real-world outcome of Oral Cavity cancer patients receiving definitive (chemo)radiotherapy without surgery

Purpose/Objective

To determine the outcome of oral cavity squamous cell cancer (OSCC) patients referred by peripheral surgical units to a tertiary oncology centre for definitive (chemo) intensity-modulated radiation therapy (IMRT), with or without concurrent chemotherapy.

Methods

OSCC patients treated radically with IMRT between January 2018 – December 2021 were reviewed in a prospectively collected database. Patients were staged using the 8thedition clinical (c)TNM classification. The standard definitive dose was 65Gy in 30 fractions over 6 weeks. Locoregionally advanced OSCC patients were considered for 2 cycles of concurrent cisplatin except for those were unfit, over age of 70, or declined chemotherapy. A 3-month post IMRT positron emission tomography (PET-CT) was done to assess treatment response as standard. The 2-year local (LC), regional (RC), distant control (DC) and overall survival (OS) were analysed.

Results

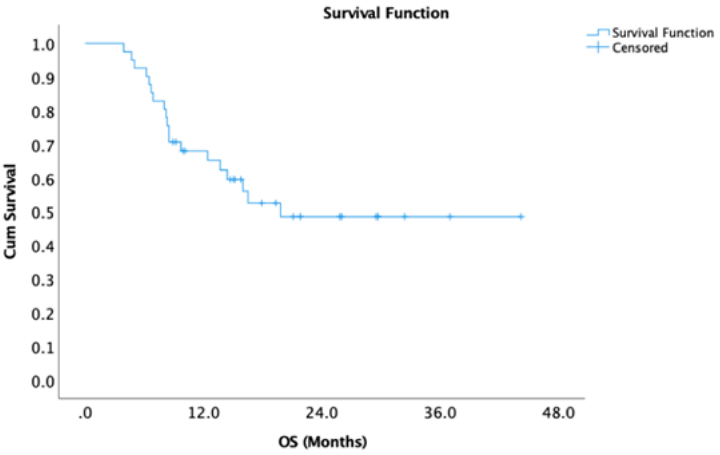
There were a total of 178 patients treated radically during the study period. Forty- one patients (23%) received non-surgical management in the form of definitive IMRT due to: attempt for preservation of oral function in view of the required extensive surgery (n=22, 53%), inadequate medical fitness for operability (n=10, 24%), patient declined surgery (n=3, 7%), delay in surgery due to COVID 19 in stages I & II patients (n=3, 7%), and previous oral cavity surgery (n=3, 7%).

Median time from histological diagnosis to the start of IMRT was 7.6 weeks (range 3.7–15.9). The median age was 65 (range 41–88). Thirty-one (76%) patients had performance status (PS) of 0-1 while 10 patients (24%) were PS2. Thirty-eight patients (93%) had locoregionally advanced disease: 6 Stage III (15%), 18 Stage IVa (44%) and 14 Stage IVb (34%). Of these patients, 32 (78%) had cT3-4 disease, and 24 (59%) had cN2-3 disease at presentation. The oral cavity subtypes included were 23 oral-tongue (56%), 7 buccal mucosa (17%), 7 floor of mouth (17%), and 4 retromolar trigone (10%). Fifteen patients (37%) received concurrent chemotherapy.

At the time of analysis, the 2-year LC, RC, DC and OS was 63%, 74%, 89% and 49% respectively. Patients with Stage IVb had lower LC, RC and OS of 46%, 59% and 31% respectively. Residual disease was detected before or at post IMRT PET-CT for 8 out of 14 (57%) primaries, and in 3 out of 9 (33%) nodal recurrences. No patients underwent salvage surgery on locoregional relapse. Only 5 patients from the 16 recurrent cases (31%) received palliative systemic treatment.

Conclusions

The departmental definitive IMRT regimen did not demonstrate satisfactory loco-regional control. Patient selection, careful disease assessment and treatment delivery are essential if definitive IMRT is considered as the radical approach in OSCC.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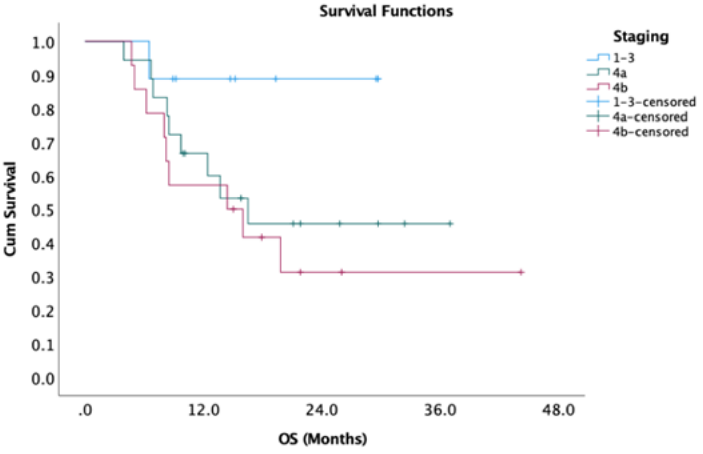
OS (Months)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OS (Months)

PO-026 | Stromal fibroblasts influence cell stiffness and metabolism of head and neck cancer cells

David Kalfert *[1]; Barbora Peltanova [2]; Hana Holcova Polanska [3]; Martina Raudenska [3]; Jan Balvan [3]; Jiri Navratil [4]; Tomas Vicar [5]; Jaromir Gumulec [4]; Martin Krater [6]; Jochen Guck [6]; Marek Grega [7]; Jan Plzak [1]; Michal Masarik [3]*

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Keywords

Head and neck squamous cell carcinomas, cancer-associated fibroblasts, biomechanical reprogramming of cancer cells

Purpose/Objective

Head and neck squamous cell carcinomas (HNSCC) are severe and highly complex malignant diseases showing a high level of variance in therapeutic response. It has been proven that cells within the tumour stroma such as cancer-associated fibroblasts (CAFs) can modulate the behaviour of tumour cells. The late stages of carcinomas may contain about 80% of CAFs. CAFs display a large heterogeneity regarding their tumour-promoting or tumour-inhibiting properties. Apart from metabolic symbiosis, CAFs are known to support cancer cell migration, invasiveness, and metastasis formation. Cell mechanic phenotypes largely impact the cell's ability to migrate and invade due to changes in the

cytoskeleton. Accordingly, the epithelial-mesenchymal transition (EMT) is accompanied by significant changes in cell stiffness. In this study, we investigated how CAFs derived from tumour tissues of different mRNA subtypes influence the metabolic, and biomechanical reprogramming of cancer cells.

Material/Methods

Tumour samples were taken from verified HNSCC; the inclusion criteria were histological confirmation and no previous oncologic treatment; each tissue specimen underwent pathology quality control.

The mRNA subtypes of tumour tissues were determined according to Lawrence et al. The basal phenotype (BA) was classified by high *TP63* and *EGFR* and low *SOX2* expression. The mesenchymal phenotype (ME) by high *VIM*, *DES*, and low *TP63* expression, the classical phenotype (CL) by high expression of *SOX2*, *NFE2L2*, and positive smoking history, and the atypical phenotype (AT) was characterised by high *SOX2* expression and p16 positivity. CAF cell lines were subsequently prepared. Conditioned media (CM) were collected from 90% confluent CAFs after 24h cultivation. As a model of cancer cells, FaDu cell line derived from hypopharyngeal carcinoma was used. Atomic force microscopy and Real-time deformability cytometry were used for the determination of cell stiffness. Young's modulus was calculated. To examine the effect of CMs derived from CAFs on cellular metabolism Real-time cell metabolic analysis (Seahorse) was performed.

Results

The coculture of FaDu cells with the BA or CL subtype of CAFs led to an increase in the stiffness of FaDu cells. The value of cell stiffness was negatively associated with mitochondrial ATP production and *MCT1* expression in FaDu cells. CAFs from ME tumours cause the most pronounced decrease in cancer cell stiffness, accompanied by minimal changes in the lactate shuttle. CAFs from

CL tumours cause the most pronounced stiffening accompanied by the highest decrease in *MCT1* expression.

Conclusion

Based on our coculture experiments, it was shown that CAFs derived from different mRNA subtypes of HNSCC tumour tissue differently modulate the mechanical properties of HNSCC cells. The resulting cancer cell stiffness was in a negative correlation with *MCT1* expression and ATP production from OXPHOS.

PO-027 | Flexible laryngoscopy is influenced by experience: HD--Narrow Band Imaging versus fiberoptics

c. Scholman [1]; Manon a. Zwakenberg [1]; Gyorgy b. Halmos [1]; Jan Wedman [1]; Jan e. Wachters [1]; Bernard F.A.M. Van Der Laan [1]; Boudewijn E.C. Plaat [1]

(1) University Medical Centre Groningen

Key Words

Videolaryngoscopy, Squamous cell carcinoma, Interobserver and Intraobserver reliability

Objectives

High Definition Laryngoscopy using Narrow Band Imaging (HDL-NBI) is superior in the visualization of pharyngeal and laryngeal lesions compared to fiberoptic laryngoscopy (FOL). The primary aim was to compare inter- and intraobserver reliability of HDL-NBI with FOL for characterizing pharyngeal and laryngeal lesions. The secondary aim was to evaluate the influence of clinical experience on precision, diagnostic sensitivity, and specificity.

Material and methods

Retrospective paired analysis in a tertiary referral hospital, assessing endoscopic videos by 12 observers with a different level of clinical experience in ENT. Observers were divided into beginners, trained observers and experts with more than 12 years of experience. Thirty HDL-NBI and FOL videos, with additional clinical information, were judged twice with an interval of 2-4 weeks in a random order. Inter- and intraobserver reliability, sensitivity and specificity for both endoscopes were calculated to detect a malignant lesion and a specific histological entity of the pharynx and larynx for beginners, trained observers and experts.

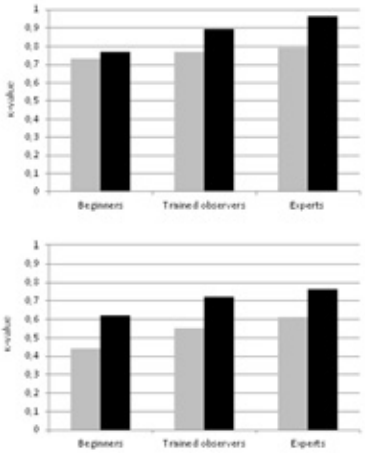
Results

By using HDL-NBI instead of FOL, interobserver reliability increased from moderate to substantial in trained observers and experts for detecting malignant lesions (HDL-NBI κ=0.66 and κ=0.77 vs FOL κ=0.51 and κ =0.56, trained observers and experts). The sensitivity of HDL-NBI was superior to FOL for recognizing a specific histological entity in all groups of observers.

Conclusion

The interobserver reliability increased with the level of clinical experience, especially when using HDL-NBI. The use of HDL-NBI results in a 16% more accurate detection and a more precise diagnosis of pharyngeal and laryngeal lesions compared to the still widely used FOL.

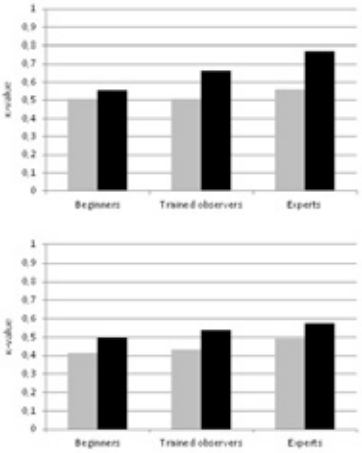
Figure 2: Sensitivity for detecting a malignant lesion and a specific histological entity for HDL-NBI (black) and FOL (grey)



Upper bar graphs: sensitivity for detecting a malignant lesion;

Lower bar graphs: sensitivity for detecting a specific histological entity

Figure 1: Interobserver reliability for detecting a malignant lesion and a specific histological entity for HDL-NBI (black) and FOL (grey)



Upper bar graphs: interobserver reliability for detecting a malignant lesion;

Lower bar graphs: interobserver reliability for detecting a specific histological entity

PO-029 | The Role of Adjuvant Radiotherapy After Salvage Laryngectomy in Laryngeal Cancer

Pantea Bayatfard [1]; Melek Tugce Yilmaz [1]; Sezin Yuce Sari [1]; Mustafa Cengiz [1]; Gokhan Ozyigit [1]; Ibrahim Gullu [1]; Sercan Aksoy [1]; Nilda Suslu [1]; Oguz Kuscu [1]; Gozde Yazici [1]

(1) Hacettepe University

Purpose

The role of second-course RT in cases with a high risk of local--regional recurrence after salvage surgery is controversial. This study aimed to determine the patient group and risk factors in which adjuvant RT is effective in patients with laryngeal cancer who underwent salvage surgery due to local-regional recurrence after radiotherapy.

Material and Method

Thirty patients who underwent curative RT±CT in our clinic for laryngeal carcinoma between 2008 and 2020 and who developed recurrence are retrospectively evaluated. One of the patients was female (3.1%) and 29 of them were male (96.7%). The median age at diagnosis is 60.5 years old (IQR: 42-78). Patients underwent total laryngectomy±lymph node dissection after local-regional recurrence. Adjuvant RT was administered to 16 patients, 10 of these patients received concomitant cisplatin (31.3%). Kaplan-Meier method was used for survival analysis and the $p<0.05$ value was considered significant.

Results

The median follow-up period after surgery due to recurrence is 26 months (IQR: 8-149). The 2- and 5- year overall survival rates (OS) were 83% and 45%, and locoregional recurrence-free survival rates (LRFS) were 64% and 50%, respectively. The characteristics of

patients stratified according to adjuvant RT are presented in Table 1. The 2- and 5-year OS of 16 patients who received RT were 76% and 49% and for the 14 patients who did not receive RT were 91% and 38%, respectively. Likewise, for patients receiving adjuvant RT vs. no adjuvant RT, the 2 and 5-year LRFS are 63% vs. 66% and 54% vs. 44%. In patients with T4 disease at recurrence, which is one of the poorest prognostic factors, the 2 and 5-year LRFS for the patients who received RT vs. no RT are evaluated as 77% vs. 66% and 61% vs. 33%. There are 9 patients with PNI in addition to the T4 stage, and 7 of these patients received RT. A comparison could not be made due to the high rate of adjuvant RT for patients with high N stage, extralaryngeal muscle invasion, extranodal extension, LVI, large tumor size, close/positive surgical margin and high tumor grade, which are known to be poor prognostic besides T stage. At follow-up, 5 of the patients developed stoma recurrence and 4 of them were in the no adjuvant RT group. Again, 1 had PNI, 1 had positive surgical margins, and 4 had a T4 tumor. The 1 patient who did not receive RT died of disease. Adjuvant RT is an important factor in survival, especially in T4 tumor recurrences, without the presence of additional poor prognostic factors.

Conclusion

In this study, patients who had salvage laryngectomy due to relapse after organ-sparing treatment were examined, and better local and regional control was achieved in the patients who underwent adjuvant RT, despite the high number of poor prognostic factors. Considering the patient characteristics, adjuvant RT is recommended especially in T4 tumors. PNI and surgical margin status are also important factors for the indication of adjuvant RT.

Table 1: Patient characteristics stratified according to adjuvant RT

	Adjuvant RT (%) (n=16)	No adjuvant RT (%) (n=14)
Tumor Differentiation		
Poor	7 (%43,8)	3 (%21,4)
Moderately	5 (%31,2)	5 (%35,7)
Well	2 (%12,5)	2 (%14,3)
Unknown	2 (%12,5)	4 (%28,6)
Median Tumor Size (IQR)	3 cm (IQR 2-5,7)	2,8 cm (IQR 1-4,2)
Presence of Lenfovascular invasion (LVI)	3 (%18,8)	2 (%14,3)
Presence of Perineural invasion (PNI)	8 (%50)	4 (%28,6)
Surgical Margin		
Positive	3(%18,8)	-
Near	3(%18,8)	1 (%7,1)
Negative	10(%43,8)	-
T classification		
T0	1(%6,3)	-
T1	-	2 (%14,3)
T2	-	-
T3	4(%25)	6 (%42,9)
T4a	11(%68,8)	6 (%42,9)
Nodal status		
Positive	6(%33,5)	1 (%7,1)
Negative	10(%62,5)	13 (%92,9)
Presence of Lymph node extranodal extension	4(%25)	-
Stage after laryngectomy		
Stage 1	-	2 (%14,3)
Stage 2	-	-
Stage 3	3(%18,8)	5 (%35,7)
Stage 4a	11(%68,8)	6 (%42,9)
Stage 4b	2(%%12,5)	1 (%7,1)

PO-030 | Treatment time has impact on outcome in patients with SCC of the floor of mouth and the oral tongue

Amrogowicz Natalia [1]; Rutkowski Tomasz [2]; Mucha-Malecka Anna [3]; Wygoda Andrzej [1]; Kentnowski Marek [1]; Ksiezniak-Baran Dorota [1]; Polanowski Pawel [1]; Bielen Agata [1]; Skladowski Krzysztof [1]

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Keywords

Oral cavity cancer, combined treatment, treatment time factors

Purpose/Objective

The aim of the study is to analyze the effectiveness of adjuvant radiotherapy (RT) or radio-chemotherapy (RCHT) in patients with squamous cell carcinoma (SCC) of the floor of mouth (FMC) or the oral tongue (OTC) treated surgically with adjuvant treatment and to identify prognostic factors influencing the effectiveness of this treatment.

Material/methods

Between 2002 and 2018 in the National Research Institute of Oncology in Gliwice (Poland) 366 patients with SCC of FMC (52%) and OTC (48%) were treated surgically with adjuvant RT alone (73%) or combined with chemotherapy (27%). Median age of the patients was 57 years (range 29-88) and majority of patients (83%) had smoked. Distribution of pathological stage of disease was as follows: pI - 2%, pII - 10%, pIII - 31% and pIV - 47%. Neck lymph nodes were involved by cancer (pN+) in 52% of patients and between them 47% had extracapsular cancer extension (pECE+). Probabilities of overall survival (OS), local control (LC), nodal control (NC)

were estimated by Kaplan-Meier method and were compared by log-rank test. Multivariate analysis was used to evaluate the impact of clinical and treatment parameters on treatment outcomes.

Results

All study endpoints have shown similar results for both cancer sites, therefore for the purpose of further analyses all cases were aggregated. The 5-year OS, LC and NC rates were: 57%, 81% and 87%, respectively. Radiotherapy treatment time (RTT) stretched from 24 to 105 days and for the patients with RTT <=45 days 5-year OS was 70% while for RTT >45 days – 50% (p=0,00001). Overall treatment time (OTT) estimated from the operation to the end of RT stretched from 76 to 203 days and when it was <=122 days 5-year OS was 67% vs 48% for OTT >122 days (p=0,0007). The 5-year OS was significantly higher for patients up to 57 years (68% vs 48%, p=0.001) and for non-smokers (62% vs 55%, p=0.02). According to pathological staging 5-year OS was 72% for stages pI-II, 60% for stage pIII and 47% for stage pIV. Within group of patients with lymph nodes involved higher 5-year OS was found for subgroup with absence of pECE+ (62% vs 40%, p=0.0001). The multivariate analysis showed that the OTT >122 days and RTT >45 days were the most independent prognostic factors of shorter OS.

Conclusion

That retrospective study is based on the experiences of oral cavity cancer combined treatment realized in one institution over the past 17 years. It is clear that such a long time has allowed many diagnostic and treatment approaches tried to achieve the best solutions. However, our results confirm that time duration of whole surgical and radio-oncological treatment always plays a crucial role for the outcome. Extending duration of combined treatment negatively affects overall survival.

PO-031 | Prognostic Value of Inflammatory Markers in Patients with HNC.

dr Jolanta Mrochem-Kwarciak Phd[(1)]; *Aleksandra Chmura, Phd*[(1)]; *Andrzej Wygoda, md Phd*[(1)]; *Dorota Ksiezniak-Baran, MD, Phd*[(1)]; *Tomasz Rutkowski, MD, Phd*[(1)]; *Joanna Huszno*[(1)]; *Prof Krzysztof Skladowski, MD, Phd*[(1)]

(1) National Research Institute of Oncology in Gliwice

Keywords

HNC, NLR, CRP, osteopontin

Purpose/Objective(s)

Inflammation is generally accompanied cancer disease. Evaluation of the inflammatory biomarkers in the treatment of head and neck cancer (HNC) patients is of potential prognostic value. The aim of present study was to assess the prognostic value of indicators calculated on the basis of initial hematology parameters: neutrophil–to-lymphocyte ratio (NLR), lymphocyte–to-monocyte ratio (LMR), platelet–to-lymphocyte ratio (PLR), leukocyte count (WBC), C-reactive protein (CRP) and osteopontin (OPN) in patients with HNC after radiotherapy alone or combined with chemotherapy.

Materials/Methods

Between 01/2009 and 06/2019 423 patients with squamous cell carcinoma of nasopharynx (8%), oropharynx (33%), hypopharynx (10%), larynx (44%) or oral cavity (5%) were treated with curative intent by RT alone or in combination with platinum chemotherapy. There were 52% patients with T1/2 and 48% with T3/4 of primary tumor stage and 43% and 57% of patients with N0 and N+ nodal stage disease, respectively. Complete blood counts (CBC), CRP and OPN were estimated in blood or serum before and after the treatment.

Results

Median follow-up was 40 months. Second primary tumor or distant metastasis were observed in 6% of patients. Patients had significantly longer overall survival (OS) when initial counts of WBC was <6,89 (p=0,0002), NLR was <2,01 (p=0,03), CRP was <2,87 mg/dl (p=0,0001) and OPN (<48,1 mg/l) (p=0,0001) were low before treatment. Additionally, significantly longer OS was found for patients with low value of NLR (<5,38), CRP (<2,87 mg/dl) or OPN (<81,73 mg/l) were low after therapy (p=0,03, p=0,02, p=0,005), respectively. No correlation was observed between LMR or PLR and OS.

Conclusion

The present results revealed that an elevated pre- and posttreatment NLR and high initial levels of WBC, CRP and OPN are associated with poor OS in patients with head and neck cancer. Low levels of inflammatory indicators like CRP and OPN after therapy may be associated with longer OS in this group of patients.

PO-032 | Real-world data on nivolumab for recurrent or metastatic squamous-cell carcinoma of head and neck

Jorge r. Rodrigues [(1)]; *Marta Almeida* [(1)]; *Diana Freitas* [(1)]; *Júlia Amorim* [(1)]; *Filipa Pereira* [(1)]; *Joana Cunha* [(1)]; *Catarina Portela* [(1)]; *Rui Nabiço* [(1)]

(1) HOSPITAL DE BRAGA

Keywords

Nivolumab, real-world evidence.

Background

In patients with recurrent, unresectable, or metastatic squamous-cell carcinoma of the head and neck, whose disease progressed within six months after platinum-based chemotherapy, and who have not undergone immunotherapy, treatment with nivolumab resulted in overall survival (OS) improvement in the CheckMate141 clinical trial.

Objective

To access real-world data on progression-free survival (PFS) and OS in patients with squamous-cell carcinoma of the head and neck treated with nivolumab.

Methods

In this retrospective observational, longitudinal single centre study, patients with recurrent, unresectable, or metastatic squamous-cell carcinoma of the head and neck undergoing nivolumab treatment during January 2017 to December 2021 where included. PFS and OS were estimated by means of the nonparametric Kaplan–Meier method. Log-rank test was applied to compare PFS and OS in subgroup analysis. Hazzard ratios (HR) and 95% confidence intervals (CI) were estimated with the stratified Cox proportional-hazard model.

Results

Whitin the study period, 37 patients began nivolumab. The mean age was 57.4 (SD 5.6) years-old; 97.3% patients were male, and 89.2% (n=33) had an ECOG-PS of 1. Twenty seven percent of the patients (n=10) had metastatic disease at diagnosis and 24% (n=9) had at least two lines of previous systemic treatment (59.5%, n=22, with cetuximab). Median PFS with nivolumab was 2.8 months (95% CI 2.1 to 3.5) and median OS was 5.9 months (95% CI 3.1 to 8.7). In patients previously treated with cetuximab median PFS (HR 0.904, 95% CI 0.450 to 1.815; P=0.773) and OS (HR 1.06, 95% CI 0.518 to 2.174; P=0.871) were not statistically different when compared with the ones that didn't receive it. Regarding toxicity, there were two cases of pneumonitis (grade 2 and grade 3) and one case of grade 3 enterocolitis. Three patients presented with sustained responses: one discontinued treatment after 26 months, with complete response; two remain on treatment, with stable disease and a follow-up time of 46 and 50 months.

Conclusions

In our population, median PFS was similar with that of the CheckMate141, but with an inferior median OS (5.9 versus 7.5 months). This may reflect a less selected population of patients (real-world evidence) than the one in the clinical trial.

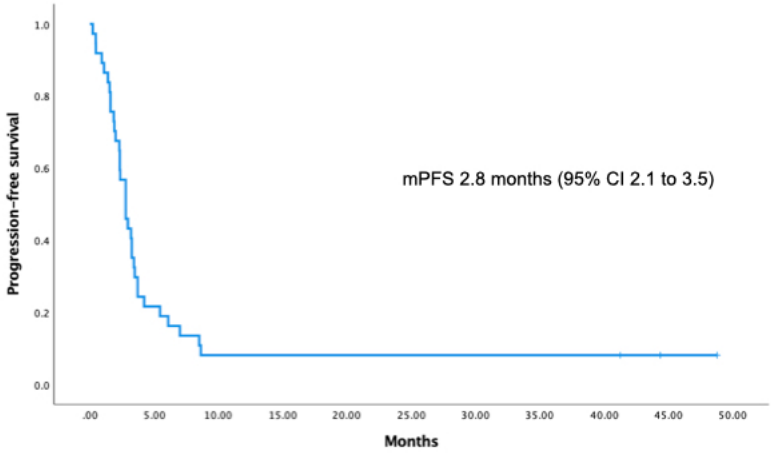


Figure 1: Progression-free survival of patients with recurrent, unresectable, or metastatic squamous-cell carcinoma of the head and neck treated with nivolumab.

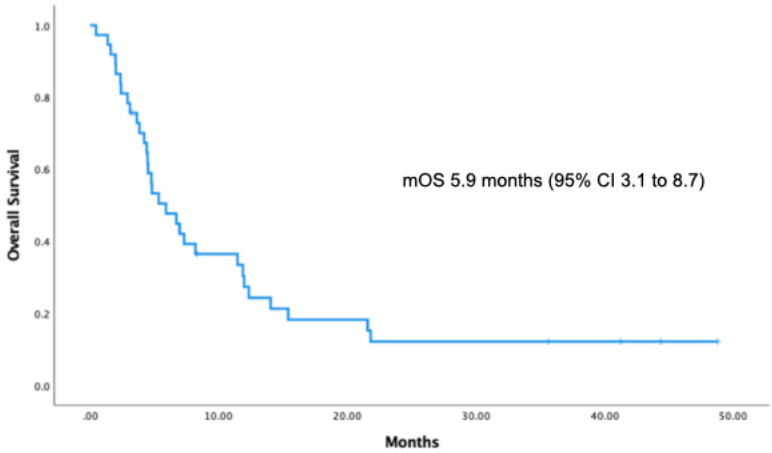


Figure 2: Overall survival of patients with recurrent, unresectable, or metastatic squamous-cell carcinoma of the head and neck treated with nivolumab.

PO-034 | The impact of HNC on informal caregivers and the interaction between caregivers and patients

Kira Van Hof [1]; Arta Hoesseini [1]; Maarten Dorr [1]; Irma Verdonck - de Leeuw [2]; Femke Jansen [2]; René Leemans [2]; Robert Takes [3]; Chris Terhaard [4]; Robert Jan Baatenburg de Jong [1]; Aniel Sewnaik [1]; Marinella Offerman [1]

(1) Erasmus MC Rotterdam (2) Netherlands Cancer Institute Amsterdam (3) Radboudumc, Nijmegen, The Netherlands (4) University Medical Center Utrecht

Objective

Evaluating the impact of head and neck cancer (HNC) on informal caregivers and how we can support them to improve quality of life and reduce psychological distress during long term follow-up.

Methods

This study used data of 234 dyads of informal caregivers and patients, participating in the ongoing multicenter prospective cohort study NET-QUBIC1. We investigated: 1) caregiver burden, 2) psychological distress and quality of life of caregivers versus patients, 3) the effect of self-efficacy and coping and 4) the supportive care needs of caregivers from time of diagnosis up to 24 months after treatment. Mixed model analyses were used to investigate the outcomes over time.

Results

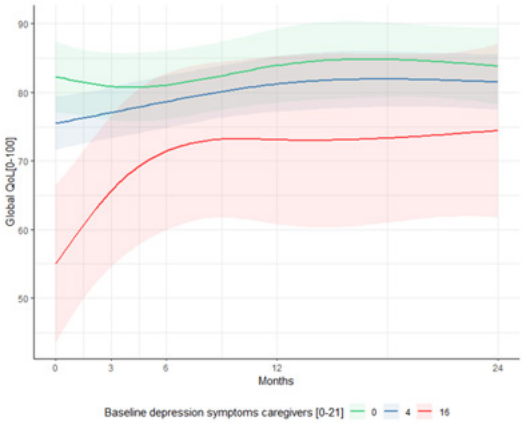
1) Caregivers reported a high level of self-esteem and at the same time a high caregiver burden, which decreased significantly during follow-up. Depression symptoms of caregivers were associated with reduced QoL of patients. 2) At baseline caregivers had higher depression symptoms than patients. 3) Passive coping and expression of negative emotions was related with higher psychological distress and reduced QoL. 4) Caregivers had high

supportive care needs, which reduced over time. However 27% of the caregivers had still unmet needs 2 years after treatment.

Conclusion

HNC has a high impact on informal caregivers. As they are the key supporters for patients, and functioning of caregivers and patients is interrelated, it is important to involve caregivers in the counseling and support that is given to patients.

Figure the interaction between functioning of informal caregivers and patients



The expected quality of life of patients when a caregiver has no depressive symptoms at baseline (green line), average depression symptoms (blue line) and high depression symptoms (red line). The models are corrected for possible confounders (age, gender, education, WHO status, comorbidity and disease stage).

PO-037 | Characterizing the spatial heterogeneity of oral squamous cell carcinoma immunohistochemically

Claudius Steffen [1]; *Simon Schallenberg* [2]; *Gabriel Dernbach* [2]; *Anastasia Dielmann* [3]; *Mihnea p. Dragomir* [2]; *Caroline Schweiger-Eisbacher* [3]; *David Horst* [2]; *Ingeborg Tinhofer-Keilholz* [3]; *Frederick Klauschen* [2]; *Max Heiland* [1]; *Ulrich Keilholz* [3]

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Keywords

Heterogeneity, tissue microenvironment, immunohistochemistry

Purpose

Intratumoral heterogeneity (ITH) is one of the elements responsible for high numbers of recurrences, metastases and diminished responsiveness to conventional therapies in oral squamous cell carcinoma (OSCC). Extensive histopathological analyses concerning the spatial heterogeneity of tissue microenvironment (TME) in OSCCs may inform clinical management, e.g. for immunotherapy strategies. This study describes the morphologic and phenotypic spatial heterogeneity of tumor cells and the TME with a focus on immune infiltration in OSCCs, revealing relevant diversity among different tumor areas.

Material and methods

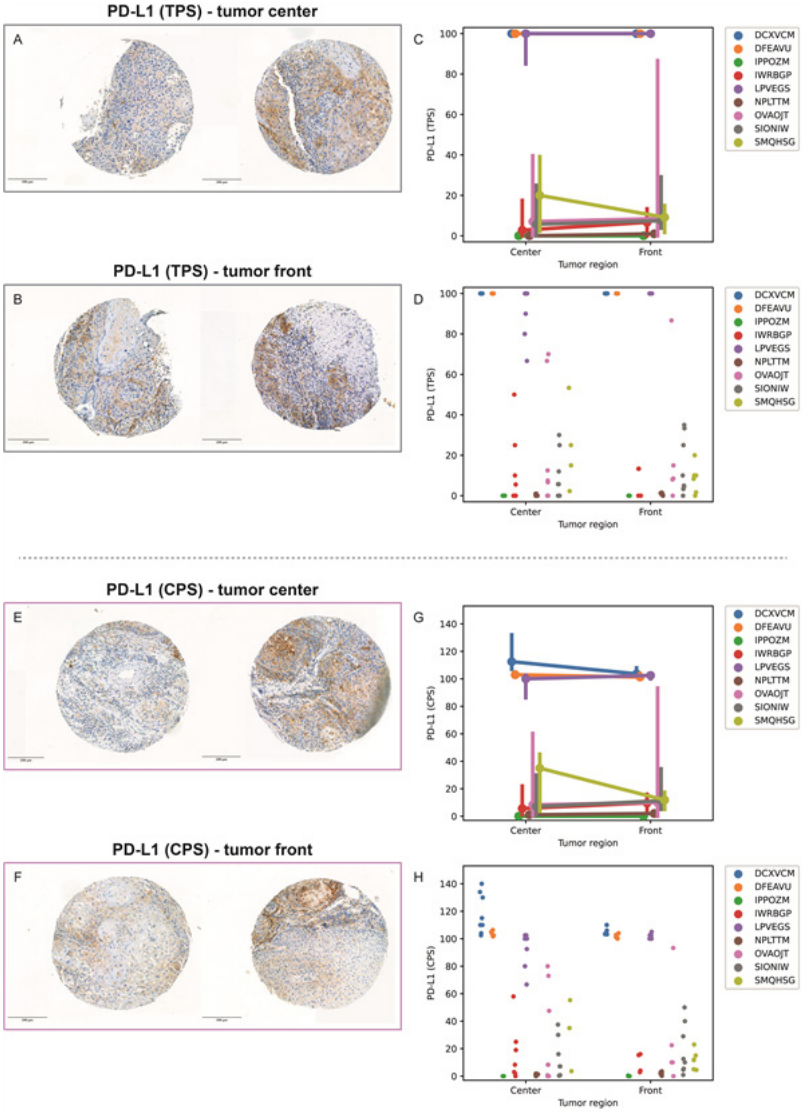
Patients with OSCCs greater than 2cm in diameter and planned surgical tumor resection were eligible for the study. During surgery, 2 biopsies each from the tumor center and the tumor rim were obtained. Immunohistochemical characterization of tumor and immune cells was performed using the following biomarkers: p53, cytokeratin KL1, Vimentin, EGFR, IDO, CAIX, CD44, CD163, PD1, PD-L1. CD3, CD4, CD8, FoxP3, CD20.

Results

From 9 patients included, (8 male, 1 female, mean age 67.3 (± 12.1) years) 36 biopsies were obtained. All patients demonstrated an individual marker expression with inter- and intratumoral heterogeneity. Comparisons between tumor center and rim revealed significant differences in the dysregulation of p53. PD-L1 demonstrated inter-tumoral two expression peaks without differences concerning the region of bioptic samples. Marker expression of patients with history of recurrences clustered similarly with especially higher expression of FoxP3, IDO, CD4, CD68, and CD163 at the tumor rim.

Conclusion

OSCCs demonstrate inter- and intratumoral heterogeneity involving both tumor cells and the TME. Evidence has been providedfor the need for analyzing multiple tumor regions for more complete tumor mapping and evaluation of biomarker significance on survival. Further studies should evaluate the prognostic impact of higher/lower expression levels of specific markers at the tumor rim.


PD-L1 (TPS) - tumor center
A
C
PD-L1 (TPS)
Tumor region
Center
Front
PD-L1 (TPS) - tumor front
B
D
PD-L1 (CPS) - tumor center
E
G
PD-L1 (CPS)
PD-L1 (CPS) - tumor front
F
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DCXVCM
DFEAVU
IPPOZM
IWRBGP
LPVEGS
NPLTTM
OVAQJT
SIONIW
SMQHSG

PO-040 | Benefits of automated gross tumor volume segmentation in head and neck cancer

Heleen Bollen [1]; Sandra Nuyts [1]; Frederik Maes [2]; Marilyn Wegge [1]; Siri Willems [2]

(1) University Hospitals Leuven (2) Catholic University Leuven

Keywords

Neural networks, Observer variability, Gross tumor volume

Purpose

Gross tumor volume (GTV) delineation for head and neck cancer (HNC) radiation therapy planning is time consuming and prone to interobserver variability (IOV). The aim of this study was (1) to develop an automated GTV delineation approach of primary tumor (GTVp) and adenopathies (GTVn) based on a 3D convolutional neural network (CNN) exploiting multi-modality imaging input from CT, PET and MRI (instead of planning CT only) as required in clinical practice, and (2) to validate its accuracy, efficiency and IOV compared to manual delineation in a clinical setting.

Methods

Two datasets were retrospectively collected from clinical cases of HNC patients containing planning CT and additional PET/CT (76 patients) or MRI (74 patients). CNNs were trained for GTV delineation with consensus delineation of two experienced radiation oncologists as ground truth, with either single (CT) or co-registered multi-modal (CT+PET or CT+MRI) imaging data as input. For validation, GTVs were delineated in on 20 new cases by two observers, once manually, once by correcting the delineations generated by the CNN. Accuracy and IOV were assessed by the volume overlap between different delineations and efficiency by the gain in delineation time. Volume overlap between delineations was

assessed calculating the Dice Similarity Coefficient (DSC), Hausdorff Distance (HD) and Mean Surface Distance (MSD).

Results

Both multi-modality CNNs (CT+PET and CT+MRI) performed better than the single-modality CNN and were selected for clinical validation. For the multimodal approaches, performance of the late fusion strategy (LF) was significantly better than early fusion. Mean DSC between the ground truth and predictions for GTVp and GTVn, respectively, was 77% and 79% for the CT+PET-LF CNN and 61% and 70% for the CT+MRI-LF CNN. Agreement between predicted and corrected delineations was 69% and 79% for CT+PET-LF CNN and 59% and 72% for the CT+MRI-LF CNN (Table 1). IOV among the two observers decreased significantly when correcting the predicted delineations (GTVp: 76% vs. 95%, GTVn: 86% vs. 96%). Time efficiency increased with 48% (8 vs. 15.5 min, $p < 10\text{-}5$). Examples of predictions are shown in Figure 1 with the ground truth in red and automated uncorrected delineations in green.

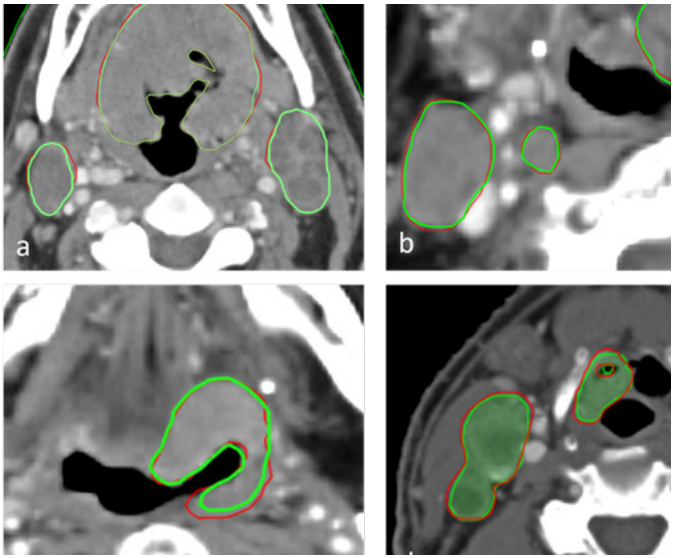
Conclusion

Multi-modality automated delineation of GTV of HNC was shown to be more efficient and consistent compared to manual delineation in a clinical setting and beneficial over a single-modality approach.

Table 1: Upper and lower bound performance (mean +/- standard deviation) of multi-modality CNNs on validation cohort

		OBSERVER 1 (HB)					
		Corrected delineations (Acc 1)			**Manual delineations (Acc$_{m}$ 1)**		
		DSC	HD95	MSD	DSC	HD95	MSD
CT+PET-LF (1:1)	GTVp	79.2(28.0)	9.4(11.6)	1.6(1.4)	70.8(24.5)	9.3(10.3)	2.4(1.0)
	GTVn	86.9(9.1)	17.0(24.2)	2.3(2.2)	79.9(10.8)	31.3(32.3)	4.2(3.5)
		DSC	HD95	MSD	DSC	HD95	MSD
CT+MRI-LF(?)	GTVp	68.9(17.7)	17.7(12.3)	3.6(2.1)	59.8(16.9)	19.4(11.2)	4.6(2.1)
	GTVn	76.9(17.5)	30.6(21.4)	5.2(5.2)	72.3(16.0)	30.3(21.1)	5.7(4.9)
		OBSERVER 2 (MW)					
		Corrected delineations (Acc 2)			**Manual delineations (Acc$_{m}$ 2)**		
		DSC	HD95	MSD	DSC	HD95	MSD
CT+PET-LF (1:1)	GTVp	82.2(20.6)	9.1(12.1)	1.4(1.4)	67.0(24.3)	11.0(11.1)	2.8(1.1)
	GTVn	91.9(6.3)	16.1(24.8)	2.0(2.3)	78.7(8.5)	31.4(31.0)	4.3(3.3)
		DSC	HD95	MSD	DSC	HD95	MSD
CT+MRI-LF(?)	GTVp	69.5(19.1)	17.8(12.3)	3.6(2.3)	58.8(18.8)	19.2(11.9)	4.7(2.3)
	GTVn	76.8(17.2)	30.6(21.4)	5.2(5.2)	71.4(13.4)	30.9(20.6)	5.4(3.8)

Abbreviations: CT+PET-LF: Network with input from planning CT and PET with late fusion; CT+MRI-LF: Network with input from planning CT and MRI with late fusion; Acc 1: Accuracy for automated delineation compared to corrected delineation for observer 1; Acc 2: Accuracy for automated delineation compared to corrected delineation for observer 2 (upper bound performance); Acc$_{m}$1: Accuracy for automated delineation compared to manual delineation for observer 1; Acc$_{m}$2: Accuracy for automated delineation compared to manual delineation for observer 2 (lower bound performance); DSC: Dice similarity coefficient (%); HD95: Hausdorff distance 95th percentile (mm); MSD: Mean surface distance (mm); GTVp: Gross tumor volume of primary tumor; GTVn: Gross tumor volume for lymph nodes.



PO-041 | A Machine Learning-Based Model for the Prediction of Xerostomia after Head and Neck Radiotherapy

Yagiz Yedekci [1]; Melek Tugce Yilmaz [1]; Sezin Yuce Sari [1]; Aysenur Elmali [1]; Mustafa Cengiz [1]; Gökhan Özyigit [1]; Gozde Yazici [1]

(1) Hacettepe University

Purpose

The aims of this study are to create an ML model using dosimetric parameters and the XI scores to predict xerostomia in patients undergoing RT, and to define the importance of the items in the XI.

Methods

Data from patients with LAHNC treated in our department between 2012 and 2017 were used in this retrospective study. The patients were selected with an aim of a minimum follow-up period of longer than two years. RIX was assessed with the XI which includes 11 questions. The ML method of random forest (RF) was used for the prediction of RIX. RF is an ensemble learning method which creates decision trees on randomly selected data samples. The prediction from each tree is evaluated and the best solution is selected by means of voting. RF can be used both for classification and regression. Also, it allows defining the relative feature importance which helps selecting the most contributing features for the target value. The RF algorithm was carried out using Python programing language version 3.8. and Scikit-Learn library (Python Software Foundation). The RF algorithm was applied to two different data;

1. To the XI, to obtain the importance of the survey questions on the total RIX score, and
2. To the dosiomics, to predict the XI scores.

Results

Eighty-seven patients were chosen for the study out of 880 treated with image-guided intensity-modulated radiation therapy (IMRT) for LAHNC. All patients were administrated the XI and the results were evaluated with our ML model which aimed to define the importance of the survey questions over the XI total score.

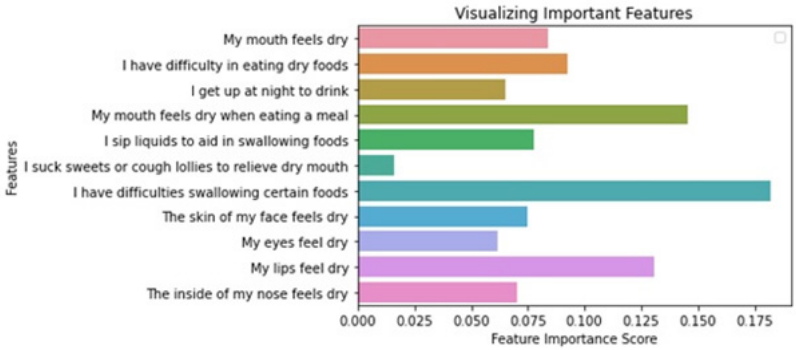
The model worked with an accuracy rate of 96.6%. The relative importance of the questions is given in Fig. 1. The question “I have difficulties swallowing certain foods” was the most effectual and “I suck sweets or cough lollies to relieve dry mouth” was the least effectual question, respectively. Fig. 2 shows the cumulative importance weights of the variables. The dashed line shows 95% of the total importance. The total importance impact of “My eyes feel dry” and “I suck sweets or cough lollies to relieve dry mouth” on the cumulative weight was less than 5%. When we omitted these questions from the questionnaire and ran the model again, the accuracy decreased to 96.3% . In the next stage, we selected the most effectual five items, and the model worked with an accuracy of 86%.

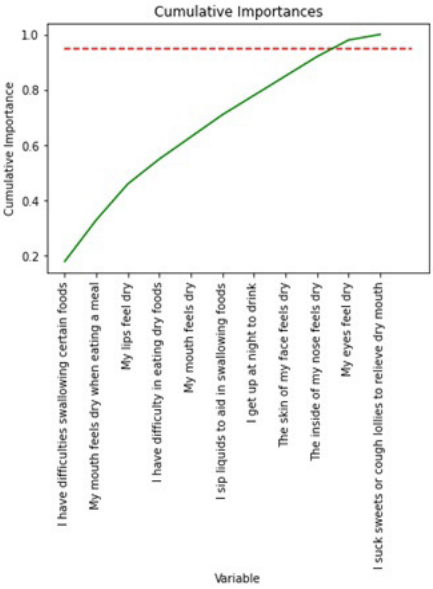
Our ML model predicted the RIX scores with an accuracy of 81% (7.1 mse and 0.91 r value). The importance of the scores ranged between 0.07 and 0.04, meaning the impact of the related DVH parameters on the total score was between 7% and 4%. After omitting the least effectual questions from the data, we recalculated the model in which the accuracy was 80.5%, and the mse and r values were 7.4 and 0.89.

Conclusion

The questions in the XI have different impacts on the total score. Our ML model showed that the XI items could be reduced from 11 to nine, costing only a 0.3% decrease in accuracy. Our proposed ML model can predict the XI score. This prediction considers the doses absorbed by the structures associated with xerostomia.

Our results also showed that the doses to the parotid stem cells have an impact on the total XI score. Therefore, we offer to delineate the parotid stem cells and record the doses to these cells for a more accurate assessment of RIX.





PO-043 | Oral Verrucous Neoplasms: Single-center Long-term oncological outcome analysis

Vimmi Gautam [1]; Smriti Panda [1]; Kuldeep Thakur [1]; Chirom Amit Singh [1]; Aanchal Kakkar [1]; Kapil Sikka [1]; Rajeev Kumar [1]; Suman Bhaskar [1]; Ahitagni Biswas [1]; Atul Sharma [1]; Alok Thakar [1]

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KEYWORDS

Verrucous neoplasms, survival

Purpose

Oral verrucous lesions have a unique clinical presentation and prognosis, however, management protocols to date are largely extrapolated from oral squamous cell carcinoma.

In this study, we aim to retrospectively analyze various factors affecting recurrence and survival in oral verrucous lesions.

Methods

A retrospective study was conducted at a tertiary care center in India on consecutive cases showing verrucous hyperplasia/verrucous carcinoma of the oral cavity in the pre-operative biopsy between January 2015 to December 2021.

Pre-operative diagnosis of squamous cell carcinoma was excluded.

All the patients underwent surgery and the post-operative histopathology report was considered the final diagnosis.

Data was collected to include subsite, DOI, perineural spread, lymphovascular emboli, margin positivity, neck dissection, and postoperative radiotherapy. Survival analysis and multivariate analysis were performed using the Kaplan-Meier method and the Cox-Proportional Hazards model, respectively.

Results

A total of 108 patients were identified (92- Verrucous Hyperplasia;16-Verrucous Carcinoma) during the above period. 104 patients were male with a median age of 48 years. Buccal mucosa was the most common subsite (57.4%) followed by tongue (17.5%). Other subsites were the lip, gingivobuccal sulcus, alveolus, and palate. 83% of the patients had some form of addiction mostly in the form of smokeless tobacco and betel quid. The histopathology report that followed were 44 patients in the verrucous hyperplasia group, 38 in the verrucous carcinoma, and 26 patients had their final report as well/moderately differentiated squamous cell carcinoma. Based on this pre-operative biopsy showed a sensitivity of 22.2 %, specificity of 95.6%, Positive predictive value of 87.5%, negative predictive value of 46.7%, and an accuracy of 52.8%. Neck dissection was performed in 58.3% of the patients, however, none of them showed nodal positivity in the final histopathology report. At the median follow-up period of 42 months, both overall survival (OS) and disease-free survival (DFS) in the verrucous hyperplasia group was 75% whereas in the verrucous carcinoma group OS was 50% and DFS was 45%.(p-value 0.01). Of all the categorical variables considered none of them showed a statistically significant association on multivariate analysis. However, on univariate analysis, the effect of post-operative radiotherapy had a significant effect on local recurrence (OR 5.4;p-value-0.004). Similar was the univariate analysis results between histopathological margins where < 5mm was considered significantly associated with local recurrence (p-value 0.001) and nodal recurrence (p-value 0.006).

Conclusion

In our study, the most important prognostic factor determining recurrence was margin positivity. Nodal metastasis though not seen in any patient, nodal recurrence is seen to be present which is independent of whether or not neck dissection was performed or post-operative radiotherapy was administered. Post-operative radiotherapy had a significant impact on local recurrence.

PO-045 | Reducing the risk of post-RT aspiration by sparing specific aspiration related organs at risk

Hans Paul Van Der Laan [(1)]; *Agata Gawryszuk* [(1)]; *Johanna G.M. Van Den Hoek* [(1)]; *Roel J.H.M. Steenbakkers* [(1)]; *Arjen Van Der Schaaf* [(1)]; *Johannes a. Langendijk* [(1)]

(1) University Medical Center Groningen

Keywords

Aspiration prevention; Outcome-guided radiotherapy

Purpose/Objective

We previously identified specific musculature related to aspiration, so-called functional swallowing units (FSUs), involved in larynx elevation and tongue base retraction (Fig. 1). These FSUs are not yet recognized as Swallowing Organs at Risk (SWOARs) in daily practice and in treatment plan optimisation. As radiotherapy (RT)-induced aspiration is a serious and potentially life-threatening side effect it should be avoided when possible. We developed a prediction model with baseline aspiration status and dose in FSUs as factors which performed well in predicting videofluoroscopy (VF) assessed RT-induced aspiration (Penetration Aspiration Scale (PAS) score 6-8), at 6 months. In the current study, we aimed to apply this model in RT treatment plan optimisation and establish its potential to reduce the risk of late RT-induced aspiration.

Material/methods

Thirty patients who previously received definitive photon RT for head and neck cancer in the larynx, pharynx or oral cavity were included in this treatment planning comparative study. Three treatment plans were automatically created with an advanced new method that we recently described (R&O 2021; 162:85). The method allows for high quality treatment plans that are optimised based

on desired toxicity-outcome profiles. The first plan was aimed at preventing xerostomia and dysphagia, but did not include FSUs as optimisation parameters. In the two other plans, the aspiration model was added as optimisation parameter to also spare FSUs and reduce the risk of late aspiration. The two FSU sparing plans were similar except the first was optimized assuming baseline aspiration and the second assuming no baseline aspiration.

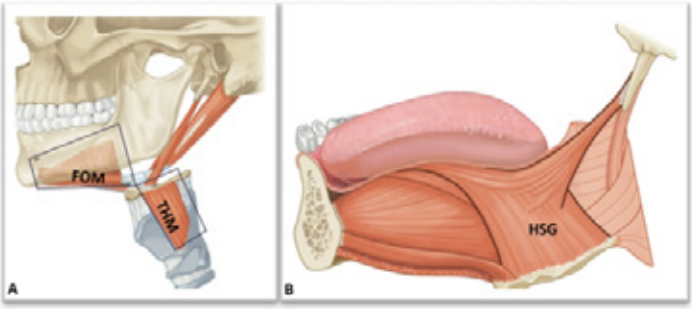
Results

All plans complied with all treatment planning quality criteria and were successful in limiting the risk of xerostomia and dysphagia (Table 1). The FSUs sparing plans reduced the risk of late aspiration significantly ($p < 0.001$) and in all 30 patients. The optimiser of the planning system increased its efforts to spare the FSUs even more when baseline aspiration was assumed. Therefore, the aspiration risk reduction was greatest in these plans (average risk reduction 13.3% versus 8.3% in plans assuming no aspiration at baseline). Aspiration risk reduction by sparing FSUs did not reduce overall plan quality. A slight redistribution of dose was seen with a minimal increased risk of xerostomia.

Conclusion

Sparing all specific aspiration related organs at risk, including FSUs, during RT has the potential to significantly reduce the risk of RT-induced aspiration, especially in patients who experience aspiration already at baseline. With automatic planning, FSUs sparing does not complicate the treatment planning process and does not compromise treatment plan quality in any way.

Figure 1. Functional Swallowing Units (FSUs) in the final NTCP model for late aspiration.



A: **Anterior Segment** consisting of two FSUs involved in hyolaryngeal elevation: FOM- floor of mouth (mylohyoid muscles, geniohyoid muscles, anterior belly of digastric muscles) and THM- thyrohyoid muscles (left and right). B: FSU involved in tongue base retraction: **HSG- hyoglossus/styloglossus muscles complex** (left and right). Illustration made by Remko van Deijk.

Table 1.

	Automatic planning n=30		
	Regular planning	Aspiration prevention (FSUs optimised planning)	
Baseline aspiration simulation		*Baseline yes*	*Baseline no*
Average mean dose swallowing units (Gy)			
Supraglottic larynx	54.73	46.19	48.76
Anterior Segment	52.98	47.76	49.69
UES unit	39.85	31.92	35.04
HSG unit	54.98	52.86	53.96
Average late aspiration risk (PAS score 6-8)			
Assuming baseline aspiration	73.9%	60.6%	
Assuming NO baseline aspiration	37.8%		29.5%
Reduction aspiration risk		-13.3% p<0.001	-8.3% p<0.001
Average risk of other common toxicities			
Patient rated			
Xerostomia (moderate-severe)	50.9%	51.5%	51.4%
Xerostomia (severe)	15.7%	16.0%	15.9%
Physician rated			
Dysphagia (grade ≥ 2)	31.6%	31.5%	31.9%
Dysphagia (grade ≥ 3)	10.4%	10.2%	10.4%

Abbreviations: PAS = Penetration Aspiration Scale; UES = Upper Esophageal Sphincter; HSG = Hyo-/Styloglossus muscles complex

PO-047 | Effectiveness of immunotherapy in platinum-refractory R/M HNSCC and its association with NLR

Rafael Bach [1]; Laura Comerma [1]; Ana Isabel Álvarez Macha [1]; Jordi Recuero [1]; David Conde-Estévez [1]; Anna Sumarroca [1]; Laura Masfarré [1]; Nil Navarro-Gorro [1]; Adriana Gómez [1]; Marta Guix [1]; Alex Corbera [1]

(1) Hospital del Mar

Introduction

Head and neck tumors are the seventh most common malignancy in the world. In Spain they account for about 12,000-14,000 cases each year. Among the choices to treat these tumors, we have surgery, radiotherapy, chemotherapy and immunotherapy. Immunotherapy entered the scene in 2016, after 10 years without new therapies, with the approval of nivolumab and pembrolizumab for recurrent or metastatic HNSCC (R/M HNSCC) refractory to platinium-based regimens. Although the approval was regardless of any biomarker, there are some that could relate with better response, such as CPS, TILS and Neutrophil/lymphocyte ratio (NLR). We propose to analyze the efficacy and safety of patients treated with nivolumab as refractory to platinium-based regimen in our center and the relation of NLR with survival.

Methods

Single center retrospective observational study with 16 patients with R/M HNSCC treated with nivolumab between 2018-2021. Demographic data, performance status (PS), stage, previous treatments received and NLR at the beginning of treatment, were collected. Tumor response, toxicities, Overall survival (OS) and Progression-Free Survival (PFS) were evaluated in general population through Kaplan-Meir analysis. Survival differences between NRL ≤ 5 and NLR > 5 were analyzed with Log-rank test and Gehan-Breslow-Wilcoxon test.

Results

A majority of patients were metastatic when nivolumab was initiated (68%). Median age was 65.6 years. Most of them had a ECOG performance status of 1 (87.5%). Median follow up was 15 months. Median OS was 5.9 months and median PFS was 2.2 months. Median NLR at the beginning of treatment was 5.8 (range 1.7-17.4). Median OS for patients with NLR ≤ 5 was 10.4 months (95%CI.1,1-14,6) vs 2.6 months for NLR >5 (95%CI. 0.1 - 7.6), Hazard Ratio (HR) was 0.38 for NRL ≤5 (95%CI. 0,1- 1,1) and 2.6 for NLR>5 (95%CI 0.9 - 7.6), not being statistically significant. We also performed a Gehan-Breslow-Wilcoxon test analysis obtaining p= 0.03, showing that survival curve was significantly different.

Conclusion

In our study we found significant relation between NLR and survival for R/M HNSCC treated with nivolumab, although Log-rank HR was not statistically significant. Also, the median OS was lower than in others reports, this may be related to the high percentage of PS1 patients and the low number of patients in our series.

PO-048 | Real-world healthcare resources utilization costs associated with R/M HNSCC patients in Portugal

Catarina Morais [1]; Maria Margarida Teixeira [2]; João Dias [3]; Teresa André [4]; Ana Joaquim [5]; Ricardo Fernandes [6]; Joana Magalhães [7]; Laura Marreiros [8]; Leonor Pinto [9]; Maria Leonor Ribeiro [10]; Mafalda Nogueira [1]

(1) MSD (2) INSTITUTO PORTUGUÊS DE ONCOLOGIA COIMBRA (3) INSTITUTO PORTUGUÊS DE ONCOLOGIA PORTO (4) CENTRO HOSPITALAR DO FUNCHAL (5) CENTRO HOSPITALAR VILA NOVA DE GAIA / ESPINHO E.P.E. (6) HOSPITAL DE BRAGA (7) CENTRO HOSPITALAR E UNIVERSITÁRIO DO ALGARVE (8) HOSPITAL GARCIA DE ORTA, E.P.E. (9) CENTRO HOSPITALAR E UNIVERSITÁRIO DE COIMBRA (10) HOSPITAL SANTA MARIA

Keywords

Healthcare resource utilization, treatment, real-world evidence

Objectives

Healthcare resources utilization (HCRU) and economic burden associated with recurrent or metastatic (R/M) head and neck squamous cell carcinoma (HNSCC) are assumed to be high, but real-world evidence (RWE) is limited in Portugal. Previous estimates reported mean total costs/patient of €24,211±€22,432 with hospitalisations and drugs as primary drivers.

This study aimed to provide RWE on HCRU costs associated with R/M HNSCC patients care in Portugal.

Material/Methods

This was a retrospective, multicenter, longitudinal study that included R/M HNSCC patients ineligible for curative treatment, diagnosed between 1JUN2017–31DEC2019, and followed for up to 1 year. It collected secondary data concerning diagnostics, treatment, clinical, and HCRU from electronic hospital databases of 9 centers.

Results

377 R/M HNSCC patients were included. 303 received systemic treatment, 73 were ineligible for systemic treatment, and 1 didn't have clinical information. Most patients were ≥50 years old (92.1%), male (92.8%), current/former (89.3%) smokers and with heavy alcohol consumption habits (72.7%). Patients were diagnosed with metastatic (62.2%) or recurrent (37.8%) HNSCC, with primary tumour location mainly in the oropharynx (33.2%).

Total HCRU costs included chemotherapy (91.4%), cetuximab (54.5%), immunotherapy (17.2%), radiotherapy (26.3%), lab tests (96.5%), imaging exams (92.0%), hospitalisations (68.1%), emergency (59.3%), outpatient consultations (94.4%) and other appointments (59.0%), were estimated as €29,401±40,535/patient and €48,499±65,388/patient/year, on average. Concomitant medication (93.4%) and surgery (9.3%) associated costs weren't estimated due to the absence of necessary information. Mean medication costs were €16,076±28,297/patient and €19,384±31,210/patient/year and mean non-medication costs were €17,323±31,834/patient and €33,935±61,249/patient/year.

HCRU costs were analysed based on patient's demographic region, disease stage and tumour location, with only the first revealing statistical differences.

Based on patient's region, total costs/patient/year were higher in south/islands and lower in north (€64,532±78,279 vs €37,910±47,624) and €46,883±69,200 in center (p=0.021). In north, estimated mean medication costs per patient (€25,029±33,818; p<0.001) and per patient/year (€28,289±35,469; p<0.001) were the highest, whereas non-medication costs were the lowest per patient (€11,377±27,266; p=0.044) and patient/year (€18,545±33,569; p<0.001).

Conclusions

In this study estimated non-medication costs accounted for 60% of total HCRU values, whereas medication was responsible for the

remaining 40%. Also, HCRU costs were different among geographic regions, suggesting different approaches for the treatment and care of these patients.

This study provides the first RWE of HCRU costs with R/M HNSCC patients care in Portugal, contributing to further understanding the therapeutic value of the different treatment modalities in clinical practice settings.

PO-049 | Real-world R/M HNSCC patients' characterization during 1st line treatment in Portugal – TRACE study

Catarina Morais [1]; Maria Margarida Teixeira [2]; João Dias [3]; Teresa André [4]; Ana Joaquim [5]; Ricardo Fernandes [6]; Joana Magalhães [7]; Laura Marreiros [8]; Leonor Pinto [9]; Maria Leonor Ribeiro [10]; Mafalda Nogueira [1]

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Keywords

Healthcare resource use, 1st line treatment, real-world evidence

Objectives

Diagnosis, management, and monitoring of patients with recurrent or metastatic (R/M) head and neck squamous cell carcinomas (HNSCC) are individualised according to tumour characteristics. Still, the best standard treatment for these patients is not consensual within Europe, including Portugal.

Thus, this study aimed to provide real-world evidence on healthcare resources use (HCRU) by first line R/M HNSCC patients in Portugal.

Material/Methods

This was a retrospective, multicenter, longitudinal study of R/M HNSCC patients who were ineligible for curative treatment, diagnosed between 1st June 2017-31st December 2019, and followed for up to one year. It collected secondary data concerning diagnostics, treatment, clinical, and HCRU from electronic hospital databases of 9 centers.

Results

This study included 377 R/M HNSCC patients, of which 303 received 1st line treatment. Most patients were between 50 and 69 years old (75.2%), male (93.1%), current (53.2%) or former (36.5%) smokers, and with heavy alcohol consumption habits (71.7%). Patients were diagnosed with metastatic (61.4 %) or recurrent (38.6%) HNSCC, with lung (39.6%) being the most frequent metastasis. The most common primary tumour location was the oropharynx (100, 33.0%). Of note, only 38 were tested for HPV, of which 7 (18.4%) were positive.

Chemotherapy was received by 269 patients, mainly carboplatin (48.0%), 5-FU (46.1%), paclitaxel (36.0%), and cisplatin (35.3%). Cetuximab was used in 151 patients. 18 patients received immunotherapy in 1st line treatment. 57 patients underwent radiotherapy, and 29 were submitted to surgery, mainly excision (75.9%) or lymph node dissection (58.6%). Systemic treatment started at 6.6±16.6 weeks after diagnosis and had a mean overall duration of 17.4±13.5 weeks.

Concomitantly to systemic treatment, patients took medications for disease management (90.1%), underwent laboratory tests (97.4%), imaging assessments (94.4%), and other exams (44.5%), such as biopsies or ECG. They also attended outpatient consultations (94.1%), including other hospital specialists (74.7%) or with a multidisciplinary team (66.0%), required emergency consultations (49.5%) or hospitalisation (44.9%), and had nutritional support (52.5%), psychological treatment (15.2%) or speech therapy (5.3%).

Conclusions

In this study, chemotherapy was the most frequent 1st line treatment modality, with only a small proportion of patients undergoing radiotherapy, surgery or immunotherapy. Nearly all patients attended oncology consultations and only 66% were followed by

a multidisciplinary team, essential for patient treatment and management due to the high complexity of the disease.

This study provides the first real-world characterization of R/M HNSCC patients undergoing first line treatment in Portugal contributing to further understanding the therapeutic value of the different treatment modalities in clinical practice settings.

PO-053 | Elective node irradiation and perineural invasion in salivary gland tumors: the MedAustron approach

Dr. Ankita Nachankar [1]; Prof. Eugen Hug [2]; Dr. Petra Georg [2]; Dr. Maciej Pelak [2]; Dr. Slavisa Tubin [2]; Dr. Joanna Gora [3]; Dr. Astrid Fraller[2]; Dr. Petra Mozes [2]; Prof. Piero Fossati [2]

(1) ACMIT Gmbh and EBG MedAustron GmbH (2) EBG MedAustron GmbH (3) EGB MedAustron GmbH

Purpose

Salivary gland cancers (SGCs) are uncommon malignancies with unique biology and natural course. In non resectable cases outcomes with photons-based RT or RT-CHT remain suboptimal as compared to squamous cell carcinoma. Carbon ions have shown promising results in non-resected SGCs in German and Japanese studies. In the German experience elective nodal irradiation (ENI) was routinely used in clinically node negative (cN0) SGCs, however Japanese centers never performed ENI and isolated neck recurrence were rare in their series. There is no consensus on need of ENI in SGCs. Perineural invasion (PNI) is at least as important as lymphatic spread in SGC. Risk of lymph node involvement and PNI in SGCs is highly variable across histologies, primary site and T stage. Here we propose recommendations for clinical target volume (CTV) with respect to ENI and PNI in cN0 SGCs.

Material/Methods

We stratified cN0, SGCs as per T stage, primary site and histologies. For ENI Tumor locations were classified into, very low risk, low risk, mid-high risk unilateral and mid-high risk bilateral groups for lymphatic spread (figure 1). SCG histologies were divided into highly lymphotropic- high and intermediate grade mucoepidermoid carcinoma, adenocarcinoma NOS and low lymphotropic- Adenoid-cystic carcinoma (ACC), salivary duct car-

cinoma, acinic-cell carcinoma, low grade mucoepidermoid carcinoma, papillary adenocarcinoma (figure 1).

For PNI, tumors were grouped into cranial and caudal primary site (figure 1, 2) and ACC were classified as neurotropic and non--ACC as non-neurotropic histologies. Twenty-three patients with SGCs treated with CIRT +/- proton therapy at MedAustron from July 2019 to September 2022 were analysed. Prescription dose CIRT (n =20) was 57 .6 - 70.5 Gy [RBE]/12 -22 fractions, with 4-5 fractions/ week. Three patients received proton therapy 50-54 Gy [RBE]/ 25-27 fractions followed by CIRT boost 12- 20 Gy [RBE]/4-5 fractions, with 4-5 fractions/ week.

Results

Median follow up was 12.2 months (range, 2.5 – 36.3). Majority of patients had advanced T stage; 1 patient had positive node at surgery. ACC was most common histology followed by mucoepidermoid carcinoma, and pleomorphic adenoma. PNI were evident in 13 patients at baseline and 1 patient developed postop facial paralysis. Two (2/23) patients had local progression, none had nodal or distant failure. 1- and 2-year loco-regional control rate is 95.7%, 81.3% respectively. Two (2/23) patient developed acute grade 3 mucositis and 1 developed grade 3 dermatitis; none developed grade >/= 3 late toxicity.

Conclusion

Isolated nodal failure in cN0, SGCs are very rare. This work can be considered a first step toward creating a consensus on ENI and PNI volumes in this population.

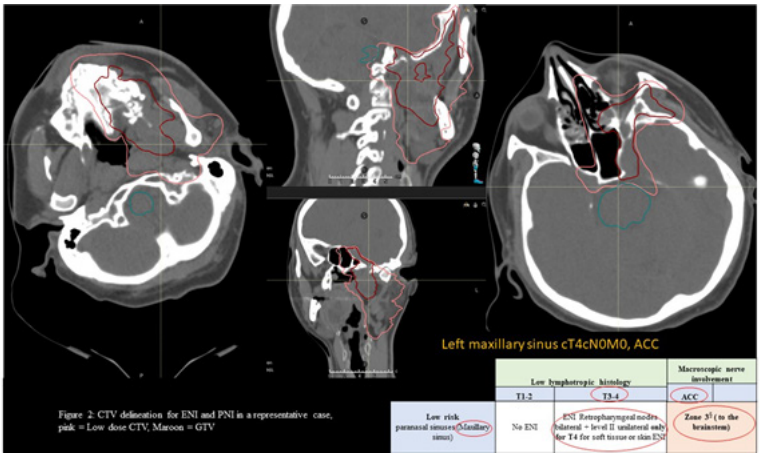

Figure 2: CTV delineation for ENI and PNI in a representative case, pink = Low dose CTV, Maroon = GTV

CTV

Location			Recommendations for ENI in cN0, SGCs: High lymphotropic histology T1-2	Recommendations for ENI in cN0, SGCs: High lymphotropic histology T3-4	Recommendations for ENI in cN0, SGCs: Low lymphotropic histology T1-2	Recommendations for ENI in cN0, SGCs: Low lymphotropic histology T3-4	Recommendations for perineural extension in CTV: Macroscopic nerve involvement ACC	Recommendations for perineural extension in CTV: Macroscopic nerve involvement Non ACC	Recommendations for perineural extension in CTV: No nerve involvement ACC	Recommendations for perineural extension in CTV: No nerve involvement Non ACC
Cranial		**Very low risk** Paranasal sinuses (Frontal sinus, Ethmoid sinus, Sphenoid sinus), middle ear	No ENI	No ENI	No ENI	No ENI	Zone 3§ (to the brainstem)	Zone 1§ (to the skullbase but evaluate single cases and possibly reduce for larynx and hypopharynx)	Zone 2§ (to the ganglia)	No expansion
		Low risk Palate, nasal cavity, paranasal sinuses (Maxillary sinus)	No ENI	Retropharyngeal nodes bilateral + level II unilateral	No ENI	Evaluate possibility of ENI Retropharyngeal nodes bilateral + level II unilateral only for T4 for soft tissue or skin ENI				
		Mid-high risk bilateral Nasopharynx, oropharynx posterior wall	Retropharyngeal level II-III-IV-V bilateral (IMRT+ carbon boost)		Retropharyngeal nodes bilateral	Retropharyngeal nodes + level II bilateral (if T4 only for nerve involvement CTV may be reduced)			Zone 2§ (to the ganglia)	
		Mid-high risk unilateral Parotid gland	Level II unilateral	Level Ib-II-III-V unilateral (Consider whether exclusive carbon or proton + carbon boost)	No ENI	Level II unilateral				
Caudal		**Mid-high risk unilateral** Submandibular gland	Level Ia-Ib, II, III unilateral	Level Ib-II-III-V unilateral (Consider whether exclusive carbon or proton + carbon boost)	No ENI	Level Ib, II unilateral				
		Middle risk bilateral Base of tongue	Level Ib-II bilateral	Level Ib-II-III-IV-V bilateral (IMRT+ carbon boost)	Level Ib-II bilateral	Level Ib-II-III bilateral				
		Middle risk bilateral Oral cavity, sublingual gland, tonsil and floor of mouth	Level Ia-Ib-II bilateral	Level Ia-Ib-II-III-IV-V bilateral (IMRT+ carbon boost)	Level Ia (for floor of mouth and sublingual gland) Ib-II bilateral	Level Ia (floor of mouth and sublingual gland)- level Ib-II-III bilateral				
		Middle risk bilateral Hypopharynx and larynx	Level II-III-IV-V bilateral (IMRT+ carbon boost)		No ENI	Level III				

Figure 1: Recommendation for ENI and PNI volumes in CTV.
Abbreviations: CTV: clinical target volume, **SGCs**: Salivary gland cancers, **ENI**: Elective nodal irradiation, **PNI**: perineural invasion **ACC** : Adenoid cystic carcinoma
*** High lymphotropic histology:** High and intermediate grade Mucoepidermoid carcinoma, Adenocarcinoma NOS
**** Low lymphotropic histology:** Adenoid cystic carcinoma, salivary duct carcinoma, acinic cell carcinoma, low grade mucoepidermoid carcinoma, papillary adenocarcinoma
§ The division of cranial nerve in zones is used as described by ***Gorayski P et al. Journal of Neurological Surgery Part B: Skull Base. 2016***
Zone 1: to corresponding the skull base foramina) but evaluate single cases and possibly reduce for larynx and hypopharynx, **Zone 2**: Zone 1 + extension to the gasserian ganglion cistern, **Zone 3**: Zone 2 + extension to brainstem

PO-055 | Follow up of head and neck cancer patients treated with TPF

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(1) Hospital del Mar

Introduction

Head and neck tumors are the seventh most common malignancy in the world. In Spain they account for about 12,000-14,000 cases each year.

Chemoradiotherapy remains the standard treatment for locally advanced tumors, but induction chemotherapy with the TPF regimen (docetaxel, cisplatin, and 5-fluorouracil) can be used in selected patients. We propose to analyze the efficacy and safety of patients treated with this scheme in our center.

Methods

Retrospective observational study from November 2003 to October 2022.

Demographic data, tumor location and histology, stage and oncological treatments received are collected (Table 1). Post-induction and end-of-treatment tumor response, toxicities, relapse, progression-free survival, and survival of the 44 patients treated with TPF are evaluated.

Results

Most of the patients (73%) underwent 3 cycles of TPF. 50% of the patients presented a partial response and 18% complete response after induction with TPF. 47% of the cases presented adverse effects ≥G3, including febrile neutropenia in 11% of the patients. There were 9% toxic deaths during induction with TPF. With a

median follow-up of 33 months (1-203), our series shows a median overall survival (OS) of 37 months, with a median progression-free survival (PFS) of 34 months.

Conclusion

Even though in most clinical trials the TPF scheme seeks the preservation of the larynx as its objective, our series found that it is a good scheme regardless of the location; both in order to reduce tumor volume and to facilitate tolerance to subsequent chemoradiotherapy. Toxic deaths in our series are 9%, in the literature they are around 5-7%; this increase may be related to the number of patients in our series.

PO-056 | Head and neck cancer treatment: is cetuximab the best option for patients unfit for cisplatin?

Sandra Silva [(1)]; *Helena Guedes* [(1)]; *Alexandra Guedes* [(1)]; *Raquel Basto* [(1)]; *Adriana Soares* [(1)]; *Enrique Dias* [(1)]; *Raquel Monteiro* [(1)]

(1) Hospital Vila Nova de Gaia

Keywords

Head and neck cancer; radical treatment; toxicities;

Purpose/Objective

To compare the toxicities of chemoradiotherapy with the use of cisplatin Vs cetuximab.

Material/methods

Single-center retrospective cohort of patients with stage II-IVb head and neck cancer, treated with chemoradiotherapy (cisplatin 21-21 days or cetuximab 8-8 days), from 2016-2022. The association between variables was evaluated using the t-test and the chi-square test.

Results

A sample of 103 patients, 87% male and 13% female, divided into two cohorts: 72 were treated with cisplatin plus radiotherapy (RT) Vs 31 patients treated with cetuximab plus RT. The mean age of the patients in the cisplatin cohort was 57 years (± 8) and 62 (± 9) in the cetuximab cohort (p=0,015). The ECOG Performance Status was ≤ 2 in the two groups, with only 1 and 2 patients with ECOG-PS 2 in the cisplatin and cetuximab cohorts, respectively. The cisplatin group had patients with fewer comorbidities compared to the cetuximab group: ACE-27 score was moderate or severe in 27,8% Vs 67,7% (p= 0,000), respectively. In general, the cetuximab cohort had more severe toxicities (≥ G3) than the

cisplatin group: 74,2% Vs 56,9%, p=0,098. The patients treated with cetuximab had significantly more radiodermatitis ≥ G3 compared to those treated with cisplatin: 25,8% Vs 8,3%, p=0,027. However, there was significantly more hematologic toxicity ≥ G3 in the cisplatin group compared to the cetuximab group: 29,2% Vs 6,5%, p=0,011. The patients treated with cetuximab had more mucositis ≥ G3 (64,5% Vs 45,8%, p=0,082) and a greater weight loss in the 12 months after finishing chemoradiation treatment (6,6 Kg Vs 4,7 Kg, p=0,818), although without statistical significance. The biggest difference in weight loss was found 3 months after the radical treatment: 8,5 Kg Vs 6,3 Kg, p=0,251 in the cetuximab cohort and cisplatin group, respectively.

Conclusion

Some patients are considered unfit for chemoradiation with cisplatin, due to some comorbidities. As an alternative, Bonet *et al* show that chemoradiation with cetuximab improves locoregional control and reduces mortality compared to RT alone. However, in this retrospective cohort, it was verified that patients treated with cetuximab plus RT had more severe toxicities, like mucositis and radiodermatitis, compared to those treated with cisplatin. Besides that, it was a greater weight loss in the year after the radical treatment in the cetuximab cohort, without statistical significance. As expected, hematologic toxicity was more frequent with the platinum. Therefore, this work found important severe toxicity with the cetuximab treatment, which makes us think that it's important to find another alternative for the patients unfit for cisplatin. However, this work also has some limitations: there is a significant difference in the sample number between the two cohorts; furthermore, despite similar performance status between the two groups, the patients, in the cetuximab group, had more comorbidities than those treated with cisplatin.

PO-061 | CSF leak in endoscopic pituitary surgery is associated with increased risk of diabetes insipidus

Palani gn[1]

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Aim

Endoscopic surgery is of increasing importance in management of pituitary region pathologies because of its superior visualisation and the increased possibility of gross total resection. As a relatively new technique that may carry a different complication profile to microscopic transsphenoidal surgery and has its own learning curve, audit of local results is imperative.

Method

Retrospective analysis of complications in 150 patients receiving transsphenoidal surgery for pituitary tumours at our centre since 2017.

Results

5% had a post-operative CSF leak requiring further treatment. Incidence of diabetes insipidus (DI) was 10%, of which 4% was permanent. There is a clear association between both transient and permanent DI in patients with CSF leak ($p<0.001$). We also note a correlation between both CSF leak and DI with postoperative meningitis.

There was an inverse correlation between CSF leak and age: CSF leak was more common in younger patients ($p=0.036$) in our cohort. Tumour size, BMI, previous radiotherapy and previous surgery were not risk factors for CSF leak in our cohort.

As with CSF leak, younger patients were at higher risk of diabetes insipidus: mean age 44.3 in patients with DI was 44.3 vs. 57.7 in those without. Histology of somatotropinoma was also a risk

factor for DI: 7/23 (30.3%) developed DI vs. 6.3% of any other histological subgroup (p=0.002).

Conclusion

Our rates of these complications are within the published range as reported in the meta-analysis by Gao et al. (Gao, 2014) with published rates of 12.8 % for CSF leak and 11.3 % DI.

The association with younger age and increased risk of CSF leak may reflect a more aggressive surgical attempt at gross total resection, which in itself might predispose to DI, as may acromegaly.

Intraoperative CSF leak predisposes to a diagnosis of DI in our series and should be a flag for increased vigilance for this complication in the perioperative period, in addition to the known risk of meningitis.

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PO-063 | Indocyanine green angiography for perfusion assessment in H&N reconstruction: a prospective study

Andrea Galli [(1)]; Leone Giordano [(1)]; Michela Nicole Melegatti [(1)]; Elisa Dolfato [(1)]; Rosa Alessia Battista [(1)]; Marco Familiari [(1)]; Mario Bussi [(1)]

(1) San Raffaele Hospital, Milan

Keywords

Indocyanine green; complications; reconstructive surgery.

Purpose/Objective

The aim of this study is describing the use of indocyanine green fluorescence video-angiography (ICGA) to evaluate the degree of perfusion of various types of reconstructive flaps in a group of patients with H&N tumors submitted to major oncological surgery. ICGA is a noninvasive technology that allows real-time intraoperative assessment of tissue vascularization in an objective, repeatable and intraoperative manner.

Material/methods

We prospectively enrolled 23 consecutive patients who underwent major ablative procedures for H&N cancer with concurrent flap reconstruction from March 2021 to May 2022 using ICGA to assess flap vascularization (Fig. 1). Inclusion criteria were the following: locally advanced head and neck cancer (stage III-IV), reconstruction with free or pedicle flaps, curative purpose of the surgery. The main outcome of the study was to evaluate postoperative flap complications (defined as any adverse event affecting the process of wound healing within 30 days after surgery). For this purpose, we compared the findings obtained in our “experimental” cohort with those derived from a comparable cohort of “historical” patients (n = 45) who underwent analogous surgical procedures (similar free/pedicled flap ratio reconstruction – $p = 0.533$ - and same surgical equipe

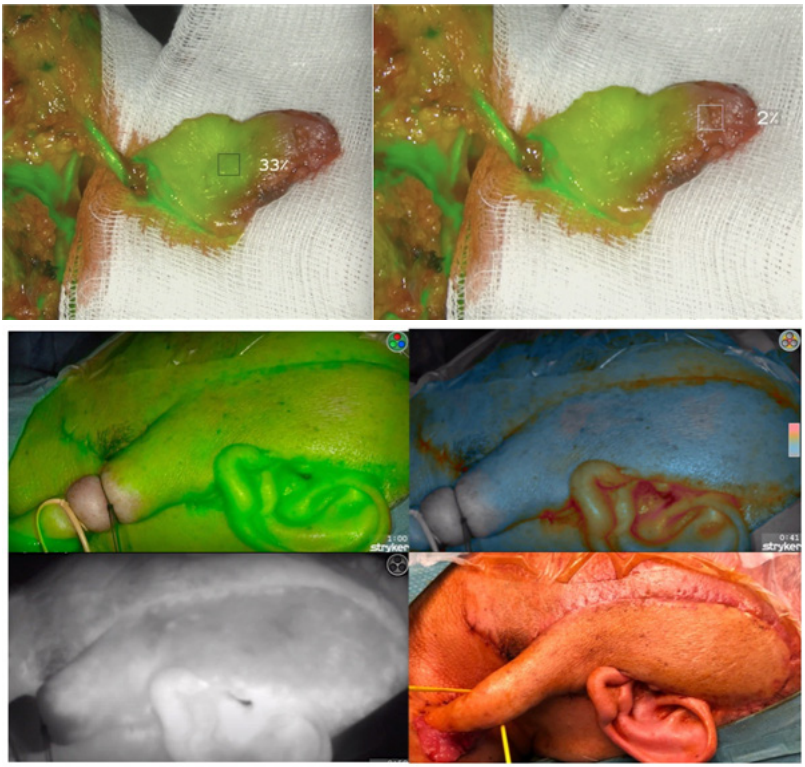
and techniques) with same inclusion criteria (stage III-IV H&N cancer, curative purpose) between January 2017 and December 2020 without the aid of ICGA. Complications were also graded using the Clavien-Dindo classification.

Results

The use of ICGA was shown to significantly correlate with a lower incidence of complications in absolute terms (p = 0.032). The ICGA cohort of patients was also proved to suffer from a significantly lower rate of major complications (Clavien-Dindo III-IV-V; p = 0.031). At multivariate analysis in a model including smoking status, previous radiotherapy, age, ASA score and cardiovascular diseases, the use of ICGA was the only independent predictor of both major (Clavien-Dindo III-IV-V) and overall compications (p = 0.041 and p = 0.037, respectively). As a matter of fact, we observed that ICGA influenced surgeons' decision algorhythm in about one third of patients (7/23): indeed, the distal part of some flaps appeared as hypovascularized/properly ischemic on ICGA assessment (despite a normal appearance on pure visual evaluation) based on predetermined cut-offs and was trimmed accordingly to obtain an adequately perfused flap (Fig. 2).

Conclusion

Due to the importance of a good perfusion for the success of reconstructive surgery in the H&N field and the influence that this type of surgery may have on patients' quality of life, the demonstrated potential role of ICGA in increasing the accuracy of such delicate procedures could be pivotal. Further studies are needed to validate these findings on a larger scale.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PO-067 | Occult metastatic disease and the role of elective nodal dissection in primary parotid neoplasms

Justin Hintze [(1)]; *Patrick Sheahan* [(1)]

(1) South Infirmary Royal Victoria University Hospital

Keywords
Salivary; malignancy; occult

Introduction

Salivary gland tumours are rare, comprising approximately 3-5% of head and neck cancers. The majority of primary salivary gland tumours arise in the parotid glands and surgical extirpation of the affected region of the parotid gland with preservation of local structures forms the cornerstone of management. Metastasis to regional nodes is rare, but variable. The management of regional control in the elective node negative setting is still debated, as the risk of occult disease is not fully elucidated. The aim of the present study was to identify the risk of occult disease from primary parotid salivary malignancies, determine the impact on recurrence and survival, and factors that might contribute to the risk of occult disease.

Methods

Retrospective case-control study of all salivary gland malignancies in a tertiary referral centre between 1998 and 2021 was carried out. Inclusion criteria included salivary gland malignancies of the parotid gland who were treated surgically. Demographic details, presenting symptoms, risk factors, pre-operative TNM staging, operative characteristics including extent of parotidectomy, neck dissection and facial nerve sacrifice, and histological diagnosis details were collected. Post-operative details including facial nerve function, adjuvant treatment, recurrence and survival data was also recorded.

Results

A total of 55 patients were available for final analysis. Mean age of the cohort was 59.7years. The nodal basin was clinically staged N0 in 70.9%. All patients underwent FNA of the parotid gland, and was reported as benign in 20% of cases and malignant in 65.5%. The most common histological diagnosis was adenocarcinoma (29.1%).

A neck dissection was performed in 34 cases (61.8%). There were seven cases of occult nodal disease, 12.7% of the overall cohort. The most common histology of these were adenocarcinoma and adenoid cystic carcinoma. The most common area of occult nodal spread were peri-/ or intra-parotid lymph nodes in 42.8%.

There were a total of 14 patients with recurrences. There was a statistically significant increase in any recurrence for patients with N+ nodal disease (p=0.025).

The overall mean survival of the entire cohort was 139.2 ± 20.1 month. There was no difference in overall or disease-specific survival depending on neck dissection, extent of parotidectomy, T or N-stage or adjuvant radio- or chemotherapy. There was no statistically significant difference in overall or cancer-specific survival between the occult cases and the rest of the cohort (p=0.618 and p=0.855 respectively).

Conclusion

The risk of occult nodal disease in primary salivary gland malignancies is 12.7%, with the most commonly involved nodes being peri-/ intra-parotid. There was a higher risk of recurrence in patients with nodal spread. A consideration should be given to performing an elective dissection in patients with primary parotid malignancies, however a limited nodal dissection could be sufficient.

PO-070 | Early outcomes of normo- and hypofractionated proton re-irradiation in recurrent head & neck tumors

Maciej Pelak [(1)]; Piero Fossati [(1)]; Slavisa Tubin [(1)]; Petra Mozes [(1)]; Ankita Nachankar [(1)]; Astrid Fraller [(1)]; Joanna Gora [(1)]; Marta Mumot [(1)]; Petra Georg [(2)]; Eugen Hug [(1)]

(1) MedAustron Ion Therapy Center (2) Karl Landsteiner University of Health Sciences, Krems

Purpose/Objective

Proton beam therapy (PBT) has shown promising results in salvage re-irradiation of head and neck tumors which recurred after the first course of radiotherapy. The use of moderately hypofractionated regimes may improve patient logistics by shortening the overall treatment time and potentially improve the outcome by applying high dose per fraction to radiation resistant disease. However, data on safety and efficacy of hypofractionated proton therapy in head & neck tumors are limited. We analyzed the outcome of our patients treated with both fractionation schemes.

Material/Methods

Thirty-eight patients treated at our institution with spot-scanning proton therapy between 2017 and 2021 were included. The median age was 61 years (range: 16-88) and the median time between previous radiotherapy and PBT was 4.1 years (range: 0.8 – 28.8). The median dose per fraction/total dose was 2.0 Gy RBE/70 Gy RBE for patients treated with normofractionated PBT (nFx, n = 17) and 3.0 Gy RBE/66 Gy RBE for patients who received hypofractionated PBT (hypoFx, n = 21). Majority of patients (92.1%) had macroscopic disease present and the most common tumor type was squamous cell carcinoma (68.4%). Only 2 patients received concomitant systemic treatment. The patient characteristics are displayed in Table 1.

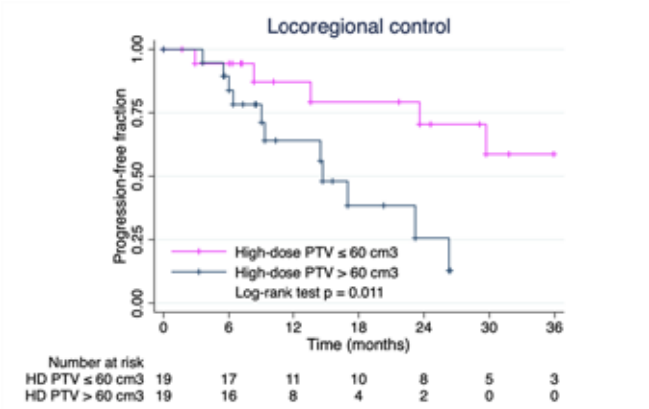
Results

The median follow-up period was 17 months (1.7 – 49.3). The actuarial 1- and 2-year local control was 85.6%/70.2%, regional control was 79.9%/64.1%, progression-free survival was 55.8%/34% and overall survival was 68.3%/51.9%, respectively. The dominating pattern of failure was local progression within the irradiated field (in 9/17 cases of tumor progression, 52.9%), followed by progression in the head & neck region outside of irradiated field (7/17, 41.1%). A significant trend towards better local control in hypoFx patients could be observed (actuarial 2-year local control for hypoFx 85.7 vs 60% for nFx, HR = 0.15, 95%CI: 0.02-0.86, p = 0.034). No differences between nFx and hypoFx for other survival endpoints were observed. In risk factor analysis we identified high-dose PTV volume as the only significant risk factor for locoregional progression with 60 cc identified as stratifying threshold. Actuarial 2-year locoregional control for the group below this threshold was 71.6% compared to 27.3% for the group above (p = 0.01) (Figure 1). No significant risk factors for other endpoints were identified.

The most common serious adverse events (CTCAE Grade ≥3) were in-field soft tissue necrosis and infections, seen in 9 (23.6%) of patients. No differences in acute and late toxicity between nFx and hypoFx were observed.

Conclusion

Our early outcomes data indicate that re-irradiation with proton beam therapy is a valuable option for patients with locally recurrent head and neck tumors after previous radiotherapy. Hypofractionated schemes appear to result in excellent local tumor control rates superior to normofractionated ones. Late toxicity, failures outside of irradiation field as well as outcome in large tumors require further improvements in treatment strategy.



Parameter	No. (%)	Median (range)	No. (%)	Median (range)
	Normofractionated (n = 17)		Hypofractionated (n = 21)	
Age		52.1 (16.3-78.7)		64.7 (40.6-87.6)
Sex				
Male	5 (29.4%)		9 (42.9%)	
Female	12 (70.6%)		12 (57.1%)	
Tumor location				
Nasal cavity and paranasal sinuses	8 (47.1%)		5 (23.8%)	
Oropharynx	6 (35.3%)		6 (28.6%)	
Nasopharynx	2 (11.8%)		7 (33.3%)	
Other	1 (5.9%)		3 (14.3%)	
Histology				
Squamous cell carcinoma p16(+)	3 (17.7%)		4 (19.1%)	
Squamous cell carcinoma p16(-)	9 (52.9%)		10 (47.6%)	
Adenocarcinoma	2 (11.8%)		2 (9.5%)	
Other	3 (17.7%)		5 (23.8%)	
High-dose PTV volume in cm^3		62.2 (11.4-238.9)		52 (12.1-222.3)
Low-dose PTV volume in cm^3		158.2 (54.9-309.2)		90.9 (51.7-591.3)
Total dose in Gy RBE		70 (60-72)		66 (54-67.5)
Dose per fraction in Gy RBE		2.0 (1.8-2.3)		3.0 (2.7-3.0)
Overall treatment time in weeks		7 (6-8)		4.4 (3.6-5)

PO-072 | Underreported consequences of oral cavity cancer treatment: a qualitative study of intimate matters

Dominique [1]; la Smeele [1]; da Young-Afat [2]; k Van Sluis [1]; le Smeele [1]

(1) Netherlands Cancer Institute Amsterdam (2) Amsterdam University Medical Center, location VUmc

Keywords

Oral cancer, quality of life, onco-sexology, qualitative research.

Purpose/Objective

The oral cavity is essential for swallowing, eating and talking. Treatment in this area can lead to functional impairments and changes in appearance, affecting patients' identity, intimacy, sexual functioning, and thus their perceived quality of life. Although professional support may help patients cope with these consequences, such intimate subjects are not regularly discussed by the treating physicians. We aim to explore if, and to what extent, patients experience changes in their identity, intimacy, and sexuality during and after curative-intent treatment for oral cavity cancer.

Material/methods

A total of fifteen patients treated for oral cavity cancer within our center in the past four years are scheduled to participate in qualitative interviews. After open coding, the retrieved constructs and themes will be visualized in a concept indicator model and analyzed thematically.

Results

So far, ten patients with a mean age of 58 years (range 25 - 70 years) were interviewed. Concerns regarding intelligibility, scars in the neck, and doubts whether to inform colleagues, influenced patients' identity. To varying extent all patients experienced changes in their intimacy and sexual functioning, mostly tempo-

rary. Although there was a lack of interest in being sexually active up to 8 weeks after treatment, the desire for intimacy seemed unaffected. A removable prosthesis, focus on survival, and doubts regarding normal healing had a negative effect on returning to normal life after treatment.

Conclusion

Consequences of treatment for oral cavity cancer on patients' intimacy and sexual functioning are rather unexplored domains. This study aims to explore the impact of treatment on sexual functioning and quality of life. By openly discussing these domains, health care professionals can normalize patients' issues, and where necessary refer them to experts.

PO-073 | Hematological Malignant Disease Presenting as Oral Lesions

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(1) CENTRO HOSPITALAR UNIVERSITÁRIO LISBOA NORTE, E.P.E.

Keywords

Mouth - Hematologic Neoplasms

Purpose/Objective

Hematologic malignancies contribute to about 9% of cancer cases diagnosed per year, with a high mortality burden associated. Underlying oral manifestations can be present, representing the first sign in the diagnosis of hematopoietic diseas. Heand and Neck Specialities must be aware of these uncommon manifestations that serve as a milestone in early diagnosis and therefore effective treatment of these patients.

Material/Methods

Our study retrospectively searched for hematological malignancies presenting with oral manifestations from 2010 to 2022, confirmed by oral cavity biopsy in the Stomatology Department of Centro Hospitalar Universitário Lisboa Norte. We excluded cases with diagnosis already known by other means or confirmed by cervical lymph biopsy.

Results

As a result, a total of 15 cases were included in the study. The sample included 6 males (40%) and 9 females (60%), ranging from 4 to 89 years of age. The most frequent diagnosis was Diffuse Large B Cell Lymphoma (7 cases – 47%), followed by Plasmablastic

Lymphoma (3 cases – 20%) in HIV positive patients. 87% of the patients presented with intra-oral swelling, affecting more frequently the mandible than the maxilla (9 cases - 60% vs. 6 cases - 40%, respectively).

Conclusion

Awareness of early-stage symptoms of hematologic malignancies can help improve mortality and morbidity of the patients. Oral cavity manifestations can account for the first symptom in some cases. Therefore, Head and Neck Specialities should be involved in order to provide most effective and precocious diagnosis and consequent treatment.

PO-075 | A retrospective single-center study of free flap transfer for head and neck reconstruction

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Keywords

Free tissue transfer, head and neck surgery, microsurgery, microvascular surgery, reconstruction.

Introduction

Objective of this presentation is to show outcomes of free flap reconstruction after head and neck tumor resection in one institution with low volume of annually raised free flaps.

Materials and methods

Data from all the patients undergoing free tissue transfers for head and neck cancer between 2011 and 2022 at Head and neck department of University Hospital for Tumors, University Hospital Center Sestre Milosrdnice in Zagreb were retrospectively analysed. Aim was to make statistical analysis, measure free flap failure rate and free flap-related complications.

Results

From 17th May 2011 to 30th June 2022, there were 102 patients who underwent free flap transfer surgeries (mean 8,50 per year) after head and neck carcinoma resection. There were 9 events of flap necrosis, and one case of partial flap necrosis which makes overall free flap success rate of 90,2%. Defects in oral cavity after tumor resection made 60,8% sites for free flap transfer, followed by oropharyngeal defects (30,9%). Most common free flap used for reconstruction was radial forearm flap (74,5%), followed by an-

terolateral thigh flap (15,9%). Most frequent complications were haematoma in the neck and orocutaneous fistula.

Conclusion

This presentation concludes that even institution with one microvascular team and low volume of annually raised free flaps for head and neck cancer reconstruction can produce positive results which are in correlation with high volume centers regarding success rate and complications.

PO-076 | National improvement of waiting times through the Dutch Head and Neck Audit

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(1) Erasmus MC Rotterdam (2) NKI-AvL, Amsterdam

Keywords

Auditing, Quality registry, waiting times

Purpose/Objective

In 2014, a quality registry for head and neck cancer in the Netherlands was established: the Dutch Head and Neck Audit (DHNA). All Dutch patients diagnosed with primary head and neck cancer are enrolled, with national coverage since 2019. The DHNA aims to transparently assess and improve the quality of care. For this study we examined how waiting times evolved since the start of the registration.

Material/methods

To assess waiting times, we determined the care pathway interval (CPI), time-to-treatment interval (TTI), and CPI/TTI-indicators. The CPI was defined as the number of days from the first visit to an HNOC or preferred partner hospital to start of curative treatment in that hospital. The TTI was defined as the number of days between histopathological biopsy and the start of curative treatment. For the CPI/TTI-indicators, the percentage of patients that started treatment within 30 days was calculated.

The Dutch national quality standard is set at a 30-day CPI for 80% of the patients. All data was extracted from the DHNA database from 2015 to 2021 for all 14 participating hospitals and the nation as a whole (benchmark).

Results

The benchmark median CPI/TTI improved from 37/37 days (2015) to 26/33 days (2021). Correspondingly, the benchmark CPI/TTI-indicator increased from 39%/36% (2015) to 67%/42% (2021). Outcomes for all hospitals improved, with three hospitals exceeding the national quality standard from 2019 onward.

Conclusions

Waiting times improved gradually over time, with three hospitals exceeding the quality standard of a 30-day CPI for 80% of the patients. On hospital-level, process improvement plans have been initiated. Systematic registration, audit and feedback of data promotes further optimization of quality of care.

PO-077 | Neoadjuvant Leukocyte Interleukin Injection (LI) extends locally advanced SCCHN overall survival

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(1) CEL-SCI Corporation (2) Boston Biostatistics Research Foundation (3) Ergomed plc (4) Semmelweis University Budapest (5) Dnipro State Medical University, Dnipro (6) Military Medical Academy, Clinic Maxillofacial Surgery, Belgrade (7) N.N. Aleksandrov National Scientific and Practical Center for Oncology and Medical Radiology of Belarus, Minsk (8) Chang Gung Medical Foundation-Kaohsiung Branch Chang Gung Memorial Hospital, Niaosong (9) Centrum Onkologii im. Prof. F. Lukaszczyka, Bydgoszcz (10) Markusovszky Lajos Teaching Hospital,Department of Oto-Rhino-Laryngology and Head –Neck Surgery, Szombathey (11) McMaster University; St-Joseph's Health Care, Hamilton (12) Colorado Head and Neck Specialists, Denver (13) Shin Kong Wu Ho-Su Memorial Hospital, Taipei

Background

The 3-week pre-surgery peri-tumoral/peri-lymphatic administration of an investigational pro-inflammatory cytokine complex biologic (LI) with CIZ (single low dose cyclophosphamide IV-bolus, 300 mg/m2), indomethacin (po 25mg tid) and Zinc as multivitamins (po 15-45mg Zinc)+Standard of Care (SOC) to oral and soft-palate SCCHN subjects, resulted in early response (CRs/PRs) prior to surgery [RECIST] (confirmed at surgery by pathology) and significantly prolonged OS in the NCCN-defined Lower risk for recurrence (LR) intent to treat (ITT) population vs SOC alone (surgery+RTx).

Efficacy and safety outcomes presented for all LR treated with radiotherapy only (RTx). These data are from the pivotal study (IT--MATTERS; Clinicaltrials.gov NCT01265849). No safety issues were noted for LI in previous phase 2 studies.

Methods

Subjects (923 ITT; 352 LR received RTx) meeting protocol entry criteria (AJCC Stage III/IVa OSCC and soft-palate, treatment naïve) were randomized 3:1:3 to treatment arms LI (+/- CIZ) + SOC or to Control (SOC alone). LI treated received ½ dose 200IU peritumorally ½ dose daily peri-lymphatically x5/week for 3-weeks before surgery. All LR subjects were to receive RTx (per NCCN Guidelines) post-surgery. Follow-up was comparable (56-57 months median) for each treatment group.

Results

Pre-surgery responders (PSR; CR/PR) in ITT LR LI RTx treated (+/- CIZ) groups were 16.5% (32/194) vs 0% (0/158) for ITT LR SOC RTx. Early response lowered death rates from 48.7% (77/158) for ITT LR SOC RTx (non-responders) in contrast to 15.6% (5/32) for ITT LR LI RTx responders (two-sided Fisher Exact p=0.0007) to 43.8% (71/152) for ITT LR LI RTx non-responders (carryover evidence). Proportional hazard ITT LR RTx treated hazard ratio (HR) was 0.70 (95% CI: [0.49-1.00]) favoring LI+CIZ+SOC vs SOC (two-sided p=0.047 controlling for tumor stage, tumor location and geographic region). An accelerating absolute OS advantage in ITT LR RTx for LI+CIZ+SOC vs SOC was 2.8%/8.3%/15.6% at 36/48/60 months (M), representing 72.3% vs 69.5% (36 M); 67.6% vs 59.3% (48 M), and 65.3% vs 49.7% (60 M) with a 33.5 M median OS advantage (101.7 M [LI+CIZ+SOC] vs 68.2 M [SOC]; 49.1% prolongation). The corresponding PFS advantage was 8.4% (60 M) for LI+CIZ+SOC vs SOC; the HR was 0.81 (95% CI: [0.58 - 1.13]) in support of multi-dimensional efficacy.

Percent treatment emergent adverse event incidences (TEAE System Organ Class) were comparable among all treated groups. No excess adverse events were reported for LI RTx vs SOC RTx during the study.

Conclusions

LI neoadjuvant immunotherapy followed by NCCN-guided surgery+RTx enabled favorable long-term efficacy outcomes (OS

and PFS) including CRs/PRs prior to surgery. No safety issues were attributed to LI. ITT LR RTx LI+CIZ+SOC absolute OS advantage over SOC increased over time; the 0.70 HR represents a 43% median survival extension in a population without any new therapy options in decades.

First author discloses financial interest.

PO-078 | Prognostic value of inflammatory parameters in early stage glottic carcinomas treated with surgery.

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Introduction

With the growing interest in the study of prognostic markers in head and neck squamous cell carcinoma (HNSCC), biomarkers have been developed that are easy to obtain from peripheral blood counts and that guide decision-making in daily practice. These include the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and the systemic inflammation index (SII). Several studies have assessed their implications many solid tumors including HNSCC, where high pre-treatment values have been found to be associated with worse prognosis in patients undergoing surgery or chemoradiotherapy.

Objective

Most studies to date include heterogeneous series with different treatments and mix tumors from different sublocations. In our study we evaluated the usefulness of these prognostic scoring systems with respect to survival outcomes in a homogeneous sample of patients with early stage glottic tumors treated surgically.

Material and methods

We selected a sample of 201 patients with glottic squamous cell carcinoma treated with transoral laser surgery at our centre between 1998 and 2019. Clinical variables and values of pre-treatment haematological parameters, obtained from the pre-operative analysis, were collected. NLR, PLR and SII ratios and their

optimal cut-off points were obtained by calculating ROC curves, using death by tumor as a status variable.

Results

191 of the patients were male and 10 were female, and 186 of them had a history of tobacco use. 180 were classified as stage I and 21 as stage II, and the surgical margins were involved in 8% of the cases. 53 patients (26%) had local recurrence, 2 (1%) regional, 6 (3%) local and regional, and 5 (2%) locoregional and distant metastases. A high NLR (above the cut-off point of 2.44) was significantly associated with lower disease-specific survival (DSS) (p=0.03). With respect to PLR (cut-off point 99.7), an association with tumour size was observed, with patients with high PLR having a larger tumour size (p=0.023), but no prognostic value in DSS. High SII (cut-off point 533) was significantly associated with recurrence (p=0.009) and worse DSS (p=0.037). None of the three ratios were associated with overall survival. In multivariate analysis (including stage, degree of differentiation, surgical margin, NLR, PLR and SII) poor tumor differentiation (HR=2.27, 95%CI=1.06-4.9, p=0.036) and high NLR (HR=3.71, 95%CI=1.4-9.6, p=0.007) had independent association with worse DSS.

Conclusions

The inflammatory response parameters assessed are easy to obtain and at no additional cost. There is growing evidence of their clinical utility given their prognostic value in multiple published series. In our sample, the prognostic utility of the NLR and SII for DSS is evident, with the NLR being an independent prognostic factor with greater prognostic ability than tumour stage.

PO-079 | A multimodal protocol combining Tilmanocept with ICG for SLNB in early-stage oral cancer

Andrea Galli [1]; Leone Giordano [1]; Stefano Bondi [2]; Carla Canevari [1]; Marco Familiari [1]; Luigi Gianolli [1]; Mario Bussi [1]

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Keywords

Tilmanocept; indocyanine green; oral cavity cancer.

Purpose/Objective

Sentinel lymph node biopsy (SLNB) is considered as viable alternative to elective neck dissection for management of cN0 oral cavity cancer. However, some difficulties were detected in sentinel lymph node (SLN) identification because of the so-called "shine-through radioactivity". We assessed the feasibility and the potential strengths of combining 99mTc-Tilmanocept with indocyanine green (ICG) fluorescence lympho-angiography in a dedicated multimodal protocol for SLNB in T1/T2N0 SCC to evaluate the synergistic role of these two tracers in such a critical anatomical subsite.

Material/methods

A left tongue margin cT1cN0 SCC was submitted to transoral glossectomy and SLNB. Preoperative lymphoscintigraphy with 99mTc-Tilmanocept was performed before surgery with SPECT/CT assessment (Fig. 1). Intraoperative lympho-angiography with ICG was used to enhance the accuracy of radio-guided SLNB procedure through a high-resolution infra-red display system.

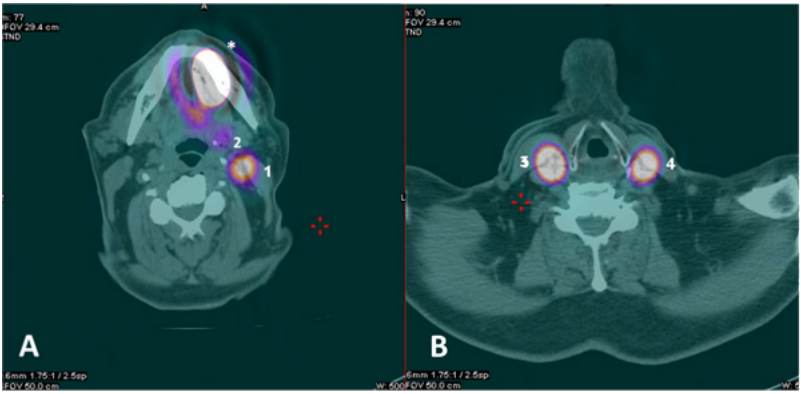
Results

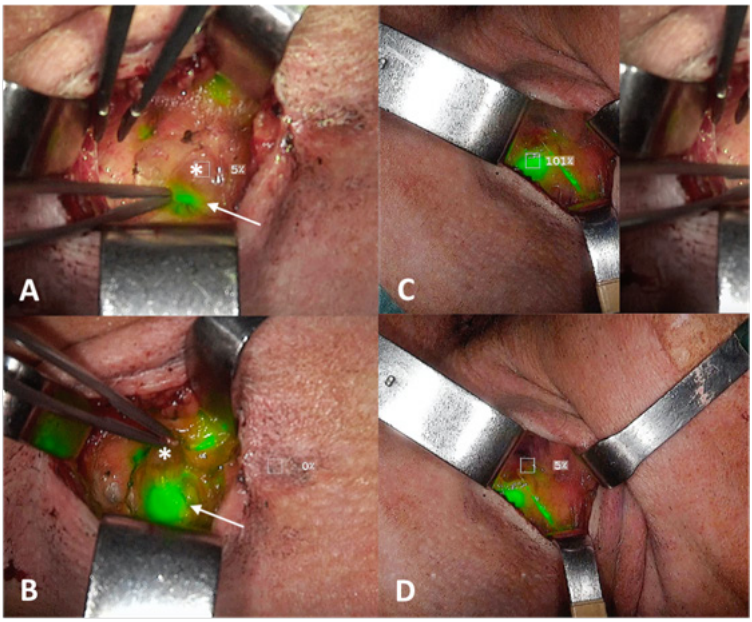
One SLN was identified and removed at left IIA, left III and right III nodal hotspots (unnecessary dissection of parasentinel nodes:

1/4, 25%) (Fig. 2). At permanent sections, a moderately-differentiated SCC was proved (depth-of-infiltration: 3.5 mm) with a micrometastasis in left IIA SLN. A completion left neck dissection was performed 3 weeks later; no other nodal metastases were found (pT1 pN1(mi)). Adjuvant therapies were not advised. The patient is without evidence of disease at 38-month follow-up.

Conclusion

The receptorial nature of 99mTc-Tilmanocept together with the optical guidance of ICG lympho-angiography with such a high--resolution infra-red display system may increase the accuracy of SLNB in T1/T2N0 oral cancer providing the appropriate sensitivity and ease of learning for its adoption on a wider scale, even for the more critical anatomical subsites.

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PO-081 | The impact of the tumour microenvironment on head and neck SCC cell viability and radiosensitivity.

Anjali Chander *[1]; Aize Pellon Rodriguez [2]; Victoria Butterworth [1]; Teresa Guerrero Urbano [1]; Anthony Kong [1]; Mary Lei [1]; Imran Petkar [1]; Tony Ng [2]; David Moyes [2]; Miguel Reis Ferreira [1]*

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Purpose/Objective

Head and neck squamous cell carcinoma (HN-SCC) is an immunosuppressive disease with functional impairment of tumour-infiltrating lymphocytes including natural killer (NK) cells, which are the main effector cells in anti-tumoural immunity and are critical in cancer immune surveillance. 2D co-culture models can be utilised to examine inter-relationships between different groups of cells in the tumour and normal tissue microenvironment, such as between cancer and immune cells. These cell culture models are also often used to study the effects of radiation in cancers and normal tissues with the purpose of improving radiobiological understanding and in turn, how to optimise treatment. However, in these settings, radiation is commonly delivered using orthovoltage irradiators in single dose fractionation schedules, which is not reflective of clinical radiotherapy applications. We have developed a 2D co-culture model of HN-SCC and NK cells using a clinically operational linear accelerator and evaluated the impact of NK cells on radiation-mediated cancer cell death.

Materials/Methods

The 2D co-culture model consists of human buccal SCC cells (TR146 cell line) and human leukaemic NK cells (KHYG-1 cell line) added either before or after irradiation at 5:1 to 10:1 NK:HN-SCC ratios. Tumour cell death was assessed using an ATP-based cell viability assay at D4-6 post-irradiation. Irradiation was carried out using a clinically-operational linear accelerator at a range of doses inclu-

ding 2Gy, 5Gy and 10Gy in a single fraction. Fractionated radiation regimens were also carried out including 6Gy over 3 fractions (2Gy per fraction) and 15Gy over 3 fractions (5Gy per fraction). Significance was assessed with the ANOVA statistical test.

Results

The addition of NK cells prior to irradiation contributed more significantly to radiation-mediated HN-SCC killing, at effector to target ratios of 5:1 ($p<0.0001$). SCC viability was significantly reduced in 5:1 and 10:1 groups compared with the TR146 alone group irrespective of single fraction radiation dose ($p<0.0001$). There was no significant difference in SCC viability between the 5:1 and 10:1 groups. Additionally, there was no significant difference in SCC viability with the different single fraction radiation doses within 5:1 group and the 10:1 group. With fractionated irradiation, SCC viability was significantly reduced in the 5:1 group compared with the TR146 alone group at both 6Gy and 15Gy ($p<0.0001$). There was no significant difference in cell viability between the TR146 groups irradiated with 6Gy or 15Gy. There was significantly reduced SCC viability in the 5:1 group at 6Gy over 3 fractions compared with 15Gy over 3 fractions ($p=0.008$).

Conclusion

We demonstrate that NK cells increase radiation-mediated cell death of radioresistant HN-SCCs. Furthermore, our findings suggest that NK cells present in the tumour microenvironment prior to irradiation are more integral to radiation-mediated SCC cell death than NK cells recruited to the tumour post-irradiation. This co-culture model will also enable the study of interactions between cancer, NK cells and the wider tumour micro-environment.

PO-082 | High-accuracy nodal staging of head and neck cancer with USPIO-enhanced MRI

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Objective

Ultrasmall superparamagnetic iron oxide (USPIO)–enhanced magnetic resonance imaging (MRI) is a potential diagnostic tool for lymph node assessment in patients with head and neck cancer. In this study, MRI signal intensity patterns of lymph nodes are (node-to-node) correlated to their histopathology to develop a new USPIO-enhanced MRI reading algorithm that can be used for nodal assessment in head and neck cancer patients.

Materials and methods

Ten head and neck cancer patients underwent in vivo USPIO-enhanced MRI before neck dissection. An ex vivo MRI of the neck dissection specimen was performed for precise co-registration of in vivo MRI with histopathology. Normal clinical histopathological workup was extended with meticulous matching of all lymph nodes regarded as potentially metastatic based on their in vivo MRI signal intensity pattern. On the basis of histopathology of resected nodes, in vivo MRI signal characteristics were defined separating benign from malignant lymph nodes.

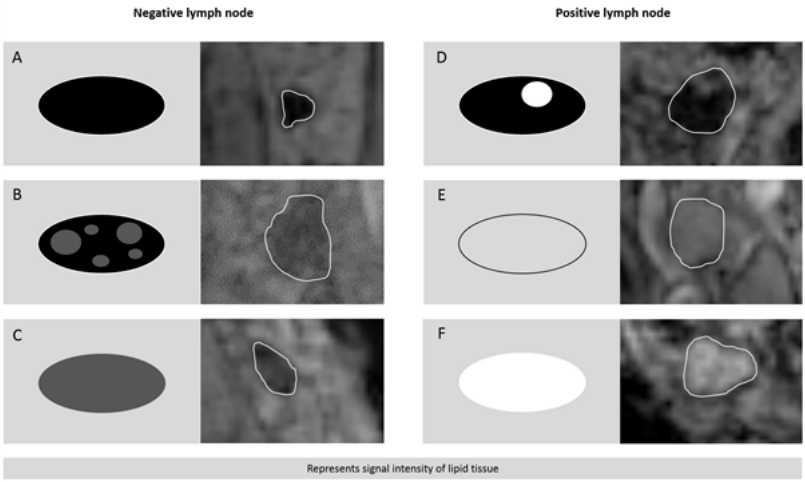
Results

Fifteen of 34 node-to-node correlated lymph nodes with remaining signal intensity on T2*-weighted MRI were histo-pathologically metastatic and 19 were benign. Radiological analysis revealed that metastatic lymph nodes showed equal or higher MRI signal intensity when compared with lipid tissue on T2*-wei-

ghted MGRE sequence (15/16 lymph nodes; 94%), whereas healthy lymph nodes showed lower (17/19 lymph nodes; 89%) or complete attenuation of signal intensity (273/279; 98%) when compared with lipid tissue on T2*-weighted MGRE. Histopathology of all resected specimens identified 392 lymph nodes. Six lymph nodes (in 4 patients) with (micro)metastases were missed with in vivo MRI, with a median metastatic size of 2 mm.

Conclusions

We developed a new reading algorithm to differentiate benign from malignant lymph nodes in head and neck cancer patients on the basis of their appearance on high-resolution T2*-weighted USPIO-enhanced MRI. Next step involves the internal validation of our reading algorithm with an independent head and neck radiologist. This validation is ongoing and we hope to present first results at ECHNO.



PO-083 | Multi-centric study on risk of complication for salvage neck dissection in head and neck recurrences

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Aims

Isolated regional recurrence (IRR) of head and neck malignancies are quite unusual, representing only 5.2% of total relapses. Surgery represents the gold standard of treatment in these patients and guarantees better survival compared to single local, concomitant loco-regional recurrences, as well as distant metastases onset; nevertheless, the high risk of surgical complications could discourage many surgeons from offering this treatment. The current evidence regarding complications after salvage neck dissection (ND) for IRCCs without concomitant local excision is still lacking.

Material and Methods

We performed a multi-centric retrospective study on 64 patients who underwent salvage ND for IRR in three Italian institutes between 2008 and May 2020.

Objectives

The aim of this study is to compare the incidence in complication rates of salvage ND after primary surgery, radiotherapy and chemoradiotherapy and to describe presentation and survival in IRRs.

Results

Fifteen patients experienced postoperative complication (23.44%) and difficult dissection was reported in 33 patients (51.56%). Acci-

dental vascular ligations or nervous injury during surgery were rarely detected (1.56-3.13%). None of the variables analysed were statistically significant in predicting the risk of complications, disease-free survival (DFS) or overall survival (OS).

Conclusions

The incidence of complications after salvage ND for IRR is higher than after primary surgery but we failed to record a difference according to primary treatment.

PO-084 | Transcervical-transparotid approach to the tumors of the parapharyngeal space

Dr. Darwin[(1)]

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Keywords

Parapharyngeal space tumors; surgery.

Purpose/Objective

Parapharyngeal space (PPS) tumors are rare with an incidence of nearly 0.5% of all head and neck tumors. About 70-80% of these are benign, having mostly neurogenic or salivary gland origins. Pleomorphic adenomas and paragangliomas are the most frequently encountered PPS tumors of salivary gland and neurogenic origin respectively. High index of suspicion is required to diagnose these tumors preoperatively so that appropriate surgical planning is possible. The main objective of this study was to determine the tumor size and locations which were amenable to be resected by the transcervial- transparotid approach.

Material/methods

A retrospective review of 12 patients. Patients were evaluated following a detailed clinical examination. Contrast enhanced computed tomography (CECT) and MRI scans were used to confirm the location and size of the tumor as a preoperative diagnosis. The important considerations included, tumor volume, distance from the skull base and the extension of the tumor into the prestyloid compartment of the parapharyngeal space, surgical challenges and histopathology. In particular, the following aspects were evaluated: tumor shape, tumor margin, tumor association with major vasculature, surrounding tissue and deep lobe of the parotid gland, as well as pre or post-styloid location.

Results

The study included 8 females (66.67%) and 4 males (33.33%) with the mean age at presentation was 33.3 years (most common age range = 20 to 40 years). The most common presenting complaint was the presence of a unilateral neck mass (83.33%) while one patient presented with hoarseness, dysphagia, diplopia and hearing loss and ear bleed in another patient. The mean distance of the tumor from the base of the skull was found to be 2.78 cm. The average tumor size was 3.72 x 2.63 x 3.42 cm. Histopathology confirmed diagnosis of schwanomma in six cases, carotid body tumor in three cases, one case of ganglioneuroblastoma, pleomorphic adenoma, warthin's tumor respectively. The nerve of origin was found to be vagus in two and cervical plexus in four cases. There was significant discrepancy in the radiological prediction as far as the nerve of origin was concerned.

Conclusion

Parapharyngeal space tumors can be successfully removed transcervical-transparotid precluding the need mandibulotomy. Current imaging modalities cannot reliably predict the origin of neurovascular neck swellings. Fine needle aspirartion may be associated with poor operative planes especially if done repeatedly.

PO-085 | Root cause analysis of the delay in head and neck cancer treatment

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Keywords

Head and neck cancer; Treatment delays.

Purpose/Objective

To investigate factors which lead to delay in head and neck cancers (HNC) diagnosis and treatment and to study time periods of the categorized delays concerning different implicated parameters.

Material/methods

This is a prospective study including all biopsy proven cases of head neck malignancy. Patients were interviewed and information was taken regarding the demographic and epidemiological factors i.e. age, gender, locality, occupation, per capita income, education and reachability of the health care centre and details of illness and related factors that would contribute to the measurement of delays was filled for each patient. The delays were categorised as Patient delay (Time is taken from the appearance of initial symptom till first ENT clinic visit), Diagnostic delay (Time taken from the day of 1st ENT visit to the day of histopathological diagnosis) and Treatment delay (Time taken from the decision of confirmatory treatment to commencement of initial confirmatory treatment).

Results

In our study, out of total 195 patients, 140 patients were included in the study. 55 patients were excluded from the study because of incomplete records and patients lost to follow up. Cumulative

delay in our study including all 140 cases came out to be 206.55 days with Patient delay, Diagnostic delay and Treatment delay being 98.54 days, 39.46 days and 68.55 days respectively.

Factors leading to different categorized delays:

1. Patient delay
    - Neglect
    - Myths
    - Dependents in the family
    - Residence outside Jodhpur district
    - Rural locality
    - Lower socioeconomic status
    - Days lost in non-ENT visits and referrals
2. Diagnostic delay
    - Operation theatre proceedings for invasive biopsies
    - Repeat biopsies
    - Biopsy reporting time
    - Radiology reporting time
    - Lost to follow up
    - Low suspicion of malignancy at the time of presentation.
3. Treatment delay
    - Waiting time for surgery/ CTRT
    - Monetary challenges
    - Social stigma
    - Delay in pre-anaesthetic checkup clearance
    - Overlapping patient factors.

Conclusion

Head and neck cancers pose a major burden on our society and its efficacious management is the need of the hour. The quality of life along with the overall survival is largely depen-

dent on the delivery of timely clinical care and attention. There are many factors at the level of the patient, hospital facilities and locoregional constraints causing a delay in treatment delivery. These delays are major targets for modulation and are in the domains of the patient, specialist care and healthcare facilities and infrastructure.

PO-092 | Local flap reconstruction of Tongue cancer defects

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Keywords

Melolabial flap, Facial artery Myomucosal flap, Submental flap, Infrahyoid flap

Objective

Resection of tongue carcinoma leads to complex defects, which cause significant changes in functional outcomes and affect patients' quality of life. Patient clinical factors and defect characteristics are important deciding factors when choosing a reconstructive option. The present study aims to retrospectively review the various types of local flaps used for reconstruction of tongue defects with their indications and complications at our Institute.

Material and Methods

The current study reviews cases of tongue cancers treated surgically and reconstructed with local flaps at our Institute between 2019 to 2020. The patient's demographical, clinical, pathological, and treatment details were recorded.

Results

In this study, we evaluated 34 patients with tongue cancers. The mean age of the population was 51 years (Range: 29-73). The male-to-female ratio was 6:1 (29:5). Majority of the patients were T2 (20, 59%), 10 were T3 (10, 29%), and four patients were T4 (12%). Melolabial flap (MLF) was the most common flap done in 25 (74%) patients, Supraclavicular flap (SCF) in 1, Facial artery myomucosal flap (FAMM) in 5, Submental flap (SMF) in 2 and Infrahyoid flap (IHF) in 1 patient. Seventy-five per cent (25) of patients were node negative.

Fifteen patients (44%) had marginal mandibular nerve paresis, and two-thirds recovered in 6 months. None of the MLF, SMF or IHF had flap necrosis. The SCF patient had complete flap necrosis, and a redo free anterolateral thigh flap (FALT) was done. One FAMM had partial, one had complete flap loss, and the remaining tongue defects were left raw. Three patients with MLF who had collection and infection at the donor site were managed conservatively. Oral feeding was started in most of the patients (81%) between 1- 2 weeks.

Six-month functional evaluation was suggestive of good outcomes. While most of the patients (91%) had a Leipzig and Pearson Scale of grade 2 or less, 9% of patients had a grade 3 score. The modified Water Swallow test was suggestive of the ability to swallow well in 88% of patients. Three per cent of patients had mild aspiration, and 9% had severe dysphagia or aspiration. Most patients had restricted (68%) Tongue range of movement (ROM) and mild to moderate Oropharyngeal dysphagia (78%).

The indications for different flaps depended upon the defect size and patient characteristics. FAMM was used to reconstruct less than hemiglossectomy defects with good mouth opening and no submucous fibrosis. MLF was used for hemiglossectomy/extended glossectomy defects. Although the facial scar became inconspicuous after a few months, females did not prefer it. SMF was used for anterior two-thirds tongue defects for low-grade tumours. The incision was concealed below the chin but was not preferred in males due to hair growth on the flap.

IHF had a tripoint with a vertical incision, and a small area was available for reconstruction. It was done for the floor of mouth (FOM) and ventral tongue defect due to the limited reach of the flap as per the position of the superior thyroid artery. The supraclavicular flap did provide a large area for reconstruction. However, there was complete flap necrosis.

Conclusion

Local flaps are a good option for reconstructing medium size tongue defects. The donor site morbidities are minimal. A careful selection of local flaps depending on the defect size and patient characteristics can provide an optimal reconstruction in selected cases.

PO-094 | Primary tonsillar lymphomas – a 10 years retrospective institutional analysis

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(1) CENTRO HOSPITALAR E UNIVERSITÁRIO DE SÃO JOÃO E.P.E.

Keywords

Tonsillar lymphomas; non-Hodgkin lymphoma; palatine tonsil malignancies

Background / Objective

Non-Hodgkin lymphoma of Waldeyer's ring constitutes a small percentage of palatine tonsil malignancies and its precise etiology remains unknown.

Lymphomas are the second most common malignancy of the head and neck and the majority of the extranodal lymphomas in this region are located in the palatine tonsil. Most of these lymphomas are of B-cell origin, with intermediate to high-grade histology.

This study aims to analyse patients diagnosed with primary tonsillar lymphoma (PTL) in our institution, in terms of clinical manifestations, type of lymphomas, treatment and prognosis.

Methods

Retrospective evaluation of patients with a diagnose of PTL in our institution from 01/01/2012 to 31/12/2021. Patients' clinical data regarding age, gender, ECOG performance status (PS), lymphoma's histology, treatment and response to treatment was collected. Progression-free survival (PFS) and overall survival (OS) rates were analysed. Statistical analysis was done using IBM®SPSS® Statistics® V27.

Results

12 patients with PTL were selected: 8 (67%) males and 4 (33%) females; median age of 63.5 years (range, 38-81 years). All of these patients had ECOG PS 0-1 and cardiovascular comorbidities were the most frequent (42%).

Only 3 (25%) patients had B symptoms and most of the PLT were diagnosed at stage I-II (58%). Five (42%) patients had a diffuse large B-cell lymphoma, 2 (17%) a high-grade B-cell lymphomas with MYC rearrangement, 2 (17%) a mantle cell lymphoma (blastoid variant), one (8%) a plasmablastic lymphoma, one (8%) a peripheral T-cell lymphoma and another a small lymphocytic lymphoma. Regarding 1st line treatment, R-CHOP was the most frequent chemotherapy scheme used (33%) followed by BURKIMAB (18%), R-daEPOCH (8%) and R-HCVAD (8%). Four (33%) patients were treated with other drugs.

More than half of patients (58%) had a complete response to treatment, 2 (17%) had a partial response/stable disease and other 2 (17%) had disease progression (DP). It was not possible to evaluated the response to treatment in one case. The 2 patients that had DP did ESHAP as 2nd line treatment, but autologous stem cell transplant was not performed due to disease progression.

Hematologic toxicity was the most common toxicity event, occurring in 4 (33%) patients (grade 2 and 3 events).

The median time of follow up was 60.5 months (range, 3-105 months). Six (50.0%) patients died, five due to disease progression. Median PFS was 65 months (IC 95%: 30.5-99.4) and median OS was 65 months (IC 95%: 60.3-69.8).

Conclusions

In this sample, patients with PTL had low ECOG PS and most of them presented with localized disease. A considerable number of aggressive lymphomas were identified. However, most patients

had a complete response to treatment, few toxicity events and a good OS/PFS.

Patients with disease progression have bad prognosis, since there seems to be a lack of effective 2nd line therapeutics to treat these aggressive lymphomas.

PO-095 | The use of thoracic skeletal muscle for sarcopenia and outcome evaluation in head and neck cancer

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Purpose

The evaluation of skeletal muscle (SM) in patients with head and neck cancer (HNC) has gained momentum in the last decade. Low SM, quantified with computed tomography (CT) images as skeletal muscle index (SMI), is known as CT-defined sarcopenia. The presence of sarcopenia in this patient population has been demonstrated to be a poor prognostic indicator, independent of weight or nutritional status. The most widely used method assesses SM in an axial slice of a CT scan at the level of the third lumbar vertebra (L3), however, this is not visible in a head and neck scan. Therfore, we used alternate SM measures at the second thoracic vertebra (T2). The aim of this study was to determine T2-SMI cut-off values for sarcopenia in patients with HNC, and investigate the impact of low T2-SMI on overall survival (OS), and weight loss during radiotherapy.

Materials and Methods

All adult patients with newly diagnosed HNC (oropharynx, larynx, hypopharynx, nasopharynx, oral cavity) who had a diagnostic PET-CT or radiotherapy planning CT scan at our facility were included. SM was analysed at T2, and a predictive formula was applied to estimate SM at L3. Patients were classified by sarcopenia status, stratified by BMI and sex. T2-SMI values were used to establish corresponding cut-off threshold values for sarcopenia with Receiver Operator Characteristic (ROC) tests for each group (Females; Males BMI<25kg/m2; Males BMI ≥25kg/m2). The T2-SMI cut-off value

using lowest quartile of the cohort was also investigated. Kaplan--Meier method was used for OS analysis based on sarcopenia status and T2-SMI, and compared using the Log-Rank test. In patients who completed radiotherapy (RT) (± other modalities), percentage weight loss during RT was compared with SM status.

Results

A total of 361 patient scans were analysed (84% males and 54% oropharynx tumours). Sarcopenia was found in 49% with 65% (n=113) having sarcopenic obesity. Kaplan-Meier survival curves showed patients who were sarcopenic had worse OS (Log Rank p=0.037). Low T2-SMI cut-off values were: females <74cm2/m2 [area under the curve (AUC): 0.89 (95%CI 0.80-0.98)], males - (BMI<25) <63cm2/m2 [AUC: 0.93 (95%CI 0.89-0.96)], males (BMI≥25) <88cm2/m2 [AUC: 0.86 (95%CI 0.78-0.93)]. Low T2-SMI using these cut-off values was found to be a predictor of sarcopenia on multivariate logistic regression analysis (HR = 67.28, CI 27.59-164.08, p<0.001), however, there was no difference in OS with T2-SMI categories using these thresholds. The lowest T2-SMI quartile value was <63cm2/m2 and these patients had worse OS (Log-Rank p=0.017). In the 335 patients who completed RT, weight loss was significantly higher in those who were not sarcopenic (6.2% vs 4.9%, p=0.023). This was also demonstrated in patients with higher T2-SMI (6.3% VS 4.9%, p=0.014), and those in the highest quartile ranges (3.6% vs 5.7% vs 7.2%, p<0.001).

Conclusions

These sex and BMI-specific T2-SMI cut-off values are effective in assessing CT-defined sarcopenia in patients with HNC. Thresholds also indicate that patients are at risk of critical weight loss (>5%) during treatment, regardless of high muscle stores, and very low T2-SMI at diagnosis may increase risk of worse OS. Further investigation into potential implementation into clinical practice is warranted.

PO-097 | Targeting MYB/MYBL1 gene rearrangements as diagnostic biomarkers in salivary cancers

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Keywords

Salivary, biomarker

Purpose/Objective

Salivary adenoid cystic carcinoma (sACC) is characterised by mutually exclusive re-arrangements of the MYB gene family members MYB and MYBL1, resulting in MYB/MYBL1 overexpression in over 90% of cases. Validating molecular pathology approaches to MYB/MYBL1 detection, therefore, has significant potential in defining diagnostic biomarkers capable of distinguishing sACC from other non-ACC salivary cancers in cases of pathological uncertainty. We sought to evaluate MYB/MYBL1 *fluorescent in situ hybridization* (FISH) probes as diagnostic biomarkers for sACC in a cohort of 62 patients with salivary cancer.

Material/methods

62 patients with histologically confirmed salivary cancer (49 sACC, 13 non-ACC) were evaluated by FISH using a MYB gene probe (ZytoLight MYB break-apart) to detect the classical ACC translocation t(6;9)(q22-23;p23-24) and other MYB variants classed as atypical (3' signal loss; 5' signal loss; partial 5' loss; and fixed split signal). sACC patients testing negative for MYB rearrangement were evaluated using a MYBL1 gene probe (Empire Genomics, MYBL1 break-apart, 20768) to detect MYBL1 variants. In a sub-group of 28 sACC patients with MYB rearrangement confirmed

by FISH, we evaluated the sensitivity of DNA-based next-generation sequencing (FoundationOne, Foundation Medicine, Roche) to detect any MYB gene rearrangement. Clinical and demographic data were collected on all patients and overall survival (OS) calculated from diagnosis. Kaplan Meier survival analysis was performed and differences between groups calculated using the log-rank test.

Results

Rearrangements in MYB/MYBL1 were identified by FISH in 44/49 sACC patients (89.8%). Signal patterns were classical MYB translocation in 24/44 (54.5%), 3'-MYB signal loss in 13/44 (29.5%), fixed split signal in 2/44 (4.5%), 5'-MYB signal loss in 2/44 (4.5%), partial 5'-MYB signal loss in 1/44 (2.3%) and MYBL1 rearrangement in 2/44 (4.5%). Of the patients with non-ACC salivary cancer, 0/13 had evidence of MYB rearrangement. For MYB-altered sACC patients, classical translocation was associated with a trend towards improved OS compared to patients with atypical MYB alterations, with 5-year OS rates of 95% vs. 54%, respectively, and median OS of 16.0 vs. 5.3 years, respectively (p=0.172). Sites of metastases were similar, irrespective of MYB status with non-pulmonary metastases present in 8/24 (33.3%) with classical MYB alteration compared with 7/18 (38.9%) with atypical MYB alterations. In a sub-group of 28 FISH-confirmed MYB-rearranged sACC tumours, only 8/28 (28.6%) had MYB gene rearrangement when analysed with DNA-based NGS.

Conclusion

We describe an approach using MYB/MYBL1 FISH probes which detects MYB/MYBL1 alterations in 90% of sACC patients. This appears to be highly specific and may be of clinical value as a diagnostic biomarker for sACC. Due to the variable break-points in MYB gene fusions, this approach has a higher sensitivity than DNA-based NGS.

PO-098 | Baseline videofluoroscopy for patients receiving curative radiotherapy for head and neck cancer

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(1) Guy's and St Thomas' NHS Foundation Trust

Keywords

Videofluoroscopy, dysphagia, radiotherapy

Purpose

Patients with head and neck cancer are at risk of dysphagia due to the impact of disease and the effect of radical curative treatment. High rates of aspiration are reported at baseline and post-treatment, and baseline function is associated with long term outcome. Detailed instrumental assessment of swallow physiology at baseline with videofluoroscopy (VFS) should identify those at highest risk of long-term impairment, and may facilitate tailored swallow intervention. In the UK VFS is typically only completed on clinical indication to investigate patients presenting with complex dysphagia due to resource limitations. We piloted the inclusion of routine VFS at baseline and three months post-treatment as standard of care for an initial cohort of 30 patients. We present the outcomes of baseline VFS and the impact on patient management.

Methods

Baseline clinical assessments (Performance Status Scale Head & Neck and 100ml Water Swallow Test) and VFS were completed for patients consented for primary curative RT from March-August 2022 (n=30). VFS was completed according to a consistent protocol and was scored with Dynamic Imaging Grade of Swallowing Toxicity (DIGEST). SLT interventions as a result of the VFS were recorded. Descriptive statistics were used to report results. Fisher's exact tests

were used to evaluate associations between patient factors and presence of baseline dysphagia (DIGEST overall grade ≥1).

Results

Patient characteristics and baseline functional scores are presented in Table 1. Only two patients (7%) presented with pharyngeal dysphagia on clinical assessment prior to the VFS including one with aspiration risk. The full VFS protocol was completed with all patients. Eight patients (27%) presented with pharyngeal stage dysphagia on VFS (DIGEST ≥1) including six (20%) who had no signs of dysphagia on clinical assessment (Figure 1). The two patients (7%) presenting with impaired swallow safety on VFS and overall moderate-severe impairment (DIGEST ≥2) were those who had presented with pharyngeal dysphagia on clinical assessment; both demonstrated silent aspiration (Penetration-Aspiration Scale=8). There was no significant association between baseline DIGEST score of ≥1 and T-stage (p=0.70) or tumour site (p=0.22).

Swallow strategies to facilitate safer or more efficient eating and drinking were identified for four (13%) patients. One patient with severe impairment (DIGEST 3) was advised to restrict oral intake for safety. All patients were advised to complete a standard comprehensive exercise programme with no specific modifications.

Conclusion

Routine baseline VFS identified dysphagia not detected by clinical assessments in a fifth of patients. Tumour site or stage was not immediately predictive of swallow presentation. In this small cohort, moderate-severe impairment was identified through SLT clinical assessment; resources for instrumental assessment could be targeted on this basis. A standard comprehensive exercise programme is appropriate for all patients.

Figure 1: Baseline DIGEST grades

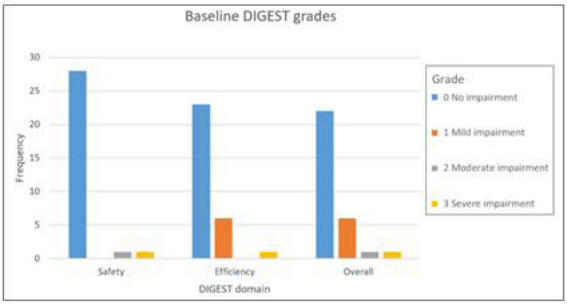

Table 1. Patient characteristics and baseline functional scores.

	n=30	(%)
Age		
Mean	60.9 years	
Range	39 – 74 years	
Gender		
Female	3	(10)
Male	27	(90)
Tumour site		
Nasopharynx	2	(7)
Oropharynx	16	(53)
Larynx	7	(23)
Hypopharynx	5	(17)
TNM stage (AJCC 7th Edition)		
I	1	(3)
II	5	(17)
III	6	(20)
IV	18	(60)
Smoking history		
Current	2	(7)
Previous	25	(83)
Never	3	(10)
Treatment plan		
Radiotherapy alone	7	(23)
Chemoradiotherapy	20	(67)
Induction chemo and CRT	3	(10)
Baseline Performance Status Scale Head & Neck		
Normalcy of Diet: Median (IQR)	100	(0)
Eating in Public: Median (IQR)	100	(0)
Baseline 100ml Water Swallow Test		
Swallow volume (ml/swallow): Mean (SD)	19.8	(7.9)
Swallow capacity (ml/second): Mean (SD)	15.1	(6.5)

PO-100 | PREMALIGNANT LESIONS IN NON-NEOPLASIC MUCOSA OF LARYNGEAL CANCER SPECIMENS

Maria Cristina Martin Villares [(1)]; *Carmen Manzanares* [(1)]; *Jesus Eduardo Ramirez* [(1)]; *Ana Rodriguez* [(1)]; *Sara Cascon* [(1)]; *Carmen Alvarez Tato* [(1)]; *Maria Jose Gonzalez Gimeno* [(1)]; *Jose Ramon Alba* [(2)]; *Ignacio Alavarez Alvarez* [(1)]

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Keywords

Premalignant, laryngeal carcinoma, prognossis.

Purpose/ objective

The objective of this work is the study of dysplastic lesions of the non-neoplastic mucosa of the laryngectomy surgical specimen.

Material and methods

We studied the non-neoplastic mucosa of 69 laryngectomy specimens to identify preneoplastic lesions (dysplasia or carcinoma in situ) at a distance from the main invasive tumor.

Results

From the study of 69 patients, we found 23 premalignant lesions (dysplasia-carcinoma in situ) in 17 patients (25%). In 6 of these patients there was more than one preneoplastic lesion simultaneously in the same laryngectomy specimen. Of the 23 malignant lesions diagnosed, 17 corresponded to carcinoma in-situ/severe dysplasia and 6 to mild-model dysplasia. The tumors that most frequently presented associated preneoplastic lesions were those of the anterior commissure (5 patients). The most frequent location of the premalignant lesions was the cord. We found no impact on the prognosis when we diagnosed simultaneous premalignant lesions with squamous cell carcinoma in the same patient.

Conclusion

25% of the patients with squamous cell carcinoma also presented associated premalignant lesions in the non-neoplastic mucosa. This histopathological diagnosis had no impact on the prognosis.

PO-101 | THE PRE-EPIGLOTIC SPACE AND TRANSORAL SUPPRAGLOTTIC LARYNGUECTOMY FOR LARYNX CANCER

Maria Cristina Martin Villares [1]; *Sergio Rodriguez Merino* [1]; *Maria Jose Gonzalez Gimeno* [2]; *Jesus Eduardo Ramirez* [1]; *Ana Rodriguez* [1]; *Carmen Manzanares* [1]; *Sara Gascon* [1]; *Jose Ramon Alba* [3]; *Ignacio Alvarez Alvarez* [1]

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Keywords

Pre-epiglottic space, laryngeal cancer, transoral surgery.

Purpose/objetive

It is difficult to study the early invasion of the pre-epiglotic space by a supraglottic cancer with laryngoscopy, computed tomography or magnetic resonance imaging. If we choose a minimal invasive transoral approach for the patient, the management of the preepiglottic space is critical. The aim of this study is to identify predictive indicators of invasion of the pre-epiglottic space.

Material and methods

We studied 25 laryngectomy specimens for supraglottic squamous cell carcinoma by whole-organ serial sections. We present the most educational histopathological preparations of our series in the present work.

Results

The preepiglottic space was invaded in 14/25 supraglottic tumors (56%). When the central regios of the laryngeal vestibule was invaded by the tumor, the preepiglottic space was invaded in 71% of the cases. Infrahyoid tumors invade this space much more frequently

(85%) than suprahyoid tumors (20%). The most frequently identified route of invasion is by infiltration of the base of the epiglottis.

Conclusions

When a supraglottic tumor is located in the central area of the vestibule and/or invades the lower region of the epiglottis, the risk of invasion of the preepiglottic space is very high, even in early stages. This fact must be taken into account in any transoral approach to the tumor.

PO-102 | DEGREE OF DIFFERENTIATION AS A PROGNOSTIC FACTOR OF LARYNX CANCER

Maria Cristina Martin Villares [(1)]; *Ana Rodriguez* [(1)]; *Mercedes Gonzalez* [(1)]; *Luis Jose Dominguez Ugidos* [(1)]; *Maria Puente* [(1)]; *Rafael Perez* [(1)]; *Jesus Eduardo Ramirez* [(1)]; *Ignacio Alvarez Alvarez* [(1)]

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Keywords

Differentation, Laryngeal carcinoma, cervical nodes.

Purpose/ objective

Degree of differentation is one of the most studied factors to understand the biological behaviour of tumours. In general, the review of the literature associates the low degree of differentiation of laryngeal cancer with aggressiveness. The aim of this study is to analyses the impact on prognosis of the differentiation degree of the laryngeal cancer.

Material and methods

We studied 85 patients with epidermoid carcinoma of the larynx. We classified the tumors in: well differentiated, moderately differentiated, and poorly differentiated.

Results

Of the 85 patients, 25 were supraglottic tumors, 33 glottic, 17 transglottic and 10 pyriform sinus. Of 85 patients, 28% patients presented lymph node metastases. 39 cases were well differentiated, 34 moderately differentiated, and 12 poorly differentiated. 64% of patients with cervical metastases had poorly differentiated tumors. If the degree of differentiation was low, there was a higher incidence of metastatic cervical nodes ($p < 0.05$), but not with a higher risk of tumor recurrence nor did it have an impact on survival.

Conclusion

The degree of differentiation was associated with the presence of metastatic nodes in our series, but had not impact on recurrence or survival.

PO-104 | MINIMALLY INVASIVE SURGERY IN EARLY GLOTICC CARCINOMA: AN HISTOPTOLOGICAL STUDY

Maria Cristina Martin Villares [(1)]; Rosa Sancho [(2)]; Maria Jesus Velasco [(3)]; Carmen Molina Ramirez [(4)]; Maria Jose Gonzalez Gimeno [(5)]; Sergio Rodriguez Molina [(1)]; Jose Ramon Alba [(6)]; Ignacio Alvarez Alvarez [(1)]

(1) Complejo Asistencial Universitario de León. Universidad de León (2) Complejo Asistencial de Zamora (3) Hospital Universitario de Avila (4) Complejo Hospitalario Universitario de Segovia (5) Hospital Infanta Sofia, Universidad Autonoma de Madrid (6) Hospital Universitario General de valencia

Keywords

Glottic carcinoma, minimally invasive surgery, vocal cord.

Purpose

The vocal cord mobility is the critical key in minimally invasive surgery for early glottic cancer. The aim of this study is to investigate the possibility of superficial infiltration of the vocal cord with a normal mobility.

Material and methods

We studied 33 surgical specimens of squamous cell carcinoma of the vocal cord treated by minimally invasive surgery, studied by whole-organ serial sections.

Patients with anterior commissure infection are excluded. The histopathological preparations of high academic interest are presented.

Results

We identified 4/33 patients with carcinoma in-situ, in which the tumor did not invade the basement membrane or the vocal ligament. In 12/33 specimens, the tumor had already invaded the basal membrane, the tumor cells reaching the vocal ligament in three of them. In 5 (15%) patients, the tumor exceeded the vocal

ligament and superficially invaded the vocal muscle, although clinically no decrease in cord mobility was identified.

Conclusion

In 15% of the patients with a glottic tumor and normal cord mobility, the tumor invaded the vocal muscle. This fact is critical when considering minimally invasive surgery in an early glottic tumor.

PO-105 | The current level of shared decision-making in Head--and-Neck Oncology: An exploratory study

Anne Heirman[1]

(1) NKI-AvL, Amsterdam

Keywords

Head-and-Neck Oncology, Patient Involvement, Physician-Patient Relations, Shared Decision Making

Objectives

Treatments for head-neck cancer are drastic and often significantly impact the quality of life and appearance of patients. Shared decision-making (SDM) beholds a collaboration between patient and doctor in which the most suitable treatment can be chosen by integrating patient preferences, values, and medical information. SDM has a lot of advantages that would be useful in making difficult treatment choices. The objective of this study was to determine the current level of SDM among patients and head-and-neck surgeons.

Methods

Consultations of patients with a non-cutaneous head-and-neck malignancy facing a treatment decision were selected and included. The consultation was recorded with an audio recorder, and the patient and surgeon filled in a questionnaire immediately after the consultation. The SDM level of the consultation was scored objectively by independent observers who judged audio recordings of the consultation using the OPTION5-scale, ranging from 0% (no SDM) to 100% (optimum SDM), as well as subjectively by patients (using the SDM-Q-9 and Control preference scale) and clinicians (SDM-Q-Doc, modified control preference scale) percentages.

Results

Five head-neck surgeons have seven recorded conversations with different patients. One of them was trained in SDM. The other four had no experience with SDM. Most patients were male (74%), and oropharyngeal carcinoma was the most common diagnosis (41%), followed by oral cancer (33%). Five patients received palliative treatment of which two patients were not treated recording guidelines. Objective SDM scores were low (33.5%). Subjective scores were overall high among patients (>85%), but also among clinicians (>75%).

Conclusion

The objective level of SDM in a tertiary head-and-neck center where patients came for counseling was found to be low. Subjective scores were high, indicating that both patients and clinicians are unaware of what SDM entails. There is room for improvement of SDM.

PO-106 | The current level of shared decision-making in Head--and-Neck Oncology: An exploratory study

Anne Heirman [1]; Song Duimel [1]; Lisette Van Der Molen [1]; Richard Dirven [1]; Julia Van Weert [1]; Michiel Van Den Brekel [1]

(1) NKI-AvL, Amsterdam

Keywords

Head-and-Neck Oncology, Patient Involvement, Physician-Patient Relations, Shared Decision Making

Objectives

Treatments for head-neck cancer are drastic and often significantly impact the quality of life and appearance of patients. Shared decision-making (SDM) beholds a collaboration between patient and doctor in which the most suitable treatment can be chosen by integrating patient preferences, values, and medical information. SDM has a lot of advantages that would be useful in making difficult treatment choices. The objective of this study was to determine the current level of SDM among patients and head-and-neck surgeons.

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Five head-neck surgeons have seven recorded conversations with different patients. One of the sugeons was trained in SDM. The other four had no experience with SDM. Most patients were male (74%), and oropharyngeal carcinoma was the most common diagnosis (41%), followed by oral cancer (33%). Five patients received palliative treatment of which two patients were not treated recording guidelines. Objective SDM scores were low (33.5%). Subjective scores were overall high among patients (>85%), but also among clinicians (>75%).

Conclusion

The objective level of SDM in a tertiary head-and-neck center where patients came for counseling was found to be low. Subjective scores were high, indicating that both patients and clinicians are unaware of what SDM entails. There is room for improvement of SDM.

PO-107 | Does Prophylactic Replacement of Voice Prosthesis Make Sense? A Study to Predict Prosthesis Lifetime

Anne Heirman *[1]; Vincent Van Der Noort [1]; Rob Van Son [1]; Marije Petersen [2]; Lisette Van Der Molen [1]; Gyorgy Halmos [3]; Richard Dirven [1]; Michiel Van Den Brekel [1]*

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Keywords

Device lifetime; prosthetic leakage; total laryngectomy; voice prosthesis; voice rehabilitation.

Objective

Voice prosthesis leakage significantly affects the quality of life of patients undergoing laryngectomy, causing insecurity and frequent unplanned hospital visits and costs.

In this study, the concept of prophylactic voice prosthesis replacement was explored to prevent leakages.

Methods

This study included all patients who underwent laryngectomy between 2000 and 2012 in the Netherlands Cancer Institute. Device lifetimes and voice prosthesis replacements of a retrospective cohort were used to calculate the number of needed voice prostheses per patient per year to prevent 70% of the leakages by prophylactic replacement.

Various strategies for the timing of prophylactic replacement were considered: adaptive strategies based on the individual patient's history of replacement and fixed strategies based on the results of patients with similar voice prosthesis or treatment characteristics.

Results

Patients used a median 3.4 voice prostheses per year (range, 0.1-48.1). We found high inter- and intrapatient variability in device lifetime. When prophylactic replacement is applied, this would become a median 9.4 voice prostheses per year, which means replacement every 38 days, implying >6 additional voice prostheses per patient per year. The individual adaptive model showed that preventing 70% of the leakages was impossible for most patients and only a median 25% can be prevented. Monte-Carlo simulations showed that prophylactic replacement is not feasible due to the high coefficient of variation (SD/mean) in device lifetime.

Conclusion

Based on our simulations, prophylactic replacement of voice prostheses is not feasible due to high inter- and intrapatient variation in device lifetime.

PO-108 | Prognostic value of FDG bone marrow and tumor uptake on PET/CT in patients with oropharyngeal cancer

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(1) Akademiska University Hospital, Uppsala

Keywords

Head and neck cancer, oropharyngeal cancer, FDG-PET/CT

Purpose/Objective

To examine the prognostic value of FDG uptake in the bone marrow (BM) for disease recurrence and survival in patients with oropharyngeal squamous cell carcinoma (OPSCC). The secondary aims were to examine the prognostic value of other PET/CT parameters of the tumor and assess the correlation of FDG uptake in the BM and tumor with serum inflammatory markers.

Material and Methods

A homogenous study cohort of 93 patients with OPSCC was included. All patients underwent a pretreatment FDG-PET/CT and blood samples were collected before treatment. Treatment was given with intention to cure and consisted of radiotherapy alone (n = 36), surgery alone (n =2), and combined chemoradiotherapy (n = 55) for patients with higher tumor stage. Blood samples were repeated at seven weeks after the start of treatment. Approximately 12 weeks after treatment termination a second FDG-PET/CT was performed followed by a clinical examination for treatment evaluation.

Blood samples were analyzed for white cell (WCC), red cell (RCC), and platelet cell counts (PCC), hemoglobin (Hb), and CRP.

Results

The univariate analysis showed that the BM uptake (SUVmeanBM) as well as tumor specific parameters (SUVmaxtumor, TL-

Gtumor, SUVmaxtotal, SUVmeantotal, TLGtotal) were significant PET parameter for recurrence-free survival (RFS). When adjusted for age, sex and stage only SUVmeanBM remained significant for RFS. Using the Spearman correlation, we found a moderate correlation between CRP and TLGtotal, WCC and TLGtotal, WCC and SUVmaxtotal, and WCC and SUVmeantotal.

Conclusion

Our results show that several FDG-PET/CT parameters could have predictive value. However, FDG uptake in the BM was shown to be the only independent PET parameter predicting RFS in the present cohort. As no correlation was seen between SUVmeanBM and the studied serum inflammatory markers we intent to extend the analysis including other proteins of interest from the OLINK immune-oncology panel in a subgroup of 34 patients with OPSCC.

PO-109 | Collaborative working in the management of head & neck lymphoedema & radiation induced fibrosis

Emma Hallam[1]

(1) Nottingham University Hospitals NHS Trust

Purpose/Objective

The head and neck cancer (HNC) population often have unmet needs as a consequence of their treatment which can lead to significant impairment and disability.

Lymphoedema and radiation induced fibrosis are common side effects that can negatively impact on a person's quality of life and early identification and management of this complex symptom provides the greatest success for rehabilitation following treatment.

Drawing on the expertise of the lymphoedema clinical nurse specialist, the Nottingham Late Effects Service has developed a collaborative and multi-disciplinary approach to the early management of lymphoedema and radiation induced fibrosis, including the use of photobiomodulation therapy, a home exercise programme, simple lymphatic drainage massage and skin care advice. This is already yielding positive early results.

This presentation will provide an overview of the service, how it offers a holistic approach to supportive care and early outcomes observed within our patients; including observed changes in appearance, improved range of movement scores and decreased psychological distress. We will also present our experience of collaborative working in this setting, how the service was established and the benefits of this for our service, including cost savings, reduced onwards referrals and a reduction in clinic visits.

Materials and Methods

Methodologies included data collection by measuring the following; change in neck rotation (degrees), change in neck extension (cm), change in mouth opening as a result of radiation induced trismus (cm), patient pain reported pain score (1-10). Patient Quality of Life testimonials were gathered in addition to this data.

Results and Conclusions

This presentation will conclude that to recommend that this collaborative approach is essential for offering excellent patient centred personalised self-supported care in the complex symptom management of the consequences of treatment. Identifying patients needs at an earlier time point along with providing education on late effects improves overall quality of life along with ensuring that the patients subjective bother is met. This approach also has a cost benefit to the patient and the health care trust in terms of reducing multiple appointments.

Neck rotation (degrees)	Neck extension (CM)	Trismus (MM)	Pain score
Average 20	Average 1.5	Average 4.5	Average -2.5
Maximum 45	Maximum 2.0	Maximum 7	Maximum -6

PO-113 | Metastasizing pleomorphic adenoma: a literature review

Carlotta Liberale [(1)]; *Andrea Sacchetto* [(1)]; *Gabriele Molteni* [(1)]

(1) University of Verona

Objectives

Pleomorphic adenoma (PA) is the most common benign tumor affecting salivary glands. PA is a mixed tumor and arises in most cases in the parotid gland. Sometimes it can undergo malignant transformation in carcinoma ex pleomorphic adenoma or, rarely, it can also metastasize to other organs, without malignant transformation.

Metastasizing pleomorphic adenoma (MPA) is an uncommon malignant tumor which can affect multiple organs with considerable temporal latency compared to the primary PA. Histologically there are no differences between PA and MPA in other organs. Up to now, there is still little knowledge about MPA and its clinical course, with poor elements about survival and relapse rate. This is a review of the literature about MPA of the parotid gland.

Materials and Methods

This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2020 guidelines. The research was carried out using the Pubmed database with the following research string: ((Metastatic) OR (metastases) OR (metastasis) OR (metastasizing)) AND (pleomorphic adenoma). All the articles found were included, without any time period restriction. Last research on the database was made in July 2022. The selected articles were analyzed, extracting different data about: authors, study design and year of the publication; age and gender of the patients; localization, imaging and histologic reports of the first parotid disease and its metastasis; type of treatment and treatment's result; eventual recurrence and related treatment; follow up.

Results

A total of 908 papers were selected using the aforementioned research string. First, an abstract reading selection was made following the inclusion criteria and 54 articles were selected. After this, a further exclusion reading full-length papers was made, with 41 articles selected, always following the pre-established criteria. From the current literature we found 43 patients with metastasizing pleomorphic adenoma of the parotid gland. The average age of the patients is 49.6 years, and the patients were 19 male and 24 female. The average time between parotid pleomorphic adenoma and first metastasis was 16.4 years. The most frequent sites of metastasis were neck lymph nodes, lungs and kidneys.

The follow up period ranges between 2 and 72 months (average 26 months), but complete data were available only for 21 patients. 8 patients of 42 underwent RT adjuvant treatment.

Conclusion

MPA is a very rare entity, with few case reports recorded in literature. Even though MPA is a benign neoplasm, it may assume aggressive behavior that can lead to death.

This literature review has the objective to collect the largest numbers of patients with MPA of the parotid gland to standardize the management of this disease, to obtain better clinical outcome in the future. To date, the gold standard treatment has not yet been defined. Further studies are needed to better characterize the disease and its management.

PO-114 | Wide tumors with orbital involvement: surgical management and main reconstructive options

Carlotta Liberale [1]; Francesca De Cecco [1]; Virginia Dallari [1]; Gabriele Molteni [1]

(1) University of Verona

Objectives

The aim of this study is to evaluate the surgical management and the reconstructive options in patients with head and neck malignancies involving the orbit.

These neoplasms often require extensive demolitive and reconstructive surgery, though the goal is always to preserve the eye and its function.

Materials and Methods

The English language literature on head and neck malignancies with orbital involvement of the past 10 years was reviewed using PubMed. Particular attention was paid to the type of reconstruction used in cases with orbital exenteration.

Different type of reconstruction can be used to fill the orbital defect and our attention focused on free flap reconstruction. We analysed different type of free flap, according to the type of surgical defect.

In the last 3 years we experienced 5 patients with extensive involvement of the orbit due to malignant neoplasm. Extensive demolition surgery was performed in all of them, using different reconstructive flaps.

Results

Different malignancies of the head and neck district, as cutaneous squamous cell carcinoma (CSCC) or sinonasal squamous

cell carcinoma (SNSCC) or sinonasal undifferentiated carcinoma (SNUC), can involve the orbit. For patients eligible for surgery, different options are available. Surgery can range from a minimally invasive approach, as in case of endoscopic resection, to an extremely demolitive one. Orbital exenteration is often required to obtain oncological radicality. Several reconstructive approaches are described. Both local pedicled flaps (as temporalis flap) and free flaps (as anterolateral tight flap or latissimus dorsi flap) can be used to restore morphological integrity of the orbital region. Depending on the type of surgical defect, the most suitable reconstructive flap is chosen. Adjuvant therapy should also be considered, according to the type and the stage of disease.

In our case series, both local pedicled flaps and free flaps were used, depending on patient's surgical defect and therapeutic perspectives.

Conclusions

Malignancies of head and neck as SNSCC or SNUC are in most cases diagnosed in an advanced stage, when symptomatic. In case of orbital invasion, radical and disfiguring surgery is often required to obtain oncological safety, so an adequate and tailor made reconstructive surgery is mandatory.

PO-116 | PET-CT guided, patient-initiated follow-up vs clinical follow-up in HNC (PETNECK2) (ISRCTN13709798)

Paul Nankivell [1]; Lauren Matheson [2]; Jo Brett [3]; Colin Greaves [3]; Joan Duda [3]; Mary Wells [4]; Ava Lorenc [5]; Denis Secher [6]; Pat Rhodes [6]; Marcus Jepson [5]; Gozde Ozakinici [7]; Eila Watson [8]; Piers Gaunt [9]; Louise Rae-Cherrill [9]; Claire Gaunt [9]; Evaggelia Liaskou [9]; Tessa Fulton-Lieuw [1]; Saloni Mittal [1]; Barry Main [10]; Hisham Mehanna [1]

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Purpose/Objective

Head and neck cancer (HNC) follow-up regimens lack evidence for their efficiency in recurrence detection and are unsustainable given rising HNC incidence. The PETNECK2 trial compares a novel PETCT-guided, symptom-based, patient-initiated follow-up (PIFU) approach against current routine follow-up. The intervention consists of a PETCT scan 1 year after completing treatment, an education session with a Nurse/AHP and written information in form of an app or booklet to understand how to look for symptoms of recurrence, and an open urgent appointment with the clinical team if patients develop worrying symptoms.

We report the results of the development phase of the programme to: i) Develop a patient-centred, evidenced-based Information and Support (I&S) resource to support PIFU; ii) Test the feasibility of delivering the intervention, before commencing the RCT.

Methods

Data from the following were amalgamated to develop the intervention: patient survey (n=144), patient interviews (n=30) and workshops with patients (n=25), caregivers (n=3) and HCPs (n=21). A modular online training package was developed for nurses and AHPs through online workshops and interviews.

The intervention was then tested in a feasibility study. Patients and their clinicians were interviewed 1-2 months after the education session to seek their opinions on and barriers to the PIFU intervention.

Results

In the surveys and interviews, patients and clinicians indicated 5 goals for the app and booklet:

1. To support patients to recognize potential symptoms of HNC recurrence, by identifying what is "normal for me" and possible deviations from this normal.

2. To educate patients to routinely check for potential recurrence symptoms.

3. To facilitate timely help seeking by patients, making a hospital PIFU appointment if needed.

4. To minimize and help patients to self-manage fear of recurrence.

5. To encourage patients to continue to engage with the above self-care behaviours and the intervention over time.

The research also identified 3 main targets for behaviour change which were incorporated into the patient education and the app:

- Regular self examination and symptom monitoring

- Seeking help from the clinical team if the symptoms persist

- Self management of ongoing long-term treatment side effects

The prospective feasibility study, recruited 32 patients from 10 NHS sites within 6 months. The online nurse training package was undertaken by HCPs (n= 27) across the recruiting sites. Patient completion rate for the baseline questionnaires was 95%.

Conclusion

We have a developed a complex intervention to support the PET-CT guided PIFU in HNC, that is acceptable to both patients and clinicians. This has been tested prior to commencing a large RCT, which will compare the effectiveness of PETCT guided PIFU to routine clinic follow-up.

PO-119 | A simple webcam-based measurement tool to assess the movements of the tongue in glossectomy patients

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Keywords

Measurement, Oral cancer, tongue motility.

Background

Head and Neck cancer is one of the most common cancers amongst men in Indian Subcontinent, and oral cancer being the commonest of it. Buccal mucosa and tongue are the commonest subsite of oral carcinoma. Tumor itself and its treatment impairs the functions of tongue including tongue motility. Though tongue motility is the most important predictor of post-treatment tongue functions, there is no standard way to measure it. Aim: To test indigenous webcam -based software to measure the motility of the tongue.

Methods

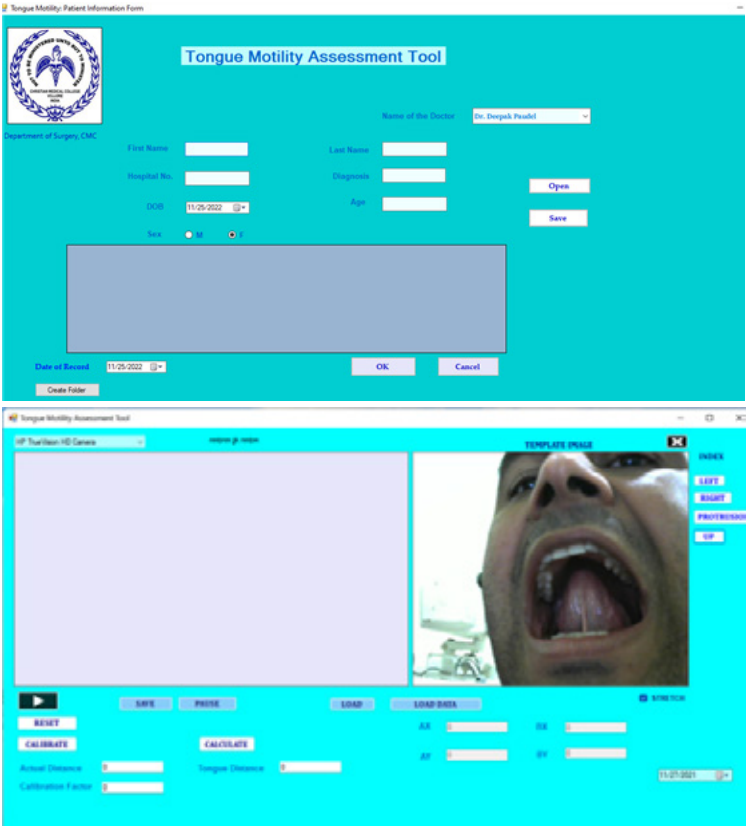
This is the validation study of newly developed webcam-based software to measure the tongue motility, done within the periods of 3 months. During the first phase of the study we measured 8 objects of the fixed dimension from 4 different distances, thus making 32 observations. After testing the utility of the software on different objects we extended the study to record the desired action of tongue on 10 healthy subjects in four different directions making 40 observations. Two different observers calculated all the observations in the objects and volunteers in two different times. Cronbach's α was used to measure the intra-observer and interobserver consistency of the measurements.

Results

There was very strong inter-rater reliability between observer 1 & 2 both for the measurement of objects and tongue motility. Similarly, both the observers have very strong intra-rater reliability for both the measurements (Cronbach's $\alpha > 0.9$ and P-value < 0.001).

Conclusion

The webcam-based tongue motility tool is easy to use, reliable and cheaper method to record the different movements of tongue. In addition, we can register the images and videos for future references.



PO-120 | Oral Squamous Cell Carcinoma: Is Sentinel Lymph Node Biopsy an alternative to Neck Dissection?

Maria Jorge Casanova [(1)]; Clara Serdoura Alves [(1)]; João Correia [(1)]; António Magalhães [(1)]; Luís Meireles [(1)]

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Keywords

Oral cavity; squamous cell carcinoma; sentinel lymph node biopsy; elective neck dissection

Purpose

In patients with oral cancer, the involvement of cervical lymph nodes decreases overall survival in 50%. Conventionally, the clinically N0 neck is approached with elective neck dissection (END) or watchful waiting. Sentinel lymph node biopsy (SLNB) has been emerging as a novel strategy in the management of early-stage oral cavity squamous cell carcinoma (SCC), as it is a more conservative approach than END, with less complications.

The goal of this study was to investigate diagnostic accuracy of SLNB for detecting neck metasthases in N0 oral SCC, as an alternative to END.

Methods

Relevant literature was systematically reviewed in Pubmed, Cochrane and Embase using search terms 'oral squamous cell carcinoma' and 'sentinel lymph node biopsy'. The review was organized considering the following PICO (population, intervention, comparison, outcome) question: What is the sensitivity of SLNB in oral SCC? 'P' was adult patients diagnosed with oral SCC without apparent lymphatic or distant metastases at the time of the study. 'I' was SLNB, 'C' was END, and 'O' was sensitivity, specificity, and negative preditive value of SLNB.

A meta-analysis was performed, and pooled identification rate, sensitivity and negative predictive value were calculated.

Results

The search retrieved 493 articles, and after exclusion criteria applied, 9 prospective studies were included in this meta-analysis, with a total of 625 subjects. The sample size varied from 16 to 222, and clinical T classification from T1 to T3.

The I2 test was used to evaluate heterogeneity between studies, and was <25% for all three diagnostic parameters assessed, showing low heterogeneity.

Pooled identification rate, sensitivity and negative predictive value for SLNB were 97.92% (95% confidence interval (CI) of 97.73-98.11), 86.37% (95% CI 85.60-87.13), and 93.79% (95% CI 93.46-94.12).

Conclusion

In conclusion, the present findings support a role for SLNB in the clinical management of oral cavity SCC.

PO-121 | Sinonasal adenocarcinoma: the experience of a northern Portuguese center

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Key words

Sinonasal adenocarcinoma, intestinal-type adenocarcinoma, non-intestinal-type adenocarcinoma

Introduction/Objective

Sinonasal carcinomas are rare accounting 3% of head and neck cancer. After squamous cell carcinoma, adenocarcinoma is the 2nd most common epithelial malignancy (10-20%). Sinonasal adenocarcinoma (SNAC) is defined as either intestinal-type (ITAC) or nonintestinal type. SNAC is related with well-described occupational risk factors like wood dust, varnishes and synthetic paints. In our center there is a high incidence of SNAC due to a prevalent woodworking population in this northern portuguese area.

This study aims to analyse patients diagnosed with SNAC treated in our center in terms of epidemiological, clinical and histopathological features, treatment type and outcomes.

Material/Methods

Retrospective analysis of clinical data of patients with histologically proven SNAC treated at a tertiary center, between March/2004-May/2022. The Kaplan-Meier method was used for survival curvess and the log-rank test and a Cox-regression for uni and multivariate analysis (SPSS® v27).

Results

Thirty-one patients were analysed, being the majority male (96,8%). At diagnosis, the median age was 63 years [42,81] and 90,3% had an ECOG PS 0-1. An occupational risk factor was present in 77,4%. The most common primary site was the nasal cavity (45,6%), followed by the ethmoid sinus (45,2%). ITAC was the most frequent histological subtype (77,4%). 35,5% of cases had a cT4 tumor and only 3,2% presented loco-regional nodal disease and 6,5% distant metastasis. Brain or orbital apex were involved in 16,1% and 45,2%, respectively. The majority (67,7%) underwent multimodal treatment. The most common modality was surgery+radiation (41,9%), while 19,4% underwent surgery+chemoradiotherapy. Margin status was negative in 29% of cases. The rate of orbital preservation was 86.1%. Disease recurrence was observed in 48,4% of the patients.

Median OS and PFS were 64 (IC95: 31,58-96,42) and 10 months (IC95: 6,28- 13,72), respectively. The median follow-up was 21 months [0-94].

OS and PFS were both correlated with histological subtype (p=0,003, p=0,019; respectively), differentiation grade (p=< 0,001; both), metastatic disease (p< 0,001, p=0,012; respectively) and macroscopic resection of the tumor (p=0,044, p=0,042; respectively). PFS was also correlated with primary site (p=0,034).

Conclusion

Despite our study limitations (sample size, retrospective nature and large period of time), the results are aligned with the literature, especially the higher incidence of men and ITAC and the association with occupational exposure. The latter stretches the role of occupational risk factors in the development of SNAC. The majority of patients did surgery+radiation with a high rate of organ preservation. However, there was a low rate of complete surgical resection with a high rate of recurrence with distant metastasis.

The diagnosis on a locally advanced stage, high rate of non-complete surgical resection and low use of chemotherapy (CT) in the multimodal treatment can justify that. Recently new multimodal approaches, such as neoadjuvant CT are being implemented with promissing outcomes. More clinical trials are needed to evaluate them, where markers like p53 may play a role.

PO-122 | Reconstructive options for large defects of the periauricular region: our experience

Francesca De Cecco [(1)]; *Virginia Dallari* [(1)]; *Carlotta Liberale* [(1)]; *Andrea Sacchetto* [(2)]; *Gabriele Molteni* [(1)]

(1) University of Verona (2) Ospedale San Bortolo, Vicenza (VI)

Introduction

Recurrent or advanced stage primary cutaneous lesions or periparotid metastatic carcinoma often demand large resections involving skin, parotid tissue and often underlying bone, including the ramus of the mandible and portions of the temporal bone.

A defect classification system has been proposed to predict the best reconstructive technique based on the size and volume of resection.

We present a case series of 15 patients affected by squamous cell carcinoma (SCC), basal cell carcinoma (BCC) and pleomorphic dermal sarcoma treated in the last 5 years. All patients showed an advanced stage of disease with facial nerve involvement in 50% of the cases. In all patients, reconstructive surgery was performed with different flaps (free of pedicled).

Materials and Methods

Between November 2017 and June 2022, we experienced 15 patients with cutaneous malignancies of the periauricolar region. All patients were male. All of them had an advanced stage of the disease. The patients were between 60 and 85 years (average 76,6). Eleven patients were affected by SCC, three of them by BCC and the last one was affected by pleomorphic dermal sarcoma.

Results

We performed extensive demolition surgery, with petrosectomy in 7 patients; facial nerve sacrifice was required in 9 of them. We

used different reconstructive flaps: 8 patients underwent reconstruction with pectoralis major flap, 4 with submental pedicled flap, 2 with anterolateral thigh flap and one with bilobed flap.

Conclusion

This study highlights the versatility of various reconstructive flaps and their security in terms of tightness. Reconstruction of facial defects makes use of different alternatives; the choice between these reconstructive alternatives depends on several factors: the location and size of the defect, the local and general condition of the patient, and the surgeon's preference and experience. In large facial skin defects, the use of local flaps is limited by the possibility of mobilizing the tissue adjacent to the defect. So, pedicle or free flaps are mainly used. The use of free flaps allows the transfer of large skin flaps, but usually involves a longer surgical time and requires the presence of experienced microvascular surgeons. Moreover, surgical outcomes are affected by vascular comorbidities.

PO-124 | Nasopharyngeal carcinoma: a therapeutic dilemma for G6PD-deficient patients.

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Keywords

Nasopharyngeal carcinoma, G6PD deficiency, chemotherapy

Purpose/Objective

Glucose 6-phosphate dehydrogenase (G6PD) is essential for oxidative processes. G6PD deficiency renders red cells susceptible to hemolysis. Low G6PD activity in patients with nasopharyngeal carcinoma (NPC) is associated with poor prognosis. The administration of chemotherapy may be challenging for G6PD-deficient patients due to the potential for anticancer drugs to trigger oxidative stress.

Material/methods

We present a case of an adult with complete G6PD deficiency, who was treated for NPC at our center.

Results

A 38-year-old Caucasian male with a deficiency of G6PD and a history of sensorineural hearing loss, was diagnosed with a nonkera-

tinizing undifferentiated NPC cT3N2M0, stage III (AJCC, 8th Ed.). He was scheduled to receive induction chemotherapy with a combination of three cycles of carboplatin (AUC 4), docetaxel (60mg/m2), and 5-fluorouracil (600mg/m2) as a continuous intravenous infusion for 4 days, followed by concurrent chemoradiotherapy including VMAT radiotherapy (Volumetric Modulated Arc Therapy) with seven cycles of platinum-based concurrent chemotherapy (carboplatin AUC 2) under close monitoring for developing hemolytic events. During the treatment administration, the patient was examined daily with complete blood count, reticulocyte count, lactate dehydrogenase, haptoglobin, peripheral smear, and urinalysis. After the second treatment course, the patient presented with disease progression at the regional lymph nodes. Induction chemotherapy was discontinued and he proceeded with concurrent chemoradiotherapy consisting of VMAT radiotherapy of the primary site, high-risk regional cervical lymph nodes, and low-risk regional cervical lymph nodes (69.96 Gy, 66 Gy, and 59.4 Gy respectively) with each dose being divided in 33 fractions, with radiosensitivity consisted of seven weekly cycles of carboplatin. The therapeutic regimen was administered safely. Neither hemolytic events nor other hematological complications were observed during the treatment course which was completed successfully, with no signs of unexpected toxicity. He demonstrated complete response and he has now been placed on regular follow-up. Three months later, there is no evidence of recurrence or adverse effects.

Conclusion

Data describing the use of chemotherapeutic agents in patients with G6PD deficiency are scarce. Although G6PD deficiency may be associated with an increased risk of complications, the patient completed the treatment course without evidence of hemolytic anemia. Since patients may have both G6PD deficiency and nasopharyngeal cancer in geographic areas with a relatively high incidence of both disorders, our report may alleviate concerns regarding the safety of patients with G6PD deficiency undergoing cancer treatment.

PO-125 | Malignant tumors of salivary glands - a case series from a tertiary hospital

Tiago Barroso [1]; *Miguel Esperança Martins* [1]; *Inês Soares Pinho* [1]; *Cecília Melo-Alvim* [1]; *Leonor Ribeiro* [1]; *Luís Costa* [1]

(1) CENTRO HOSPITALAR UNIVERSITÁRIO LISBOA NORTE, E.P.E.

Introduction

The World Health Organization recognizes 23 subtypes of salivary gland tumors. They have low incidence and a high morphological and genetic diversity. The over-expression of androgen and HER2 receptors is clinically relevant and predicts response to targeted treatment.

Treatment is based on surgery with or without adjuvant radiotherapy (RT). In metastatic disease, systemic therapy consists of chemotherapy (ChT), targeted therapy and immunotherapy.

Objectives

The primary aim of our study was to describe the characteristics of malignant tumors of the salivary glands followed at a Tertiary Hospital regarding patient characteristics, tumor characteristics and treatment. Our secondary objective was to compare overall survival as a function of tumor site.

Methods

We reviewed all patients followed at our department between January 2011 and April 2022 with a malignant tumor of the salivary glands. Comparison of Kaplan-Meier survival curves according to the tumor site were done using the pairwise logrank test with Bonferroni correction for multiple comparisons (alpha = 0.05, which requires $p < 0.008$ for statistical significance).

Results

We identified 49 patients, 53% male, with median age 63 years old, with a mean follow-up time of 3 years (maximum 12 years). Of these patients, 55% had parotid tumors, 18% had minor salivary gland tumors, 16% submandibular tumors and 10% sublingual tumors. The most frequent histologic types were cystic adenoid carcinoma (22%) and mucoepidermoid carcinoma (20%).

Regarding staging, 40% of tumors were T4. Most (72%) were N0, with 9% N1 and 20% N2. *De novo* metastatic disease was present in 4%.

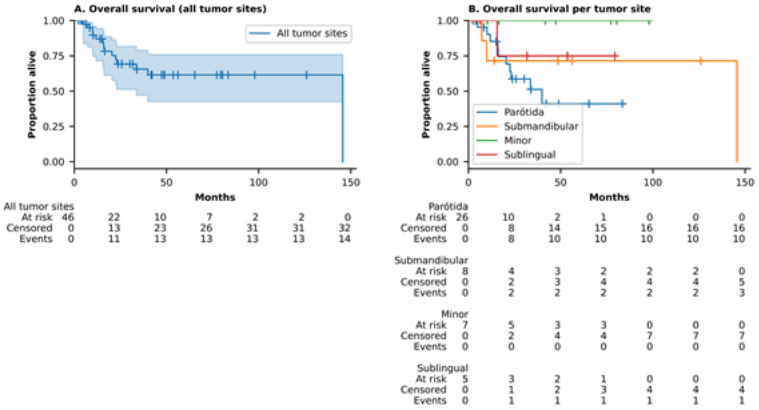
Androgen receptors were tested for in 7 patients, and were positive in 3. HER2 was tested for in 7 patients, and was negative in all of them. Forty-two patients had surgery: 64% with lymph node dissection (LND), 29% without LND and 2% with no information regarding LND. A total of 29 patients had adjuvant treatment: 93% with RT and 7% with ChT and RT. The tumor relapsed in 23 patients (9 local relapses, 14 distant relapses). Nineteen patients had palliative treatment (RT, systemic treatment and best supportive care). For 1st line of palliative treatment (11 patients), 1 patient had antiandrogen therapy and the remainder had platinum-based ChT.

Overall survival among all patients was 65% at 3 years. Overall survival seems lower for parotid tumors compared to minor salivary gland tumors, but without statistical significance after Bonferroni correction ($p > 0.008$).

Conclusions

The most frequent histologic subtypes were similar to the ones described in the literature. Most patients were treated with local treatment. The small sample size didn't allow for comparison of survival according to tumor location. The low incidence of these cancers requires individual and institutional experience in patient management.

Figure 1. Kaplan-Meier curve for overall survival of patients based on primary tumor location. Logrank test non-significant. Logrank p = 0.03 when comparing survival for parotid gland tumors vs minor salivary glands. This doesn't reach statistical significance when correcting for multiple comparisons. The other pairwise comparisons have p > 0.1.



PO-126 | Role of autophagy and its modulation in Head and neck cancer

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(1) San Raffaele Hospital, Milan

Keywords

Autophagy, head and neck cancer

Purpose

Autophagy is a highly conserved catabolic cellular pathway with a well-known double-edged sword in cancer. On one hand, it expresses a tumor suppressive activity in the tumorigenesis, but on the other, once the tumor has been established, it exerts a tumor-promotive activity. Our study aim is to elucidate the role of autophagy in tumor cells and tumor microenvironment as a prognostic factor and possible therapeutic target.

Material/methods

We conduct preclinical studies on head and neck cell lines to investigate how inhibition of autophagy may affect the response to three commonly used chemotherapeutic agents (in particular 5-fluorouracil, cisplatin and docetaxel). Analyzing genomic data accessible on C-Bioportal, we conducted a mutational study on the genes involved in autophagy. Moreover, we conducted a retrospective analysis on previously surgically treated patients affected by oral cancer, the most common head and neck cancer, and the 6th most common cancer worldwide.

Results

Autophagic machinery was found overactivated in tumor cell lines. Of note, both pharmacological and genetic inhibition of autophagy led to the restoration of chemosensitivity in resistant cell

lines. Autophagic genes were found mutated in a small percentage of head and neck cancers, with a tendency of better survival rate in mutated patients. Moreover autophagic marker p62 demonstrated to have a possible prognostic role in patients according to recurrence rate.

Conclusion

Autophagy may be considered a possible targetable mechanism in head and neck cancer

PO-127 | Outcomes of oral cavity carcinoma patients following surgery and post-operative (chemo)radiotherapy

Lauren Sidon [1]; Najah Nizam [1]; Yatman Tsang [1]; Hannah Price [1]; Ashita Ashraf [1]; Shagun Juneja [1]; Kevin Chiu [1]

(1) Mount Vernon Cancer Centre, Northwood, London

Aims

To evaluate outcomes of advanced oral cavity cancer (OSCC) patients undergoing primary surgery at peripheral secondary surgical units followed by post-operative (chemo) radiotherapy (PORT) in a tertiary oncology centre.

Methods

Patients with OSCC treated between January 2018 and December 2021 were reviewed in a prospectively collected database. Patients were staged pathologically using the 8th edition TNM classification. The 2-year local control (LC), regional control (RC), distant control (DC) and overall survival (OS) were analysed. Patients were also stratified according to time from surgery to PORT being less than 6 weeks, 6 to 8 weeks and over 8 weeks.

Results

There were a total of 137 patients and the median age was 63 years (range 34 to 82). Oral cavity subtypes included 47 tongue (34%), 35 lower alveolus (26%), 21 buccal mucosa (15%), 15 upper alveolus (11%), 13 retromolar trigone (9%), 5 floor of mouth (4%) and 1 hard palate (<1%). Postoperative pathology demonstrated 116 (84%) Stage 4 disease, with 65 (47%) at Stage 4a, and 51 (35%) at Stage 4b.

At time of analysis, 38 patients (28%) had recurrent disease and of these 19 patients (50%) developed distant disease. The overall 2-year LC, RC, and DC was 96%, 86%, and 86% respectively. Of the

recurrences, 12 patients (32%) had Stage 4a and 17 (45%) had Stage 4b disease at presentation. Of the 47 patients with pathological node negative (pN0) disease post-surgery, 31 (66%) received no neck PORT. Two of these (6%) developed ipsilateral regional recurrence. Additionally, 2 pN0 patients (4%) developed contralateral neck recurrence despite having lateralized buccal and lower alveolus OSCC.

The OS of all patients was 79% at one year and dropped to 68% at two years. The 2-year OS for stage 4a and 4b patients was 85% and 45% respectively (p=0.003) (Figure 1). The 2-year RC and DC for Stage 4b patients was 82% and 73% respectively. All stage 4b patients were upstaged due to pathological extranodal extension, with 26 (51%) underwent concurrent chemotherapy with PORT.

The median time from histological diagnosis to surgery, and from surgery to PORT was 4.7 (range 0.7–14.6) and 7.7 weeks (range 3.9–13.7) respectively. OS at two years was 82% in those receiving PORT within 6 weeks from surgery (n=24), compared to 65% in the 6 to 8 week (n=66) and 67% in over 8 weeks cohort (n=44). The difference was not statistically significant (p=0.535) (Figure 2).

Conclusions

Stage 4b patients had a significantly worse prognosis than earlier stage disease. In this subgroup, careful disease and patient assessment should be considered about whether major surgery followed by PORT should be the default management given the poor outcomes.

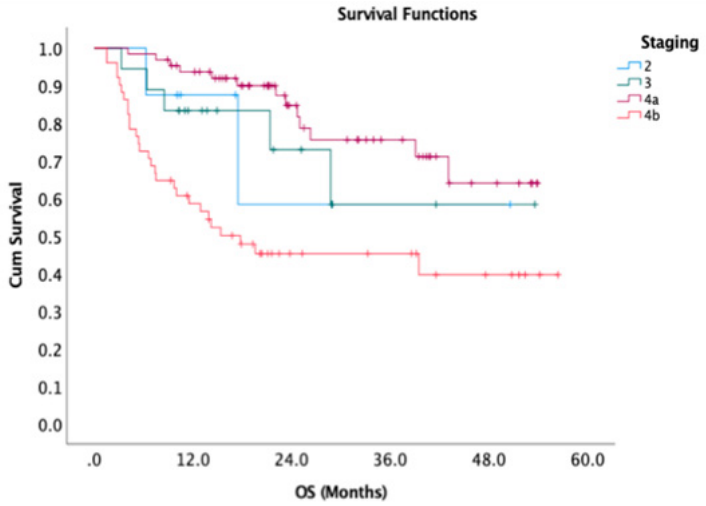

Figure 1 – Effect of staging on overall survival

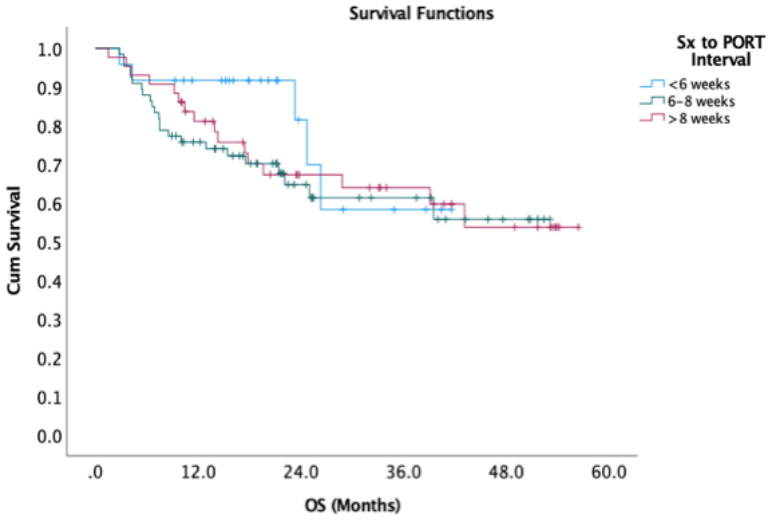

Figure 2 – Effect of time from surgery to (chemo)radiotherapy on survival

PO-129 | Head and neck cancer surgery in elderly patients: the role of frailty assessment

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Keywords

Elderly, Frailty, Postoperative complications, Head and neck surgery

Objectives

To study whether any risk model, frailty index, patients' comorbidities, or demographic characteristics correlate with postoperative morbidity in elderly patients who underwent surgery for head and neck cancer (HNC). A secondary objective was to compare between frailty indexes that are used at our medical center.

Methods

A retrospective analysis of head and neck cancer patients operated between 2007 and 2021 was performed.

Results

One hundred and fifteen patients were included and divided into three age groups: 50–69 years, 70–79 years and≥80 years. Although most elderly patients had a significantly higher rate of comorbidities and lower Norton scores, no statistically significant difference was found between the groups in postoperative morbidity rates, intensive care unit (ICU) or internal medicine department admissions, re-hospitalization in 1–3 months, and in falling risk (MFS—Morse Fall Scale). On multivariate analysis there was a positive correlation between preoperative cerebrovascular accident (CVA), dementia, and cardiac arrhythmias, and the probability for developing postoperative complication. The latter findings were not related to the patients' age.

Conclusions

In this study, we did not find higher postoperative morbidity rates among elderly population in comparison to younger age groups, and therefore, our current evaluation system could not assist in identifying elderly at risk. However, prediction of operative risk based on physiologic reserve or frailty is an important tool in the evaluation of elderly head and neck cancer patients. Future studies are needed to assess the role of frailty index in the elderly head and neck cancer population.

PO-131 | Intragenic NF1 deletions in sinonasal mucosal malignant melanoma.

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Keywords

Sinonasal cancer; mucosal melanoma; NGS; mutation; intragenic deletion; NF1

Purpose/Objective

Sinonasal mucosal melanomas (SNMM) are rare and aggressive tumors in which, despite the effectiveness of local therapies, recurrence and metastasis are still frequent, resulting in a 5-years overall survival rate of 20-40%. As it becomes increasingly recognised that mucosal melanomas behave as systemic diseases, interest in understanding their genetic and molecular characteristics is growing. This study is aimed to identify actionable genetic alterations in a sample of SNMM by next-generation sequencing (NGS).

Material/methods

15 SNMM samples were analyzed by NGS and Sanger sequencing. Gene copy number alterations were analyzed by MLPA. Mutation status was correlated with pERK and Ki-67 expression and follow-up data.

Results

Inactivating mutations and intragenic deletions in *NF1* were identified in 3 and 2 cases, respectively (in total 5/15, 33%) and activating mutations in *NRAS* and *KRAS* in 3/15 cases (20%). Other mutated genes included *CDKN2A, APC, ATM, MITF, FGFR1* and *FGFR2*. *BRAF* and *KIT* mutations were not observed. Cases with

NF1 alterations tended to have worse overall survival. The mutational status was not associated with pERK, pAKT or Ki-67 immunostaining.

Conclusion

SNMM carry frequent gene mutations activating the MAPK pathway. Intragenic *NF1* deletions have not been described before and may go undetected by sequencing studies. This finding is clinically relevant as *NF1* mutated melanomas have worse survival and could benefit from therapy with immune checkpoint and MEK inhibitors.

PO-132 | CURRENT MANAGEMENT OF MALIGNANT TUMORS OF PAROTID GLAND AREA. SURGICAL TIPS AND CONTROVERSIES

Milan Stankovic [1]

(1) Outro

Key words

Malignant tumors, surgery, parotid gland, temporal bone, skull base, facial nerve

Objective

To present current surgical tretamnt options for parotid area malignant tumors.

Surgical treatment of different malignant tumors affecting parotid gland and its surroundings (temporal bone, skull base, parapharynx) includes: superficial, total, radical, and extended radical parotidectomy. Such surgery often includes flaps, reconstruction, and can be aided by harmonic scalpel, and endoscopic approach. Management of the facial nerve is essential while performing such surgery. Anterograde, retrograde facial nerve identification, and facial nerve monitoring enable facial nerve preservation. Important questions concerning facial nerve and malignant tumors are: nonfunctional nerve and surgery, occult temporal bone facial nerve involvement, and perineural spread, as well. Controversial subjects are: parotidectomy and malignant tumor of auricle or surrounding skin, and deep lobe parotidectomy for metastases. Temporal none invasion is surgically treated by subtotal or total petrosectomy. Surgery includes elective, modified radical, radical, or extended radical neck dissection.

Results

We present current reference data concerning malignant tumors in parotid area, and surgical tips in solving each of the affected

structure with indications, surgical technique, and reconstruction of defect. The size and propagation of the tumor determines the type and extension of resection, ability to obtain negative surgical margins, preservation of vital structures, prevention of complications, better survival rate, and postoperative quality of life.

Biological markers and molecular targeted therapy are discussed. Tissue engineering and new technologies in contemporary and future treatment of malignant tumors affecting parotid gland area are presented.

Conclusion

Malignant tumors affection parotid gland, temporal bone, skull base, and parapharynx are difficult to treat surgically. Adequate surgical technique, and new technologiaes have improved the results of surgery.

PO-133 | Reducing cancer diagnosis times by the introduction of rapid-access Head & Neck lump imaging

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(1) Bedfordshire Hospitals NHS Foundation Trust

Keywords:
Diagnosis, ultrasound, biopsy

Objective

Reduction of time to diagnosis and treatment in head & neck cancer is consistently associated with improved patient outcomes. However, the COVID-19 pandemic has delayed patient presentation to head and neck services and the effects of the pandemic are still being felt. Though guidelines have long-recommended ultrasound-guided needle sampling, ideally in a one-stop setting, this has not always been within the reach of large tertiary general hospitals. Given this setting, our aim was to improve the time taken to diagnose head and neck cancer (or to reassure of a non-cancer diagnosis), by introducing a rapid-access clinic for head and neck lumps including same day ultrasound scanning with fine needle aspiration/core needle biopsy. We wanted to determine whether this could mitigate delays in diagnosis by making our part of the diagnostic pathway more efficient.

Based on a risk-stratification calculator that was used across the UK during the COVID-19 pandemic, referrals were triaged to this rapid-access clinic if they reported a new persistent lump in the neck or salivary gland region. To maximise the efficiency of resource use, we further specified the necessity for an externally visible or palpable lump, and excluded patients with a previous ultrasound or needle aspiration diagnosis.

Methods

Data was collected in two rounds: 3 months prior to (May – July 2022) and 3 months after (September – November 2022) the introduction of the rapid-access clinic. Data collected included reason for referral (to determine the quality of triage), time from referral to specialist review, time from referral to ultrasound imaging, and time from referral to the diagnosis being communicated to the patient. Patients not fitting the agreed criteria for the rapid-access clinic were excluded.

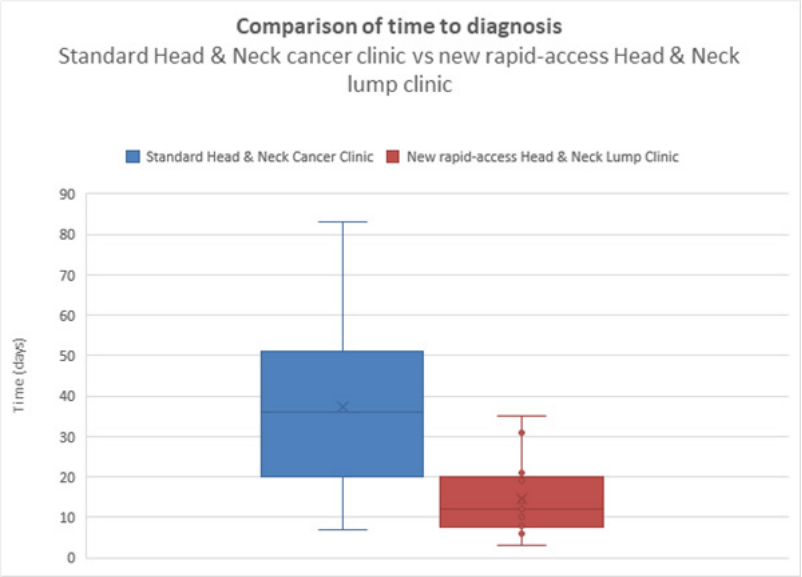
Results

In the first round 39 suitable patients had reached a diagnosis at the time of analysis: the median time to diagnosis was 36 days (interquartile range 21.5-50.5); the median time to ultrasound imaging in the first round was 28.5 days (IQR 23.25-37.75). In the second round 13 patients had reached a diagnosis at the time of analysis: the median time to diagnosis was 12 (IQR 8-19); median time to ultrasound imaging in the second round was 9 (IQR 7-14). The Wilcoxon rank sum test was applied showing a statistically significant difference in the time to diagnosis of 24 days (p-value < 0.001), and a statistically significant difference in the time to ultrasound of 19.5 days (p-value < 0.001). There was no statistically significant difference in the time between referral and first clinical review.

Conclusion

This preliminary data shows a 66% reduction (24 days) in the median time to diagnosis and a significant reduction in ultrasound delays. This was despite an equivalent duration between referral and the first clinical review showing that it was the availability of same-day ultrasound that generated the improvement. This suggests that a one-stop clinic model with same day ultrasound imaging may significantly reduce the time to diagnosis in head and neck cancer presenting via neck lumps. These results should

encourage other tertiary head & neck services based in large general hospitals that the establishment of rapid-access clinics with the availability of same-day USS-guided needle biopsy can help reduce the impact of post-pandemic delays on cancer diagnosis and treatment.



PO-134 | Development of a reusable metal 3D-printed Heat and Moisture Exchanger

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(1) Netherlands Cancer Institute Amsterdam (2) Mobius 3D Technologies

Keywords

Heat and Moisture Exchanger, total laryngectomy, pulmonary rehabilitation

Purpose/Objective

Due to sub-optimal humidification performance and compliance of small disposable Heat and Moisture Exchangers (HMEs), often consisting of a plastic cassette and foam core coated in hygroscopic salt, pulmonary complaints remain prominent in patients with a tracheostomy or permanent tracheostoma after total laryngectomy. Metal 3D printing could enable the development of both higher-performing and reusable HMEs while maintaining acceptable breathing resistance and size and enabling accurate optimization of these parameters. This study assesses the humidification performance of three all-metal 3D-printed HME prototypes.

Material/Methods

Under standardized conditions, we measured the humidification performance (water exchange) of three stainless steel HME prototypes with different core designs, with similar low breathing resistance and size compared to a commercially available disposable HME. We chose stainless steel because it can store and release a lot of heat needed for water exchange (the condensation and evaporation of water) and because of its biocompatibility, durability, and reliability in 3D printing.

Results

All three HME prototypes have a humidification performance that exceeds that of the disposable HMEs under ambient conditions. The HME prototypes are much heavier than disposable HMEs, even though they have a similar size, due to the high density of the stainless steel.

Conclusion

A 3D-printed metal HME could provide a higher-performing and reusable alternative to disposable HMEs, potentially positively affecting overall HME compliance and experienced pulmonary complaints in patients with a tracheostomy or permanent tracheostoma. Therefore, we recommend a long-term clinical assessment of the metal HME to assess patient compliance and acceptance as the next step.

CONFLICT OF INTERESTS AND FUNDING

Mobius 3D Technologies (Nieuw-Vennep, The Netherlands) has filed a patent application for the additive manufacturing of HMEs (P6105500NL). The authors have no other funding or conflicts of interest to disclose.

PO-135 | Response pattern under palliative chemotherapy in R/M HNSCC

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Purpose

Cytotoxic chemotherapy in combination with cetuximab has been the standard of care for patients in the recurrent metastatic setting of head and neck cancer until the introduction of immunotherapy and remains a treatment option for some patients. The majority of patients have an objective response to treatment and 4-6 cylces are considered as standard of care followed by cetuximab maintenance. Many patients experience excessive toxicities with impaired quality of life. We investigated treatment response after two or three cycles of chemotherapy and evaluated whether continuation of treatment after interim staging led to further tumor reduction.

Methods

Patients treated at Charité university Cancer Center, Berlin Germany were included in the retrospective study. Inclusion criteria consisted of recurrent metastatic head and neck squamous cell carcinoma having received either platinum, 5-FU, cetuximab (PFC) or docetaxel, cisplatin, cetuximab (TPEx) 6 or 4 cycles respectively. Imaging had to be complete for baseline, interim and final evaluation. Response to treatment was assed by an radiologist according to RECIST1.1 criteria. The institutional ethic board approved the study. IBM SPSS Statistics 27 was used to perform descriptive and exploratory analysis.

Results

638 patients were screened of which 69 met the eligibility criteria. 56 patients were treated with PFC, 13 patients received TPEx. Treatment results at interim were stable disease 22 (31.9%) patients, partial remission 46 (66.7%) patients and complete remission 1 (2.7%) patient. Out of 69 analyzed patients only 3 patients (4.3%) showed further regression of tumor volume comparing interim with final staging at the end of chemotherapeutic treatment. No patient with stable disease at interim imaging had a further reduction in tumor size over the continued course of therapy.

Conclusion

Out of 69 patients only three showed a further reduction of tumor size over the continued course of therapy. It is unclear whether the continuation of chemotherapy over 2/3 cycles translates in a survival benefit. Especially in the light of the treatment associated toxicities and quality of life, short courses of therapy compared with SoC should be prospectively evaluated.

PO-137 | Socioeconomical factors of HNC pacients in Czech Republic – HEADSpAcE project

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Objective/Porpuse

Head and neck cancer (HNC) is the seventh most common type of cancer worldwide and fifth most common type in Czech Republic. Predominant risk factors have used to be tobacco use and alcohol abuse. In last decades other factors like human papillomavirus plays still more and more important role. With this change also the socioeconomical profile of the HNC patients became different, especially in lower age, higher number of non-smokers, sex behaviors, e.g. The goal of our study, which is part of the large international HEADSpAcE project, is to find and summarize new patterns of HNC patients for improving cancer screening and prevention.

Methods

78 patients with HNC were diagnosed and treated at ENT surgical center in Prague. Socioeconomical information like age, level of education, family status, diet and sex behavior, general health and comorbidities were obtained from the questionnaire and analyzed.

Results

65% of male and 35% female patients were treated with HNC, in average age 63 years, when diagnosed. Only 38% were active smokers, 34% stopped more than 3 years ago, 27% have never smoked. 73% were active or former alcohol consumers, only 27% have never drunk alcohol. Average number of sex partners were 2-5. 73% of patients refer their health as good or very good, most frequent comorbidity

was cardiac disease in 44%. Most frequent localities of tumor were tonsil (32%), tongue base (25%) and larynx (24%).

Conclusion

New knowledge in pathophysiology of head and neck cancer in last decades has changed traditional patterns of patients with type of cancer. Gaining actual and precise profile of current HNC patient will help with better screening, early diagnosis and treatment, that is crucial for good prognosis of this disease.

PO-138 | Malignant tumors of Major Salivary Glands: a clinicopathologic review of cases over a 25-year period

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Keywords

Salivary Gland; Cancers

Purpose/Objective

Malignancies of major salivary glands are uncommon, accounting for 2% to 5% of all head and neck cancers. They are distinguished by diverse histological subtypes and wide range of clinical and biological behaviors. This retrospective study aims to describe the clinical behavior of major salivary gland cancers treated at a tertiary oncology center in the last 25 years.

Materials/Methods

A data line search was made of all patients who had treatment for major salivary gland cancers at a tertiary center from June 1997 to June 2022. Patient, tumor, and treatment characteristics were recorded from a retrospective analysis.

Results

A total of 276 patients were included. Data are shown in Table 1 and 2.

Median age at diagnosis was 64 years. 142 (51.4%) were male. Site of primary tumor was parotid in 223 patients (80.8%), submandibular in 50 (18.1%), and sublingual gland in the remaining 3. A palpable mass was noted as the first symptom in 221 (80.1%) patients. 176 patients performed FNA, from which 73.3% revealed

malignant cytology. Regarding TNM classification, an equitable distribution was seen through the 4 stages.

Majority (90.9%) underwent surgery as first treatment approach. 208 parotid surgeries were performed – 110 (53%) superficial parotidectomies and 94 (45%) total or extended parotidectomies – 42 with facial nerve sacrifice (either partial or total). Also, majority of submandibular cancers (94%) underwent surgery as first treatment. 29 (11.6%) had an elective neck dissection and 44 (17.5%) had a therapeutic neck dissection.

With respect to parotid cancers, the most common histology was salivary duct carcinoma (17.3%), followed by mucoepidermoid carcinoma (16.4%). Regarding submandibular gland cancers, the most common histology was adenoid cystic carcinoma (46%), followed by salivary ducts carcinoma (14%). Perineural invasion was present in 86 (45.3%) surgical specimens, vascular invasion, in 56 (29.5%); close or positive margins, in 145 (60.6%); and high-grade in 97 (51.6%) tumors.

The expression of HER2 and androgen receptors was investigated in 40 patients, mostly in the context of recurrent or metastatic disease.

In the adjuvant setting, 176 patients (70.1%) performed radiation therapy.

With a median follow-up of 46 moths, 86 (32.5%) patients showed recurrence of the disease. Median time to first recurrence was 13 months. The most common site of distant recurrent disease was the lung, followed by the bone and the liver.

Involved margins were considered a significant prognostic factor for recurrence ($p<0.05$). Stage grade and margins are, in univariated analyses, independent prognostic factors.

The 5-year overall survival, disease-free-survival and disease-specific survival rates were 59%, 63.8%, and 67%, respectively.

Conclusion

With the limitations that a 25-year setback entails, we present a considerable sample of salivary cancers. Patients and histopathologic characteristics are similar to those described in the literature. In our experience, FNA has a high sensibility (73.3%) eventually allowing a better staging and therapeutic adequacy. Although surgery remains a powerful tool, high recurrence rates (32.5%) remain a concerning challenge. Classic prognostic factors like stage, grade and margins should be considered in the risk stratification of patients. Awareness to specific histopathologic particularities can help to optimize both local and distant control of these aggressive cancers.

Clinical features	
Male	142 (51.4%)
Age at diagnosis - median, years (range)	64 (6-93)
Salivary Gland	
Parotid	223 (80.8%)
Submandibular	50 (18.1%)
Sublingual	3 (1.1%)
FNA	176
Malignant	129 (73.3%)
Symptomatic at time of diagnosis	233
Palpable Mass	221 (94.8%)
Pain	52 (22.3%)
Facial nerve compromise	26 (11.2%)
Stage at diagnosis	
Stage I	61 (22.4%)
Stage II	79 (29%)
Stage III	59 (21.7%)
Stage IV	73 (26.4%)
IV a	37 (13.4%)
IV b	26 (9.4%)
IV c	10 (3.6%)
First treatment approach	
Surgery	251 (90.9%)
Chemotherapy	10 (3.6%)
Radiation Therapy	3 (1.1%)
Chemotherapy + Radiation	5 (1.8%)
Symptomatic	7 (2.5%)
Initial Surgery (n= 251)	
Parotid Gland	
Enucleation	4 (1.6%)
Superficial parotidectomy	110 (43.8%)
Total parotidectomy	
w/ facial nerve preservation	52 (20.7%)
w/ facial nerve sacrifice	37 (14.7%)
w/ facial nerve sacrifice + mastoidectomy	5 (2%)
Submandibulectomy	47 (18.7%)
Sublingual gland excision	3 (1.2%)
Neck lymph node dissection	71
Elective	29 (11.6%)
Therapeutic	44 (17.5%)

Table 1: Clinical, first treatment approach and initial surgery features.

Histopathological findings (n=251)	
Tumor dimension – median, mm	27
Perineural invasion	86 (45.3%)
Vascular invasion	56 (29.5%)
Lymphatic invasion	40 (15.3%)
High-grade tumors	97 (51.6%)
Close margins	62 (25.9%)
Involved margins	83 (34.7%)
Investigation of HER2 and androgen receptor expression (n=40)	
Androgen Receptor +	16 (40%)
HER2 +	9 (22.5%)
Adjuvant treatment after surgery	
Radiation therapy	176 (70.1%)
Radiation + chemotherapy	13 (5.2%)
Chemotherapy	2 (0.8%)
None	60 (23.9%)
Recurrence (n=121)	
Time until recurrence – median, months	13
Local	48 (39.7%)
Regional	6 (5%)
Locoregional	6 (5%)
Systemic	38 (31.4%)
Local and systemic	10 (8.3%)
Regional and systemic	7 (5.8%)
Treatment	
Surgery	28 (23.1%)
Surgery + radiation therapy	15 (12.4%)
Surgery + Chemotherapy	3 (2.5%)
Chemotherapy	26 (21.5%)
Radiation therapy	12 (9.9%)
Radiation + Chemotherapy	10 (8.3%)
Radiation + Chemotherapy + Surgery	4 (3.3%)
Immunotherapy	1 (0.8%)
Cryoablation	1 (0.8%)
Symptomatic	19 (15.7%)

Table 2: Characteristics regarding histopathology, adjuvant treatment and recurrences.

PO-139 | Laryngeal cancer detection algorithm for self-screening test based on convolutional neural network

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Keywords

Laryngeal mass, Convolutional neural network, Deep learning, Patient safety

Purpose/Objective

Early detection of laryngeal cancer without periodic visits to hospitals is essential for improving the possibility of full recovery and the long-term survival ratio after prompt treatment, as well as reducing the risk of clinical infection.

Material/methods

We utilized an NVIDIA Geforce RTX2060 board, Anaconda 3.7, Python 3.6.10, Tensorflow 1.13, Keras 2.0.8, and CUDA 10.0 on Ubuntu 18.04.4 LTS for model development.

Results

We first propose a convolutional neural network model for automated laryngeal mass detection based on diagnostic images captured at hospitals. Thereafter, we propose a pilot system, composed of an embedded controller, a camera module, and an LCD display, that can be utilized for a home-based self-screening test. In terms of evaluating the model's performance, the experimental results indicated a final validation loss of 0.9152 and a F1-score of 0.8371 before post-processing. Additionally, the F1-score of the original computer algorithm with respect to 100 randomly selected color-printed test images was 0.8534 after post-processing while that of the embedded pilot system was 0.7672.

Conclusion

The proposed technique is expected to increase the ratio of early detection of laryngeal cancer without the risk of clinical infection spread, which could help improve convenience and ensure safety of individuals, patients, and medical staff.

PO-142 | Outcomes of curative treatment in elderly patients with locally advanced oropharynx cancer

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Keywords

Oropharynx, elderly, outcomes

Purpose/Objective

The incidence of head and neck cancer is rising worldwide, as is the number of elderly patients with this disease, in part because of life expectancy. However, the representation of this population in clinical trials is scarce and therefore the outcomes may be different from general population. These differences may be explained by medical comorbidities and performance status to endure treatment toxicities. Our goal was to understand if elderly and non-elderly patients with locally advanced oropharynx cancer treated with definitive chemoradiation had comparable outcomes.

Material/Methods

This is a retrospective unicentric cohort of patients with diagnosis of oropharynx cancer between January 2017 to December 2022. Demographic data, OS and PFS were collected from patients' medical files and analysed using SPSS V26. Patients above 65 years old were considered elderly.

Results

A total of 27 patients were diagnosed with locally advanced oropharynx cancer between January 2017 to December 2022. From these, 9 were considered elderly with a median age of 72.89 years,

the majority being male (n=8) and p16+ (n=6). In the group of the non-elderly (n=18) the median age was 49.83 years, most of them were also males (n=15) and p16+ in 9 of them.

Most patients (n=24) underwent definitive chemoradiation consisting of 3 cycles of 3-weekly cisplatin concurrently with fractionated external radiotherapy. Two patients were treated with carboplatin and one with cetuximab instead, simultaneously with radiotherapy.

When analysing outcomes, we found a statistical difference between groups in PFS (*p= 0.03*) with the elderly group having a median PFS of 16.33 months compared to 27.99 months. Regarding OS, the elderly group had a median OS of 35.61 months compared to a median OS of 37.11 months in the non-elderly group, without statistical difference (*p=0.42*).

Conclusion

We can conclude that the PFS in elderly oropharynx cancer patients is worse than in the younger population, submitted to the same treatment regimen. This could be explained by the lower compliance of these patients to withstand treatment toxicities which can lead to treatment interruptions and affect disease control.

However, the same conclusion cannot be taken about OS. The absence of statistical difference in OS between the two groups might be justified by the new upcoming treatment strategies, for instance immunotherapy, that may prolong patients' survival despite initial disease progression. There are some limitations of this study that should be noted, first the low number of patients, the lack of analysis of medical comorbidities and treatment interruptions because of toxicities.

To sum up, the literature is not consensual about outcomes in elderly patients and more evidence is needed to take further conclusions.

PO-143 | Clinical parameters associated with immunotherapy outcomes in metastatic cutaneous SCC

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(1) The Christie NHS Foundation Trust (2) The Univeristy of Manchester (3) University Hospitals of Leicester NHS Foundation Trust (4) Portsmouth University Hopsitals NHS Foundation Trust (5) University Hospitals of Leicester NHS Foundation Trust

Purpose

Drug therapies blocking the programmed death 1 (PD1) receptor have transformed the management of recurrent/metastatic cutaneous squamous cell carcinoma (R/M-cSCC) with durable responses seen in most patients. However, around 30% of patients derive no meaningful benefit from treatment and there is a need to develop predictors of response and resistance to therapy. Immunohistochemistry for the PD1 ligand (PD-L1) has no defined role as a predictive biomarker. We therefore sought to evaluate clinical parameters in a cohort of patients with R/M-cSCC treated with the anti-PD1 therapy cemiplimab to identify clinical parameters predicting response/resistance to therapy.

Method

88 patients with R/M-cSCC were treated with cemiplimab 350mg every 3 weeks at 3 UK cancer centres until progression or toxicity as per physician assessment. Clinical characteristics, including immunocompromised status, site of disease and treatment outcomes were recorded for all patients. Overall survival (OS) was calculated from the date of confirmed recurrent, metastatic or locally advanced disease. Locally assessed progression free survival (PFS) was calculated from the date of cycle 1. Univariate Kaplan Meier survival analysis was performed, and differences calculated using log rank test. Toxicities were asses-

sed as per common terminology criteria for adverse events version 5 (CTCAE v5).

Result

Of 88 R/M-cSCC patients (73% male, 27% female), median age was 71 years (range 34 to 93 years). Prior surgery was performed in 66% and prior radiotherapy in 57%. The primary site was of the head and neck region in 65%, the remainder were torso (7%), upper limb (7%), lower limb (18%) and unknown primary site (3%). The median number of cycles was 8 (range 1 – 36) and median duration of follow up 14 months. The overall response rate (ORR) was 60% (53/88). For the entire cohort, the median OS and PFS was not reached, and the 2-year OS rate was 60%. 40% (35/88) of patients developed immune-related (IR) toxicities of any CTCAE grade, while 13% (11/88) developed grade 3 or above. Patients with head and neck (HN) primary site had significantly improved OS and PFS compared with other sites combined. For HN primary site, median OS was not reached versus 25.8 months and 1 year OS rate was 83% versus 52% (p=0.035) and median PFS was not reached versus 6.5 months (p=0.006). No differences in survival outcomes were identified based on other clinical parameters.

Conclusion

Cemiplimab treatment demonstrated significant clinical benefit with a manageable side effect profile. Patients with R/M-cSCC with a head and neck primary site have a significantly improved OS and PFS compared with other primary sites when treated with cemiplimab, and future work should be undertaken to investigate this further.

PO-144 | Early detection of recurrent HPV-positive HNSCC by ctDNA analysis

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Keywords

ctHPVDNA, HNSCC, biomarker

Purpose/Objective

Plasma circulating tumor DNA (ctDNA) is a potential biomarker of cancer diagnosis and disease monitoring. We previously developed and tested a next generation sequencing assay for ctDNA analysis in head and neck cancer that allows assessment of copy number changes and human papillomavirus DNA (HPV) by low coverage whole genome sequencing, as well as mutations in frequently changed cancer genes by target-enrichment deep sequencing. To increase sensitivity of HPV DNA detection we included high-risk HPV-E7 sequences in the target-enrichment panel. The aim of this study is to demonstrate performance of the adapted assay and to demonstrate that this assay allows longitudinal monitoring of ctHPV-DNA in plasma and oral rinse during post-treatment follow-up and accurately predict residual disease or disease recurrence

Material/Methods

Parental test performance was analyzed in plasma of 10 patients with HPV-positive tumors and 20 non-cancer controls1. The adapted test was analyzed on baseline plasma and oral rinse of 27 HPV-positive OPSCC patients and 27 non-cancer controls; matched for age, smoking and alcohol use. For the longitudinal monitoring study plasma samples were analyzed of 9 patients with HPV-positive head and neck cancers with recurrent disease and

of 18 patients who remained disease-free, matched for stage and treatment. Blood plasma and oral rinse samples were available at baseline, 6 months, 12 months and 24 months and collected within the framework of the NETQUBIC study.

Results

With the parental lcWGS assay HPV-DNA in plasma was detected in 100% of patients with HPV-positive tumors, and not in plasma of 9 patients with HPV-negative tumors and 20 non-cancer controls. Performance of the adapted assay as compared to the parental assay is underway and the data will be presented. Results for disease monitoring in 9 patients with recurrent disease and 18 patients who remained disease-free will be discussed in addition.

Conclusion

Monitoring for HPV DNA in plasma is highly sensitive and specific, and ctHPVDNA testing holds promise as screening assay after treatment for early diagnosis of recurrent disease.

PO-145 | Implementation of free flap head and neck reconstruction: from zero to the standard of care

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Keywords

Reconstruction, microsurgery

Purpose/Objective

Immediate microsurgical free flap reconstruction after tumor resections is a gold standard approach for head and neck cancer surgery. Free tissue transfer is preferred compared to local flaps, as it provides significantly improved functional and aesthetic restoration and reduces morbidity at the donor site. However, free flap reconstructions are complex and challenging procedures, therefore their initial implementation at the unexperienced departments is an ambitious endeavor.

Material/methods

Having successfully established microsurgical head and neck reconstructions at the National Cancer Institute (Lithuania) over the past four years, in this presentation we will delineate the essential steps that are essential for successful start. We highlight the importance of knowledge transfer from experienced world-wide Head and Neck departments as well as hands-on training to acquire specific skills required to perform free flap raising and microsurgery.

Results

Reconstructive surgeries for medium, large and complex head and neck defects performed in our department from 2018 to 2022 using the radial forearm, anterolateral thigh, deep circumflex iliac artery (DCIA), and scapula system flaps will be presented in detail.

Conclusion

Our experience provides the guidance for any other surgical departments aiming to introduce free flap surgeries as their standard of care. Furthermore, we reveal the enhanced reconstructive capacity of multidisciplinary teams, such as ours, consisting of two maxillofacial surgeons and two ear, nose and throat (ENT) surgeons.

PO-147 | Experience in microvascular reconstruction of a Portuguese reference centre on head and neck cancer

Henrique Messias *[1]; Miguel Vilares [1]; Sandra Bitoque [1]; Patricia Santos [1]; Inês Salgado [1]; Luisa Sequeira [1]; Ricardo Nogueira [1]; Carina Semedo [1]; Pedro Gomes [1]*

(1) INSTITUTO PORTUGUÊS DE ONCOLOGIA LISBOA

Keywords

Head and Neck Cancer, Maxillofacial Reconstruction, Microvascular reconstruction.

Purpose/Objective

Microvascular free-tissue transfer significantly changed reconstructive capacity and outcomes in patients with head and neck cancer. The experience with this technique in patients with head and neck cancer in Portugal is still poorly reported. Here, we present the experience and lessons learned in microvascular reconstruction of a Portuguese reference centre on head and neck cancer.

Material/Methods

The medical records of a tertiary referral center for head and neck cancer were retrospectively evaluated. All patients undergoing reconstruction with free flaps were selected and information was collected on the characteristics of the population, free flap, comorbidities, complications and follow-up.

Results

Between 2013 and 2021, 227 free flap reconstruction procedures were performed. The majority were radial forearm (60%) and fibula (37.5%) free flaps. The majority of patients were male (71%), age ranged between 16 and 79 years, most tumors located in the oral cavity (95%) most being squamous cell cancers. An overall

success rate of over 90% for free-tissue transfers is reported, in line with reports in the literature.

Conclusion

Reconstruction of head and neck defects with free flaps is a reliable procedure in head and neck oncology.

PO-148 | Multimodal approach to rare and aggressive neuroendocrine carcinoma of paranasal sinuses

Andreia Ponte [1]; Rita Vitorino [1]; Frederico Sarmento [1]; Teresa Alexandre [2]; Eduardo Netto [2]

(1) HOSPITAL SANTO ESPIRITO | ILHA TERCEIRA (2) INSTITUTO PORTUGUÊS DE ONCOLOGIA LISBOA

Purpose/objective

Neuroendocrine carcinoma (NEC) is a rare disease of nose and paranasal sinuses. In contrast to other regions NEC of this area has been reported to be recurrent and locally aggressive, and unlike squamous cell carcinoma which is most commonly seen in maxillary sinus, NEC is mostly observed in ethmoid sinus. No definite treatment has been established till date because of rarity of this disease and sparse literature about this topic is available, but multimodality approach is recommended. Our purpose with this work is to describe a case treated at our institution and perform a literature revision at the same time.

Material/methods

Literature revision and clinical case description.

Results

A non-smoker 46-years-old male presented with 2 months history of anosmia, nasal obstruction, right nostril bleeding, watering and right periorbital edema. Examination revealed a bleeding mass in the right nasal cavity (middle nasal meatus). Computed tomography (CT) and magnetic resonance imaging scans revealed an expansive mass in the right anterior nasal cavity, frontal and ethmoid – maxilar region, with skull base and right orbita invasion, and a suspicious right submandibular lymph node. Biopsy revealed carcinoma with neuroendocrine

differentiation. AE1/AE3 positive, focal positive for chromogranin A, synaptophysin, P40 and negative for S100, HMB45. The patient had no evidence of distant metastasis (CT scan and PET FDG). A right partial maxillectomy ressection with orbital exenteration, right sphenoidotomy, right skull base exeresis and reconstruction, right cervical lymph nodes dissection (level I-IV) was performed. The pathology analysis confirmed poorly differentiated neuroendocrine carcinoma, with cerebral invasion and cervical nodal involvement, staged as pT4bN2bM0 ECE+, R1. He was started on adjuvant concurrent chemo radiotherapy, but shortly afterward, local recurrence was documented. The treatment was maintained, with definitive intention, with cisplatin along with a total radiotherapy (RT) dose of 70Gy in 33 fractions, delivered by intensity modulated radiotherapy (IMRT) technique. The patient had 3 cycles of adjuvant cisplatin and etoposide chemotherapy (ChT). Two months later, the patient presented to us with multiple rapidly growing skin scalp nodules. The biopsy report revealed subcutaneous metastization. He was restarted on ChT with two different regimens with clinical progression, so we decided to treat him with radiotherapy (30Gy/10fr) with a significant decrease on size and number of the lesions, which had impact on his quality of life and body image. Unfortunately few months after he developed the same lesions on both sides of the neck. We performed the same radiotherapy scheme with partial clinical response and improvement on his ability to swallow. The patient died 14 months after his initial diagnosis.

Conclusion

Head and Neck NEC is a rare but aggressive neoplasm, with no demographic preference, no correlation with smoking or radiation, with strong propensity for locoregional recurrence and distant metastasis. Extra-pulmonary NEC has proven to be a fatal disease having poor prognosis with a 13% five year survival rate. This case demonstrates the poor outcome of this disease, but

despite of that it also proves that we have some tools to palliate the symptoms and increase the quality of life of our patients. Further investigation is needed to improve the outcomes of this aggressive disease.

PO-149 | Reconstructive surgical procedures for the management of salvage laryngectomy complications

Septimiu Sever Pop [1]; *Cristina Tiple* [1]; *Mirela Cristina Stamate* [1]; *Magdalena Chirila* [1]; *Valentin Muntean* [2]; *Marius Fodor* [3]; *Lucian Fodor* [4]

(1) ENT Department, "Iuliu Hatieganu" University of Medicine and Pharmacy Cluj-Napoca (2) Surgery Department, "Iuliu Hatieganu" University of Medicine and Pharmacy Cluj-Napoca (3) Vascular Surgery Department, Clinical County Emergency Hospital Cluj-Napoca (4) Plastic and Reconstructive Surgery Department, Clinical County Emergency Hospital Cluj-Napoca

Keywords

Salvage laryngectomy, reconstructive procedures, pharyngocutaneous fistula

Purpose/Objective

Salvage total laryngectomy (STL) remains the only hope for survival for patients with recurrences after chemoradiation protocols. A higher rate of postoperative complications is expected after STL, the most frequent being pharingocutaneous fistula (PCF). Various surgical reconstructive procedures are required in the management of these complications.

Material/methods

We performed a retrospective analysis of all patients who underwent a salvage total laryngectomy after organ preservation protocol failures in our Department between 2016 and 2020. We assessed the incidence of pharyngocutaneous fistula and the available management options.

Results

30 patients were included in this study. 17 (56,66%) patients developed a pharyngocutaneous fistula in the postoperative pe-

riod. No significant differences have been found between the subgroup that received chemoradiotherapy compared to radiotherapy alone. Six patients (35,29%) with minor fistulae were successfully treated with conservative measures. Of the 11 patients (64,70%) with major fistulae requiring surgical repair, 5 (45,45%) underwent a pectoralis major flap reconstruction, 5 (45,45%) underwent a free flap reconstruction, and in 1 patient (9,09%), a gastric transposition was performed. In the free flaps group, we used a free jejunal flap in 4 patients (80%) and a free fasciocutaneous flap harvested from the arm in 1 patient (20%). All flaps survived. Bleeding requiring surgical hemostasis was noted in 1 patient (9,09%). All patients achieved 100% oral intake after surgery.

Conclusion

Using loco-regional axial and free flaps is a reliable reconstructive option for patients with major pharyngocutaneous fistulae after salvage total laryngectomy. A multidisciplinary team is the key for success.

PO-151 | Mold-based pulsed dose rate brachytherapy for early stage nasal vestibule squamous cell carcinoma

Julius Scheurleer [1]; Johannes Rijken [1]; Remco de Bree [1]; Mischa de Ridder [1]; Homan Dehnad [1]; Weibel Braunius [1]; Luuk Janssen [1]; Bernard Tijink [1]; Gerben Breimer [1]; Ernst Smid [1]; Lot Devriese [1]

(1) University Medical Center Utrecht

Keywords

Nasal vestibule, squamous cell carcinoma, brachytherapy

Objective

Cancer of the nasal vestibule is a rare type of malignancy constituting less than one percent of all head and neck cancers. These tumors are typically diagnosed at an early stage. Both surgery and radiotherapy provide excellent oncological results, but aesthetic results are better after radiotherapy. The aim of this study was to evaluate the long-term oncological follow-up after brachytherapy for early stage squamous cell carcinoma of the nasal vestibule.

Methods

Retrospective analysis of patients with carcinoma of the nasal vestibule who were treated with primary brachytherapy in the Utrecht University Medical Center.

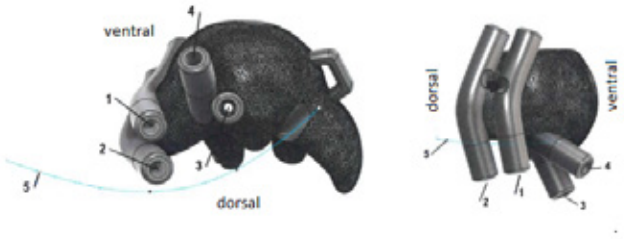
Results

In this single center experience over a 17-year period 68 patients with early stage squamous cell carcinoma of the nasal vestibule were treated with brachytherapy. Two patients had lymph node metastases at first clinical presentation. Median follow-up duration was 46.5 months. Five-year locoregional recurrence-free survival, disease-specific survival, and overall survival were 91.1%,

96.1%, and 66.2%, respectively. All recurrences occurred within the first three years of follow-up.

Conclusion

Brachytherapy offers excellent oncological outcomes and is a safe and effective treatment for early stage carcinoma of the nasal vestibule. Recurrences typically occur within three years after treatment.



PO-153 | PRAME staining in sinonasal mucosal melanoma: A single-center experience

Julius Scheurleer [1]; Weibel Braunius [1]; Bernard Tijink [1]; Karijn Suijkerbuijk [1]; Miranda Dierselhuis [1]; Ruud Meijers [1]; Willeke Blokx [1]; Remco de Bree [1]; Gerben Breimer [1]; Johannes Rijken [1]

(1) University Medical Center Utrecht

Keywords

Sinonasal Mucosal Melanoma – Field-Melanomization – PRAME

Background

Sinonasal mucosal melanoma (MM) is a rare, aggressive melanoma subtype. Complete surgical excision, with or without adjuvant radiotherapy, remains the cornerstone of treatment and yields adequate locoregional control. Metastatic MM is managed similarly to metastatic cutaneous melanoma but with poorer survival. PReferentially expressed Antigen in MElanoma (PRAME) has been identified as a potential diagnostic marker and therapeutic target in the treatment of cutaneous melanoma.

The objective was to determine the prevalence of PRAME expression in sinonasal mucosal melanoma and establish a better understanding of the biomolecular profile of these tumors.

Methods

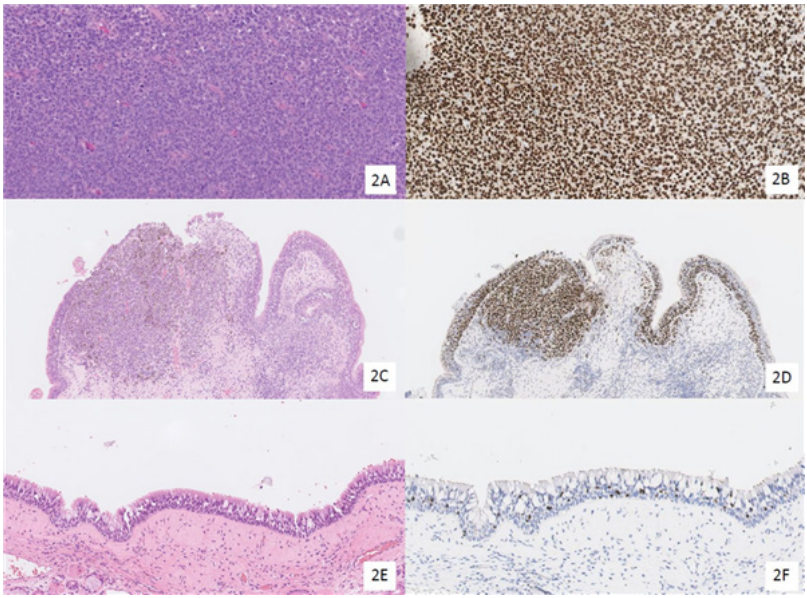
Retrospective analysis of the clinical characteristics and immunohistochemical features of all sinonasal MM patients referred to the department of Head and Neck Surgical Oncology, UMC Utrecht Cancer Center, between 2011 and 2021 was performed. Single Nucleotide Polymorphism (SNP) array and Next-Generation Sequencing (NGS) were performed in selected cases.

Results

A total of 26 patients with an MM were included. The median follow-up duration was 15 months. At the end of follow-up, 13 patients had died due to progression of their disease, and one patient died of intercurrent disease. PRAME immunohistochemistry was performed in 23 out of 26 cases, all displaying PRAME expression. In two cases PRAME expression was present both within the melanoma cells and in melanocytes in adjacent mucosa. SNP array showed ≥ 5 copy number variants (CNV) in all tested cases, with a median of 29.5 CNVs (IQR: 23.25 – 40). The three most common mutations identified by NGS were *NRAS* (7 cases) and *NF1* (2 cases).

Conclusion

We show that expression of PRAME is common in sinonasal MM, making PRAME a useful ancillary diagnostic tool and a potential therapeutic target in sinonasal MM. The demonstrated occurrence of extensive presence of PRAME-positive melanocytes in the surrounding mucosa of sinonasal MM, might explain the multifocal nature of melanoma in the (sinonasal) mucosa, and would be an extra argument for a PRAME targeting treatment in preventing local disease recurrence.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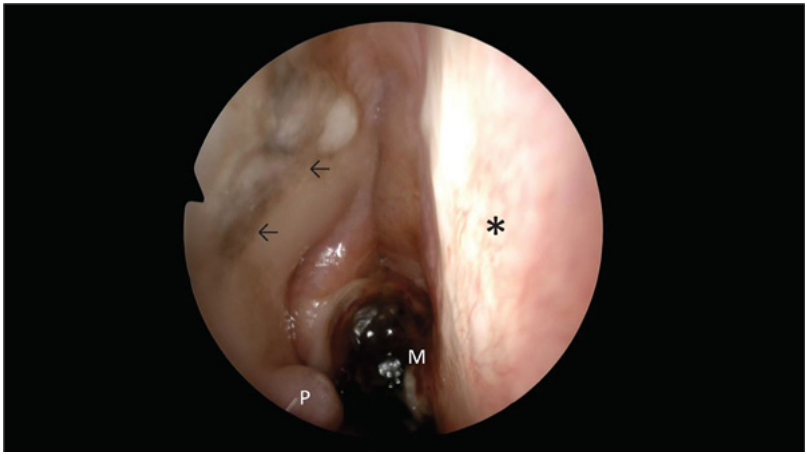
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PO-154 | Treatment of Basal Cell Carcinoma of lower eyelid with High-Dose-Rate Brachytherapy

Catarina Novalio Oliveira [1]; Cláudia Viveiros [2]; João Fonseca [1]; António Silva Mota [3]; Catarina Travancinha [4]; Miguel Labareda [5]; Inês Pino [1]; Tiago Madaleno [1]; Susana Esteves [1]; Filomena Santos [1]

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Keywords

Eyelid; basal cell carcinoma; high-dose-rate brachytherapy

Purpose/Objective

To report the outcomes with high-dose-rate (HDR) brachytherapy (BT) treatment in patients with lower eyelid basal cell carcinoma (BCC) and to analyse the association between dosimetric parameters and acute and late toxicities.

Material/methods

Retrospective unicentric study with patients diagnosed with lower eyelid BCC treated with HDR BT between January 2012 and December 2019.

58 patients with a median age of 76 years (range 39 – 89) were included.

Among these patients, 55.2% received adjuvant HDR BT and 44.8% radical HDR BT.

The prescribed dose was 36 Gy to 40 Gy in 9 to 10 fractions, twice daily, over 5 days.

Local control, acute and late toxicities (according to CTCAE v5.0) and cosmetic result (using CAIB qualitative scale) were evaluated.

Results

At a median follow-up of 44 months there were 4 local relapses, achieving a 4-year local control rate of 95% and 100% in the adjuvant and radical groups, respectively.

Dermatitis (44.8%), conjunctival hyperemia (31.0%) and eyelid edema (24.1%) were the most common acute toxicities. Hypopigmentation grade 1 (20%), epiphora grade 1 (17.2%) and conjunctival hyperemia grade 1 (17.2%) were the most common late toxicities. There were 7 patients with grade 3 cataracts. Cosmetic results were excellent and very good in 93.1% of patients.

There was no statistical association between the volumes of 150%, 200% and 300% of the prescription dose and acute and late toxicities. However, acute conjunctival hyperemia is strongly associated with the dose received by the ocular globe (volumes of 0.1cc, 1cc and 2 cc) ($p<0.05$).

Conclusion

Interstitial HDR BT in the treatment of lower eyelid BCC is a technique associated with excellent local control, acceptable long-term side effects and good cosmetic results.

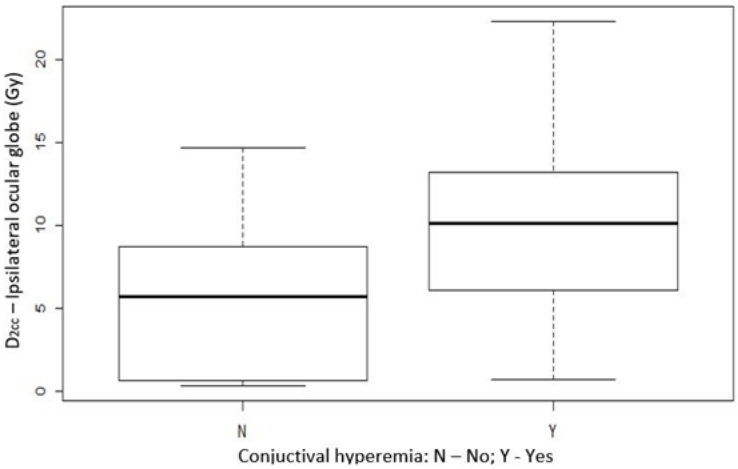

Figure 2. Vertical boxplot: D2cc – Minimal dose (Gy) received in 2cc volume of ipsilateral ocular globe according to the presence of conjunctival hyperemia.

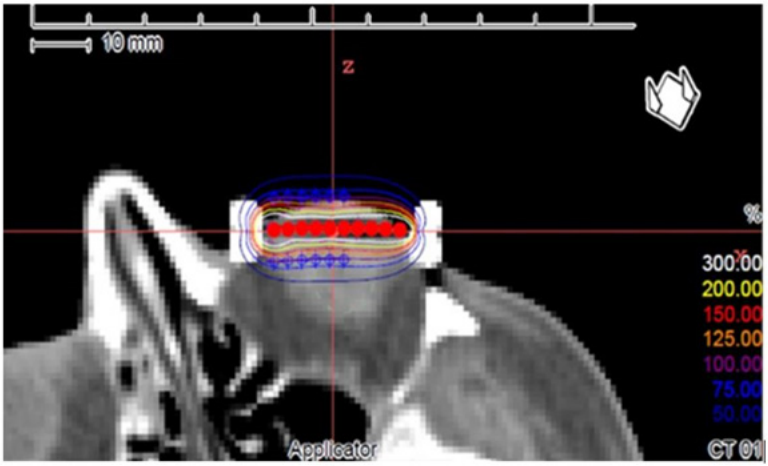

Figure 1. Dosimetry of interstitial high-dose-rate brachytherapy in basal cell carcinoma of lower eyelid.

PO-155 | Diode laser partial arytenoidectomy and cordotomy (DPAC) a novel treatment of vocal cord paralysis

Mostafa Magdy Donia [(1)]; *Hisham Mostafa Abdel-Fattah* [(1)]; *Alaa Eldin Hazem Gaafar* [(1)]

(1) faculty of medicine, Alexandria university

Keywords

Vacal cord paralysis, laser, cordotomy, diode laser

Purpose/Objective

Bilateral vocal cord paralysis is a well known and dreaded complication of Thyroidectomy, negatively affecting the quality of life and can be life threatening. Diode laser is a relatively less expensive tool than CO2 laser, however, it has not been commonely used in laryngology. We aimed to evaluate the results of using diode laser partial arytenoidectoy and cordotomy (DPAC) in the management of bilateral postthyroidectomy vocal fold paralysis.

Material/methods

After obtaining proper consents and ethical approval, 25 consequetive patients presenting with permenant bilateral vocal cord paralysis were included. DPAC was performed for the patients. All patients were assesed clincally and using video laryngosopy preoperative and during the follow up. Breathing was assessed using dyspnea symptom score and voice was assessed using voice handicap index-10 (VHI-10) preoperative and postoperative during the follow up period. Cases were followed up for up to 20 months.

Results

28 procedures were performed, the procedure is described and its rsults are presented. success rate with single surgery was 88%,

reaching 96% with revision surgeries. the quality of voice was negatively affected by the procedure

Conclusion

DPAC is a vaible technique for management of bilateral vocal cord paralysis with comparable results to published data with the standard CO2 laser

PO-156 | Analysis of the expression of immune regulators of checkpoints in head and neck cancer

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(1) Department of Head and Neck Surgery, Poznan University of Medical Sciences The Greater Poland Cancer Centre

Keywords

Head and neck squamous cell carcinoma, immunotherapy, immune checkpoint inhibitors

Objective

To broaden the knowledge about the expression of immune checkpoints in head and neck tumors. Assessment of changes in PD-1 and CTLA-4 expressions on peripheral blood leukocytes of patients depending on the performed surgical treatment compared to clinical data. Determination of PD-1, PDL-1, and CTLA-4 expression in neoplastic tissue.

Material and metods

30 patients with squamous cell carcinoma of the oral cavity were treated surgically. The control group was 20 healthy people. The materials were peripheral blood and neoplastic tissue. Only peripheral blood was collected from the control group.

Results

The relationship is directly proportional between PD-1 and PDL-1 expression and nicotinism. Negative correlation between the lymph node ratio and PD-1 expression. Intensification of PD-1 expression in blood of patients prior to surgical treatment, showing no tumor keratosis, high differentiation of neoplastic tissue, no perineural infiltration, and no nodal metastases lymph in the neck. Positive correlation between the lymph node rate and PD-1

expression in a blood test after treatment. Higher CTLA-4 expression in the control group and the blood test of patients with T1 tumors prior to surgical treatment. Perineural infiltration led to higher CTLA-4 values before treatment, as did the surgical margin below 2mm. The depth of neoplastic infiltration and the severity influenced the value of FoxP3. A decline in T helper cells was noted after treatment in patients with stages T3 and T4.

Conclusions

The expression of immune checkpoints in head and neck tumors depends on the stage of the disease and histopathological data. Changes in the percentage of PD-1 and CTLA-4 require analysis on individual subpopulations of peripheral blood lymphocytes and should be further studied.

PO-157 | Cutaneous head and neck squamous cell carcinoma gain benefit from weekly hypofractionated RT

Francesca De Felice [(1)]; *Maria Serpone* [(1)]; *Lavinia Grapulin* [(1)]; *Annalisa Magnante* [(1)]; *Rossella Caiazzo* [(1)]; *Nadia Bulzonetti* [(1)]; *Daniela Musio* [(1)]; *Vincenzo Tombolini* [(1)]

(1) University of Rome La Sapienza, Policlinico Umberto I

Keywords

Cutanous squamous cell carcinoma; radiotherapy; elderly

Purpose/Objective

Elderly population is increasing over years and the incidence of cutaneous squamous cell carcinoma (cSCC) of the head and neck region rises steeply with age. Emerging evidence shows that hypofractionated radiotherapy (RT) lead to durable responses in a variety of cancers, including cSCC. This study evaluated the role of definitive weekly hypofractionated RT in elderly patients with cSCC of the head and neck region.

Material/methods

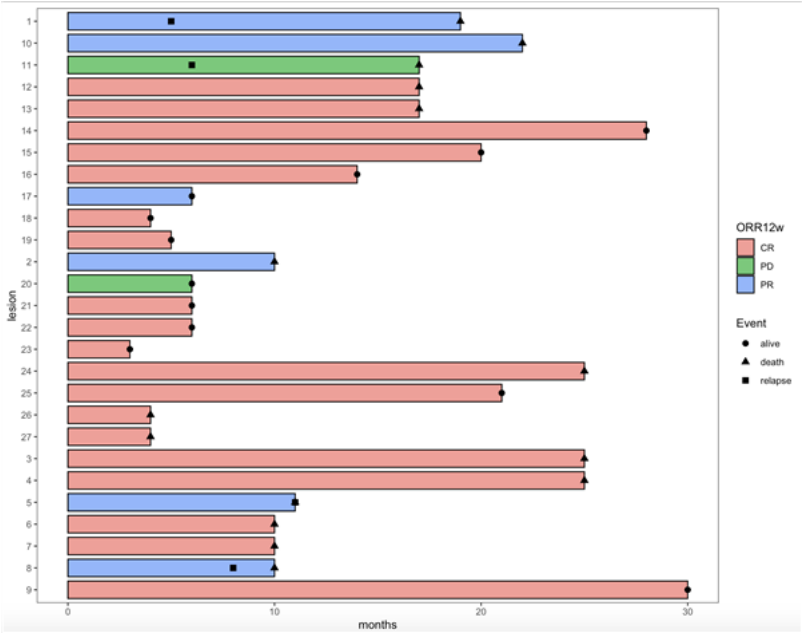
Data of surgery-ineligible elderly (≥ 75 years) patients with cSCC lesion(s) treated with definitive weekly hypofractionated RT (8 Gy per week per 7-8 weeks) were prospectively collected.The primary endpoint was overall response rate at 12 weeks (ORR12w) according to Response Evaluation Criteria in Solid Tumors (RECIST) criteria. ORR12w was defined as the proportion of lesions which have a partial or complete response to therapy and was assessed 12 weeks from the completion of RT. Secondary end-point included toxicity profile (according to the Common Terminology Criteria for Adverse Events, version 5.0), RT response self-reported pain score, overall survival (OS) and disease-free survival (DFS). OS and DFS were calculated in months from the date of the start of RT to the first event, including date of the last follow-up or death (OS) and/or relapse (DFS).

Results

A total of 19 consecutive elderly patients (median age 87 years), accounting 27 cSCC lesions of the head and neck region were treated with curative intent. All patients received the planned treatment: compliance with weekly hypofractionated RT was excellent. The ORR12w was 92.6%. Both bleeding and pain relief were achieved in all cases. Severe toxicity was not recorded. The 1-year OS and DFS rates were 70.8% (95%CI 0.391-0.881) and 59.7% (95%CI 0.301-0.802), respectively.

Conclusion

Definitive weekly hypofractionated RT represents a safe, efficient and cost-effective treatment option in surgery-ineligible elderly patients with cutaneous squamous cell carcinoma of the head and neck region.



PO-158 | The impact of HPV status on TNM staging and patients' survival

Piotr Machczynski [1]

(1) Greater Poland Cancer Centre, Poznan, Poland

Keywords

HPV, orpharyngeal cancer, TNM classification

Purpose

Due to the fact that patients with p16-positive oropharyngeal squamous cell carcinoma have better survival outcomes, the aim is to analyze patients diagnosed with oropharyngeal squamous cell carcinoma in the context of HPV infection and in the context of the seventh and the eighth edition of the TNM staging system.

Materials and methods

There were 233 patients treated due to oropharyngeal squamous cell carcinoma included in the study.

All patients with a known stage according to the 7th TNM staging system were reclassified according to the 8th TNM staging system.

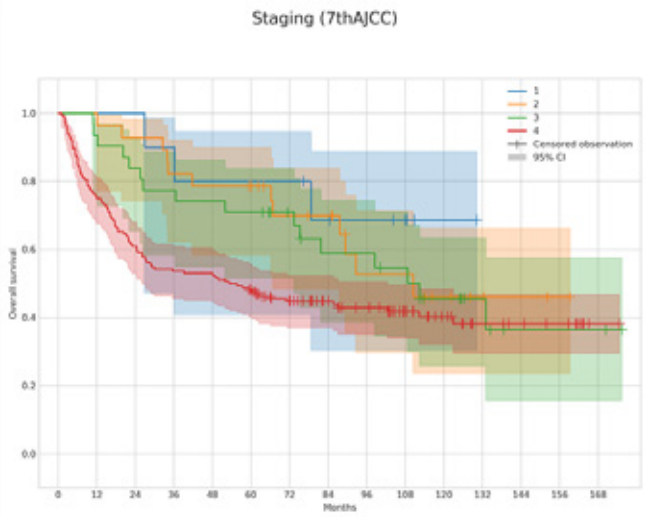
Results

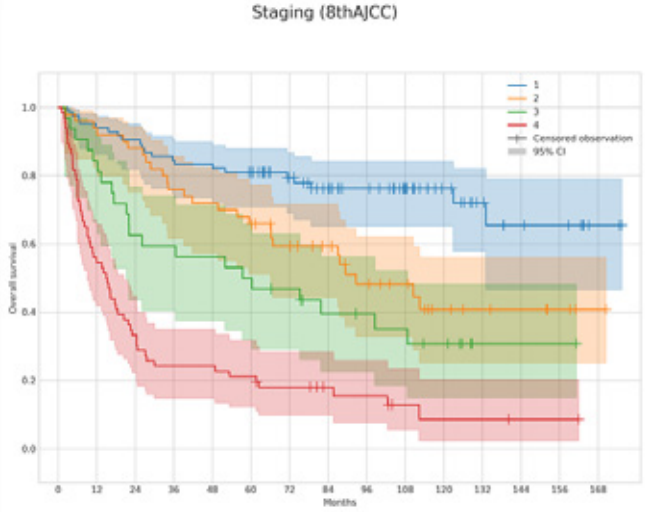
Under the seventh TNM edition the 5-year OS rates for stage I, II, III and IV were 80%, 79%, 71% and 48%, respectively, while under the eighth edition the 5-year OS rates for stage I, II, III and IV were 81%, 66%, 50% and 21%, respectively.

While ENE and the number of metastatic lymph nodes did not affect the survival rates, the occurrence of bilateral lymph node metastasis had a negative effect on both OS and PFS.

Conclusion

The eighth edition of the TNM staging system stratifies the risk better than the seventh edition. Therefore it should entirely replace the former edition, which does not discriminate well between the stages of the disease.





PO-160 | Therapy and prognosis of salivary gland carcinoma

Elena Hofmann [(1)]; Janine Priebe [(1)]; Annekatrin Coordes [(1)]; Heidi Olze [(1)]; Veit Hofmann [(1)]; Max Heiland [(1)]; Benedicta Beck-Broichsitter [(2)]

(1) Charité - Universitätsmedizin Berlin (2) Katharinenhospital Klinikum Stuttgart

Keywords

Salivary gland carcinoma, therapy, prognosis

Objective/Porpuse

The rare occurrence and heterogeneity of salivary gland carcinomas pose a challenge to the diagnosis and therapy and complicate the derivation of evidence-based recommendations from prospective studies.

Materials and Methods

The aim of this work was the retrospective study of all patients that presented with malignant salivary gland tumors between 2010 and 2020 at the Departments of Oral and Maxillofacial Surgery and Otorhinolaryngology at Charité – Universitätsmedizin Berlin and were followed-up for at least five years to identify potential influencing factors on prognosis. This study included 167 patients. Adenoid cystic carcinoma (n = 27; 16.2%) was the most common tumor entity. Other histopathological diagnoses were squamous cell carcinoma (n = 26), adenocarcinoma not other specified (NOS) (n = 23), mucoepidermoid carcinoma (n = 16), epithelial-myoepithelial carcinomas (n = 15), acinic cell carcinomas (n = 12) and carcinomas in pleomorphic adenomas (n = 12).

Results

The parotid gland was affected in 77% of all cases and 14 patients showed facial paralysis at the time of initial diagnosis. A total of 64 patients received surgical treatment without adjuvant thera-

py, while 69 patients received a combination of surgical therapy and adjuvant therapy (radiation and/or systemic therapy). The majority of surgically treated patients (74%) received a neck dissection. Positive lymph node involvement was documented in 34 cases and distant metastases were evident in 23 cases. Reduced survival depended on tumor grading as well as nicotine abuse as a risk factor. Ten patients died during the follow-up period of five years with nine cancer-associated deaths. However, there was a recurrence rate of 38% within five years after initial diagnosis.

Conclusion

Recurrence was significantly associated with positive lymph node involvement, higher tumor grade and lymphatic vessel invasion. The study provides important insights into the management of salivary gland carcinomas. Considering the high risk of recurrence, an aggressive therapy regimen and close follow-up care seem reasonable in the case of positive lymph node involvement and high grading.

PO-162 | Percutaneous tracheostomy - challenging the contraindications, our experience

Yotam Shkedy [1]; Natalia Gvozdev [1]; Muhamad Zahalka [1]; Roni Barzilai [1]; Emad Khoury [1]

(1) Rambam Healthcare Campus

Keywords

Percutaneous Tracheostomy; Anticoagulant Therapy; Airway Obstruction

Purpose/Objective

Tracheostomy is the most common procedure performed in intensive care patients requiring prolong ventilation., Establishing a secure airway in case of emergency is also a not uncommon indication. Open and percutaneous dilatational tracheostomy (PDT) are both well-known and widely used techniques. Obesity, emergent tracheostomy, coagulopathy, previous neck surgery, inability to extend the neck and high ventilator demand were initially thought to be contraindications for PDT. The aim of our study was to describe our experience in PDT on patients with “contra-indications” for this approach.

Material/methods

Retrospective analysis of cases in which PDT was performed during the period of 2012-2021 with analysis of surgery indications, anatomical features of patients and intra- and postoperative complications.

Results

PDT was performed on 323 patients on anticoagulant therapy (81% aspirin, 17% Plavix, 1 patient warfarin and 2 patients under direct factor Xa inhibitors). We did not observe an increase in ble-

eding complications in this population. In 7 cases PDT was performed for an acute airway obstruction, with successful airway control in all cases. In one case PDT was performed for re-tracheostomy with no complications.

Conclusion

Our experience suggests that the current relative contra-indications should be reexamined. As always, clinical judgment is recommended in each case before deciding on the surgical approach.

PO-163 | Tongue and floor of mouth reconstruction: to flap or not to flap?

Nicolacornale [(1)]; Rita De Sousa Rebelo [(1)]; Bassani Sara [(1)]; Molteni Gabriele [(1)]

(1) University of Verona

Keywords

SCC tongue and floor of mouth, pull-through, flap reconstruction

Background

Tongue and floor of mouth cancer has always presented itself as an oncologic challenge in the field of head and neck surgery. In the last decades several studies have reaffirmed the importance of tumor and cervical nodes (T-N track) resection by en bloc approach as a sound oncological treatment in these patients, with an improvement in overall and disease-free survival. This anatomically-based surgery has shown better loco-regional particularly in tumors with a depth of infiltration ≥ 10mm. The importance of this approach relies on the simultaneous removal of tongue and related floor of mouth, clearing the neck lymph nodes in continuity with the T-N tract. Furthermore it may potentially reduce metastatic dissemination and concurrently preserve the function of the healthy residual tongue. It can be achieved by a pull-through or transmandibular technique and must be associated with an adequate flap reconstruction.

Objective

The aim of this study is to review the clinical and functional outcome of tongue and floor of mouth reconstruction in patients who underwent en bloc resection, analysing pitfalls of flap reconstruction by comparing the use of pedicle versus free flap. Exposing our experience of a patient who underwent pull-through CS and reconstruction with Radial Forearm Free Flap (RFFF).

Methods

A systematic review of the English language literature was performed using PubMed database based on predetermined inclusion/exclusion criteria. The analysis was conducted according to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines. Inclusion criteria were squamous cell carcinoma (SCC) of the tongue and floor of the mouth, en bloc resection via pull through and flap reconstruction. Exclusion criteria were non SCC tongue tumors, resection with transmandibular approach and T4 oral cavity staging.

Results

We selected 153 articles, several describe en bloc tongue tumor resection, but few describe the optimal reconstruction approach. The content of the articles varied widely, focusing on aspects such as oncologic outcome, surgical technique and type of reconstruction. According to our exclusion criteria 141 articles were excluded. Our final final sample included 12 articles. From the final sample we confronted the particularities for each type of flap, analysing the advantages and pitfalls of each type of reconstruction.

Conclusion

Studies have come to establish en bloc tongue resection as the most valuable treatment option in tongue and floor of mouth tumors with a DOI ≥ 10 mm. This surgery allows for a strict control of local disease, limits dissemination pathways by T-N track en bloc resection and has the potential of reducing distant dissemination. Nevertheless a major oral cavity resection requires a suitable repair. However a gold-standard reconstruction has not yet been defined. In literature both free and pedicle flaps have been proposed as valid method.

In the cases analysed from our center RFFF was chosen as it may represent an adequate surgical option given its reproducibility and consistent anatomy. However a consensual reconstruction

option has not yet been established for tongue tumors. As it happens in other reconstructions of the head and neck region the decision of the right approach is influenced by numerous factors, such as patients' clinical status, type of resection, operating team and a greatly dependent on the surgeon skills.

PO-168 | Radiation therapy for nasopharyngeal carcinoma: a thirteen-year experience.

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Keywords

Nasopharyngeal cancer, Radiotherapy, Chemotherapy.

Purpose/Objective

To evaluate the disease characteristics and outcome of patients with nasopharyngeal carcinoma (NPC) treated with radiation therapy.

Material/Methods

Between January 2008 and December 2021, 30 newly diagnosed NPC patients were treated with external radiotherapy.

Three-Dimensional Conformal Radiation Therapy (3D-CRT) was applied in 3 patients and Intensity-Modulated Radiation Therapy/Volumetric Arc Therapy (IMRT/VMAT) was applied in 27 patients.

The disease was Stage I in 3 (10.0%), Stage II in 3 (10.0%), Stage III in 12 (40.0%) and Stage IV in 12 (40.0%).

The median prescribed dose was 68.98 Gy to the gross tumor volume, 67 Gy to the positive neck nodes and 59.7 Gy to the clinically negative neck.

Twenty-five patients were submitted to concomitant radiochemotherapy, 2 patients underwent neoadjuvant chemotherapy and 13 patients underwent adjuvant chemotherapy. Five patients were submitted only to radiotherapy.

Acute and late normal tissue effects were graded according to the Radiation Therapy Oncology Group radiation morbidity scoring criteria.

Local relapse-free survival (LRFS), nodal relapse-free survival (NRFS), distant metastasis-free survival (DMFS), and overall survival (OS) were estimated using the Kaplan-Meier method.

Results

With a mean response evaluation of 9.5 weeks (range 2–24 weeks), 19 patients developed a complete response, 6 patients developed a partial response, 2 patients did not respond local or regionally and 3 patients did not undergo response assessment. Two patients with initial partial response developed complete response after 46 and 93 weeks, respectively.

With a mean follow-up of 52.6 months (range 4–163 months), 21 patients with complete response no developed local in-field failure, 1 patient developed regional relapse and 6 patients developed distant metastasis.

Six patients with persistent disease after first response evaluation developed locoregional progression or distant metastasis.

The 3-year actuarial LRFS, NRFS, DMFS and OS were 95.7%, 89.7%, 71.1%, and 77.3%, respectively.

The worst acute mucositis was Grade 1 or 2 in 15 (50.0%) and Grade 3 in 1 (3.3%) patient. Acute dysphagia requiring tube feeding occurred in 1 (3.3%) patient. The proportion of patients with Grade 1-2 xerostomia was 50%.

Conclusion

Our experience of using external radiotherapy in the primary treatment of NPC showed a very high rate of locoregional control and favorable toxicity profile.

Table 1. Characteristics (n= 30).

Characteristics	n	%
Age (years)	Median 57 (range 23-86)	
Gender		
Male	22	73.3
Female	8	26.7
Histology		
Undifferentiated carcinoma	13	43.3
Nonkeratinizing squamous cell carcinoma	12	40.0
Keratinizing squamous cell carcinoma	1	3.3
squamous cell carcinoma	3	10.0
neuroendocrine small cell carcinoma	1	3.3
ECOG		
0	28	93.3
1	2	6.7
T stage		
T1	10	33.3
T2	6	20.0
T3	5	16.7
T4	9	30.0
N stage		
N0	9	30.0
N1	5	16.7
N2	13	43.4
N3	3	10.0
Clinical Stage		
I	3	10.0
II	3	10.0
III	12	40.0
IVA	10	33.3
IVB	2	6.7
EBV tumor	8	26.7
Unknown EBV	22	73.3
Induction ChT	2	6.6
Concomitant RTChT [a]	25	83.3
RT	5	16.6
Adjuvant ChT [b]	13	43.3

ECOG - Eastern Cooperative Oncology Group; ChT- Chemotherapy; RT-External Radiotherapy; [a] Platin; [b] 5-FU and platin.

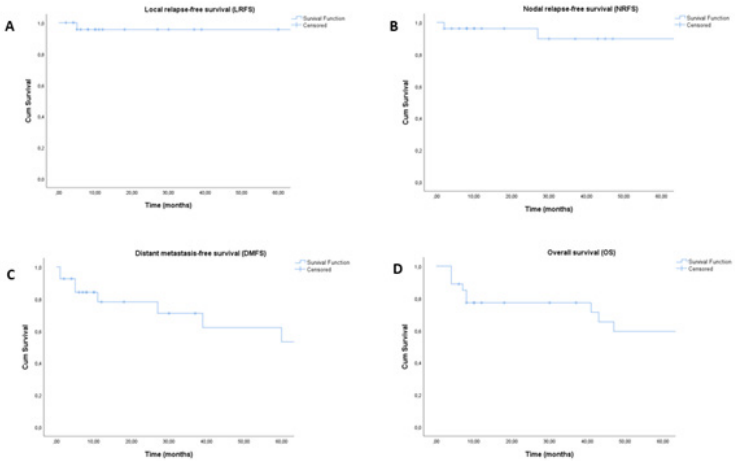

Figure 1: Oncologic outcomes. (A) Local relapse-free survival. (B) Nodal relapse-free survival. (C) Distant metastasis-free survival. (D) Overall survival.

PO-170 | Thyroglossal duct cyst carcinoma and concurrent thyroid cancer in an adolescent: a rare case report

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Keywords

Thyroglossal duct cyst carcinoma, thyroid carcinoma, papillary carcinoma

Purpose/Objective

Thyroglossal duct cysts (TDC) represent approximately 70% of all congenital neck masses and up to 1% of them have been proven to contain thyroid tissue malignancies. Up to 90% of these are papillary-type thyroid carcinomas (PTC). The median age at the time of initial diagnosis is 40 years. The clinical manifestations of a TDC carcinoma are commonly indistinguishable preoperatively from benign tumors. An association with coexisting PTC has been observed in approximately 25–40% of patients.

Material/methods

We present a case of papillary carcinoma of TDC coexisting with PTC in an adolescent.

Results

A 16-year-old previously healthy Caucasian woman presented to our institution with a painless, gradually enlarging lump at the

middle line of the neck. Physical examination revealed a well-circumscribed, rubbery, non-tender, and non-mobile mass at the middle line of the neck, anterior to the hyoid bone. The rest head and neck examination, including flexible upper airway endoscopy, was normal. The thyroid function tests were normal. The imaging findings suggested that the most likely diagnosis was TDC. The patient underwent a Sistrunk procedure under general anesthesia and the postoperative course was uneventful. The permanent histopathology of the mass revealed a BRAFV600E-positive papillary carcinoma in a TDC. A thyroid gland and neck ultrasound described a right level VI lymph node with characteristics highly suspicious for malignancy. Fine needle aspiration cytology (FNAC) of the lymph node revealed no malignant elements and FNAC thyroglobulin lavage (FNAC-Tg) was negative. Under general anesthesia, total thyroidectomy and central compartment lymph node neck dissection were performed. The postoperative course was uneventful. Histopathological findings revealed a parenchymal locus of PTC and three lymph nodes infiltrated by thyroid papillary carcinoma. Radioactive iodine (131I) ablation therapy was administered as adjuvant treatment and the patient is now closely followed.

Conclusion

Few case reports of TDC carcinoma coexisting with PTC in young patients exist. The clinical diagnosis of a TDC should always be followed by a thorough head and neck examination and detailed imaging. A high level of suspicion for coexisting thyroid malignancies must always be maintained when treating a patient for a TDC. When a TDC carcinoma is diagnosed after surgery (typically a Sistrunk procedure), further surgical management and/or adjuvant therapy are controversial among clinicians.

PO-172 | Nivolumab for Head and Neck Squamous Cell Carcinoma - Retrospective Multicenter Real-World Data

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Key words
Real-World Data; Nivolumab

Purpose/Objective

Analysis of median overall survival, progression-free survival, and side effects of treatment with nivolumab for platinum-resistant persistent, recurrent and/or metastatic head and neck squamous cell carcinoma (HNSCC), and its comparison with the data of CheckMate 141 trial.

Material/Methods

All consecutive patients treated in a group of Medical Oncology Departments of a single European country with nivolumab for HNSCC over a 4-year period (august 2018 to august 2022) were in-

cluded. Patients treated with platinum more than 6 months prior to nivolumab and tumors of the nasopharynx, salivary glands, nasal and perinasal sinus, thyroid and skin, were excluded. Data analysis and visualization were done in Python using the *lifelines* and *matplotlib* libraries.

Results

We included 310 patients, 90% male, median age 58 at diagnosis (min 24, max 83). The most common tumor location was the oropharynx (30%), followed by the oral cavity (28%), hypopharynx (23%) and larynx (18%). Most tumors were stage IV at diagnosis (82%), followed by stage III (10%), stage II (5%), stage 0 (2%) and stage I (1%). Of the 94 oropharyngeal tumors, only 13% were p16-positive (positivity for p16 wasn't tested in 30%).

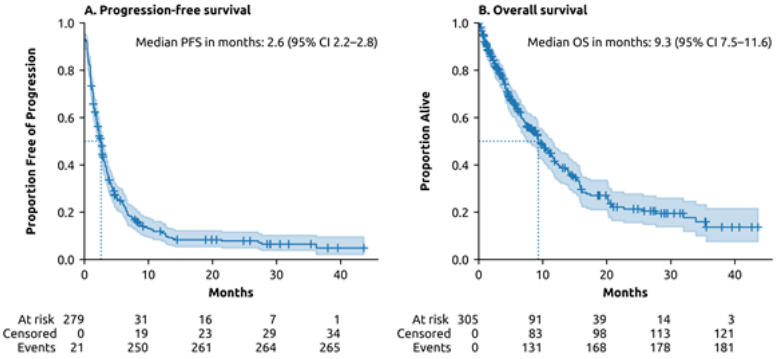
Most tumors were subject to curative treatment (81%), mostly definitive chemoradiation (ChT/RT) (41%) and surgery with adjuvant ChT/RT (25%). Among patients who underwent curative treatment, 60% had local relapse, 18% had disease persistence and 58% had distant relapses. Nivolumab was used as 1st line for non-resectable or metastatic disease in 35% of patients, as 2nd line in 55% and as ≥ 3rd line in 10%.

Median progression-free survival (PFS) was 2.6mo (95% CI 2.2-2.8) and median overall survival (OS) was 9.3mo (95% CI 7.5-11.6) (Figure 1). Immune-mediated adverse effects (iAEs) were present in 32% of patients, with 6% of patients with grade ≥ 3. Endocrine toxicity was most common (12% of patients).

Conclusion

The number of patients was slightly superior to the treatment arm of the CheckMate 141 trial (310 vs 236). Median PFS was 2.6mo (2.2-2.8), similar to 2.0mo (CI 1.9-2.1) in the CheckMate 141 nivolumab arm. Median OS was 9.3mo (CI 7.5-11.6), compared to 7.5mo (CI 5.5-9.1) in CheckMate 141. Toxicity was lower in our data than in the CheckMate 141 trial (all iAEs 32% vs 58.9%, grade ≥ 3 events 6% vs 13.1%), probably due to the retrospective nature of data col-

lection. Thus, effectiveness and toxicity profile of nivolumab is comparable in this real-world cohort to the data of CheckMate 141 trial. Standard forms for reporting AEs could help more accurate reporting in the real world.



PO-174 | Pre-vascular facial nodes in GBCC: Incidence and clinico-pathological predictors

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Introduction

Pre-vascular lymph nodes are supra-mandibular lymph nodes above the inferior border of mandible. Pre-vascular lymph nodes are not part of routine neck dissection done for OCSCC (either selective or comprehensive).

Metastatic lymph nodes at this station can be responsible for regional recurrences. Aim of the study is to report incidence and clinico-pathological predictors.

Materials and Methods

Patients with GBCC (T1-T4) were prospectively recruited in this study between June 2020 to June 2022 with an intent to evaluate the incidence of pre-vascular facial node metastasis and clinico-pathological factors predicting it.

Results

137 GBCC patients were enrolled; pre-vascular nodal metastasis were seen in 26 patients – (18.9%; n=26/137). 46% (n=12/26) were isolated while 54% were with cervical nodes. 80.7% were pathological T4. On multivariate analysis, depth of invasion (>10 mm; $p<0.008$), tumour grade (MDSCC; $p<0.04$), pathological N+ disease($p<0.045$, skin involvement ($p<0.009$) and male sex ($p<0.03$) are significant predictor of pre vascular facial node metastatic involvement in our study.

Cconclusion

Incidence of pre-vascular facial node metastasis is high (18.9%) in GBCC, which can be potentially the first echelon node in the lymphatic drainage pattern in this sub-site. Meticulous clearance of this nodal basin is of paramount importance during neck dissection in this subsite to prevent regional recurrences.

PO-177 | Elective neck irradiation guided by sentinel node biopsy in larynx & pharynx cancer: the PRIMO trial

Van Den Bosch [1]; Kaanders [1]; Takes [1]; de Ridder [2]; de Bree [2]; Al-Mamgani [3]; Schreuder [3]; Karssemakers [3]; Elbers [4]; Hardillo [4]; Hoebers [5]; Van Weert [6]; de Jong [7]; Jansen [7]; Langendijk [8]; Plaat [8]

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Rationale

Squamous cell carcinoma of the upper aerodigestive tract comes with a substantial risk for cervical lymph node metastases. Elective neck irradiation is performed in patients receiving (chemo)radiotherapy aiming to eradicate nodal metastases that are under the diagnostic detection level. Most toxicity and permanent long--term radiation side effects are caused by elective neck irradiation. In particular xerostomia and dysphagia are notoriously known to negatively and permanently affect quality of life. Sentinel lymph node biopsy (SLNB) has emerged as a staging procedure that can reliably detect microscopic metastases by histopathological examination of sentinel lymph nodes (SLN) and the pathologic status of the SLN accurately reflects the status of the remaining nodal basin. A recent meta-analysis demonstrated an excellent diagnostic test accuracy of SLNB in patients with cancer of the oropharynx, larynx and hypopharynx (sensitivity 0.93 and negative predictive value 0.97). It is conceivable that personalized elective neck irradiation can be performed guided by the results of SLNB.

Objective

To compare safety and efficacy of treatment with SLNB guided elective neck irradiation versus standard elective neck irradiation in patients receiving definitive (chemo)radiotherapy for

stage cT1-4N0M0 squamous cell carcinoma of the oropharynx, larynx or hypopharynx for whom bilateral elective neck irradiation is indicated.

Design

This is a multicenter, randomized controlled, non-inferiority trial. In total 242 patients will be randomized in ratio 1:1 to the control arm with standard bilateral elective neck irradiation or to the interventional arm with SLNB guided personalized elective neck irradiation. During a 2 year follow-up, data on toxicity, quality of life and oncologic outcomes will be collected (Figure 1).

Intervention

Patients randomized to the intervention arm will undergo SLNB (flexible endoscopic tracer injection under topical anesthesia, SPECT/CT-scan, and surgical removal of identified SLNs). Based on the histopathologic status of the SLN(s), patients will receive no elective neck irradiation (if all SLNs are negative), unilateral only (if a SLN is positive at one side of the neck) or bilateral (if SLNs are positive at both sides of the neck) (Figure 2).

For patients randomized to the control arm SLNB will not be performed and all will receive standard bilateral elective neck irradiation.

Endpoints

The primary safety endpoint (non-inferiority) is the number of patients with recurrence in regional lymph nodes within 2 years after treatment. The primary efficacy endpoint is patient reported xerostomia-related quality of life measured by the xerostomia symptom scale of the EORTC QLQ-H&N35 at 6 months after treatment. Other endpoints are acute and late radiation toxicity, quality of life, local and regional control rates, disease specific and overall survival, and cost-effectiveness.

Expected outcomes

Futile elective neck irradiation can be omitted to one or both sides of the neck in 9 out of 10 patients. This will enabling better sparing of normal tissues from radiation resulting in a major decrease of permanent long-term radiation side effects with better quality of life after treatment compared to standard elective neck irradiation.

Current status

Funding has been obtained. A SLNB training program will be initiated for participating centers. Start of accrual is expected in October 2023.

Figure 1 - Flowchart giving an overview of the trial design

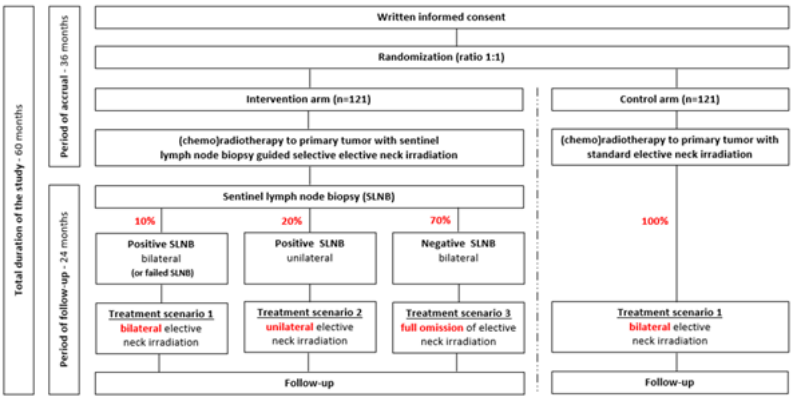
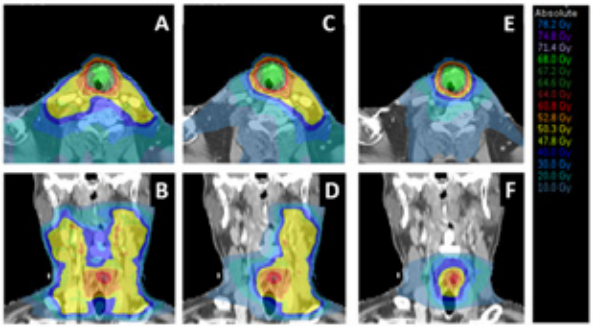


Figure 2 - Transverse and coronal views of dose planning with bilateral (A-B), unilateral (C-D) and no elective neck irradiation (E-F) for a case with cT3N0 laryngeal cancer, illustrating the major dosimetric gains to uninvolved tissues with sentinel lymph node biopsy guided elective neck irradiation.



PO-178 | Modalities of laryngeal cancer treatment during the COVID-19 pandemic in the Republika Srpska - BiH

Vanja Nežic, Sonja Dujkovic [(1)]; *Mirjana Gnjatic* [(1)]; *Zorica Novakovic* [(1)]

(1) UKC RS Banja Luka

Keywords

Carcinoma of the larynx, surgical treatment, laryngoscopy, retrospective study

Introduction

Carcinoma of the larynx accounts for 1-2% of all malignant tumors in humans and is the most common localization of malignant tumors of the head and neck. About 95–99% of all malignant tumors of the larynx consist of squamous cell carcinomas. It is rare in younger people, and most often occurs after the age of 50 and up to 10 times more often in men than in women. The most important risk factor is smoking, so smokers have a 10 to 20 times higher risk of laryngeal cancer than non-smokers, and it is an independent risk factor for disease recurrence. Alcohol, alone or in combination with smoking, is also an important factor in the development of cancer.

Aim

To define and determine the frequency of laryngeal cancer, according to gender and age structure, in hospitalized patients who underwent surgical treatment during 2021 at the Ear, Throat and Nose Clinic of the University Clinical Center of the Republic of Srpska.

Methods

A retrospective study conducted in the period from January 1, 2021 to December 31, 2021, related to the collection of data on

hospitalized patients who underwent surgical treatment and were diagnosed with laryngeal cancer.

Results

The research included 102 hospitalized patients diagnosed with laryngeal cancer.

Carcinoma was predominantly represented in men, 88.3% of patients, while 11.7% werewomen. The most represented age group is between 60 and 69 years (40%), followed by the period from 50 to 59 years, i.e. 35.30% of the total number of hospitalized patients. The youngest hospitalized patient was 41 years old, while the oldest was 82 years old, in both cases it was a male. Total laryngectomy was performed in 15.70% of patients, while partial laryngectomy was performed in 57.85%. No operative intervention was performed in 17.65% of patients. Almost all hospitalized patients were smokers, i.e. 99%.

Conclusion

Carcinoma of the larynx is a fairly common cancer, and in the general structure of malignant tumors it accounts for 2.6% of cases. Among malignant cancers of the head and neck, this cancer ranks first in terms of frequency of occurrence. Primary prevention of malignant tumors should be applied in order to educate the public about the risk factors for their occurrence, to eliminate the risk, i.e. to reduce exposure, and to preserve and improve the general state of health.

PO-179 | Early and substantial decline in lean body mass during (chemo)radiation in HNC patients

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Purpose

The primary aim was to investigate the rate of decline in total body weight (BW), lean body mass (LBM), fat mass (FM), muscle strength, and functional performance during treatment (Tx) in head and neck cancer (HNC) patients with good performance status.

Secondly, to investigate the association between loss of LBM and muscle strength and functional performance. Finally, to test the hypothesis that chemoradiation (CCRT) induces a larger loss of LBM compared to radiation alone.

Methods

Fourty-eight HNC patients (all tumour sites) and performance status 0-1 were included. Patients received either 6 wks of radiation alone (n=16) with 66-68 Gy in 33-34 Fx, 5-6 Fx/wk or concurrent chemoradiation (n=32) adding 40 mg/m2 cisplatin weekly. BW, LBM and FM were evaluated pre-Tx and bi-weekly until two wks post-Tx by Dual-energy X-ray Absorptiometry. Maximal muscle strength in leg- and chest press (1 Repetition Maximum, RM) and functional performance (30 s chair rise and arm curl test) were assessed pre- and post-Tx. Rates of decline during Tx as well as all associations were analyzed using linear regression. Pre-Tx to post-Tx changes in muscle strength and performance were analyzed using Students´ Paired T-tests.

Results

BW and LBM declined significantly already at wk 2, before the onset of radiation side effects, and continued to decline significantly through wk 4 and 6 before levelling off from wk 6 to 8. Every two weeks from Tx start to wk 2, wk 2-4 and 4-6, LBM declined 1.22±0.40 kg ($p=0.002$; 95% CI: 0.44;2.01), 2.01±0.40 ($p<0.0001$; 95% CI: 1.23;2.80) and 1.42±0.40 ($p=0.001$; 95% CI: 0.62;2.22). FM declined with a two-week delay compared to BW and LBM with significant and continuous reductions from wk 2-8. 1RM leg- and chest press both declined by 12.5%, by 7.2±1.4 ($p<0.0001$; 95% CI 4.4;10.0) and 5.0±1.1 ($p=0.0001$; 95% CI 2.8;7.2) from pre to post Tx, whereas 30 s chair rise and arm curl performance were unchanged. The total loss of LBM from pre-Tx to post-Tx was significantly associated with muscle strength impairment; 1RM leg press ($p=0.002$; $R2= 0.3$) and chest press ($p=0.0001$; $R2= 0.4$). According to the unadjusted linear regression patients receiving chemoradiation lost 3.1±0.8 kg of LBM ($p=0.0001$; 95% CI 1.5;4.7) more from pre-Tx to two wks post-Tx compared with patients receiving radiation alone. This difference was confirmed in analyses adjusted for tumour site, stage, nimorazole and baseline BMI.

Conclusion

Lean body mass declined significantly and substantially in HNC patients before the onset of radiation-induced side effects, such as mucositis, suggesting that LBM depends on multiple factors including concurrent cisplatin. Loss of LBM was correlated significantly with loss of muscle strength. The present findings emphasize the importance of early and prophylactic interventions to combat LBM loss, e.g., nutritional support and onset of resistance training; particularly in patients treated with concomitant chemoradiation.

Fig. 1

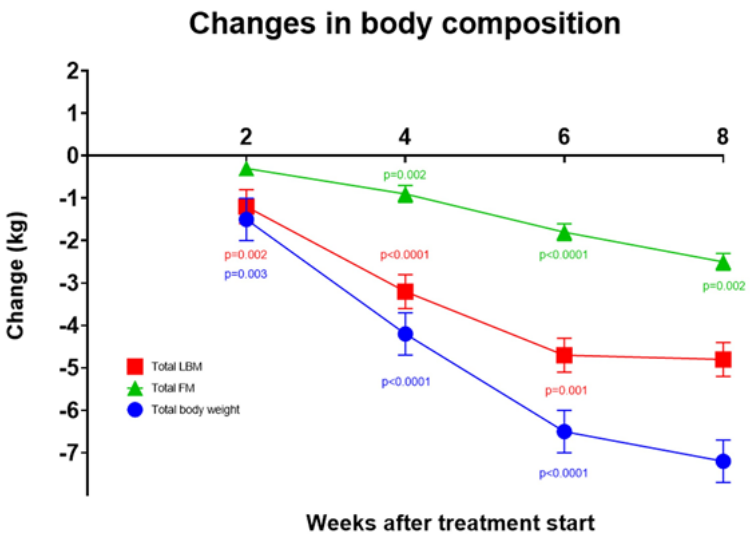

Fig.1.: Changes in body composition during treatment. LBM: Total body lean body mass; FM: Total body fat mass; BW: Total body weight. Data presented as mean values ± SEM. Specific p-values denotes significant change compared with previous timepoint according to linear regression analyses.

PO-183 | Analysis of patterns of locoregional failure in advanced oral cavity cancer following radiotherapy

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Keywords

Recurrence, Deformable, OSCC

Purpose/Objective

To assess the volumetric pattern of failure in oral cavity cancer (OSCC) patients who developed locoregional recurrences after primary surgery and post-operative radiotherapy (PORT) at a tertiary centre.

Material/methods

OSCC patients who received PORT between January 2018 and December 2021 were identified from a prospectively collected database. All patients were treated to established clinical guidelines and radiotherapy peer review. Individual recurrence gross tumour volumes (rGTV) on the recurrence scans of either CT, MRI or PET-CT were contoured by a Clinical Oncology Registrar, and checked by a Consultant Head and Neck Oncologist. These scans were co-registered to the original planning scans with rigid (RIR) and deformable (DIR) image registration using VelocityTM (Varian Medical Systems), and rGTVs were deformed and transferred onto the planning CT for analysis.

Each individual rGTV was assessed separately even in patients with multiple rGTVs. The centre of the rGTV (centroid) was measured in relation to the nearest treatment planning target volumes (PTV) and dose to 95% of the volume (D95%) of each deformed rGTV was measured. Failures were classified into 5 types: A (central high dose), B (peripheral high dose), C (central elective dose), D (peripheral elective dose), and E (extraneous dose).

Results

A total of 142 OSCC patients were identified, of which 24 (17%) patients had developed locoregional recurrences at the time of analysis. Six (25%) of them also developed synchronous distant metastasis. Two patients were excluded from the analysis due to considerable uncertainty of the degree of co-registration.

From the 22 patients, 41 individual rGTVs were assessed; 12 patients had 1 rGTV, 6 patients had 2 rGTVs, 2 patients had 3 rGTVs, 1 patient had 4 rGTVs, and 1 patient had 7 rGTVs. Nine (22%) of the rGTVs were local relapse, with 32 (78%) regional recurrences. Of note, 3 patients (14%) underwent adaptive replan during radiotherapy.

Overall, there were 4 type A, 6 type B, 7 type C, 5 type D and 19 type E failures (Figure 1). Within type B, 2 out of 5 local relapse (40%) were new OSCC primaries. Five of the type C failures (71%) were regional recurrences and 3 of which (60%) were present at initial planning as sub-centimetre nodes. 3 of 4 type D regional failures (75%) presented clinically with skin nodules from the nodal relapse. All type E failures were regional recurrences, with 7 (37%) contralateral recurrences despite being clinically node negative (cN0), 6 (32%) ipsilateral recurrences despite pathologically node negative (pN0), and 4 (21%) recurrences in areas that would not routinely be irradiated i.e. parotid and level VI neck. Figure 2 shows the average D95% from radiotherapy per failure type, normalised to nearest PTV prescription. Types A and C consistently received clinical dose and B, D and E did not, though this is expected due to the parameters of categorising each type (D95%>95% required for types A and C, D95%<95% for B and D). Most notably is the D95% for type E, which varied the most and averaged around 18.9% of prescription dose.

Conclusion

There were disproportionately higher numbers of out-of-field type E failures in comparison to the overall locoregional rate of all

patients. The clinical complexity and pattern of individual OSCC case must be given consideration during radiotherapy planning.

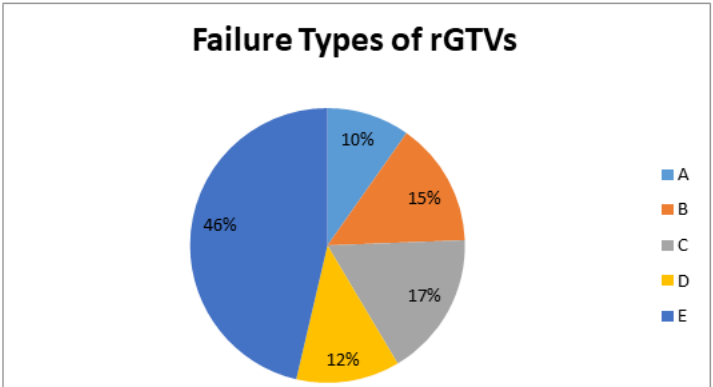

Figure 1: Chart to show the percentage of overall rGTVs per failure type

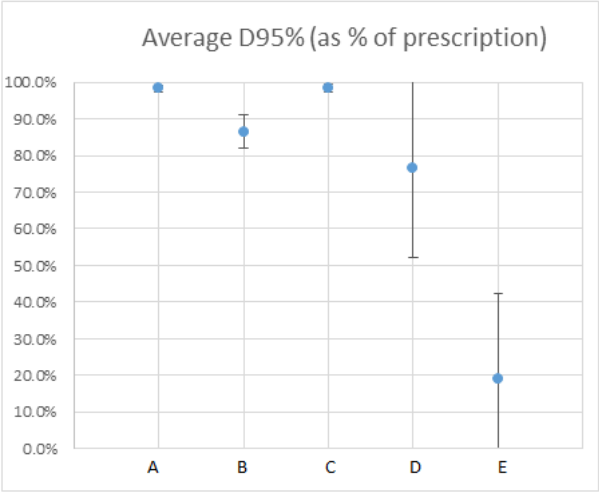

Figure 2: Average D95% of each failure type

PO-184 | The pattern of lymph node metastasis and its determinants in parotid carcinomas: Prospective study

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Keywords

Elective neck treatment, parotid gland cancer, Lymph node metastasis

Purpose/Objective

Intra-glandular (IGLN) and peri-parotid lymph nodes are sentinel nodal basins in parotid cancer before metastasizing to cervical lymph nodes. In this prospective study, we seek to determine the true incidence of intraglandular, peri-parotid, occult, and overt lymph node metastases in primary parotid carcinomas (PPC). This study also looks for various primary tumor factors responsible for nodal metastases.

Material/methods

FNAC/ core biopsy-proven PPC patients were enrolled between July 2020-May 2022. Work-up included clinical and radiological evaluation using ultrasonography and CEMRI of the primary tumor and cervical lymph node stations. NCCT Chest was done for all stage III and IV diseases. Patients were planned for surgery as per the tumor stage. The post-parotidectomy facial nerve grading system (PPFNGS) documented the facial nerve function.

Results

Thirty-four patients were screened initially with parotid gland tumors. 11 patients were excluded after the initial workup. Twen-

ty-three patients entered the final analysis. Twelve male and 11 female patients ranged from 19-75 years (mean: 45.7 years). 91.3% (n=21/23) presented with pre-auricular swelling/mass. 26% (n=6/23) had facial nerve palsy at presentation. 52.1% (n=12/23) had clinically palpable nodes at presentation. Twelve patients had T4 disease at presentation. 65.2% (n=15/23) patients underwent total conservation parotidectomy (TCP), and 34.7% (n=8/23) patients underwent radical parotidectomy. Selective neck dissection was performed in 60.8%(n=14/23) patients, and comprehensive neck dissection in 39.1% (n=9/23). 13% (n=3/23) and 8.6% (n=2/23) patients had metastatic lymphadenopathy in IGLN and peri-parotid lymph nodes, respectively. 30% (n=7/23) had overt cervical lymphadenopathy, while only 4.3% (n=1/23) had occult lymphadenopathy. Level II (30.4%) and level V (21.7%) were the most involved lymph node stations.

Primary tumor factors responsible for metastatic lymphadenopathy were T4 stage (p-value: 0.001) and high-grade histology (p-value: 0.007). Facial nerve palsy at presentation is also a statistically significant predictor for metastatic lymphadenopathy (p-value: 0.0049). Perineural invasion and lymphovascular emboli were not statistically significant but showed a trend (p-value: 0.06). MRI has high sensitivity (100) and high NPV (100) for metastatic cervical lymphadenopathy. All 23 patients followed up with a mean duration of 8.4 months, with a range of follow-up from 6 to 18 months. Postoperatively 56.5 % (n=13/23) of patients received adjuvant radiotherapy. Four patients (17.4%) died within 12 months follow-up period, and all were stage IVB disease. However marginal mandibular branch had significant paresis after surgery. 53.3% (n=8/15) had slight paresis (M3), and 13.3% (n=2/15) patients had pronounced paresis (M2) after six month.

Conclusion

PPC initially metastasizes to intra-glandular and peri-parotid lymph nodes, which act as sentinel lymph node basins. In this

prospective study, 17% of patients had a demonstrable association. Facial nerve palsy at presentation, T4 stage, and high-grade tumors are statistically significant risk factors for cervical metastatic lymphadenopathy. MRI is the investigation of choice for primary tumor extent determination and metastatic lymphadenopathy.

PO-186 | Intraoperative imaging techniques to improve surgical resection margins of oropharyngeal carcinoma

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Keywords

Oropharyngeal cancer; intraoperative imaging; margin analysis.

Purpose/Objective

Inadequate resection margins in head and neck squamous cell carcinoma surgery necessitate adjuvant therapies like re-resection and radiotherapy with or without chemotherapy, and imply increasing morbidity and worse prognosis. On the other hand, taking larger margins by extending the resections also leads to avoidable increased morbidity. Oropharyngeal squamous cell carcinomas (OPSCCs) are often difficult to access, and resections are limited by anatomy and functionality and thus carry an increased risk for close or positive margins. Therefore, there is a need to improve intraoperative assessment of resection margins. Several intraoperative techniques are available, but these often lead to prolonged operative time and are only suitable for a subgroup of patients. In recent years new diagnostic tools have been the subject of investigation.

Material/methods

This study reviews the available literature on intraoperative techniques to improve resection margins for OPSCC. A literature search was performed in Embase, PubMed and Cochrane.

Results

Narrow band imaging (NBI), high resolution microendoscopic imaging, confocal laser endomicroscopy, frozen section analysis (FSA), ultrasound (US), computed tomography scan (CT), (auto) fluorescence imaging (FI) and augmented reality (AR) have all been used for OPSCC.

Conclusion

NBI, FSA and US are most commonly used and increase the rate of negative margins. Other techniques will become available in the future, of which Fluorescence Imaging has high potential for OPSCC.

PO-190 | Esthesioneuroblastoma: A single institution's experience with 20 patients

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Keywords

Nasal tumor; esthesioneuroblastoma

Purpose/Objective

Esthesioneuroblastoma (ENB), or olfactory neuroblastoma, is a rare malignant of the sinonasal tract, originating from the olfactory neuroepithelium. ENB corresponds to 2-6% of nasal and paranasal sinus cancers. There are no standard guidelines regarding its treatment. The few available studies reported favorable outcomes with a multimodal approach. This study aimed to review our institute's experience in the treatment of ENB.

Material/Methods

Unicentric retrospective study of 20 patients with ENB, treated in our Institution between 1984 and 2022. Overall survival (OS) and Progression Free Survival (PFS) were estimated by the Kaplan-Meier method.

Results

The median age was 51 years old (20 to 76), with 40% being over 60 years at diagnosis. Sixty-five percent of patients were men. Presenting symptoms included: nasal obstruction (78%), recurrent epistaxis (56%), headache (28%), rhinorrhea (28%), hyposmia (28%), proptosis (17%), facial/neck mass (17%), followed by dizziness (6%) and diplopia (6%). According to the modified Kadish staging system, there were: 1 stage A patient (5%), 7 stage B patients (35%),

11 stage C patients (55%) and 1 stage D patient (5%). Regarding the TNM staging (8th edition), 3 patients presented with early-stage disease (T1-2) and 17 with advanced disease (T3-4) one of latter had cervical metastasis (N3).

Six patients were treated with surgery alone, 8 with surgery and adjuvant radiotherapy (RT), 3 with surgery and adjuvant chemo-radiotherapy (ChRT) and the remaining 3 were treated with ChRT, chemotherapy (ChT), alone or combined with RT, respectively. RT was delivered to the tumor bed and local extension, in the dose of 50 to 70 Gy (1 patient was treated with Cobalt-60, in the dose of 80Gy). ChT consisted of the combination of cisplatin (100 mg/m2) and etoposide (100 mg/m2), with dose adjustment if needed. After the first line of treatment, the recurrence rate was 35% (6 with locoregional and 1 with distance disease), while 15% had persistence disease.

The median follow-up was 59.7 months (1.8 to 287). The median time from the end of first treatment to recurrence was 20.9 months. At the time of the study, 8 patients had died, 1 patient was alive with evidence of disease and 10 patients were alive and free of disease. The Kaplan-Meier analysis estimated a survival of 83.9% and 77.9% at two and five years of follow-up. The two and five-year PFS rates were 76.7% and 61.0%, respectively.

Conclusion

The different approaches of our institute in the treatment of ENB follow the progressive scientific understanding of the disease. A multimodal approach appears to be the best strategy for most patients, with unimodal treatment being an option in selected patients. Given the rarity of this entity, further studies, with larger samples, are needed to optimize the management of patients with ENB.

PO-191 | Assessment of quality of life and functional swallowing outcomes following major glossectomy

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Keywords

Glossectomy; quality of life

Aim

Quality of life and functional swallowing outcome in patients undergoing major glossectomy have not been studied extensively in literature. Our primary objective was to assess individual subscale parameters contributing to post-glossectomy QoL. Secondarily, we aimed to correlate the two subjective scoring systems individually to penetration aspiration scale scores.

Methodology

29 patients who underwent major glossectomies between January 2022 to August 2022 were assessed post-operatively. All patients undergoing subtotal (STG) or near total glossectomy (NTG) were included in our study. Patients who have received prior radiotherapy or chemoradiation; prior oral cavity or oropharyngeal surgery were excluded. Subjective quality of life was assessed based on Functional Assessment of Cancer Therapy-Head and Neck (FACT-H&N) Scale and The M.D. Anderson Dysphagia Inventory (MDADI). Functional swallowing outcome was assessed by Fibreoptic Endoscopic Evaluation of Swallowing (FEES), which was interpreted according to Penetration Aspiration Scale (PAS). The self-administered questionnaires and FEES were recorded beyond two weeks post-surgery.

Results

The baseline characteristics of the patients are shown in Table 1. The mean scores of FACT-HN were found to be lower in HNCS, FWB, SWB subscales (15.4, 16.91 and 17.95 respectively) (Fig 1). The median FACT-HN and MDADI scores were found to be 88.12 and 55.42 respectively. There is statistically significant positive correlation between the FACT-HN and MDADI scores (p value 0.02). However, there is negative correlation between the QoL scores and PAS score (p value 0.5 and 0.3 for FACT-HN and MDADI respectively) suggesting aspiration is not the exclusive indicator determining post-glossectomy quality of life. Furthermore, poorer functional and social well-being subscale scores emphasize upon the non-swallowing related aspects which contribute to the overall quality of life of a post-glossectomy patient.

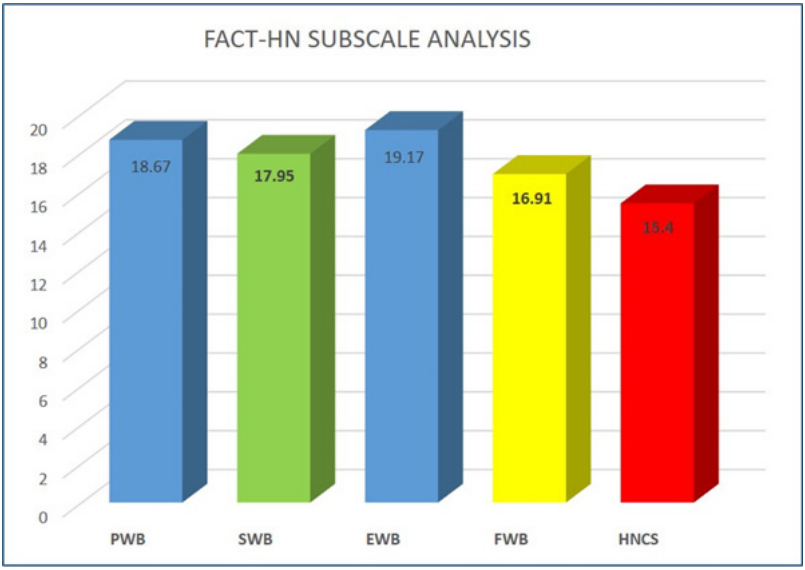
Discussion

Post-glossectomy quality of life domains which were maximally affected were functional (FWB) and social well-being (SWB), apart from expected swallowing related morbidity. Even patients with no penetration or aspiration were found to have low FACT-HN scores implying dysphagia is not the sole factor affecting post-major glossectomy QoL. Direct visualization of the swallowing process by FEES not only aids in analysis of the post-surgical swallowing limitations but also helps in planning of the compensatory rehabilitative maneuvers.

Conclusion

Non-dysphagia related facets of quality of life, which are often overlooked, need to be equally rehabilitated in patients undergoing major glossectomy.

AGE (YRS) (MEAN ± S.D)	SEX (M:F)	T		N		TYPE OF GLOSSECTOMY		HYOMANDIBULAR SUSPENSION
39 ± 7.7	27:2	T4a	25	N0	13	STG	22	5
				N1	8			
		T3	4	N2b	3	NTG	7	
				N2c	2			
				N3b	3			



PO-192 | Establishment of patient-derived organoids from HNSCC for analyzing mechanisms of radioresistance

Anne-Sophie Fisch [(1)]; Ana Pestana [(1)]; Vanessa Sachse [(1)]; Max Heiland [(2)]; Christian Doll [(2)]; Steffen Dommerich [(1)]; Theresa Obermüller [(1)]; Veit Maria Hofmann [(1)]; Konrad Klinghammer [(1)]; Iris Piwonski [(1)]; Simon Schallenberg [(1)]; Daniel Zips [(1)]; Ingeborg Tinhofer [(1)]

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Keywords

Organoids, translational oncology, 3D cell culture

Objective/Porpuse

Achieving personalization in treatment of head and neck squamous cell carcinomas (HNSCC) requires adequate models. Biomimetic *ex vivo* cultures such as organoids increasingly replace simplistic monolayer cell cultures, and are in line with the 3R principle. The study aims at the establishment of patient-derived organoids (PDOs) from HNSCC, and the assessment of their potential value in biomarker discovery for radioresistance and screening for radiosensitizing agents.

Methods

The ethics committee of the Charité University Hospital approved this study (EA1/152/10). Tumor tissue from patients with informed consent was collected during diagnostic or curative surgery. After mechanic and enzymatic dissociation and expansion in monolayer cultures, tumor cells were seeded in Matrigel® to form organoids. Interference of clinical parameters with organoid engraftment was analyzed using SPSS. Formaldehyde-fixed and paraffin-embedded organoid sections were haematoxylin-eosin and immunohistochemically stained for p40, CK5/6 and Ki67. A protocol for *ex vivo* assessment of radiosensitivity was established using 3D cultures of radioresistant / -sensitive subclones from the

HNSCC cell line FaDu. The protocol was then applied to PDO models. Effects of irradiation on organoid volumes, their metabolic activity (Cell Titer Glo®) and clonogenic potential were analyzed.

Results

Overall efficiency of PDO generation from primary tumor specimen (n=174) from HNSCC patients (n=164) was 45% (n=78). Histopathological characterization confirmed the SCC-phenotype. The majority of models were from male patients (64%) and current or former smokers (71%). Tumors were diagnosed at the oral cavity (n=56), oropharynx (n=13), hypopharynx (n=2), larynx (n=3) or other anatomical sites (n=4). Neither the tumor localization nor the sample type (biopsy *vs.* surgical specimen) was decisive for successful organoid generation. Samples from recurrent or persistent tumors after radiotherapy showed a significant lower engraftment rate (n= 10, 33.3%) compared to treatment naive specimens (n= 68, 80%) ($p<0.001$). With our *ex vivo* irradiation protocol, we were able to distinguish radiosensitive from resistant cells in the FaDu model. Preliminary results from PDOs (n=3) showed a dose-dependent decrease in proliferation, cell-viability and clonogenic potential, and a considerable interpatient variability in radiosensitivity.

Conclusion

To our knowledge, this is the largest collection of HNSCC PDO models established so far. Multi-omics characterization (exome, transcriptome and proteome) of the organoids and matching primary tumors is currently ongoing. Our first results suggest that PDOs might be valuable models to investigate individual responses to radiation therapy and the molecular mechanisms underlying radioresistance. In future studies, we will also focus on improving organoid engraftment from radioresistant tumors.

PO-193 | Supraclavicular flap: a reliable and versatile solution in head and neck reconstruction

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(1) CENTRO HOSPITALAR E UNIVERSITÁRIO DE SÃO JOÃO E.P.E.

Keywords

Supraclavicular flap; head and neck reconstruction

Objective

Head and neck reconstruction after oncologic resection is challenging given the size and complexity of the defects, the functional and aesthetic requirements and the limited locorregional options. In the last decades, the supraclavicular flap has emerged as a useful and versatile reconstructive solution for head and neck defects, since it is a reliable and technically simple flap with low donor site morbidity. This works aims to expose the multiple applications of this reconstructive technique based on a single centre experience.

Methods

A retrospective analysis of all patients who underwent head and neck reconstruction with a supraclavicular flap in our institution was performed. Data collection included demographic information, medical history, diagnosis, characteristics of the defect, surgical report, post operative complications and outcomes.

Results

21 pedicled fasciocutaneous supraclavicular flaps were performed in 20 patients. Surgical indications included 5 pharyngocutaneous fistulae, 3 tracheoesophageal fistulae, 6 skin defects (5 mandibular and cervical defects, 1 retroauricular defect), 3 intraoral defects (1 mouth floor defect, 2 thongue base and oropharynx

defects), 1 pharyngoesophageal defect, and 1 cutaneous and intraoral defect. All flaps survived and allowed partial or complete resolution of the patients' problem. Only 2 patients required a major revision procedure with a second flap. Overall the functional and aesthetic outcomes were very satisfactory.

Conclusion

The supraclavicular flap is a reliable, easy to harvest and versatile option for head and neck reconstruction since it provides good quality tissues, has a wide arc of rotation and has low donor site morbidity. It must be included in the reconstructive armamentarium of the head and neck reconstructive surgeon either as a primary solution and for secondary plasties.

PO-194 | The role of perioperative antibiotics in total laryngectomy?

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(1) General Hospital of Thessaloniki ''G'Papanikolaou''

Keywords

Head and neck, , Head and neck cancer, Head and Neck Surgery, Larynx, Squamous cell carcinoma

Objective

The purpose of this study was to evaluate the formation of a pharyngocutaneous fistula (PCF) after total laryngectomy in the early postoperative period.

MAterial/Methods

A retrospective analysis of all patients who underwent total laryngectomy in General Hospital of Thessaloniki ''G'Papanikolaou'' between January 1998 and September 2021 was performed. Analysis included both praimary and salvage cases.

Results

Two-hundred twenty five patients were identified. Our results demonstrate that the use of ampicillin/sulbactam at least one hour preoperatively significantly reduced the incidence of PCF in salvage laryngectomies (p=0.038). In primary laryngectomies, PCF formation was also reduced in patients that received perioperative antibiotic coverage, but it was not considered statistically significant (p=0.618).

Conclusion

Patients undergoing a salvage total laryngectomy should be routinely administrated with perioperative antibiotics to reduce the incidence of a postoperative PCF formation.

PO-196 | The role of salvage in patients with adenoid cystic carcinoma. Single institution experience.

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(1) National Research Institute of Oncology in Gliwice

Purpose/Objective

Adenoid cystic carcinoma (ACC) is a rare tumor of secretory glands. We present treatment results achieved in relatively large group of patients treated because of ACC in single institution. The role of salvage was especially assessed.

Material/Methods

The group consisted of 122 patients treated due to ACC in National Research Cancer Institute in Gliwice between 2000 and 2020. There were 43 (35%) men and 79 (65%) women in the median age of 53 years. In 98 (80%) cases treatment consisted of surgery followed by radiotherapy. In most cases primary tumor site was sinonasal region followed by oral cavity and large salivary gland in 44 (36%), 27 (22%) and 36 (29%) cases respectively. Over 60% patients presented advanced primary tumor (T3 or T4) but nodal involvement was found only in 5 (4%) cases. Loco-regional control has been defined as the recurrence in primary tumor site or regional lymph nodes. Distant failure has been defined as the recurrence elsewhere. Overall survival (OS) was calculated as the time since the end of radical treatment till the death or last control. Salvage treatment was defined as an attempt to apply the radical management of persistent tumor or recurrence after the completion of primary radical therapy. Successful salvage was reported when the treated tumor was either no longer observed for at least 3 months or remained stable for at least 6 months after the salvage procedure. Overall survival, loco-regional recurrence-free survival (LRC), metastases-free

survival (MFS) was estimated using the Kaplan-Meier method and compared using log-rank test.

Results

Five- and 10- years OS, LRC and MFS were 77% and 58%, 74% and 56%, 78% and 60% respectively. Locoregional primary treatment failure was found in 50 (41%) patients. In 41 (82%) patients from this group salvage treatment was performed. Radiotherapy alone, surgery alone or combined salvage approach was used in 18 (45%), 6 (15%) and 16 (40%) patients respectively. Five- and 10- years OS for patients who had successful salvage and who failed salvage were 95% v 55% and 68% v 47% respectively (p=0.03). Distant metastases were found in 47 (38,5%) patients and OS was not worsened in this group because of salvage surgery or radiotherapy given in most of them (80%).

Conclusion

For patients with ACC combined surgery and radiotherapy gives good results. Despite of high ratio of locoregional failure and metastatic disease effective salvage may provide significant benefit in such patients.

PO-197 | The Value of PET/CT in the treatment plan of stage II supraglottic laryngeal cancer

Alexandros Poutoglidis [1]; Paraskevi Karamitsou [1]; Antonios Skalias [1]; Evropi Forozidou [1]

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Introduction

Laryngeal supraglottic squamous cell carcinoma (SCC) has the tendency to metastise early and bilateral. A clinical lymph node negative neck does not always eliminate the presence of occult metastasis.

Objective

The purpose of this study was to assess the value of the positron emission tomography / computed tomography (PET/CT) in the pre-treatment plan of patients with laryngeal SCC supraglottic stage II patients.

Method

A retrospective analysis of all laryngeal SCC patients of our department, who underwent a routine PET/CT after staged as supraglottic cT2N0M0 between January 2017 and June 2022, was performed.

Results

Ten patients were identified. PET/CT detected a single occult neck metastasis in 50.0 per cent of patients with negative CT scan or Magnetic Resonance Imaging (MRI). Level II was involved in 4/5 (80.0 per cent) of cases. Patients with positive neck were upgraded to stage III and treatment plan was changed significantly. Up to date all patients are alive and disease free, with a median follow up of 16 months.

Conclusion

Half of our patients would have undergone an inappropriate treatment, if they had not taken a PET/CT. The value of PET/CT is obvious and is strongly recommended as a routine examination in all clinical stage II supraglottic laryngeal SCC cancers.

PO-200 | Automatic segmentation of 3D ultrasound volumes by deep learning of resected tongue carcinomas.

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(1) Netherlands Cancer Institute Amsterdam

Keywords

3D Ultrasound, Deep learning, Tongue carcinoma

Purpose/Objective

To develop an AI model for automated 3D segmentation of the tumor and healthy regions in intra-operatively acquired 3D ultrasound volumes of resected tongue carcinomas.

Material/methods

Using electromagnetic tracking of the ultrasound (US) transducer, 113 3D US volumes were acquired from 27 resected tongue carcinomas. The reconstruction software in CustusX enables the reconstruction of the acquired 2D images into a 3D US volume. In each 3D US volume, the regions representing tumor and healthy tissue were manually annotated by a trained technical physician. A ResNet based on 2.5D convolutions with a top-k, focal, binary cross-entropy dice loss was trained using a 16GB NVIDIA Tesla T4 GPU. Training on 150 epochs and a 5-fold cross-validation (stratified per patient)) developed the final 2.5D ResNet model. The performance of the model was evaluated on a withheld test set containing 20% of the dataset by 1) the dice surface similarity score, 2) the dice volumetric similarity score, 3) the Hausdorff distance, and 4) the average surface distance. To compare the performance of the model, the well-known nnUNet was trained with the same dataset as a benchmarking model. The variability of manual annotation in the dataset is assessed by repeatedly annotating the tumor in one 3D US volume for 8 times.

Results

The 2.5D ResNet results in a dice score of 0.90 for the healthy tissue and 0.61 for the tumor region. The nnUNet performed a dice score of 0.96 for the healthy tissue and 0.72 for the tumor. The variability of manually annotating the tumor in the same 3D US volume for 8 times results in a mean dice of 0.82. The automation of annotating the 3D US volumes by deep learning reduces the annotation time to 5 minutes compared to 25 minutes of manual annotation.

Conclusion

The nnUNet model performs superior over the 2.5D ResNet, with a dice score of 0.96 for the healthy tissue region and 0.72 for the tumor region. Automated 3D annotation is 5 times faster than manual annotating. In the future, less variability in annotations is required to improve the performance of the model.

PO-201 | HEAD & NECK SARCOMAS. A SINGLE INSTITUTION 15 YEARS EXPERIENCE

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Keywords

Sarcomas, microsurgery

Purpose/Objective

Head and neck sarcomas are a complex, heterogeneous group of tumors, that present a diagnostic and therapeutic challenge to plastic surgeons, as they have many overlapping clinical and imaging features, while their treatment requires wide surgical resection and complex reconstructive methods. The purpose of this presentation is to review our experience and evaluate the results on head and neck sarcomas, which have been treated, during the last fifteen years, in our Plastic and Reconstructive Surgery Department.

Material/Methods

In this period, totally 15 patients were examined at Oncology Head and Neck Clinic, (13 male, 2 female), with an average age of 50 years. The histopathology varied, including two leiomyosarcomas, five malignant fibrous histiocytomas (MFH), one malignant peripheral nerve sheath tumor (MPNST), three dermatofibrosarcomas (DFS), two osteosarcomas, one angiosarcoma and one solitary fibrous tumor (SFT). Surgical resection included maxillectomy, craniectomy and mandibulectomy. Modified radical neck dissection was performed in all patients. The reconstruction was performed with one rectus abdominis flap, five radial forearm flaps, two latissimus dorsi flaps, one vascularized fibula flap, three

temporalis flaps, one nasolabial and four scalp flaps. The average follow-up period was 10 years.

Results

The state of patient hospitalization was smooth, followed by postoperative radiotherapy. Finally, 11 of the 15 patients are still alive and disease free. There were three recurrences treated with palliative radiotherapy.

Conclusion

The surgical approach for head-neck sarcomas is challenging, as the achievement of a functionally acceptable result, by maintaining noble organs, is crucial for the smooth integration of these individuals into society. Wide surgical resection in combination with postoperative planned additional radiotherapy or chemotherapy, along with appropriate reconstruction, particularly with microsurgical techniques, offer improved prognosis and quality of life to patients.

PO-204 | The role of microvascular flap reconstruction in palliation for head and neck cancer

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Keywords

Palliation, microvascular reconstruction

Purpose/Objective

Salvage surgery is the best option for many patients with recurrent cancer of the upper aerodigestive tract (UADT) especially when original therapy included irradiation.

The primary objective of this study was to fully assess the value of salvage surgical procedures in the treatment of local and regional recurrence and also to evaluate the role of surgery for symptom palliation in patients with advance head and neck malignancy.

Material/Methods

41 patients were examined at the head and neck combined oncology clinic and as they fulfilled the salvage survey criteria, it was decided for them to undergo further wide surgical resection and free flap reconstruction, after previous definitive treatment.

The recurrent site was primarily the tongue and floor of mouth (FOM) in 18 cases.

Resection included mandibulectomy and glossectomy in the majority of the cases (21) and total glossectomy in 18 cases. Reconstruction was performed with various types of free flaps, predominately radial forearm flap (RFF).

Results

20 patients died during the first 2 years of follow up from local disease recurrence mainly. 21 patients are still alive and 3 patients are in less than a year follow up.

Conclusion

Salvage surgery of T1, T2 recurrent tumors and microvascular reconstruction offers patients' improvement in quality of life and also quality of dying, while being in T3 and especially T4 tumors alleviating symptoms such as bleeding, pain, dysphagia, non-healing ulcers, airway obstruction and pathological fractures.

PO-205 | Characterization of clonal evolution by chemoradiation in head and neck squamous cell carcinoma

Vanessa Sachse [(1)]; *Theresa Eder* [(2)]; *Korinna Joehrens* [(3)]; *Ingeborg Tinhofer* [(2)]

(1) Charité - Universitätsmedizin Berlin (2) Charité – Universitätsmedizin Berlin; German Cancer Research Center (DKFZ), Heidelberg (3) University Hospital Carl Gustav Carus

Keywords

Radioresistance, clonal selection, head and neck cancer

Purpose

Despite multimodal treatment by surgery combined with adjuvant chemoradiation or definitive concurrent chemoradiation less than 50% of patients with locally advanced head and neck squamous cell carcinoma (HNSCC) can be cured. Upon relapse, the disease characteristics change towards an even more aggressive phenotype, with much lower responsiveness to currently available treatments. Clonal evolutionary processes induced by curative-intended chemoradiation remain largely unexplored. Their characterization will not only identify potential candidate genes for improvement of curative treatment regimens but also guide future efforts for treatment optimization in the recurrent/metastatic disease setting.

Patients and Methods

Patients with locally advanced HNSCC (n=12) who progressed within less than 2 years after initiation of the curative-intended therapy, applied as either surgery followed by adjuvant radiochemotherapy or definitive radiochemotherapy, were included in this pilot study. Mutational profiling by NGS targeting the exonic regions of 327 genes was applied to paired primary/recurrent tumor samples. Somatic mutant variants with allelic frequencies

(AF) of ≥ 10% as well as copy number variations in primary and/or recurrent tumors were considered in further analysis.

Results

Within the 12 matched pairs, 119 single nucleotide variants (SNVs) predicted as tumor drivers were identified across 51 of the 327 targeted genes, including *TP53, FAT1, NSD1, KMT2D, CDKN2A and PIK3CA*. Considering only pathogenic driver gene variants, the degree of concordance in mutations between primary and relapsed tumors was low, with shared SNVs detected only in 2 of the 12 matched pairs (16,6%). Copy number alterations (n=47) were found in 28 of 327 genes, with amplification of CCND1 observed in at least one of the matched sample pairs in 6 of 12 cases (50%). Again, high variablity between primary and recurrent samples was observed, with only 20 of 47 (43%) numerical alterations shared between primary and recurrent tumors.

Conclusion

Our preliminary results confirm previous results from others [1,2] that clonal selection by chemoradiation is a frequent event and may lead to significant changes in the molecular landscape of HNSCC tumors. Such changes have to be considered in the current development of personalized treatment decisions support systems. The functional consequences of clonal selection by concurrent chemoradiation for the efficacy of subsequent treatment remain unclear and will be investigated in an ongoing study in patient-derived organoid (PDO) models from head and neck cancer patients.

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PO-207 | Adenoid cystic carcinomas of salivary glands treated with carbon ion radiotherapy at CNAO

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Keywords

Salivary glands, carbon ion radioterapy.

Purpose/Objective

To report outcome of head and neck adenoid cystic carcinoma (ACC) patients (pts) treated with carbon ion RT (CIRT) at the National Center for Oncological Hadrontherapy (CNAO).

Material/methods

Between 2013 and 2020, 184 ACC pts (Males/Females 89/95) were treated with active CIRT. Pts median age was 54 yrs (range 20 – 87). Tumour site was minor salivary gland in 112 (61%) and major salivary gland in 72 (39%) pts. Majority of pts were naïve (71%), 53 pts (29%) were recurrent never irradiated. Definitive and postoperative RT were performed in 68 and 116 pts (63%), respectively, among these latter 85 pts (73%) had surgical positive margins (R1), and 31 (27%) macroscopical residual disease (R2). Overall, before starting CIRT 153 pts (81%) had macroscopical gross tumor volume (GTV) detected at the simulation MRI. Prescribed total dose was 65.6-68.8 Gy(RBE) in 16 fractions (4.1-4.3 Gy(RBE)/fr, 4 fr/week). Local relapse free survival (LRFS), progression free survival (PFS), overall survival (OS), and distant metastasis free survival (DMFS) were estimated by the Kaplan–Meier method and compared using the Log-rank test. Toxicity was evaluated according to the CTCAE v.4.0.

Results

With a median follow-up of 45 months (range: 7-90), 5 yrs- LRFS, OS, PFS and DMFS were 52.2%, 64.6%, 35.5% and 63%, respectively. At univariate analysis prognostic factors for both LRFS and OS were tumor site (p <0.0001 and 0.054 respectively), stage (p <0.0001 and 0.0005 respectively), and surgery before CIRT (p=0.042 and 0.042). Performance status (p<0.0001), age (p=0.006) and GTV (p<0.0001) were additional prognostic factors for OS. Interestingly, worse OS was reported for pts with any GTV at preCIRT MRI compared to macroscopically resected pts (p=0.008), with shorter OS in pts after debulking surgery and unresected pts (43% and 54% 5 yrs OS) compared to R1 postoperative pts with macroscopic disease at pre CIRT MRI (78% OS) and pts with microscopic disease (93%, p=0.014). At multivariate analysis prognostic factors for OS were large GTV volume (0cc, vs <50cc, vs >50cc, p=0.006), site (higher risk for sub-lingual glands vs others, p=0.02), stage (IV vs <IV, p=0.03) and age (risk factor, p=0.006), for LPFS stage (IV vs <IV, p=0.003) and site (higher risk for sub-lingual glands & paranasal sinuses p<0.00001). At the end of CIRT no toxicity >G3 was reported. Interestingly, higher acute toxicity was reported for the patients with tumor located at the minor salivary glands (p=0.03) and with flap reconstruction after surgery (p=0.04). Late maximum toxicity reported during follow up was G0 in 11%, G1 in 23%, G2 in 48%, G3 in 15%, G4 in 2% and G5 in 1% of the pts.

Conclusion

CNAO data for ACC are in line with other CIRT facilities. A multidisciplinary effort is required for better selecting pts for CIRT. Our results point out that CIRT might be offered as an alternative curative option to surgery in locally advanced cases deemed to be R2.

PO-209 | Is there an over-indication for elective tracheostomy in patients with oral cavity cancer?

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Keywords

Elective tracheostomy; tracheostomy scoring system; complications

Purpose/Objective

Temporary tracheostomies are often used in oral oncologic surgery to secure postoperative airway management and avoid emergency tracheostomies. Even when planned electively, tracheostomies can cause severe and life-threatening complications. Our aim was to evaluate the morbidity associated with elective tracheostomy in patients undergoing oral and orophayngeal tumour resection performed at our institution. Additionally, we intend to identify those patients who may avoid elective tracheostomy.

Material/methods

A retrospective cohort study was undertaken. Inclusion criteria included patients with oral and orophayngeal squamous cell carcinoma in which resection with curative intent and prophylactic tracheostomy intended for short-term removal was performed. Variables collected included demographics and co-morbidities, ASA grade (American Society of Anaesthesiologists), TNM stage, tumour site, extent of resection, type of reconstruction, time until decannulation, complications and possible need for recannulation. Additionally, we applied the Cameron and TRACHY tracheostomy scoring systems to evaluate their utility for tracheostomy recommendations.

Results

A total of 116 elective tracheostomies were performed between January 2019 and December 2020. The mean age was 63.8 years (range 39–91), with a total of 91 (78.4%) males and 25 (21.6%) females. Most tumours were situated in the tongue (37.9%), mandibular alveolus (22.4%) and floor of mouth (19.8%). Of the 116 patients, 103 (88.8%) underwent resection of more than one site. Median time to decannulation was 7 days, with a range from 2 to 66 days, excluding 8 patients who were discharged with cannula still in situ. Two patients died during hospitalization, one due to medical complications and another with a progressive paraneoplastic syndrome. Tracheostomy associated complications were observed in 14 patients (12.1%), most commonly pneumonia. In 42 patients (36.2%) complications not associated with tracheostomy were verified. According to the Cameron scoring system and the TRACHY score, recommendation for tracheostomy coincided in only 54.3% and 45.7%, respectively. Median scores of our cohort were 5 for the Cameron scoring system and 3 for the TRACHY score.

Conclusion

Postoperative airway management in our institution is performed in a safe and controlled manner with an overall tracheostomy--associated complication rate that coincides with the literature. Nevertheless, there appears to be an over-indication for elective tracheostomy in our patients with oral cavity and oropharyngeal cancer. Although screening based on the tracheostomy scores could help guide preoperative planning, they proved insufficient for our sample. We propose revisions that would more effectively identify the patients that most benefit from elective tracheostomy.

PO-210 | Chemoradiotherapy in Oropharyngeal Malignancies -Are we ready to De-escalate Radiotherapy protocols?

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Background

Radical Chemoradiotherapy is the modality of choice for Non--Metastatic Squamous cell Oropharyngeal malignancies. In our study, we have tried to analyzed the local control rates and overall survival for the same.

Primary Aim

To evaluate:

a. Local control rates with Radical chemoradiotherapy in Non-Metastatic Squamous cell Oropharyngeal malignancies.

b. Radiation Toxicity assessment according to RTOG common toxicity criteria.

Materials and Methods

A total of 56 patients diagnosed with Non-Metastatic Squamous cell Oropharyngeal malignancy between January 2019 to December 2021 were considered. Patient, tumor and treatment related details were collected retrospectively using hospital records. All the patients received 70Gy/35#/7weeks + concurrent Inj. Cisplatin/ Carboplatin. The local control rates were evaluated clinically and radiologically using contrast enhanced CT scan. Patients were followed up every month for the first 3 months and 3 monthly after that.

Results

The median age was 60 years (range 39-75 years) Male : female ratio was 13:1, 35.7%% had comorbidities. 77% patients had locally advanced disease. The most common site of malignancy was Base of tongue (50%). Local control rate was found to be 62.5% at 3 months, and 34% at 1 year. About 12.5% patients were lost to follow up after completion of chemoradiotherapy.50% of the patients had grade 2 toxicities, 25% of the patients had grade 3 toxicities while 18% of the patients required Nasogastric tube insertion.

Conclusion

In our study we would like to conclude that, radical chemoradiotherapy is a very effective modality of treatment for Non-Metastatic Squamous cell Oropharyngeal malignancies. However, the grade 2 reactions were around 50% , grade 3 reactions were above 20%, and above 15% of the patients required insertion of nasogastric tube. Hence, with the advent of HPV related Oropharyngeal malignancies, the concept of de-escalation of Radical chemoradiotherapy regimens is warranted, to decrease chemoradiotherapy related toxicities.

PO-212 | Efficacy of relative intact parathormone levels in predicting hypocalcemia after total thyroidectomy

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Keywords

Hypocalcemia; Thyroidectomy; Parathormone; Thyroid cancer

Purpose

Transient or temporary hypocalcemia is a very common sequalae of total thyroidectomy leading to significant morbidity and prolonged hospital stay. Prediction of post-operative hypocalcemia is dependent upon clinical symptoms and signs, biochemical markers including intact parathormone (iPTH), ionized calcium levels or corrected serum levels. However variability exists in literature with regard to timings of conducting these tests. Prophylactic calcium and vitamin D supplementation is also practiced in many centers. We conducted a prospective study to determine whether relative decline in iPTH levels (pre-operative iPTH levels minus post-operative iPTH levels) measured at 1 hour and 1 day after total thyroidectomy predicts biochemical hypocalcemia early and guide regarding initiation of calcium supplementation before development of distressing clinical symptoms.

Methods

70 patients were enrolled over a period of 2 years from January 2021- December 2022 who underwent total thyroidectomy/ completion thyroidectomy. Female to male ratio was 2:1 with mean age of 38years (range: 19-82 years). 51.4% (n=36/70) patients had only thyroid swelling at presentation, 45.7% (n=32/70) patients had nodal metastasis at presentation while 2 patients had distant metas-

tasis at presentation. 73.9% of the patients had PTC, 13% had MCT, Follicular neoplasm in 8.6% and goiter in 4.3%. 40 patients has early disease (T1, T2) and 27 had advanced disease (T3, T4). 3 patients had benign disease. Pre-operative iPTH , vitamin D , ionized calcium and magnesium levels was done for each patient. Relative decline in iPTH and ionized calcium levels at postoperative 1 hour and 1 day was determined and analysed with regard to development of biochemical versus clinical hypocalcemia.

Results

In this cohort, 40% (N=28/70) patients developed post-operative hypocalcemia. Patients with post-operative hypocalcemia had significantly greater decline in parathyroid hormone levels at 1hour than normocalcemic patients (85.71% vs 35.6 % , P=0.001). 96.4% (N=27/28) of hypocalcemic patients had >50% decline in relative iPTH levels at 1hour. On other hand only 25% (n=7/28) developed clinical symptoms with 12 hours and 60.7% (n=17/28) after 12 hours. Relative ionized calcium decline at 1 hour was also statistically significant (p value< 0.02).

Study also revealed that female sex (n=21 , 65.73 % , p value= 0.05) and age < 40yrs(p value= 0.017) are risk factors for developing hypocalcemia. Preoperative vitamin D levels (p value=0.139) and serum magnesium (p value= 0.393) were not found to be risk factor for hypocalcemia in this study group.

Conclusion

Relative decline in iPTH levels at 1hour is better biochemical marker for patients who are going to develop clinical hypocalcemia later on and to prevent distressing morbidity. Relative iPTH levels should be utilized for initiating calcium supplementation rather than prophylactic supplementation.

PO-214 | Determining the efficacy of Nimotuzumab as a radio-sensitizer in head and neck malignancies.

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Background

In this study, we attempted to determine the efficacy of Nimotuzumab as a radio sensitizer in locally advanced squamous cell malignancies of head and neck.

Objectives

The primary objective was to assess local control rates and secondary objective was to evaluate the overall survival and disease free survival.

Methods

28 patients with locally advanced squamous cell malignancies of head and neck who underwent chemoradiotherapy with Nimotuzumab as a radiosensitizer between January 2013-October 2021 were considered. Patient, tumor and treatment related data were collected retrospectively. Local control rates were evaluated clinically and radiologically at 3 months, 6 months & 1 year.

Results

Median age was 58 years (range 36-73years). 75% of patients had a stage III or IV disease. 40% patients had a malignancy of the hypopharynx. 64% patients received a platinum based chemotherapy along with Nimotuzumab as radiosensitizers and 36% of our patients received Nimotuzumab alone. The local control rates achieved at the end of 3 months, 6 months and 1 year was 96%, 85.7% and 71%. Statistically significance was seen in terms of local

control rates with respect to tumor site, patient's age and N stage ($p<0.05$). Statistical Significance in terms of overall survival was found with tumor site($p<0.05$).

Conclusion

In our study, we were able to demonstrate better local control rates in locally advanced squamous cell malignancies of head and neck with addition of Nimotuzumab to conventional chemoradiotherapy when compared to chemoradiotherapy alone with respect to Local control and overall survival. However, a larger study with more number of patients and a longer follow up would be required to confirm the same.

PO-215 | Negative pressure wound therapy: salvage option for pharyngocutaneous and tracheoesophageal fistula.

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Keywords

Negative-pressure wound therapy, pharyngocutaneous fistula, pharyngoesophageal reconstruction.

Introduction

Pharyngocutaneous fistula is a common complication of laryngopharyngeal surgery, being associated with increased morbidity and mortality.

Beyond the classical management with regional flaps and free flaps, negative-pressure wound therapy (NPWT) can be an alternative and effective treatment.

Clinical Report

4 patients with laryngeal squamous cell carcinoma were subjected to total laryngectomy and pharyngoesophageal reconstruction. All of them developed a pharyngocutaneous fistula and NPWT was used.

A significant decrease of the fistula aperture and exudate was observed after 20 to 30 days of NPWT.

After that standard wound care was instituted and closure of the fistulae was accomplished in a average of 10 days.

Conclusion

Negative-pressure wound therapy can be an effective treatment for pharyngocutaneous fistula closure, either in the setting of fistulae that persist besides multiple surgical revisions using muscle flaps or as a first-line therapy when fistulae develops.

Authors

Gonçalo Gandra, MD; Sergio Teixeira, MD; Joana Costa, MD; Bernardo Correia, MD, and Ricardo Horta, PhD.

PO-216 | Impact of nutritional counseling for Head and Neck Cancer patients undergoing radiochemotherapy

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Keywords

Nutrition; radiochemotherapy; supportive care

Purpose/Objective

We aimed to determine the impact of dietary counselling in a prospective cohort of patients with Head and Neck Cancer (HNC) undergoing radio-chemotherapy.

Material/methods

Between November 2020 and March 2021, we conducted this single-centre prospective study on 17 consecutive patients treated with radio-chemotherapy or radiotherapy for HNC. At baseline, nutrition risk assessment was performed using the Malnutrition Universal Screening Tool (MUST). Nutritional outcome and morbidity, during and 1 month after the end of treatment, were evaluated.

Results

Seventeen patients were prospectively enrolled. The majority of patients were male (77.5%). Mean age was 66,6 years (range 56-81 years). Patient, clinical and treatment characteristics are summarised in Table 1.

At baseline, the most commonly observed issues were inadequate oral intake and involuntary weight loss, with inadequate energy intake as the most frequent cause (38%).

The mean body weight and BMI trend were collected during the whole observation. At the same time, data on variation in energy and protein intake were collected to evaluate the effect of nutritional intervention over establishment and progression of nutrition-related symptoms (Table 2).

At mid-treatment (T1), mean body weight showed a reduction from baseline, with a little increase at the end of therapy. Globally, we observed body weight stability during the treatment period and a recovery from the observed minimum weight (mean 74.3 vs 74.4 kg, min 59 vs 57.3 kg).

Conclusion

Our data suggest that nutritional counseling should be adopted to increase dietary intake and to prevent therapy-associated weight loss and treatment adherence reduction.

Tab. 1: Patient's Baseline characteristics.

	N°	%
Patients	17	100
Age		
mean	66,6	
range	56-81	
Sex		
Male	13	77,5
Female	4	23,5
Performance Status (ECOG)		
0	15	88
1	2	12
2	0	
Tumor Site		
Oral Cavity	3	17,65
Salivary Gland	2	11,76
Larynx	3	17,65
Oropharynx	7	41,17
Rhynopharynx	1	5,88
Unknown Primary	1	5,88
Smoker Status		
Non smokers	4	23,5
Smokers	13	76,5
Inactive	7	
Active	6	
HPV Status		
Positive (all oropharynx)	7	39
Negative or not tested	10	61
Chemotherapy		
No	6	35
Yes	11	65
CDDP/q7	5	
CDDP/q21	5	
Cetuximab	1	
Treatment setting		
Adjuvant	4	18
Radical	13	82
Surgical intervention	4	18
No surgical intervention	13	82
Treatment		
Radiotherapy	6	35
Chemo-Radiotherapy	11	65

Abb: ECOG, Eastern Cooperative Oncology Group;HPV, human papilloma virus; CDDP, cisplatin.

Tab. 2. Principal nutritional parameters evaluated during observation.

Parameters	Baseline (T0) (n=17)	T 1 (n=17)	T2 (n=14)	T3 (n=9)
Weight (Kg)				
Mean	75,2	73	74,4	70,4 (74,3†)
Min	55,5	54,5	57,3	56 (59†)
Max	94,5	95	93,5	92,3 (92,3†)
BMI (Kg/m2)				
Mean	25,7	25	25,3	23,23
Intake E (Kcal)	1734	1711	1753	1953 (2078†)
Intake P (g)	72	74	77	88
ONS (% pz)	29	65	78	22

BMI:Body Mass Index; ONS: oral nutritional supplements
† The data in brackets refer to the sample without the two patients with severe late toxicity (G3 mucositis)

PO-217 | Paranasal sinus and nasal cavity carcinoma: experience of a tertiary hospital

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Keywords

Sinonasal carcinoma, nasal cavity carcinoma, multimodal treatment

Background/ Objective

Primary malignant tumors of paranasal sinus and nasal cavity (PSNC) are rare. Near 60% of these are squamous cell carcinomas (SCC).

Major SCC risk factors are smoke and human papillomavirus, while occupational exposures to inhaled wood dusts, glues and varnishes (WDGV) are more related with adenocarcinoma (AC).

PSNC carcinomas treatment remains challenging. Recommendations are based on observational case series due to lack of randomized trials. Most patients are diagnosed in advanced stage and the outcomes remain poor. The introduction of neoadjuvant (NA) chemotherapy (CT) has shown to be promising.

This study aims to analyse patients diagnosed with PSNC carcinomas treated in our institution in terms of clinicopathological features, treatment and outcomes.

Methods

Retrospective analysis in a tertiary hospital between 03/2004 to 05/2022. PSNC carcinomas with histological confirmation were included and data was collected from patient's clinical file. Statistical analysis was done using SPSS® v27.

Results

Forty-nine patients with PNSC carcinoma were analysed: 46 males (93.9%), median age of 64 years [38-84]. The majority (87.7%) had ECOG PS 0-1 at the time of diagnosis. 30.6% were or had been tobacco smokers and 55.5% had occupational exposure to WDGV.

The most common type of carcinoma was AC (63.3%), mostly intestinal type (ITAC; 77.4%), followed by SCC (24.5%). 87.5% of ITAC patients had occupational exposure to WDGV.

63.3% had a locally advanced tumor at the time of diagnosis (stage III-IVB). A multimodal treatment was done in 69.4%: 44.2% did surgery+radiotherapy (RT), 26.5% surgery+chemoradiotherapy (CRT) and 20.6% radical CRT. From patients who did CT, 84.2% was platinum-based. The rate of orbital preservation was 86.1% and 30.6% had a complete resection.

44.9% of patients had disease recurrence (DR), 17.4% of them with distant metastasis.

Median follow-up was 17 months [0-94]. Median progression free survival was 35 months (IC 95%: 13.0-57.0) and median overall survival (OS) was 53 months (IC 95%: 24.6-81.3). The 3-year OS was similar between SCC and AC (57.7% and 67.1%, respectively; p=0,266). Patients who did platinum-based CT had significantly better OS (p=0.035).

Conclusions

In our study there was a predominance of ITAC mainly due to the high occupational exposure to WDGV, which is prevalent in northern of Portugal, where patients of this study are from. This reinforces the importance of occupational risk factors in the development of AC and the importance of preventive measures in those workplaces.

More than half of our patients did a multimodal treatment, mainly surgery+RT. The rate of orbital preservation was 86.1%, but less

than one-third (30.6%) had a complete resection. 44.9% had DR (near 20% with distant metastasis), which was higher than that reported in literature, probably due to the late diagnosis and high rate of an incomplete surgical resection.

Our study has some limitations due to its retrospective nature and the large period of time of patients' inclusion, which may lead to differences in treatment modality selection criteria, RT techniques and CT schedules along the years. Recently, new sequences on multimodal therapies, such as NACT are being applied with impressive results on organ preservation and survival outcomes. More clinical trials are needed to prove the benefit of these treatments in order to improve patient's outcomes that remain poor.

PO-218 | Chemoradiotherapy with curative intent in head and neck cancer – experience from a cancer center

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Keywords

Head and neck cancer; radical treatment; chemoradiotherapy;

Purpose/Objective

Curative treatment options for Oropharynx, Hypopharynx, or Larynx cancers include an association of Radiotherapy (RT) and Chemotherapy (CHT). This approach allows tumor eradication, preserving the organ and improving functional outcomes. Improvements in RT, CHT, and supportive care have been shifting the patterns of survival and disease control. We aimed to assess the clinical outcomes of our hospital (a tertiary center) in terms of overall survival (OS), progression-free survival (PFS), and disease-specific survival (DSS).

Material/methods

Retrospective review of patients diagnosed with squamous cell carcinoma of the Oropharynx, Hypopharynx, and Larynx between January 2015 and December 2020. All the patients completed RT treatment with curative intent at our hospital (a tertiary center). Exploratory and descriptive statistics were used.

Results

334 patients were identified. The mean age at diagnosis was 57.2 years. The most common primary site of cancer was Oropharynx (60.5 %), followed by Hypopharynx (28.7 %) and Larynx (10.8 %). The majority of patients presented with stage IVa (54.8 %), followed by stage IVb (19.8 %) and III (18.0 %). Only 21.0 % received induction

chemotherapy, but 93.4 % undergo concomitant chemotherapy (mainly Cisplatin). The median OS was 38.3 months (39.4, 32.4, and 35.2 months, for Oropharynx, Hypopharynx, and Larynx cancers respectively). The median PFS was 92.3 months (92.3 and 81.0 months, for Oropharynx and Hypopharynx cancers respectively). The 5-year OS was 38.0 % (42.5 %, 28.2 %, and 39.8 % for Oropharynx, Hypopharynx, and Larynx cancers respectively). The 5-year PFS was 61.7 % (63.5 %, 55.9 %, and 71.2 % for Oropharynx, Hypopharynx, and Larynx cancers respectively). The 5-year DSS was 55.2 % (56.1 %, 51.2 %, and 59.2 % for Oropharynx, Hypopharynx, and Larynx cancers respectively).

Conclusion

Casuistic studies use past experience to improve our intervention today. The singularities in the treatment approaches of this population emphasize the importance of referral to reference centers. This study provided the clinical outcomes at our hospital (a tertiary center). Our results are according to the published data, however, there's always margin to improve.

PO-219 | Internal mammary artery perforator (IMAP) flap for head and neck oncological defects reconstruction

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Keywords

Head and Neck surgery; Reconstructive surgery; IMAP flap

Purpose

To report different scenarios of the usefulness of internal mammary artery perforator (IMAP) flap in reconstruction of head and neck oncological defects, particularly small and medium sized pharyngoesophageal defects or defects near tracheostoma.

Material/methods

Retrospective study of 6 patients, corresponding to 8 IMAP flaps, submitted to head and neck oncological and reconstructive surgery in a Portuguese tertiary hospital between 2016 and 2020.

Results

Seven male patients aged between 60 and 77 years underwent head and neck surgery, where one IMAP flap (or two IMAP flap in two patients) were used to reconstruct the different defects. IMAP flaps were used in the following scenarios: primary reconstruction of partial pharyngectomy (2); tracheoesophageal fistulas closure (2); tracheostoma reconstruction (2); and cutaneous defects reconstruction (1). The use of IMAP flaps was successful in 8 cases (follow-up period of at least 6 months). In one patient, submitted to total laringectomy and partial pharyngectomy for a recurrence of a supraglottic SCC after treatment with chemo-ra-

diotherapy, the IMAP flap became necrotic two weeks after The patient needed additional surgical treatment.

Conclusion

IMAP flaps are a reliable and versatile alternative to local flaps such as dectopectoral and pectoralis major flaps for reconstruction of small and medium cutaneous and pharyngoesophageal defects of the lower neck region. They are also an alternative to free microvascular flaps because they require less surgical skills and less surgery time.

PO-220 | Reirradiation with particle therapy in recurrent sinonasal carcinoma: a single institution results

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Keywords

Sinonasal carcinoma, reirradiation, particle therapy

Purpose/Objective

Although surgery represents the mainstay of treatment for recurrent sinonasal carcinoma (SNC), only few selected patients with resectable tumors are eligible for salvage surgery. Unresectable and inoperable cases are usually managed with re-irradiation (re--RT). However, the best re-RT approach in terms of techniques and fractionation is still far from being defined. In this scenario, due to their favorable dosimetry and the ability in overcoming radioresistance, charged particle radiotherapy (RT) including proton (PT) and carbon ion (CIRT) could represent a treatment option. We aim to investigate the clinical outcome and toxicity profile of a series of recurrent sinonasal patients retreated with particle therapy .

Material/Methods

Fourteen consecutive patients with inoperable recurrent, previously irradiated, sinonasal carcinoma curatively treated at our Institution between 2013 and 2020 were included in this retrospective analysis. All patients has been clinically evaluated at baseline, during RT, at treatment completion, and every 3 months for the first 2 years after the end of RT, and then at 6-months intervals, with clinical visit and local imaging with MRI (or CT if contraindication to MRI). Local control (LC) and Overall Survival (OS) were estimated

by the Kaplan–Meier method. Acute and late toxicities were scored according to the National Cancer Institute's Common Terminology Criteria for Adverse Events CTCAE version 5.0.

Results

Seven out of 14 patients were Intestinal-Type carcinoma (ITAC), 3 Esthesioneuroblastoma (ENB), 2 Squamous cell carcinoma (SCC), 1 Sinonasal undifferentiated carcinoma (SNUC), and 1 Adenocarcinoma. First radiotherapy course was delivered with photon Intensity Modulated RT (IMRT) in 13 cases and with cyberknife in 1 case with a median dose of 60 GyRBE. The median time from first RT course was 36 months (range 10-213). Thirteen patients received CIRT, only one patient PT. Median reRT dose was 54 GyRBE (range 45-64 GyRBE) delivered in 3 or 4 GyRBE/fr for the CIRT and 2 Gy (RBE)/fr for the PT schedule. After a median follow-up time of 19,5 months (range 6-95), LC rates was 47,6% (95% CI 20-75,2) at 1-year, and 38,1% at 2- and 3-years (95% CI 10,1-66,1) . OS rates at 1-, 2- and 3-years were respectively 92,3% (95% CI 77,5-100) 76,9% (95% CI 53,5-100) and 46,2% (95% CI 15 - 77,4). Thirteen patients developed G1-G2 acute toxicity, mostly dermatitis and mucositis, no patients developed G3-G4. Regarding late toxicity 9 patients developed G1-2 events (G2 neuropathy, asymptomatic brain radionecrosis and dysphagia) and 5 patients did not experience any toxicity.

Conclusion

To our knowledge, despite the small number of patients, our study is the first series of recurrent SNC reirradiated with particle therapy. Our preliminary data shows that reRT with particle therapy is safe and feasible with acceptable outcome results.

PO-221 | Intratumoral necrosis in head and neck cancer following hadrontherapy: the role of dose, RBE and LET

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Keywords

Soft tissue necrosis, hadrontherapy and head and neck

Purpose/Objective

To understand the potential role of RBE-weighted dose (DRBE), RBE modelling and dose-averaged LET (LETd) in the development of intratumoral necrosis after proton (PT) and carbon-ion (CIRT) treatment of head and neck (HN) tumors.

Material/Methods

For this analysis we considered all HN cases, definitively treated with PT or CIRT between 2013 and January 2022, free of local recurrence during follow-up, which experienced soft tissue necrosis starting at the treated tumor site (STN).

The STN volume was contoured on the planning CT, rigidly registered with MRI study showing STN at the first occurrence. PT plans were recalculated with RBE=1.1 and the McNamara model with variable a/b ratio (2 and 10 Gy); CIRT plans with the local effect (LEM) and microdosimetric kinetic model (MKM). DRBE and LETd distributions in the STN were analysed in comparison with GTV values, looking at percentage deviation in near-to-maximum (D1%) and median DRBE (D50%), for each RBE model, and LETd (L1%, L50%) values. We finally analysed the incidence of STN, per particle type, in relation to fractionation schedule variations during the study period.

Results

Five PT and 9 CIRT cases developed SNT at a median follow up of 6 and 16 months, respectively. All patients, except one CIRT case, had adenoid cystic carcinomas (ACC). In total, 152 ACC patients received definitive CIRT; since 2017 up-to-date, 54 patients were treated with PT. In the STN group, the median prescription dose was 69.96 Gy(RBE) (range 66-70) in 33 fractions for PT and 68.8 Gy(RBE) (65.6; 70.4) in 16 fractions for CIRT.

DRBE was not significantly different in the STN with respect to the GTV, (median DD1%= -0.1% [-0.2%; 0.1%] for PT; 0.6% [-0.8%;0.7%] for CIRT), with no influence of RBE modelling. LETd was lower (median DL1%= 10.6% [-14.1%;-6.1%] for PT; -13.0% [-17.4%;-11.4%] for CIRT), being the necrotic area mainly located in the target centre (Figure 1).

Due to the annual incidence of SNT after CIRT in 2015 (6%), the prescription dose was reduced to 65.6 Gy(RBE). The PT scheme (1,8-2 Gy(RBE)/fraction) was implemented in 2017 for ACC invading large part of the oropharyngeal mucosa infiltration. The subsequent introduction of a moderate hypofractionated schedule (2.12 Gy(RBE)) could have been one of the factors contributing to the increase of the PT toxicity rate (7%) for this critical group. Assuming a higher sensitivity of the involved tissue, the McNamara (a/b 2 Gy)--based calculation indicated a 9.5% increase in the median target DRBE, which would correspond to 2.32 Gy(RBE)/fraction.

Conclusion

Our preliminary results seem to find a relationship between STN, tumor histology, prescribed dose and fractionation schedule, for both PT and CIRT. Further analyses are mandatory to confirm our findings, including evaluation of potential clinical dose-modifying factors, histological subtype and individual patient radiosensitivity profiles, possibly in comparison with a control patient pool.

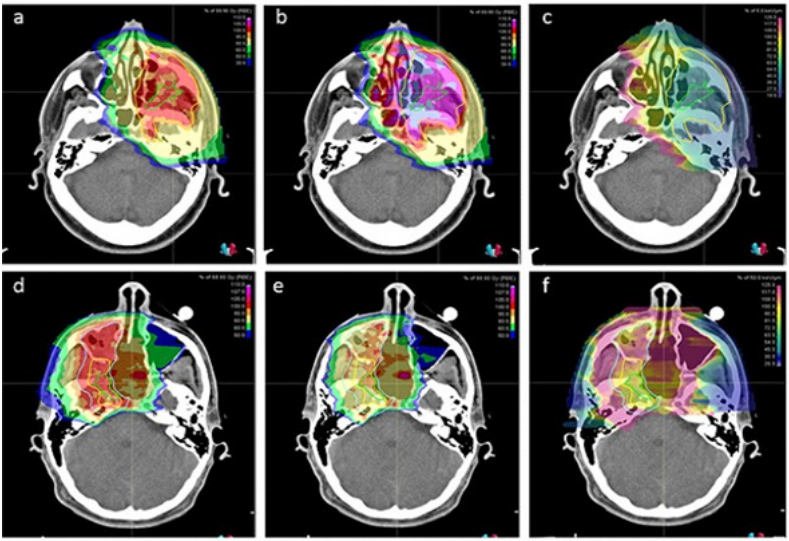

Figure 1. Axial CT-scan of two STN cases: a) PT D_{RBE} RBE=1.1; b) PT D_{RBE} recalculated with McNamara α/β 2 Gy, both normalized to the prescription 69.96 Gy (RBE); c) PT LET_d distribution normalized to 3 keV/µm; d) CIRT D_{RBE} LEM; e) CIRT D_{RBE} recalculated with MKM, both normalized to the prescription 68.8 Gy (RBE); f) CIRT LET_d distribution normalized to 50 keV/µm. The yellow contour indicates the GTV, the green contour the STN volume and the light blue the high-risk Clinical Target Volume (CTV).

PO-222 | Laryngeal chondrosarcoma, the experience of an oncologic center

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Keywords

Larynx Chondrosarcoma; Larynx chondroma; Larynx cancer

Purpose/Objective

Laryngeal chondrosarcoma is a rare pathology of the larynx. It arises from the cartilaginous structures. IT's more frequently located at cricoid cartilage followed by thyroid cartilage, epiglottis, and arytenoid cartilages. Their symptoms are variable, depending on the size and location, and may include hoarseness, dyspnea and stridor. The treatment of choice is surgery which may be endoscopic or open surgery. They have low tendency to metastatic diffusion and the prognosis is generally good. This study investigates presentation, treatment modalities and patient outcomes of a oncologic center in Lisbon, Portugal. The aim of this work is to understand more about this rare entity that we still don't know the ethiology.

Material/Methods

Estudo retrospectivo de casos de condrossarcoma de laringe acompanhados de 1992 a 2022 no serviço de Otorrinolaringologia de um centro oncológico - Instituto Português de Oncologia de Lisboa. A análise estatística foi feita com o Microsoft Excel® e SPSS®.

Results

Seventeen cases were identified. 2 in 3 of the patients were male and the average age of this population was 59.6 years. Just 24% oh these patients had smoking story. Most of the patients had insidious dysphonia and/or dyspnea. The posterior arch of cricoid cartilage was the most common origin place. Histopathology after biopsy suspected of this pathology but it was not diagnostic. Imagiology, mainly CT, helped to do this diagnosis showing calcifications. The primary treatment was surgery for all studied patients. The most common surgical approach was larynx microsurgery with debulking of the lesion (47%) followed by partial laryngectomy (24%). The latter one was more common in the first years analyzed of this study. None did adjuvant radiotherapy or chemotherapy. 23% had residual tumor after the surgery. Half of them were in watchful waiting and the other half were submitted to other surgey. Just one patient that had recurrence did radiotherapy. Disease-specific survival rates for 1 and 5 years were 97% and 91% respectively.

Conclusion

Laryngeal chondrosarcomas are rare and the etiology is still uknown. Various surgical approaches were done with a good prognosis. Nonsurgical approaches weren't used primarly for these lesions. The main concern regards their propensity to relaps.

PO-223 | Feasibility study of Infrahyoid flap in oral tongue reconstruction after compartmental glossectomy

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Keywords

Infrahyoid flap; carcinoma tongue; compartmental glossectomy; oral cancer

Purpose

Compartmental glossectomy for lateralized carcinoma tongue has been an important surgical procedure due to its oncological sound basis but has been associated with reconstruction need. This prospective study focuses on feasibility of infrahyoid myocutaneous flap for reconstruction and speech and swallowing outcomes with this flap after compartmental glossectomy.

Methodology

40 patients were enrolled prospectively from January 2021 - November 2022. Male to female ration was 3.4::1. Mean age of the cohort was 44 years. T-stage for 40 patients was T2:17; T3:20 and T4a: 3 respectively. 32 patients had compartmental glossectomy; 3 had subtotal glossectomy, 4 had partial glossectomy and 1 had hemi-glossectomy. Outcomes was noted objectively for swallowing by cinefluoroscopy and subjectively for speech. Also flap outcomes were evaluated in terms of complete survival, partial necrosis and complete failure.

Results

All the patients were evaluated for the surgical outcome in terms of flap survival. Complete flap survival is seen in 72.5% (n=29/40).

The complete and partial loss of flap was noted in 5.2% (n=2/38) and 23.6% (n=9/38) respectively. The cumulative survival was this study group was 96.1%. Intraoperatively flap had to be discarded twice because of advanced nodal stage (involvement of Internal Jugular Vein) and inadvertent injury to pedicle. All the patients could be started on oral feeds at average 3 weeks post operatively (ranging from 2 to 4.5 weeks). Cinefluoroscopy was utilized for evaluation of swallowing which showed acceptable results. Speech was comprehensible for all of the patients and correlated with the extent of resection.

Conclusion

Infrahyoid myocutaneous flap is a viable alternative for tongue reconstruction after various types of glossectomies with excellent cumulative survival It provides both muscle bulk and skin lining to reconstructed tongue. Infrahyoid myocutaneous flap is an alternative option to free flap reconstruction after compartmental glossectomy in a resource constrained settings and in patients unfit for free flap reconstruction.

PO-224 | VEGF-A gene -460 C/T polymorphism – potential genetic marker for overall survival in OSCC patients

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Purpose/Objective

The vascular endothelial growth factor A gene (VEGF-A) is located on 6p21.1 and its product induces proliferation and migration of vascular endothelial cells. The objective of this study was to evaluate vascular endothelial growth factor A (VEGF-A) gene polymorphism -460 C/T (rs833061) as potential genetic marker for overall survival in oral squamous cell carcinoma (OSCC) patients.

Material/methods

In total, 61 samples of paraffin-embedded tissue taken during the surgery from patients diagnosed with OSCC, served for further molecular testing. All patients were older than 18 years and total follow up period was for 3 years. Adequate adjuvant therapy related to postoperative risk was applied. Data were collected on the overall survival of the patients. Genomic DNA was isolated using the QIAamp DNA FFPE Tissue Kit (Qiagen). Region including polymorphism of the VEGF-A gene at the position -460 C/T was amplified and PCR amplicons were sequenced. Sequence analysis was performed in BioEdit (Hall, 1999), and the genotypes were scored. All of the statistical analyses were performed using IBM SPSS Statistics. The Chi-square test of independence was used to determine if there is a significant relationship between two categorical variables.

Results

The VEGF-A -460 C/T genotype was successfully determined for all 57 patients. The mean age of patients was 65.4 ± 10.1. The most frequent genotype was CT 24 (42.1%), followed by CC 20 (35.1%), while TT genotype was detected in 13 (22.8%) patients. There is statistically significant relationship between VEGF-A -460 C/T genotype and overall survival (chi-square=6.550, df=2 p=0.038). More than half of non-survived patients in 3 year follow up period had genotype CT, while most of survived patients after 3 year follow--up period had CC (47%). Only 14% of non-survived patients had genotype CC, while one third of them had TT genotype.

Conclusion

Homozygotes CC at VEGF-A -460C/T polymorphism (rs833061) showed longer overall survival. This SNP is located in the promoter region of VEGF-A gene and previous association studies including different cancer types yielded conflicting results. In our study we showed that this polymorphism might be potential new marker for overall survival in OSCC patients. In order to further evaluate it, it would be beneficial to conduct a survey in healthy control and to increase study population size.

PO-227 | A dynamic, cancer specific patient reported experience measure item-bank: a mixed method approach

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Objective

Since the introduction of value based healthcare there is an increased attention for the use of Patient Reported Experience Measures (PREMs) for quality improvement. However, currently most used PREMs are generic and static, while healthcare is dynamic and contains a wide variety of aspects that contribute to quality of care. In order to continue improving the healthcare process at a department, it is important to react to opportunities for improvement pointed out by the PREM data. Therefore, the aim of this study was to propose a PREM-item bank to dynamically evaluate the provided care at the outpatient clinic.

Methods

In co-creation with head and neck cancer patients, a mixed methods study was conducted: an explorative review of literature, qualitative focus group analysis with patients, and a quantitative item selection by patients and healthcare professionals through prioritization.

Results

A total of eight validated generic and cancer specific PREMs were included. After removal of duplications 141 single items were obtained. Nine themes were formulated after qualitative analyses of the focus group: '*Organization of healthcare', 'Competence of healthcare professionals*', *'Communication', 'Information & services', 'Patient empowerment', 'Continuity & informal care', 'Environ-*

ment' and 'Technology'. After mapping of the single items underneath the themes, 7 patients and 11 professionals were asked to prioritize the most important items. Eventually, an itembank with 76 items was proposed.

Conclusion

Together with head and neck cancer patients and healthcare professionals, we proposed a patient reported experience measure itembank to evaluate patients experience with provided cancer care in the outpatient clinic. This PREM itembank can be used to dynamically evaluate the given cancer care at an outpatient clinic.

Figure 1. Development of the PREM-itembank

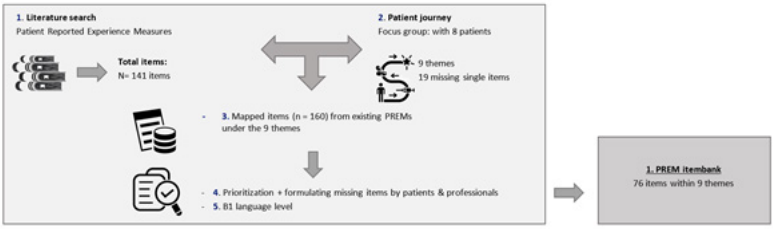
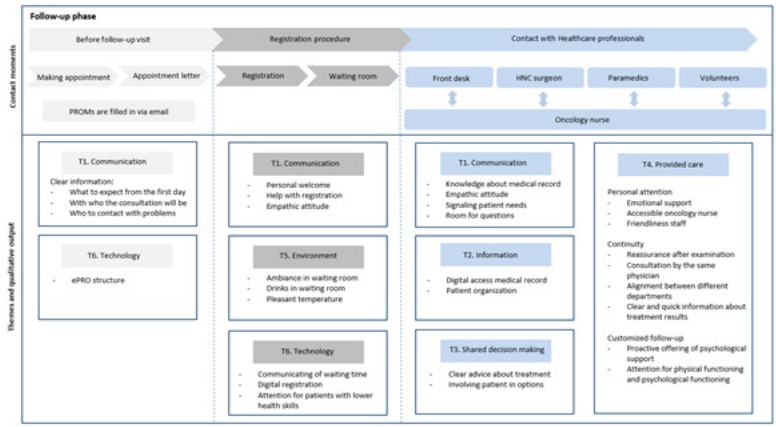


Figure 2. Contact moments in the follow-up phase of the patient journey for HNC patients



PO-228 | IMAP flap: a reliable option for neck reconstruction

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(1) CENTRO HOSPITALAR E UNIVERSITÁRIO DE SÃO JOÃO E.P.E.

Keywords
IMAP flap; Neck reconstruction

Purpose/objective

There are limited locoregional flaps for head and neck reconstruction. The most used is the supraclavicular flap. However, its pedicle may be compromised during neck dissection. The purpose of this work is to show the utility of internal mammary artery perforator (IMAP) flap on neck reconstruction.

Methods

A female patient with an extensive tumor of head and neck was proposed to palliative surgery. The plan consisted of debulking of tumor and postoperative radiotherapy. The tumor invaded the level V on neck dissection and the cervical transverse artery was sacrificed during the excision of the tumor. After excision, the skin defect measured 8 x 5cm on the neck. It was reconstructed with an IMAP flap.

Results

A good aesthetic reconstruction was achieved with no postoperative complications. The donor area was closed directly, causing low donor site morbidity. The patient started the radiotherapy as scheduled.

Conclusion

The IMAP flap is a reliable locoregional option on neck reconstruction. It is associated with low donor site morbidity, making it a solution to be considered.

PO-230 | Transoral Ultrasonic Surgery (TOUSS): a safe and effective alternative for Head and Neck tumors.

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Keywords

TOUSS

Purpose/Objectives

In recent years, transoral endoscopic surgery has been intensively developed for benign and malignant pathologies of the upper aerodigestive tract. In 2015, the first experiences with Transoral Ultrasonic Surgery (TOUSS) were published, as an alternative to robotic surgery. We present the experience of our institution in the last five years.

Material and Methods

A retrospective review of the reports of patients treated with ultrasonic endoscopic transoral surgery is carried out since its incorporation in September 2017. Those patients who have at least one month of follow-up will be considered.

Results

Between September 2017 and October 2022, 28 procedures were performed on 27 patients. 8 (29,6%) women and 19 (79,4%) men with an average age of 61 years (range 14-84 years old). 8 (28,5%) procedures were performed on benign lesions and 20 (71,5%) were malignant (1 lymphoma, 1 low-grade liposarcoma and 18 squamous cell carcinomas). No conversion to open surgery was observed. Regarding malignant cases, no positive mucosal margins were registred but 2 (10%) had deep margin involvement. 27

patients were able to restart the oral diet, 23 (85,1%) of them with a satisfactory swallow (FOSS 0-2). 10 (35,7%) tracheostomies were performed, of which 7 could be closed. 4 patients experienced complications related to surgery: 1 mild local bleeding that could be controlled conservatively and 2 bleedings that could be controlled in the operating room were recorded.

Conclusion

TOUSS seems to be a safe and effective technique for the treatment of benign and malignant pathologies of the upper respiratory tract, with good functional results.

PO-231 | 3D printed immobilization devices for radiotherapy dedicated MRI of head and neck cancers

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Keywords

3D printing, magnetic resonance imaging, radiotherapy

Purpose/Objective

Radiotherapy (RT) of head and neck cancer (HNC) patients requires high precision and reproducibility. The standard RT setups consists of individualized five-points head and shoulders masks, foam headrests, individualized spacers and/or wedges, and a baseplate. The same setups should be used during planning computed tomography (CT) and magnetic resonance imaging (MRI), with the latter one routinely used for better soft tissue resolution and delineation improvement. Unfortunately, as most of immobilization devices are made of carbon fiber they are not compatible with MRI. High cost of MRI-safe solutions limits their use in small radiotherapy departments as well as in multispeciality hospitals with many MRIs requiring buying dedicated immobilization set for each. 3D printing technique allows to create objects of desired shape from wide range of materials. The aim of our research was to explore the feasibility of 3D printing of immobilization devices for RT dedicated MRI of HNC patients.

Material/methods

We used an open-source parametric 3D modeler FreeCAD (© The FreeCAD Team) to develop a set of digital structures

compatible with the commercial immobilization devices used in our department. A Creality Ender 5 Plus 3D Printer with an ecoPLA white and transparent filaments (3DJAKE, Poland) was used for 3D printing. We printed two sets of spacers and wedges, and a baseplate (Image 1). The rest of immobilization set - mask and foam headrests, were MRI-safe. MRI planning images were acquired using a 1.5 or 3 Tesla Siemens Magnetom Vida MRI (Siemens Healthcare, Erlangen, Germany). Due to incompatibility of standard head and neck immobilization with the head coil we used two flexible 18-channel coils (Image 2) with additional spine coils in the table. The sequences used in our institutional protocols for acquisition of MRI images for RT planning were: 1. non-enhanced and contrast-enhanced isometric VIBE sequence with Dixon technique in T1-weighted images (WI) in the sagittal plane, 2. Turbo spin-echo sequence in T2-WI in the transverse plane, 3. Diffusion-WI in the transverse plane, 4. Turbo spin echo sequence with Dixon technique in T2-WI in the transverse plane.

Results

In April 2022 we utilized our 3D printed immobilization devices for the first time for RT dedicated MRI acquisition. They fit commercial ones perfectly. Quality of the images was accepted by our team of head and neck radiologists. Acquired images were co-registered with planning CT. As we did not find any problems with the use of printed accessories, we have decided to implement MRI imaging in treatment position for HNC RT planning into institutional protocol. The cost of materials used for 3D printing of one set of immobilization devices (3 pieces of spacers and wedges, and a baseplate) was below 40 euro.

Conclusion

We found that 3D printed immobilization devices can be safely used for RT dedicated MRI of HNC. The low cost of 3D prin-

ting, which in our research was below 40 euro for one set of accessories, may allow broader use of the treatment position during RT dedicated MRI, even in small radiotherapy departments. The quality of MRI images acquired with the use of 3D printed immobilization devices and flexible coils is acceptable.

PO-232 | Voice Outcome After Uncomplicated Thyroidectomy in Patients With Papillary Carcinoma

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(1) KBC Zagreb

Key Words

Voice change, total thyreoidectomy, papillary carcinoma

Introduction

Thyroidectomy is a standard treatment for thyroid cancers. Injury of the inferior laryngeal nerve is not the only cause of voice alteration after thyroidectomy; many patients notice minimal changes immediately after operation, without evidence of inferior laryngeal nerve damage. The aim of this study was to promote understanding of voice change after uncomplicated thyroidectomy by analysing the results in patient with papillary carcinoma after total thyreoidectomy in our institution.

Materials and methods

Forty patient with papillary carcinoma who underwent total thyroidectomy were studied. We evaluated voice parameters including the Voice Handicap Index-10 (VHI-10), the vocal efficacy index, the fundamental frequency (F0), the maximum phonation time (MPT), jitter, shimmer, preoperatively and at the second, fourteenth postoperative days and first and third postoperative months. All patients underwent stroboscopy preoperatively and first postoperatively day.

Results

No complications occurred during operation or in the postoperative period. Immediately after surgery, significant decreases in MPT (p=0.002) and significant increases in F0, jitters and shim-

mers, (p=0.009, 0.02, and 0.02, respectively) were observed. In F0, statistically significantly higher on the second day after surgery than on the 14th postoperative day. VHI is the highest on the second postoperative day with a slight decrease on the 14th postoperative day and is elevated on the third postoperative month in those patients who have elevated parameters of acoustic analysis

It is visible that the greatest voice changes were recorded on the second day after the operation, and each subsequent measurement shows a decreasing intensity of voice changes.

Conclusions

Voice changes after uncomplicated thyroidectomy occur and can be objectively measured. F0 , shimmer, and MPT significantly worsened in the early and not in the late postoperative period.

PO-233 | Reconstruction of large skull base defects after tumor resection

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Keywords

Skull base reconstruction, Free microvascular flap; Interdiscplinary endoscopic skull base surgery

Purpose/Objective

Larger anterior skull base defects with lateral extension or reaching the middle cranial fossa, involvement of the orbit, nose or maxilla or after radiation may require reconstruction with free microvascular flaps. In recent years, endoscopically assisted insertion has gained in importance.

Material/methods

In the period from 2019 to 2022, we performed 6 skull base reconstructions with free grafts after resection of extensive malignant tumours of the skull base together with our neurosurgical department. Tumors treated were 3 carcinomas and 3 sarcomas of the paranasal sinuses with invasion of the orbita and skull base. For reconstruction we used a forearm flap four times and an ALT twice. In three patients, flaps were inserted endoscopically assisted. The anastomosis was made to branches of the external carotid artery. Flap pedicles were placed transpteriogoidal parapharyngeal.

Results

Skull base reconstruction was succesful in all cases without occurrence of CSF-leak. No major complications occured.

Conclusion

Endoscopic assisted insertion can be helpful in reconstructing large skull base defects with microvascular flaps. The choice of flap, pedicle routing and recepient vessels depends on the size and location of the defects.

PO-234 | Pharyngocutaneous Fistula Following Total Laryngectomy

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Purpose

The development of a pharyngocutaneous fistula (PCF) is the most common and troublesome postoperative complication following laryngectomy. The management of PCF can considerably increase hospitalization time and expense, delay the initiation of adjuvant radiation therapy. The purpose of this study was to evaluate the potential risk factors for Pharyngocutaneous Fistula Following Total Laryngectomy

Material and methods

A retrospective case-control study was designed. In the period between 2011 and 2021 we performed 387 total laryngectomies for advanced squamous cell carcinoma of larynx at the University ORL Clinic Nis, Serbia.

Primary total laryngectomy (PRT) was applied in 316 patients, while in 38 patients initial radiotherapy (60–70Gy), and in 33 patients chemotherapy (cisplatin-5 fluorouracil) with radiotherapy were introduced becauce of refusal of primary surgery, and they later received salvage total laryngectomy (STL).

Results

The most frequent tumor site was glottic with 49.1%, followed by supraglottic in 33.9%, and subglottic or transglottic localization in 17.0%. T3 stage (57.1%) was more frequent than T4 stage of the disease. N2 stage predominated with 43.7%, while N3 and N1 were less frequent. The overall fistula rate was14% in patients with primary closure. Majority of leaks manifested within first 2

weeks and most appeared in the lateral part of the suture line. In most patients the fistula healed with conservative management alone. All the laryngectomies were performed by four surgeons, using the same routine surgical technique. Briefly, pharynx was closed linearly or in T shape, with 3-0 Vicryl single stitches, muscular reinforcement was made using the same material, and nasogastric tube was used for 7 days.

The mean time for spontaneous closure of fistulas was 25±3 days. Totally 88.4% of fistulas closed spontaneously, with local care and specific antibiotic treatment. Generally, PCF develops just above the tracheostoma, at the weakest point of the suture line of the pharyngeal mucosa. The involved neck skin becomes tender and dark red. In our series, history of previous radiotherapy, and positive surgical margin were significantly associated with fistula formation. Statistical analyses showed a significant correlation between PCF and preoperative radiotherapy, which might be attributed to the diminished healing capacity of the irradiated tissues.

Conclusion

Based on our results we concluded that pharyngocutaneous fistula remains a troublesome complication of the postoperative period after total laryngectomy.

Our data showed that the, previous radiotherapy, and positive surgical margins can all be important predisposing factors, or at least underlying causes. Our experience confirmed that most fistulas can be successfully managed with conservative treatment.

PO-238 | Electrochemotherapy in Head and Neck Melanoma - Review of the Literature

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Keywords

Melanoma; electrochemotherapy; head and neck

Objectives

Cutaneous malignant melanoma of the head and neck region represent 15 to 20% of all melanomas. Surgical treatment of these tumors with this location is sometimes limited by functional and aesthetic issues. Electrochemotherapy (ECT) is a weapon therapy that fuses chemotherapy with electroporation, thus increasing the cytotoxic effect of the drug. Our aim is to review the literature concerning the use of ECT as a therapeutic strategy in patients with head and neck melanoma.

Material/Methods

A medical literature review using PubMed, Scopus, and Cochrane databases were screened with a combination of keywords and medical subject headings to identify relevant studies. Additionally, we present a case of a 94-year-old patient with multiple melanoma lesions of the face with severe comorbidities that underwant ECT in our institution.

Results

ECT is an effective procedure in locoregionally advanced melanoma. It is considered a safe, low toxic palliative therapeutic option for unresectable lesions or for high-risk surgical patients. Results

in studies show high and consistent response rates, with adequate local response and tumor control. Some case reports have also shown that efficacy is possibly maintained even with a reduced dose of Bleomycin, the drug of choice for ECT. Specifically in our case, the patient had an acceptable response to ECT with good regression of tumour. Local complications were not observed.

Conclusions

ECT produces favorable results in terms of local response, local tumor control and low toxicity, emerging as a therapeutic option for patients with head and neck melanoma who do not meet the conditions for other treatments.

PO-239 | E-learning's effectiveness in surgical training of medical students and trainees:A systematic review

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Keywords

E-learning, surgical training, medical education, medical students, resident doctors.

Purpose/Objective

As the landscape of medical education alters with rapid rhythm, training curriculum is frequently challenged by several obstacles, that abrogate natural participation. E-learning is a salutary asset that gains more and more ground in the field of healthcare teaching. Nevertheless, its effectiveness is tested when it comes to surgical skills instruction. The aim of this study is to evaluate the efficacy of computer-based modalities in the surgical training of novice medical students and surgical trainees.

Material/Methods

A systematic search of four bibliographic databases (MEDLINE, Cochrane Library, Scopus and Web of Science) was conducted, looking for articles published during the last decade, according to the PRISMA statement. Eligibility criteria included prospective studies correlated to online surgical education of medical students or surgical trainees.

Results

A total of 511 studies were identified from the initial search, accompanied by 480 records that were identified from citations

searching. Finally, 18 studies (2 RCTs and 2 observational cohort studies), with a total of 1172 participants, were considered eligible and underwent further review. Types of e-learning modalities included were video projection, in the majority of them, attended by other type of multimedia, such as web-based platforms, mobile learning modules and online presentations. Overall, e-learning methods, manage to achieve either superior or comparable results comparing to other teaching methods or no intervention at all. A meta-analysis was not possible to be conducted due to the lack of homogenous quantitative data.

Conclusion

Despite significant heterogeneity among the included studies, e-learning modules appear to be a beneficial supplement to the conservative tuitional approaches, rendering the educational curriculum more effective.

PO-240 | S-100 as a differentiation marker in olfactory neuroblastoma treatment and its impact on prognosis

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Keywords

Olfactory neuroblastoma, S-100, Kadish, Hyams, esthesioneuroblastoma.

Purpose/Objective

Olfactory neuroblastoma (ONB) is a rare tumor originating from the paranasal sinuses and the nasal cavity (it accounts for 3% of tumors in this location), with specific clinical and pathological features, as well as a diverse clinical and natural course. So far, several clinical staging systems have been used, none of which has been finally recognized as valid. The Hyams system is currently the most widely used malignancy grading system, with the advantage of being able to be used as a prognostic factor. We present one institution's experience with this tumor and the results of therapy.

Material/methods

Nineteen patients treated for ONB at Maria Sklodowska-Curie National Research Institute of Oncology, Gliwice Branch between 1999 and 2018 were retrospectively reviewed and analyzed in terms of the use of the S-100 marker as a prognostic factor determining differentiation between neuroendocrine and neuromatous tissue structure.

The diagnosis of ONB was histologically confirmed for each patient.

Results

The mean follow-up was 9.16 years. In 78,9% of cases, patients received treatment with surgery followed by postoperative radiotherapy. Fifty eight percent received chemotherapy as part of initial treatment. Overall 5-year and 10-year survival rates were 90% in S-100 (+) group but overall 5-year and 10-year survival rates were 50% and 40% in S-100 (-) group (p=0.027), respectively.

Compared to these results, using Kadish classification, overall 5-year survival rates were 100% and 100% and 60% for Kadish A, Kadish B and Kadish C , respectively (p=0.43) but overall 10-year survival rates were 100% and 100% and 53% for these groups (p=0.43).

Using Hyams classification system, overall 5-year survival rates were 100% and 88% and 49% for Hyams 1, Hyams 2 and Hyams 3, respectively (p=0.19) but overall 10-year survival rates were 100% and 77% and 49% for these groups (p=0.19).

Five patients whose disease was initially stage Kadish C and also S-100 (-) had a recurrence. The mean time for recurrence was 3.08 years.

We recorded 3 cases of posttreatment failure, 3 cases of distant metastases and 2 second malignancies.

Conclusion

In the presented group of patients, the S-100 marker interpreted as a differentiation indicator was the most sensitive prognostic indicator.

PO-243 | Durable response after neoadjuvant immunotherapy in resectable CSCC: The MATISSE trial (NCT04620200)

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Purpose

Nivolumab alone (MONO) or combined with Ipilimumab (COMBO) has demonstrated promising results when administered prior to curative surgery across multiple solid tumors. In stage III/IVa CSCC, immune checkpoint blockade (ICB) employing neoadjuvant aPD1 induces a 75% pathological response rate at time of surgery1. However, the efficacy of aPD1 combined with aCTLA4 ICB has not yet been investigated in this setting.

Methods

Patients with T1-4N0-3M0 or TxN1-3M0 CSCC of all body sites with an indication for extensive or mutilating surgery w/wo adjuvant RT are included in the MATISSE trial and randomized for either ARM A: NIVO (3 mg/kg, weeks 0&2, N=24) or ARM B: NIVO (3 mg/kg, weeks 0&2) + IPI (1mg/kg, week 0, N=19) prior to extensive surgery (week 4). Primary objective is efficacy in terms of pathological response. A major pathological response (MPR) is defined as ≤10% residual viable cancer cells in the surgical resection specimen. Toxicity in terms of CTCAE v.5.0. Performing WES and RNA sequencing to identify predictive biomarkers for response. Furthermore, a quality-of-life and cost-effectiveness analyses will be done.

(Preliminary) results

44 of 50 patients with a T1-4N0-3M0 CSCC (median age 76) were enrolled in the MATISSE trial. Grade 3-4 irAEs occurred in 3/44 (6%) patients and were well manageable. 34 of 44 (77%) patients underwent standard of care surgery w/wo adjuvant RT. Of these 34

patients, 24 (74%) patients had a primary tumor (T1-4a), of whom 13 (52%) patients reached an MPR at the primary tumor site. Eleven patients with a T0N1-3M0 CSCC underwent surgery, of whom 4 (36%) reached an MPR. Two of 44 patients with clinically progressive disease refused mutilating surgery after all, of which 1 patient reached complete remission 2 months later. Another 8 patients chose not to undergo surgery and RT as they themselves experienced a significant clinical tumor remission upon immunotherapy (5 MONO and 3 COMBO patients). These nine patients have reached a durable complete remission without relapse, with a median FU of 10,6 months (range 3 to 26 months). Taken these patients into account, overall MPR rate at the primary tumor site 20 / 31 (65%) (MONO: 52% and COMBO: 79%). Patients with only lymph node metastases, overall MPR rate was 6 / 13 (46%) (MONO: 50% and COMBO: 40%).

Conclusion

In the MATISSE trial, so far, overall MPR rates after neoadjuvant in CSCC ranges from 46 - 65%. MPR at primary tumor after MONO and COMBO are 52% and 79%, respectively. Importantly, 9 patients have proven the concept that only 2 infusions of Nivolumab w/wo Ipilimumab can lead to durable complete responses in well-selected elderly CSCC patients normally treated with extensive and mutilating standard of care surgery and RT.

REFERENCE:

Ferrarotto R, et al. Pilot Phase II Trial of Neoadjuvant Immunotherapy in Locoregionally Advanced, Resectable Cutaneous Squamous Cell Carcinoma of the Head and Neck. Clin Cancer Res. 2021 Aug 15;27(16):4557- 4565. doi: 10.1158/1078-0432.CCR-21-0585. Epub 2021 Jun 29. PMID: 34187851; PMCID: PMC8711237.

PO-245 | Voice prosthesis rehabilitation: complications and costs - our experience from 2015 to 2021

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Keywords

Total laryngectomy, voice rehabilitation, voice prosthesis, tracheoesophageal puncture, adverse events, life quality, head and neck cancer.

Purpose/Objective

Voice rehabilitation after a total laryngectomy could be a challenge with techniques such as esophageal speech and electrolarynx. Tracheoesophageal voice prosthesis is the most recent voice rehabilitation technique and is considered the gold standard for voice rehabilitation after total laryngectomy due to its higher success rate, easier learning process, improved voice and life quality. Nevertheless tracheoesophageal voice prosthesis is related with complications during the procedure as well as during the postoperative period.

This study aims to summarize adverse events and health care costs associated with voice prosthesis placement in patients with head and neck cancer.

Material/Methods

Retrospective study using clinical records of adults submitted to total laryngectomy at Hospital Garcia de Orta between January 2015 and December 2021. Inclusion criteria were defined: larynx or hypopharynx malignant cancer submitted to total laryngectomy by ENT department, voice rehabilitation with primary or secondary voice prosthesis placement, esophageal speech or lisping voice. Lost of follow-up was considered an exclusion criteria.

Adults were distributed into two groups (voice prosthesis *versus* without prosthesis) for statistical validation. Statistical analysis was performed by using the SPSS v25 program.

Results

56 total laryngectomies were performed, 25 with voice prosthesis placement. From which 94 adverse events were extracted. The most common adverse events were leak (67%), local infection (10.64%), granulation tissue formation (7.44%), detached brush tip (6.38%), torn plug (5.32%). In 3% of patients the voice prosthesis was removed due to non-adaptation.

The health care costs were significant higher in the voice prosthesis group, related to more medical appointments and device costs.

Conclusion

Adverse events associated with tracheoesophageal puncture and voice prosthesis placement often are attributed to improper use. Interventions aimed at improving patient education may help reduce adverse events attributed to improper use. Health care costs are higher with voice prosthesis rehabilitation but is associated with substantial improvements in quality of life related to earlier voice speech.

PO-246 | Bilateral neck dissection in N0 contralateral well lateralized T3/T4 oral cavity carcinomas

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Keywords

Well-lateralized squamous cell carcinoma of the oral cavity; N0 contralateral T3/T4 tumors; Bilateral cervical lymph node dissection.

Purpose/Objective

To understand the benefit of performing a bilateral cervical lymph node dissection in a N0 contralateral well-lateralized T3/T4 tumor of the oral cavity.

Material/Methods

We performed a unicentric longitudinal study in the Head and Neck Surgery service of the Lisbon's Instituto Português de Oncologia (IPO), from 01/06/2017 to 30/06/2019 (median follow-up of 48 months). Oral cavity tumors data collection was obtained prospectively based on a retrospective database. Exclusion criteria included T1/T2 tumors; recurrent tumors; lip, tongue and floor of the mouth tumors; tumors extending the midline; oral cavity tumors followed by other specialties and lesions that were wrongly classified as malignant before surgery. Statistical analysis was outsourced after defining the study variables.

Results

33 patients were included after applying exclusion criteria to a total of 123 initial patients. After data gathering, it was verified that there was no comparison group, since all patients included in the

study only underwent ipsilateral cervical lymph node dissection. Of the patients eligible for the study, the majority were T4 tumors (90.9%), occurred on gingiva (57.6%) and received adjuvant treatment (85%). About 66.7% (22 out of 33) were men and 33.3% (11 out of 33) were women. A total of 45.45% relapsed (15 out of 33) and most of these relapses (53.3%) were ipsilateral (8 of 15) with only 20% (3 of 15) being contralateral. We were unable to identify possible risk factors for contralateral ganglionic recurrence due to the reduced number of cases. The disease-free survival rate and the overall survival rate were, respectively, 54.5% and 36.4%.

Conclusion

Although we were unable to demonstrate statistically significant results, we verified that the incidence of contralateral ganglionic recurrences is very low and, therefore, there appears to be no benefit in doing a bilateral cervical lymph node dissection on a N0 contralateral well lateralized T3/T4 tumor. Stratification of risk factors for recurrence and contralateral recurrence needs more studies. According to the literature review, this is the first study that analyzes only well-lateralized T3/T4 tumors (located in the buccal mucosa, gingiva, and retromolar triangle).

PO-248 | Small cell neuroendocrine carcinoma of tongue: a review of a rare entity

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Keywords

Neuroendocrine neoplasm, small cell carcinoma, oral cavity neoplasm

Purpose/Objective

Starting with a rare case of small cell neuroendocrine carcinoma of the tongue, a review of the literature about this entity in head and neck is made.

Material/methods

An electronic search with no date restriction was undertaken in different data base. Eligibility criteria included publications containing enough clinical, radiological and histopathological information to confirm a definite diagnosis of these lesions. Data were evaluated descriptively.

Results

Neuroendocrine tumour of the head and neck are extremely rare neoplasms, and they are divided into 2 categories: well-differentiated neuroendocrine tumors and poorly differentiated neuroendocrine carcinomas, where we cand find the small cell carcinoma. There is limited data regarding the frequency, treatment, prognosis, and site of this entity and stronger studies are necessary.

Conclusion

Neuroendocrine neoplasms of the head and neck are a rare entity, which when diagnosed, must be treated promptly to prevent potential life-threatening compromise given the primary site and concern for airway compromise.

PO-249 | Squamous Cell Carcinoma of Unknown Primary: Tonsillectomies, Radiotherapy, and Primary Emergence

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Keywords

Unknown Primary, Radiotherapy, Lingual Tonsillectomy

Purpose/Objectives

Even with advanced imaging techniques, identification of small primary sites in the mucosa of the pharynx can be difficult, particularly in the tonsil or base of tongue. While surgical techniques such as tonsillectomy or lingual tonsillectomy can improve the identification rate, the utility of these approaches particularly for radiosensitive human papilloma virus positive malignancies remains in question. We reviewed our experience of patients treated with radiotherapy for squamous cell carcinoma of unknown primary in the head and neck.

Materials/Methods

After IRB approval was obtained, a database of head and neck cancer patients treated with radiotherapy was queried. Relevant features were abstracted from the charts. Local control (LC) was calculated from the end of RT and estimated via Kaplan-Meier method.

Results

A total of 59 patients with squamous cell carcinoma in a cervical lymph node treated as unknown primary head and neck cancer were identified. Imaging routinely included CT Neck with contrast, and PET/CT, complemented by physical exam with flexible laryngoscopy. P16 was assessed in 93.2% (n=54) of patients; and was positive in 72.2% (n=39) and negative in 27.8% (n=15) All pa-

tients were taken to the operating room for direct laryngoscopy. Bilateral palatine tonsillectomies were performed in 33.9% (n=20) patients, unilateral palatine tonsillectomy in 6.8% (n=4) patients, and neither in 59.3% (n=35) patients (3 of which had a documented remote history of tonsillectomy). Lingual tonsillectomies were not performed in any patient. The oropharyngeal mucosa was targeted with radiotherapy in 89.8% (n=53), tonsil mucosa only in 1.8% (n=1), oropharynx and nasopharynx in 1.8% (n=1), and the mucosa was not targeted directly in 6.8% (n=4). When the mucosa was targeted, it was bilateral in 65.5% (n=36) and unilateral in 34.5% (n=19). Excluding patients with mucosal prescriptions of greater than 60 Gy (n=10), median prescription dose (EQD2) to the mucosa was 50 Gy (range 40.32 – 58.55 Gy). Most patients also received concurrent systemic therapy, primarily platinum based (n=46) or cetuximab (n=1). At a median follow-up of 2.6 years (range 0 – 7.96 years), no primary site has emerged to date, for a LC of 100%.

Conclusions

In this cohort of patients with squamous cell carcinoma of unknown primary of the head and neck, none of whom underwent lingual tonsillectomy, and the majority of whom did not undergo palatine tonsillectomy, there was no patient with primary site emergence on follow-up. These data suggest there is a potential opportunity to minimize surgical procedures and restrict radiotherapy mucosal targets and doses, particularly in patients who present with p16/HPV positive disease.

PO-250 | Predictors of Post-Operative Hypocalcemia after Thyroidectomy at an Apex Care Centre in India

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Key words

Hypocalcemia, Thyroidectomy, Vitamin D

Objective

Post operative hypocalcaemia is the most frequent complication following thyroidectomy. It can be permanent or transient hypoparathyroidism of which the incidence of permanent hypoparathyroidism is less than 3 %. This study aimed to evaluate and identify the predictors of postoperative hypocalcaemia in patients undergoing thyroidectomy.

Methodology

A prospective cohort study was conducted on 52 patients at an apex care institute. Preoperative testing for serum calcium, Parathormone (PTH) and Vitamin D were done on the day of surgery. These patients were subjected to surgery as per standard protocol. Postoperative testing for PTH was done 24 hours after surgery and serum calcium on day 0 and 1. All patients were assessed clinically for signs and symptoms of hypocalcemia till 48 hours post operatively and they were correlated with biochemical parameters and season in which surgery was performed.

Results

A total of 52 patients were operated in our institute over a period of 18 months in the midst of COVID 19 outbreaks. Both hemi

thyroidectomy (40) and total thyroidectomy (12) patients were included in the study. One significant finding was the low levels of preoperative Vitamin D values among 90% of the subjects. Out of the 52 patients, 12 underwent total thyroidectomy and 40 underwent hemi thyroidectomy as per standard protocols. 54% of the patients of total thyroidectomy and 52% of the patients of hemi thyroidectomy developed clinical as well as biochemical hypocalcemia over a period of 48 hours and were managed as per standard protocol. 38% of the patients were having low calcium values preoperatively and a statistically significant correlation was found between preoperative low calcium value and development of postoperative clinical hypocalcemia (P value 0.001). There was no statistically significant correlation between Pre operative Vitamin D level and season of surgery with postoperative clinical hypocalcemia.

Conclusion

All patients being planned for surgery, whether it is total or hemi thyroidectomy should undergo preoperative serum calcium evaluation and necessary correction if required, since preoperative low calcium is a clear predictor of post thyroidectomy clinical hypocalcemia. Further studies are required to correlate relation between Vit. D level and postoperative hypocalcemia

PO-251 | Correlation Between Expression of MMP-9, MMP-13 and Differentiation of HNSCC: A Prospective Study

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Introduction

The expression of matrix metalloproteinase-9 (MMP-9) and MMP-13 in head and neck squamous cell carcinoma (HNSCC) could be a useful predictor of tumour differentiation, nodal metastasis, and invasiveness.

We conducted this study to ascertain the correlation between the expression of these markers and the differentiation of tumour cells.

Materials and methods

A prospective observational study was conducted in a tertiary care centre. Forty-three cases of proven HNSCC were recruited after obtaining informed consent. Using the surgically excised specimen, tumour differentiation and invasiveness were assessed and correlated with rates of expression of the markers.

A Chi-square test was done to correlate immunohistochemical (IHC) marker positivity and the degree of differentiation of the tumour, lymph node metastasis, and invasiveness.

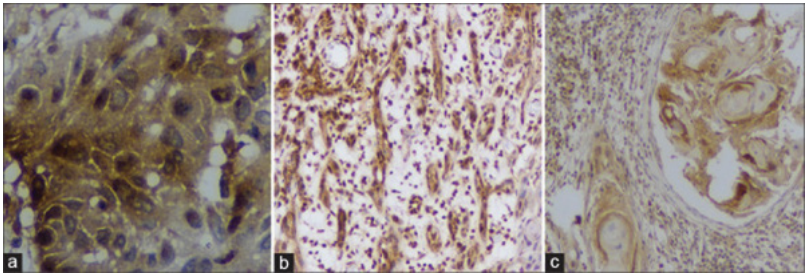
Results

MMP-9 and MMP-13 were expressed in 72% and 34% of cases, respectively. MMP-13 expression correlated with poorer tumour differentiation (p = 0.03), and relatively younger age at diagnosis (p = 0.01).

However, there was no correlation with lymphovascular or perineural invasion or lymph node metastasis.

Conclusion

In our study, MMP-13 expression correlated with poorer tumour differentiation and younger age at diagnosis, giving indirect evidence of tumour aggressiveness. IHC markers can provide additional information to prognosticate HNSCC. Identifying potential targets for newer biological therapy is essential in the Indian population as there are biological differences in cancer behaviour—increased expression of the proteolytic MMP-13 correlated with poorer differentiation of HNSCC.



PO-254 | PROGNOSTICATING ORAL CANCERS BY CO-RELATING PATHOLOGICAL GRADE, LVI, PNI AND LYMPH NODE METASTASIS

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Keywords

Prognosis, oral cancer

Background

Selective neck dissection electively is the procedure of choice in clinically N0 neck. When addressing level IIB, traction and manipulation of spinal accessory nerve causes shoulder dysfunction well elaborated in literature. No consensus is given in literature for omitting this step in literature. We present our experience on incidence of occult level IIB metastasis in clinically N0 neck in oral cavity cancers.

Material and methods

Retrospectively from January 2019, clinically N0 patients included in study where level IIB was separated intra operatively (n=32) and their radiological findings were also noted.

Results

On clinico-radiological evaluation out of the clinically N0 necks (n=32) 25 were radiologically N+ and 7 were N0. While, pathologically 17 were N0 in radiologically N+ cases. All radiologically N0 were pathologically N0. The incidence of level IIB metastasis was 2/32 (6.02%).

Conclusion

Our findings (6.02%) Co-relate with the literature findings, that metastasis in level IIB does occur in cN0 neck. In our experience

occult metastasis was not noted in early lesions. Further research in a prospective manner with a larger sample size will reveal more evidence.

PO-256 | Regulatory B cells producing IL-10 are increased in human tumour draining lymph nodes.

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Keywords

Sentinel node, B cells, B regulatory cells

Purpose/Objective

The contribution of different immune cell subsets, especially T cells, in anti-tumour immune response is well established. In contrast to T cells, the anti-tumour contribution of B cells has been scarcely investigated. B-cells are often overlooked, even though they are important players in a fully-integrated immune response and constitute a substantial fraction of tumour draining lymph nodes (TDLNs) known also as Sentinel Nodes.

Material/methods

Samples including TDLNs, non-TDLNs and metastatic lymph nodes (LNs) from 23 patients with oral squamous cell carcinoma (OSCC) were analyzed by multicolour flow cytometry with a focus on B cells populations.

Results

TDLNs were characterized by a significantly higher proportion of B cells compared with nTDLNs (p= 0,0112). TDLNs associated B cells contained high percentages of naïve activated B cells, in contrary to nTDLNs which contained significantly higher percentages of memory B cells. Patients having metastases in TDLNs showed a significantly higher presence of B regulatory cells among TDLNs associated B cells (p=0,0008) compared with N0 patients. B cells derived from TDLNs were characterized by sig-

nificantly higher expression of an immunosuppressive cytokine - IL-10 compared with non-TDLNs (p= 0,0077).

Conclusion

Our data indicate that B cells in human TDLNs differ from B cells in nTDLNs and exhibit more naïve and immunosuppressive phenotypes. We identified a high accumulation of regulatory B cells within TDLNs which may be a potential obstacle in achieving a response to novel cancer immunotherapies in HNSCC. Elevated levels of regulatory B cells in TDLNs are associated with the advancement of the disease. Detailed knowledge of pre-existing antitumor immune responses in human TDLNs is needed in order to fully understand the mode of action of novel immunotherapeutics.

PO-257 | InGReS: Intra-treatment Image-Guided Adaptive Radiotherapy Dose-escalation - a Phase 1 study

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Keywords

Radiotherapy, adaptive, dose-escalation

Purpose/Objective

The InGReS study will assess the feasibility and safety of adaptive radiotherapy (RT) dose-escalation (DE) to locally advanced head and neck cancer (HNC), guided by intra-treatment FDG-PET-CT and MRI. To date, this is the first study using both imaging modalities to guide RT dose-escalation in HNSCC. We report the early progress of this multi-institutional phase 1 study.

Material/methods

Patients requiring chemo-RT (CRT) for intermediate-to-high risk oropharyngeal, or hypopharynx, SCC are eligible. The primary endpoint is the incidence of grade ≥3 late mucosal toxicity (RTOG/EORTC), or feeding tube retention rate, at 12 months post-CRT. A rate of >14% would be regarded as unacceptable.

At fraction (#) 11 +/-1 of standard treatment (ST; 70 Gy/35#) patients undergo a FDG-PET-CT(+ contrast) and MRI for response assessment. Patients without residual disease continue with ST. Those

with residual disease proceed to re-planning and DE to the gross tumour volume (GTVTboost). Residual disease criteria is: residual SUVmax of ≥4.0 and/or MRI disease ≥1cm in maximum/long and minimum/short axial dimensions with intermediate T2 signal. All intra-treatment imaging is acquired in RT position and mask to allow optimum delineation. All MRI-based GTVTboost delineation is peer-reviewed by HN radiologists. The FDG-PET boost is delineated using an isocontour of 50% of SUVmax, followed by manual adjustment as necessary.

Adaptive re-planning occurs during # 12 to 20, without treatment breaks. The GTVTboost is planned to receive 2.46 Gy/# from # 21-35, to a total dose of 76.9 Gy/35#, using a simultaneous integrated boost technique. The standard planning target volumes (PTV), PTV70 and PTV56, continue to receive conventional doses.

Results

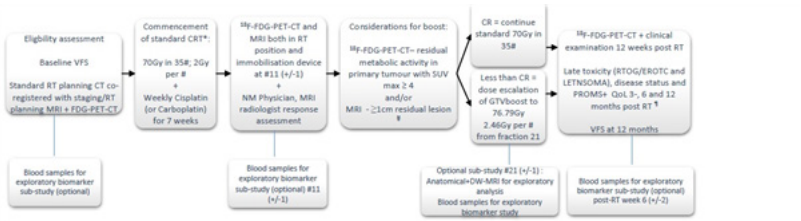
Between August and December 2022, 3 patients completed RT within InGReS. All patients had HPV negative oropharyngeal tumours. Median age was 63 (60-65). Disease stages were T2N2c (n=1) and T4N2b (n=2).

Intra-treatment MRI occurred at # 11 (n=3), and FDG-PET-CT at # 11 (n=2) and #12 (n=1). The first patient had almost complete response on intra-treatment MRI and continued with ST. Patients 2 and 3 had residual disease and proceeded to DE. The GTVTboost was well visualised and segmented on both imaging modalities. The percentage volume reduction of the MRI-based GTVTboost was 67.3% and 41.1%. Percentage reduction in SUVmax was 28.7% and 25.7%. Final boost volumes were 5.5cm3 and 51.4cm3. Target volume objectives were met in all patients. Normal tissue tolerances, including swallowing structures for dysphagia-optimisation, and standard PTV hotspot constraints were respected. All DE treatment commenced at #21.

Median follow-up was 7 weeks (1-9) post CRT. All patients completed RT without treatment breaks or delays. All patients received at least 200mg/m2 of concomitant cisplatin. Maximum CTCAE acute toxicity for all patients was: grade 3 anorexia (patient 1, RT-related), grade 3 dysphagia (patient 2, RT-related), grade 3 thromboembolic event (patient 3, non-RT related).

Conclusion

The present findings demonstrate feasibility of the InGReS study intra-treatment imaging schedule and adaptive RT technique. This approach can potentially be adopted by any tertiary oncology centre. Further recruitment and follow-up data is required to establish safety of the DE approach.



*MRI and PET-based volumes will be combined to generate a single GTVTboost.
¶Acute toxicity assessment (Common Terminology Criteria for Adverse Events [CTCAE] version 5.0); weekly during CRT and weeks 1-4, 6 & 12 post-CRT. PROMS + QoL at baseline, weeks 3 & 7 of CRT, then 6 and 12 weeks post-CRT. Clinical 100ml water swallow assessment 6 weeks; 6 and 12 months post RT.

PO-258 | CEACAM7 promotes oral cancer cell metastasis through targeting BST2

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Keywords

CEACAM7, BST2, oral cancer, metastasis

Purpose/Objective

Oral cancer is the most common head and neck malignancy. Failure to control primary cancer and lymph node metastasis are the main causes of death among patients. Carcinoembryonic antigen-related cell adhesion molecule 7 (CEACAM7), one of CEA gene family member, regulates normal cellular differentiation. In recent years, many studies have found that the expression of CEACAM7 is closely related to the process of carcinogenesis. For example, the expression of CEACAM7 is significantly lower in colorectal cancer compare to normal tissues. Interestingly, although the expression of CEACAM7 is lower in colorectal cancer than in normal tissue, the expression of CEACAM7 significantly increased during liver metastasis. Moreover, CEA and CEACAM7 double-positive gastric cancer patients have poorer survival rates than CEA and CEACAM7 double-negative patients. However, no studies have explored the effects of CEACAM7 expressions and oral cancer metastasis.

Material/methods

The clinical status and survival rate was analyzed by GEO database. The growth curve of oral cancer cell was detected by MTT assay. The cell cycle of oral cancer cell was analyzed by flow cy-

tometry. The cell migration and invasion ability was analyzed by Transwell assay. The protein expression of CEACAM7 and BST2 was analyzed by western blot. The RNA expression of CEACAM7 and BST2 was analyzed by RNA sequencing.

Results

In this study, we found that in the GEO database, patients with oral cancer with a high stage of cancer or lymph node metastasis had higher expression of CEACAM7, and patients with higher CEACAM7 had poorer survival rates. Next, we established a CEACAM7 overexpression vector and found that CEACAM7 overexpression does not affect the growth ability of SAS and TW2.6 cell lines, but can promote their migration ability. We also found CEACAM7-overexpression increasing bone marrow stromal cell antigen 2 (BST2) expression in RNA sequencing data. Moreover, BST2 overexpression increased migration ability in SAS and TW2.6 cells.

Conclusion

In conclusion, these results suggest that the increase of BST2 by CEACAM7 overexpression contributes to oral cancer metastasis.

PO-259 | Patients' communication and adaptation after total laryngectomy

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Keywords

Total laryngectomy, Communication, Compensation

Purpose/Objective

After a total laryngectomy, the upper and lower airways are separated, the natural voice is lost, and the patient breathes through a tracheostoma. Tracheoesophageal speech is the most common speech rehabilitation technique in the western world. This study aimed to explore the communication and adaption in verbal (syntactic complexity) and nonverbal (the use and type of co-speech gestures) communication after total laryngectomy.

Material/methods

Previously obtained interviews of eight laryngectomized women (patients) were analyzed and compared with healthy controls. For syntactic complexity, we explored around 1000 words per patient and control. Strings of words were labeled as utterances, C-Units, clauses, prepositional phrases, and noun phrases.

Mazes, also known as dysfluencies, were also counted and compared. For co-speech gestures, time sampling was used, resulting in five minutes of annotation per patient. The number of produced speech gestures and the type of gesture was classified. For statistical analysis, a Mann-Whitney U test was used.

Results

Focussing on dysfluencies, the patients uttered 8.8% (SD=3.1) in mazes versus 16.1% (SD=3.0) in the control group (U=4, Z=-2.9, P=0.002). In the syntactic complexity, the patients had an average of 6.4 words (SD=0.9) per C-unit, while the control group averaged 7.5 words per C-unit (SD=0.8) (U=10.5, Z=-2.2, P=0.014*). For the Noun Phrases, patients showed an average of 1.5 words (SD=0.1) versus 1.7 in the control group (SD=0.1) (U=1.0, Z=-3.2, P=0.001**). Concentrating on co-speech gestures, we found that the patients produced an average of 5.8 co-speech gestures (SD=2.1) versus 5.5 (SD=1.3) in the control group. The gesture-type Beats were observed as the most frequent.

Conclusion

This study found indications that patients use different techniques to compensate for their physical disabilities. Firstly, patients seem to be a bit more certain and careful in planning an utterance. Secondly, patients appear to reduce their syntactic complexity of utterances, and lastly, they seem to use co-speech gestures to support their verbal communication. Further research is needed because knowledge of such compensatory strategies would help improve speech and language therapy and better inform patients and their loved ones about what to expect after the surgery and how to compensate in communication after the procedure.

PO-261 | Scapular tip free flap for mandibular reconstruction

Giuseppe Perlangeli [1]; *Silvano Ferrari* [1]; *Andrea Ferri* [1]; *Ginevra Catola* [1]; *Micol Bellinato* [1]

(1) University hospital of Parma

Keywords

Scapular flap, mandible reconstruction, microsurgery

Purpose

Application of scapular tip chimeric free flap for reconstruction of mandibular defects has been recently popularized in literature but its role in the bone containing free flaps arsenal is still debated. Purpose of this study is to discuss how the technique changes in the last years, focusing on the technical issues that makes this flap a second choice for mandibular reconstruction and suggesting some solution developed to address these issues. Finally, the analysis of a case series will be used to present morphological and functional results.

Material/methods

Patients treated for mandibular reconstruction using STFF between 1st January 2014 and 1st June 2022 were retrospectively considered. Data about chimeric flap selection, bone management, vascular pedicle and final outcome were collected.

Results

Thirty-one patients (13 men and 18 women) with a mean age of 68 years (range: 38-85 years) were enrolled. According to Urken Classificiation, 15 patients had a body defect (B), 7 patients a ramus defect (R), 7 patients a symphysis defect (S) and 2 patients a combination of ramus + body defects (R+C).

In 5 cases STFF was harvested with the scapular angle component alone as a composite osteomuscular flap, in 26 cases a chi-

meric STFF was preferred. Circumflex pedicle was included in 8 patients. A single osteotomy was performed in 6 of the 7 patients with symphyseal defect. Average length of the harvested bone measured on OPT was 69.92 mm with a maximum value of 104 mm. Average height of the transplanted bone was 26.78 mm with 44.2 as the highest value recorded.

Conclusion

STFF should be considered an excellent second option for mandibular reconstruction when other flaps are not available, in elderly patients, in those in poor general condition or more in general when we need to reduce morbidity related to bone reconstruction. The evolution of surgical technique made this flap feasible in a large cohort of patients allowing for bone reconstruction also in those previously candidate to alternative procedure such as reconstruction with soft tissue free flap with or without titanium plate.

PO-262 | Hispolon induces apoptotic cell death via upregulation of HO-1 expression in OSCC cells

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Keywords

Hispolon, Apoptosis, Heme oxygenase 1

Background

Oral cancer is the most prevalent cancer for middle-aged men in Taiwan, and its delayed diagnosis has been shown to be associated with poor survival rates. Thus, development of nature drug or drug therapy was important topic. Hispolon is among the most crucial functional compounds which was identified from Phellinus linteus. It has been reported to possess antioxidant, antiinflammatory, anti-proliferative activities, and antitumor activities. Heme oxygenase-1 (HO-1) is a microsomal enzyme, which regulates the degradation of heme to carbon monoxide (CO), free iron, and biliverdin. HO-1 was reported to be overexpressed or downregulated in different cancer types and has a multifaceted role in cancer development through regulating apoptosis, angiogenesis and metastasis. However, whether HO-1 are involved in the anticancer properties of hispolon against oral squamous cell carcinoma cells (OSCC) remains unclear.

Hypothesis/Purpose

The aim of this study was to investigate the anticancer effects and underlying mechanisms of hispolon against OSCC.

Methods

The effect and potential mechanisms of hispolon against OSCC were explored by an MTT assay, flow cytometry, Western blot as-

say, apoptosis antibody array, and genetic knockdown by small interfering RNA. The TCGA database was used to investigate the prognosis of hispolon-targeted genes.

Results

Hispolon was demonstrated to suppress cell proliferation via simultaneously inducing S-phase arrest and cell apoptosis. Mechanistic investigations found that upregulation of HO-1 via MAPK pathway activation were critical for hispolon-induced caspase-8/-9/-3 activation and apoptotic cell death.

Conclusions

Overall, the current study showed that caspase-dependent apoptosis is induced by hispolon through activating the HO-1 expression, which supports a role for hispolon as part of a therapeutic approach for OSCC.

PO-263 | PREDICTED ANTICIPATED DIFFICULT MASK VENTILATION & ITS ACTUAL OCCURRENCE: AN OBSERVATIONAL STUDY

Swati Chhabra [1]; JAYAN ROY [1]; Pradeep Bhatia [1]; Rakesh Kumar [1]; Sadik Mohammed [1]; Darshana Rathod [1]; Kamlesh Kumari [1]; Nikhil Kothari [1]

(1) All India Institute of Medical Sciences, Jodhpur

Keywords

Difficult mask ventilation, difficult airway, airway management

Purpose/Objective

Facemask ventilation remains the basic and an essential skill in airway management. Successful mask ventilation gives anaesthesia providers a back-up plan in the event of failed laryngoscopy attempts or unanticipated difficult airway scenarios as in head and neck cancers. The incidence of difficult mask ventilation (DMV) is approximately 2–6 in 300. So predicting DMV is important to reduce morbidity and mortality. The primary objective was finding association between clinically anticipated and actual difficult mask ventilation using capnographic grading based objective scoring system. The secondary objective was to compare the objective capnographic score before and after neuromuscular blockade, to internally validate the objective capnographic scoring system.

Material/methods

Patients of either gender, belonging to ASA physical status 1 to 4, aged more than 18 years scheduled to undergo surgical/diagnostic procedure under general anaesthesia were included in the study. Patients with anticipated difficult mask ventilation were identified based on various group indices (BONES, MOANS). After induction of anaesthesia, a qualified anaesthesiologist with at least one-year experience performed mask ventilation and marked

the best capnographic waveform achieved with the manoeuvres/adjuncts before and after administering NMBD. After mask ventilation the operator's assessment (easy/difficult/very difficult) was also noted before and after administering NMBD. The observation period ended with completion of the mask ventilation and rest of the anaesthetic procedure was continued as planned by the attending anaesthesiologist.

Results

We found that difficult mask ventilation was more common in elderly patients, patients with higher weight/BMI group and higher ASA status patients. The specificity and sensitivity of the capnographic scoring system (if the score >3 is defined as difficult mask ventilation) was 91.5% and 78.7% respectively. If the score >5 is defined as difficult mask ventilation, the specificity and sensitivity was 39.2% and 96.4% respectively. The specificity and sensitivity of the operator assessment of difficult and very difficult mask ventilation was 93.8% and 76.4% respectively. The specificity and sensitivity of the operator assessment of very difficult mask ventilation was 97% and 39.2% respectively. We found that before administering NMBD, the specificity and sensitivity of the scoring system (with score > 3 defined as difficult mask ventilation) was 98.4% and 91.6% whereas, the specificity and sensitivity of the scoring system (with score > 3 defined as difficult mask ventilation) was 97.3% and 86.3% after administering NMBD. We also found that there was a significant decrease of the number of difficult mask ventilation cases after administering NMBD according to the capnographic scoring system as well as according to the operator assessment.

Conclusion

We concluded that according to the scoring system if the score > 3 is defined as difficult mask ventilation, it is highly associated with the clinically anticipated difficult bag and mask ventilation. After

administering NMBD, the mask ventilation becomes easier than before administering NMBD. The newly devised capnographic scoring system for mask ventilation has good specificity and sensitivity for difficult mask ventilation when the score is more than 3.

Before Neuromuscular blockade			**After Neuromuscular blockade**		
Score		**Patient's score**	**Score**		**Patient's score**
Best capnograph achieved			*Best capnograph achieved*		
1	 Plateau present		1	 Plateau present	
2	 No Plateau, EtCO2 ≥ 10 mmHg		2	 No Plateau, EtCO2 ≥ 10 mmHg	
3	 EtCO2 ≤ 10 mmHg		3	 EtCO2 ≤ 10 mmHg	
4	 No EtCO2		4	 No EtCO2	
No of hands engaged for holding mask			*No of hands engaged for holding mask*		
1	One handed		1	One handed	
2	Two handed		2	Two handed	
3	Three handed		3	Three handed	
Airway used			*Airway used*		
0	No		0	No	
1	Yes		1	Yes	
Total Score _____	❑ **Grade A Easy (2-3)** ❑ **Grade B Difficult (4-5)** ❑ **Grade C Very Difficult (6-8)**		**Total Score** ____	❑ **Grade A Easy (2-3)** ❑ **Grade B Difficult (4-5)** ❑ **Grade C Very Difficult (6-8)**	

PO-265 | Oral cancer in young adults - should we approach these patients differently?

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(1) Poznan University of Medical Sciences

Keywords

Oral cancer; young adults; risk factors

Purpose

Oral cancer generally affects men in the 6th and 7th decades of life, predominantly smokers and heavy drinkers. In recent years, the incidence of oral cancer has increased in younger patients (age < 45), rising from 3%-5% in the 1970s and 1980s to approximately 10% at present. The main aim of the present study was to determine the prevalence of oral cancer in younger adults in our cohort/region/hospital. A second aim was to compare treatment outcomes in these two groups (young adults vs. older adults). Finally, we sought to identify the risk factors present in young adults who developed oral cancer.

Material/methods

This was a retrospective study of 284 patients diagnosed and treated for oral squamous cell carcinoma from 2010 to 2021 at our institution. The following clinical parameters were registered: age; sex; smoking habit; alcohol use; comorbidities; disease stage; T status; N status; number of positive metastatic lymph nodes; PNI; LVI; ENE; and final margin status. The type of recurrence and/or type of second primary tumour was also assessed. Disease-free survival and overall survival rates were calculated. The primary analysis included the entire group stratified by age (< or ≥ 45). These two groups were then compared to assess for differences in clinical parameters. Next, all patients under age 45 (n=44) were

matched 1:1 by sex and local and regional disease stage with older patients (55 – 70 years). The groups were compared according to the following clinical and demographic variables: smoking and alcohol history; comorbidities; tumor grade; PNI; LVI; ENE; adjuvant treatment; final surgical margin status; recurrence (yes/no); type of recurrence; neutrophil-to-lymphocyte ratio (NLR); and platelet-to-lymphocyte ratio (PLR).

Results

Of the 284 patients, 188 were males (66%). The mean patient age was 58 (11.9) years (range, 23–97). Of these 284 patients, 240 (84.5%) were age 45 or older while 44 patients were younger than age 45. At baseline, the only statistically significant difference between the groups was in the number of comorbidities, which were more prevalent in the older group ($p<0.001$). A trend toward significance was observed in N status ($p=0.08$), with a higher percentage of older patients presenting with N0 (59% vs. 50%) In the matched pair analysis a higher proportion of older patients were smokers (75% vs 54 %; $p=0.0446$), with more comorbidities in the older group (47.7%; $p=0.007$). The mean (SD) PLR and NLR values were significantly higher in young adults (157.72 [64.8] vs 118.24 [41.29]; $p<0.001$; and 3.19 [1.52] vs 2.70 [1.88]; $p=0.018$, respectively). No significant between-group differences were observed in tumor grade, PNI, ENE, LVI, final surgical margin status, use of adjuvant RT/ CRT; or recurrence. In the matched pair analysis, no between-group differences were observed in survival outcomes (OS and DFS).

Conclusion

Our study shows, in contrast to some previous reports, that initial disease stage and treatment outcomes are similar in older and younger patients diagnosed with oral cancer. Although older patients tend to smoke more, this does not appear to significantly impact treatment outcomes. The reasons underlying the growing

incidence of oral cancer in younger patients remain unknown, although data from several studies, including ours, suggest that it might be related to an impaired immune system. Nevertheless, more research is needed to better understand this phenomenon.

PO-266 | Genetic intratumor heterogeneity and the implication for targeted therapy in head and neck cancer

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(1) Department of Otorhinolaryngology, Head & Neck Surgery and Audiology, Rigshospitalet, University of Copenhagen (2) Center for Genomic Medicine, Rigshospitalet, University of Copenhagen (3) Department of Oncology, Section of Radiotherapy, Rigshospitalet, University of Copenhagen

Keywords

Intratumor heterogeneity, targeted therapy, ESCAT.

Purpose

Genomic profiling is increasingly used both in therapeutic decision making and as inclusion criteria for trials testing targeted therapies. However, the mutational landscape may vary across different areas of a tumor and intratumor heterogeneity can thereby challenge treatments or decisions based on single tumor biopsies. The purpose of this study was to explore genetic intratumor heterogeneity in head and neck squamous cell carcinomas (HNSCC) and assess clinical relevance for patient management using the ESMO Scale for Clinical Actionability of Molecular Targets (ESCAT).

Material/Methods

This prospective study included 33 whole tumor specimens from 28 patients with HNSCC referred for surgery. Three tumor blocks were selected from central, semi-peripheral and peripheral positions, respectively, mimicking clinically biopsies in three different locations. Genetic analyses were performed on the three biopsies using Oncoscan with 45 preselected HNSCC genes. To assess clinically relevance the ESCAT scale was used to assess if decisions and possible treatments would change between the three biopsies.

Results

Several differences were found in somatic copy number alterations (SCNA) in the 45 preselected genes between each of the three tumor biopsies taken from the same tumor. Please see the heatmap in Figure 1. Twenty-eight of the tumors had one or more change in SCNA between the three biopsies and only five of the 33 tumors were homogenous and had no differences between the three biopsies. Assessed with ESCAT scale 36% of the patients had differences that potentially could change choice of treatment or clinical decisions based on a single tumor biopsy. Table 1 depicts the specific genes and alteration along with ESCAT score, potential drug and potential therapeutic relevance. Recurrent tumors had significantly more differences in SCNA than primary tumors (p=0.023) but no significant correlation between tumor size and intratumor heterogeneity (p = 0.7) was observed.

Conclusion

There is an increasingly focus on intratumor heterogeneity, however potential impact on patient management is not well known. Here, in this study intratumor heterogeneity with potential clinically relevance for patient management was observed in 36% of the patients. This emphasizes that future studies should focus more on the actual consequences of intratumor heterogeneity rather than on the concept itself.

Tumor	Gene with heterogeneity	ESCAT score	Drug	Potential therapeutic relevance
1	PTEN deletion	IIIA	Resistance to EGFR mAB	Lack of efficacy of cetuximab
2	EGFR amplification	IIA	EGFRi	Efficacy of EGFR targeted therapy
	TP53 Y220C	IIB	PC14586	Efficacy of TP53 Y220Ci
3	Inactivating PTEN mutation	IIA	EGFRi	Lack of efficacy of cetuximab
5	FBXW7 LOH	IVB	GAKi	Efficacy of GAKi
	PD-L1 amplification and LOH	IIIB	IO	Efficacy or lack of efficacy, respectively, of immune checkpoint inhibitor
7	FBXW7 D+LOH	IVB	GAKi	Efficacy of GAKi
11	PD-L1 amplification	IIIB	IO	Efficacy of immune checkpoint inhibitor
13	FGFR1 amplification	IIIA	FGFRi	Efficacy of FGFR1i
20	PIK3CA amplification	IIIB	PIK3i	Efficacy of PIK3i
	FBXW7 D or D+LOH	IVB	GAKi	Efficacy of GAKi
	PD-L1 D or D+LOH	IIIB	IO	Lack of efficacy of immune checkpoint inhibitor
	PTEN D+LOH or LOH	IIIA	Resistance to EGFR mAB	Lack of efficacy of cetuximab
24	PD-L1 D+LOH	IIIB	IO	Lack of efficacy of immune checkpoint inhibitor
27	FBXW7 LOH			Efficacy of GAKi

Figure 1: Heatmap representing aberrations detected in 45 preselected genes in all 99 biopsies from the 33 tumors. The Y-axis depicts the 45 preselected genes and the X-axis depicts the 99 biopsies grouped and ordered by tumor number. Primary tumors and lymph node metastases are indicated with P and L respectively. The colour bar to the right displays the actual aberration in the specific gene. Abbreviations: A: amplification, D: deletion, LOH: loss of heterozygosity, NA: no aberration. The genes above the dashed horizontal line correspond to Table 1 and the results marked with a dotted rectangle indicate heterogeneity in genes in Table 1 as well.

PO-267 | Cetuximab Treatment Beyond Progression in Recurrent or Metastatic Head and Neck Cancer

Mengche, Hsieh *[1]; Muh-Hwa Yang [2]; Ming-Yu Lien [3]; Jin-Ching Lin [4]; Jo-Pai Chen [5]; Hsueh-Ju Lu [6]; Tai-Lin Huang [7]; Chia-Jui Yen [8]; Hui-Ching Wang [9]; Pei-Jen Lou [10]; Hung-Ming Wang [11]*

(1) E-Da cancer hospital (2) Taipei Veterans General Hospital (3) China Medical University Hospital (4) Changhua Christian Hospital (5) National Taiwan University Hospital Yunlin Branch (6) Chung Shan Medical University Hospital (7) Kaohsiung Chang Gung Memorial Hospital (8) National Cheng Kung University Hospital (9) Kaohsiung Medical University Hospital (10) National Taiwan University Hospital and College of Medicine (11) Chang Gung Memorial Hospital, Linkou

Keywords

Cetuximab; recurrent or metastatic head and neck squamous cell carcinoma; treatment beyond progression

Objective

Cetuximab based chemotherapy is one of the first-line treatment for recurrent or metastatic head and neck squamous cell carcinoma (R/M HNSCC). Little was known regarding the continuation of cetuximab after first progression in patients with R/M HNSCC.

Methods

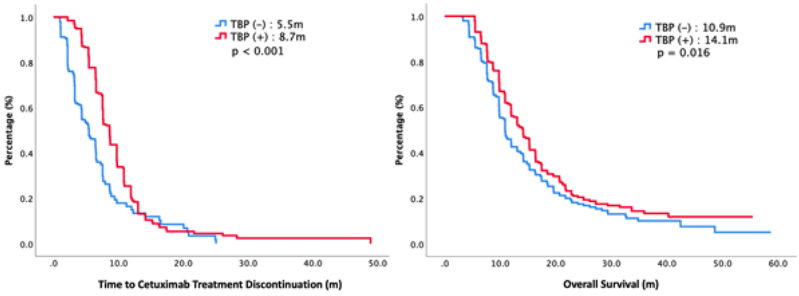
Patients who were treated with cetuximab based chemotherapy as first-line treatment for R/M HNSCC between 2015 and 2020 were retrospectively identified from Taiwan Head and Neck Society Cancer Registry. Patients received second-line treatment were enrolled into our study and classified into (1) cetuximab treatment beyond progression (TBP (+)) if they continued cetuximab in second-line treatment and (2) non-treatment beyond progression (TBP (-)) if they discontinued cetuximab in second-line treatment. The oncologic outcomes were presented with time to cetuximab treatment discontinuation (TTD) and overall survival (OS).

Results

A total of 498 patients were analyzed for outcomes comparison with 259 patients in TBP (+) group and 239 patients in TBP (-) group. Basic characteristics were similar between these two groups. The most common first-line chemotherapy were EXTREME regimen in both groups. As for second-line treatment, the most common regimen were TPEx in TBP (+) and other single chemotherapy agent in TBP (-). Median TTD were 8.7 months in TBP (+) and 5.5 months in TBP (-) ($p < 0.001$). In terms of survival, median OS were significant longer in TBP (+) then those in TBP (-), accounting for 14.1 months versus 10.9 months ($p = 0.016$), respectively. Multivariate analysis demonstrated cetuximab TBP was an independently factor associated with OS.

Conclusions

Cetuximab TBP is effective and can be a treatment option for highly selected patients with R/M HNSCC. Further prospective randomized studies are warranted to confirm our results.



PO-268 | Senescence as a contributor in HNSCC pathogenesis: preliminary results of the SASP factors

Patryk Niewinski [1]; Kamila Ostrowska [1]; Igor Piotrowski [1]; Julia Ostapowicz [1]; Sabina Koczot [1]; Wiktoria M. Suchorska [1]; Pawel Golusinski [2]; Michal M. Masternak [3]; Wojciech Golusinski [1]

(1) Greater Poland Cancer Centre, Poznan, Poland (2) Department of Otolaryngology and Maxillofacial Surgery, University of Zielona Góra (3) Burnett School of Biomedical Sciences, College of Medicine, University of Central Florida

Keywords

Head and neck cancer; Senesence; SASP factors; Head and neck biomarkers

Purpose/Objective

Cellular senescence is characterized by cell-cycle arrest, apoptotic resistance and may be oncogene- or therapy-induced. Senescent cells may promote the cancer development by secreting a collection of proinflammatory factors, collectively termed the senescence-associated secretory phenotype (SASP). SASP factors can enhance carcinogenesis in a variety of ways, including proliferation, metastasis, and immunosuppression. In this study, our goal is to determine the level of selected cellular senescence markers in tumor tissues and histopathologically unchanged adjacent tissues through the analysis of senescence markers p16 and LMNB1 and SASPs IL-6, IL-1b, CXCL-1 and TNF-α. Moreover, to correlate this data with patients' clinical features.

Material/methods

In this cohort study we have measured the mRNA transcript level of selected SASPs IL-6, IL-1b, CXCL-1 and TNF-α in 76 cancerous tissues and 65 histopathologically unchanged adjacent tissues from the larynx and oral cavity, using qPCR method. The correlation between the studied variables was determined using the

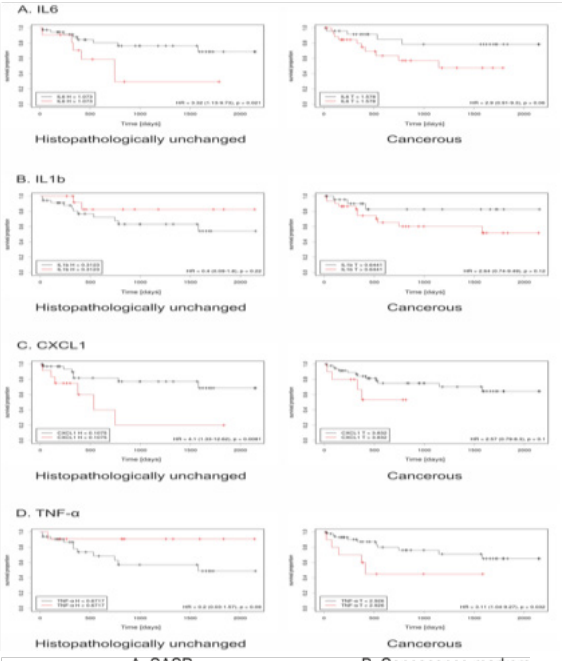
Spearman correlation. The patient's survival analyses were estimated by the Kaplan–Meier method. To evaluate the accuracy of using gene expression to distinguish cancerous tissue from histologically unchanged tissue, we produced the receiver operating characteristic (ROC) curves and calculated the area under the curve (AUC), sensitivity, and specificity for each ROC curve.

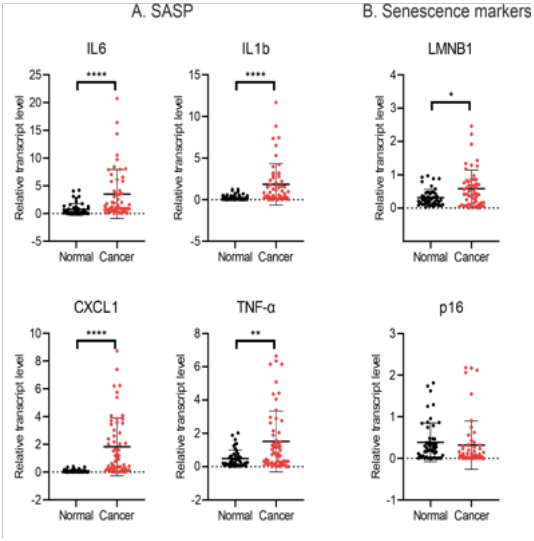
Results

Our results showed statistically higher mRNA transcript levels of the selected SASPs: IL6, CXCL1, TNF-α and IL1b between cancerous and histopathologically unchanged tissues. We noticed that IL6 and IL1b was significantly higher in cancerous tissue across all age groups, in the larynx and oral cavity mainly in T2-T3 for IL6 and T3-T4 for IL1b. CXCL1 showed a statistical difference for almost every clinical feature while TNF-α predominated in the oral cavity, in men over 60 and N1, G1-G2 stage. The higher transcript levels of these SASPs in cancerous tissue correlated with lower OS of patients. Furthermore, ROC curves showed CXCL1 and IL6 as the strongest candidates for distinguishing cancerous from normal tissue.

Conclusion

SASPs as well as senescence related processes may potentially affect the HNSCC pathogenesis and may be considered as a biological marker for tumor progression. However, to better understand the impact of this process in HNSCC patients, further studies are required.


A. IL6
Histopathologically unchanged
Cancerous
B. IL1b
Histopathologically unchanged
Cancerous
C. CXCL1
Histopathologically unchanged
Cancerous
D. TNF-α
Histopathologically unchanged
Cancerous


A. SASP
B. Senescence markers
IL6
IL1b
LMNB1
CXCL1
TNF-α
p16
Relative transcript level
Normal
Cancer

PO-271 | Insights into the interactions between head & neck cancer drivers and the immune microenvironment

Jean-Pierre [1]; Francesca D. Ciccarelli [2]; Hrvoje Misetic [3]; Mohamed Reda Keddar [4]

(1) Guy's and St Thomas' NHS Foundation Trust (2) The Crick Institute London, UK. (3) The Crick Institute London UK. (4) Kings College, London UK.

Purpose/Objective

The interaction between cancer and the tumour immune microenvironment (TIME) has attracted significant interest because of its impact on cancer evolution and response to treatment. TIME interactions and their molecular mechanisms in individual cancer patients are still poorly understood.

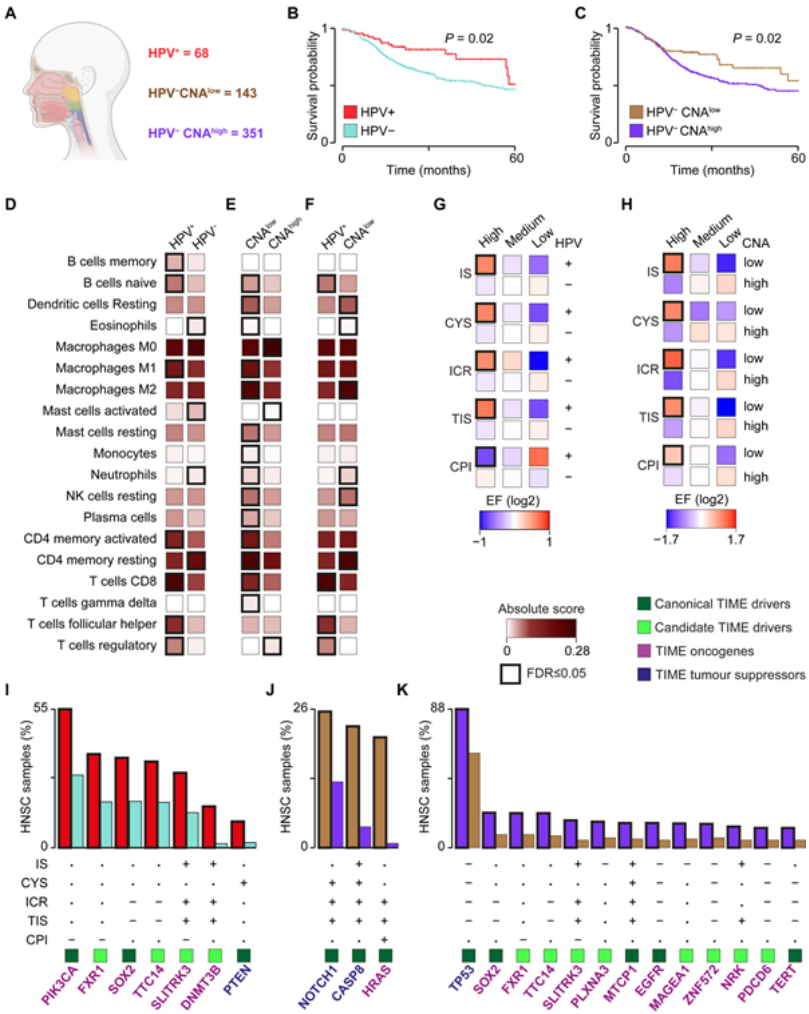
Material/method

We applied Lasso-regularised ordinal regression and artificial intelligence modelling to identify cancer-specific genetic drivers interacting with anti- and pro-tumour TIME features drivers. The antitumour TIME driver burden of a cancer type is predictive of its overall response to immunotherapy. Focusing on head and neck squamous cell carcinoma (HNSCC), we rebuilt the functional networks linking specific TIME driver alterations to the TIME states of the corresponding HNSC molecular subtypes. We showed that TIME driver alterations predict the immune profiles of HNSC subtypes, and that deregulation of keratinization, apoptosis and interferon signalling underpin subtype-specific driver-TIME interactions.We intergated The Cancer Gene Atlas (TCGA) HNSCC cohort to and the Clinical Proteomic Tumour Analysis Consortium (CPTAC) to create a series of 562 patients with matched genomic and transcriptomic data.Of these 68 were HPV+ and 494 HPV-ve patients.. Based on the levels copy number alterations (CNAs, we further divided the 494 HPV negative (HPV-) HNSCs

into 351 CNAhigh and 143 CNAlow samples.We confirmed that HPV+ HNSC patients have better overall survival and, within the HPV- group, high levels of aneuploidy confer worse prognosis.

Conclusion

Overall, our study provides a comprehensive resource of TIME drivers giving mechanistic insights on their immune-regulatory role in head and neck cancer. Amongst the HPV-ve group known to have a worse prognosis, we have found that a subset of these that have high mummer of mutations have a worse overall survival. Our analyses provided a comprehensive resource of TIME drivers and elucidated their mechanistic role that can be further investigated in experimental and clinical setting.


A
HPV+ = 68
HPV-CNAlow = 143
HPV- CNAhigh = 351
B
P = 0.02
Survival probability
HPV+
HPV−
Time (months)
C
P = 0.02
Survival probability
HPV- CNAlow
HPV- CNAhigh
Time (months)
D
HPV+
HPV-
B cells memory
B cells naive
Dendritic cells Resting
Eosinophils
Macrophages M0
Macrophages M1
Macrophages M2
Mast cells activated
Mast cells resting
Monocytes
Neutrophils
NK cells resting
Plasma cells
CD4 memory activated
CD4 memory resting
T cells CD8
T cells gamma delta
T cells follicular helper
T cells regulatory
E
CNAlow
CNAhigh
F
HPV+
CNAlow
G
High
Medium
Low
HPV
IS
CYS
ICR
TIS
CPI
EF (log2)
H
High
Medium
Low
CNA
low
high
EF (log2)
Absolute score
FDR≤0.05
Canonical TIME drivers
Candidate TIME drivers
TIME oncogenes
TIME tumour suppressors
I
HNSC samples (%)
PIK3CA
FXR1
SOX2
TTC14
SLITRK3
DNMT3B
PTEN
J
HNSC samples (%)
NOTCH1
CASP8
HRAS
K
HNSC samples (%)
TP53
SOX2
FXR1
TTC14
SLITRK3
PLXNA3
MTCP1
EGFR
MAGEA1
ZNF572
NRK
PDCD6
TERT

PO-273 | PEDIATRIC THYROID SURGERY: WHEN IS NECK DISSECTION AND/OR COMPLETION THROIDECTOMY NEEDED?

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Key words

Pediatric thyroid, neck dissection, ultrasonography

Introduction

The objective of this study is to report our thyroidectomy experiences in pediatric patients. We also aim to evaluate the requirements of neck dissection and completion thyroidectomy in pediatric thyroid surgeries.

Material and Methods

A retrospective review of patients aged 18 and younger who underwent thyroid surgery at a tertiary medical center between 2011 and 2019. The indications of surgery, preoperative and postoperative tests results of patients, the surgical technique used and complications were reviewed and analyzed.

Results

A total of 34 pediatric patients were included. 73.5% (n=25) were females, 26.5% (n=9) were males. The age range was between 8 and 18. The major complaint was a mass in the neck in 25 patients (73.5%). A Thyroid nodule was detected by sonography in 6 patients (17.6%) only in right thyroid lobe; in 13 patients (38.2%) only in left thyroid lobe; and 12 patients (35.2%) in both lobes of the thyroid. In the sonographic evaluation, 14 patients (41.1%) had lymphadenopathies. Fine needle aspiration biopsy was done in 27 patients (79.4%). Completion thyroidectomy was done in 9

(26.4%) and neck dissection was done in 7 patients (20.5%). Malignant disease in final pathology was reported in 23 patients (67.6%).

Conclusion

Pediatric thyroid diseases that required thyroidectomy with or without neck dissection are rare. In pediatric population the risk for malignant thyroid pathology is higher than adults. Therefore, preoperative evaluations is important for correct surgical decisions making to avoid risk of second surgery and potential morbidity.

PO-274 | A single centre experience with neck dissections in the management of head and neck cancers

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Keywords

Neck dissection, head and neck cancer, metastatic lymph nodes

Introduction

Neck dissections (ND) are necessary in the surgical management of head and neck cancer. We investigate the epidemiology and patterns of neck dissections performed in our institution. Extensive ND of multiple levels of the neck often result in profound morbidity for patients should complications arise.

Methods

A retrospective study of ND in a single institution over 7 years was undertaken. Half of the done ND were selected in a blinded, random manner and analyzed. Data from these patients including demographics, primary tumor type, location, extent of ND and number of lymph nodes removed were tabulated. This study was approved by the institution ethics review board.

Results

114 ND procedures were undertaken in 83 patients, for which 31 patients underwent bilateral ND. All ND were done with appropriate resection of primary tumor. The median age was 58 (range 24-81) years and majority of the patients were male (n=62, 74.6%). Primary tumors originated most commonly from the tongue (n=32, 28.1%), larynx (n=28, 24.6%), oral cavity (n=11, 9.6%), thyroid (n=17, 14.9%), major salivary glands (n=11, 9.6%) and nasopharynx (n=5, 4.4%). Majority of cancers were squamous cell carcinomas (CA) (n=67, 58.8%).

Lymph nodes in 14/866 (1.6%) of primary tongue CA, 10/371 (2.7%) of oral cavity CA, 16/740(2.2%) of laryngeal CA, 8/99 (8.0%) of nasopharyngeal CA were histologically proven to have cancer involvement postoperatively. Most notably, none of the lymph nodes resected at level 5 for tongue, laryngeal, thyroid and nasopharyngeal CA or level 4 and 5 for oral CA were histologically proven to have no cancer involvement, regardless of pre-operative T and N staging.

Conclusion

ND are a commonly practiced surgical procedure for cancer treatment for multiple primary tumour sites in the head and neck. Our data suggests that less extensive ND can be proposed in certain cancer subtypes which may lead to decreased morbidity for patients, although more extensive studies with bigger sample sizes may be required to confirm this.

PO-275 | Aplication of Liquid Biopsies and Next Generation Sequencing in Oral Cancer follow-up - Pilot study

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Keywords

Oral cancer: Cell-free DNA, Liquid biopsies, Next Generation Sequencing

Purpose/Objective

The aim of this pilot study was to explore the applicability of liquid biopsies to detect the mutational landscape of oral tumors as well as to monitor the disease course, as In the clinical management of oral cancer there is a lack of biomarkers available for relapse and metastasis detection and treatment selection.

Material/methods

A total of 140 samples of plasma and tissue were collected from 22 oral cancer patients before and at several timepoints after initiation of treatment. After cell-free DNA (cfDNA) isolation, concentrations were determined, compared between patients and monitored throughout the patients' clinical course. The ctDNA mutational profile was compared with the profile of the corresponding tumor tissues and monitored at different timepoints using Next Genera-

tion Sequencing (NGS) in five patients .. The data was correlated with the patients' clinicopathological features.

Results

The levels of plasma cfDNA seem to increase right after initiation of treatment in all patients, before decreasing. Five patients developed metastasis/relapses and a slight increase in plasma cfDNA levels was observed in some of these patients during clinical follow up, being needed more patients and studies to correlate this data with the prognosis capability of liquid biopsies. Sequencing of ctDNA of 5 patients (4 of them with metastasis, relapses or second primaries) showed not only pathogenic variants in pivotal genes for carcinogenesis process such as *TP53, EGFR, KRAS,* and *PIK3CA* but also the identification of new alterations that seem to arise during the treatment course, like in *SMAD4*. Interestingly, some variants were found both in tumor tissue and biofluid samples, while others were only detected in biofluid samples, which suggest the capability of liquid biopsies to reflect individual tumor heterogeneity and clonal evolution.

Conclusion

Our results suggest that liquid biopsies may evolve into a useful tool in the clinical management of oral cancer patients, especially if NGS is applied.

PO-276 | Long-term outcomes and surgical complications of endonasal endoscopic surgery in ITAC

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Objective

To describe the long term outcomes and surgical complications of intestinal-type adenocarcinoma (ITAC), treated with endonasal endoscopic approach (EEA) or external surgery (ES), followed by adjuvant IMRT. Previously, we reported that EEA was feasible in T3-T4 tumors with a trend of improved survival (p=0.10). We provide an update of a retrospective cohort study a referral centre in Belgium, with an analysis of long term outcomes, surgical complications, and TME analysis with focus on tumor infiltrating lymphocytes (TILs).

Material and methods

A single-centre retrospective cohort study was performed on all patients diagnosed with ITAC between 1998 and 2018. Survival curves were obtained using Kaplan-Meier method and compared with the log-rank test. We used Fisher's exact test to compare incidence of postoperative complications between surgical groups. Tumor-infiltrating lymphocytes were assessed following the IIBWG guidelines with hemathoxylin/eosin stain and CD3+ and CD8+ IHC (DAKO).

Results

92 patients were treated with endonasal endoscopic approach (EEA, n=40) or external surgery (ES, n=52), followed by adjuvant IMRT. With a median follow-up of 16 years, median overall survival (OS), disease specific survival (DSS), local relapse free survival (LRFS) and disease free survival (DFS) were 8.1years [95%CI 6.0-

11.1], 6.5years [95%CI 4.1-21.0], 9.1years [95%CI 4.1y-9.1y] and 6.9years [95%CI 3.5y-10.5y] respectively. DSS was significantly longer in the EEA cohort (HR 0.51, 95%CI 0.27-0.96) (see table 1). There was no statistically significant difference in surgical complications, but the duration of hospitalization was significantly shorter for EEA (median 4 days), compared to ES (median 8 days) (p=<0.001) (table 1). High CD3+ (4+; HR=0.26 [95% 0.07-0.96]; P = 0.0432) or CD8+ TIL count (2+ or higher; HR=0.11 [95%CI 0.02-0.58]; P = 0.0090) were associated with improved DSS (fig 1).

Conclusions

EEA is a feasible and safe surgical approach in ITAC, with good long term survival. Surgical complications are rare in reference centers, and duration of hospitalization is shorter for EEA compared to ES. High CD3+ and CD8+ TILs are associated with an improved prognosis, and merit further investigation.

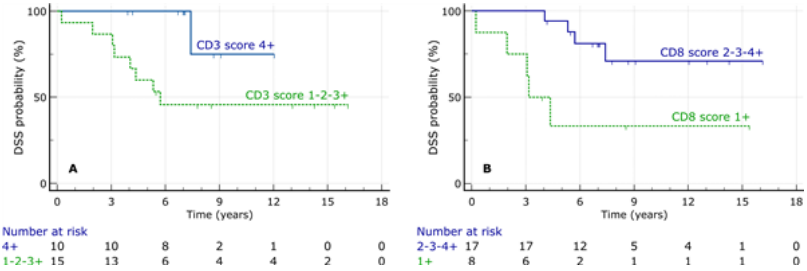

Table 1: Survival estimates and complication rates in patients undergoing surgery for ITAC				
Parameter	ES (n=52)	EEA (n=40)	HR [95%CI]	P
mOS (years, 95%CI)	7.4 (4.0-11.1)	10.1(6.1-12.0)	0.86 [0.51-1.45]	0.563
mDSS (years, 95%CI)	4.0 (2.8-7.4)	12.7(6.1-12.7)	0.51 [0.27-0.96]	0.037
mLRFS (years, 95%CI)	9.1 (2.5-9.1)	NR(NR-NR)	0.77 [0.41-1.43]	0.407
mDFS (years, 95%CI)	4.3 (2.3-9.1)	7.1(2.9-10.5)	0.87 [0.50-1.52]	0.615
Major bleeding*	1/52 (2%)	1/40 (3%)		1.000
Post-operative CSF leak	2/52 (4%)	1/40 (3%)		1.000
Post-operative infection (local)	1/52 (2%)	0/40 (0%)		1.000
Post-operative infection (other)	1/52 (2%)	0/40 (0%)		1.000
Any post-operative complication	5/52 (10%)	2/52 (5%)		0.694
Positive surgical margins	21/52 (40%)	18/40 (45%)		0.734
Duration of hospitalization in days (IQR)	8 (6-12)	4d (3-5)		<0.001

*major bleeding: requiring revision, RBC transfusion, hemodynamically instable, Hb drop >2g/dL
CSF, cerebrospinal fluid; EEA, endonasal endoscopic approach; ES, external surgery

PO-279 | Non-intestinal type sinonasal adenocarcinoma: A case report

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Keywords

Non-ITAC, bleeding, sinonasal tumor.

Introduction

Primary adenocarcinomas of the sinonasal tract are a group of malignant neoplasms that represent 10%-20% of all primary malignant neoplasms of the nasal cavity and paranasal sinuses and are classified into salivary types (5%-10%) and non-salivary, within this last group they are classified as intestinal type adenocarcinoma (ITAC) and non-intestinal. Non-ITAC tumors are divided into high-grade (solid growth patterns and are usually aggressive) and low-grade (form papillary and glandular structures). Non--ITACs do not express the anterior gut-specific markers and are considered to be of heterogeneous origin. It has been associated with the human papilloma virus (HPV) although the risk factors are not clear. They are more frequent in men and in the 6th decade of life and the most common symptoms are: unilateral nasal obstruction, epistaxis, facial pain and visual disturbances.

Material and methods

We present the case of an 87-year-old female patient with a medical history of hypertension, type II diabetes mellitus, breast cancer and knee replacement who was referred by the Radiology Service due to the discovery of a mass in the skull and nostril right. The patient had previously been seen by a private otolaryngologist for an occupying and bleeding lesion in the right nostril

with a progressive evolution of one year and causing right nasal respiratory failure, for which a CT scan of the paranasal sinuses was requested. Nasofibroscopy revealed a bleeding mass that occupied the entire right nostril. A biopsy of the mass was taken and sent for analysis. An MRI of the paranasal sinuses and head was also requested.

Results

Computed tomography revealed a solid frontobasal extraaxial hyper-uptake mass of the right anterior cranial fossa that entered into the right nasal fossa and extended to the right ethmoid air cell, cavum, and extraconal fat infiltration of the right orbit, in addition to signs of intracranial expansiveness. . On the other hand, the biopsy revealed the result of infiltrating adenocarcinoma, compatible with "non-intestinal type" sinonasal adenocarcinoma of intermediate grade with positivity in immunohistochemistry for CKAE1-AE3, CK7, SOX10; estrogens (only 30% of cells with mild-medium intensity). The patient was taken to the tumor committee, however, before making a therapeutic decision for the patient, she died. There is no standardized treatment algorithm for sinonasal non-ITAC; however, surgery followed by radiation is a mainstay in the treatment of these tumors.

Conclusion

In summary, the etiology and risk factors of these types of tumors remain unknown today and despite some studies having related them to HPV and exposure to tobacco, it remains unconfirmed. In addition, non-intestinal sinonasal adenocarcinomas are rare tumors, so the literature is scant and there are not enough cases to develop a standardized treatment algorithm. However, the usual treatment usually includes both surgery and radiotherapy.

PO-281 | Outcome and toxicity analysis of head and neck cancer patients treated in phase I clinical trials

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Keywords

Trials, Score

Purpose/Objective

AntiPD(L)-1 agents have improved overall survival (OS) in patients (pts) with recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC). The availability of new immunotherapy (IT) combinations in early drug development (EDD) has increased the number of pts treated within phase 1 clinical trials (Ph1 CT) even before having exhausted standard of care (SOC) therapies. Several prognostic scores have been proposed to select pts that are likely to benefit from Ph1CT.

We evaluated the outcome of R/M HNSCC pts treated within Ph1 CT at the EDD Unit of Institut Català d'Oncologia (ICO) - Hospitalet and explored predictors of survival.

Material/methods

Retrospective cohort analysis of pts with R/M HNSCC treated in Ph1 CT at ICO Hospitalet between December 2017 and May 2022. Clinical, laboratory data and grade (G) 3-4 treatment-related adverse events (TRAEs) were collected. Overall response rate (ORR) was assessed according to RECIST 1.1. Clinical benefit rate (CBR) was defined as complete/partial response + stable disease for ≥6 months (m). Progression-free survival (PFS) and overall survival (OS) were estimated by Kaplan–Meier method. A multivariate

analysis (MVA) Cox regression model was performed for OS, including LDH, NLR and regional disease. MVA results were used to build a new prognostic score for OS (including LDH and regional disease). Reported mOS and mPFS of alternative SOC by line of treatment at time of study entry according to historical data were recorded.

Results

Out of 43 pts reviewed, 5 (12%) were screen failures (4 due to clinical deterioration and 1 due to lack of biopsiable disease) and 38 (88%) were included in the analysis. Cohort characteristics and type of treatment received are described in Table 1.

G3-4 TRAEs occurred in 8 pts (21%). ORR and CBR were 24% (10.5% complete responses) and 29.0% respectively. With a median follow up of 13.5 m, estimated mPFS and mOS were 3.5m (95% CI 1.7-4.4) and 10.4m (95% CI 7.8-18.2), respectively. In pts with available SOC, a total of 57.1% and 67.7% achieved a higher mPFS and mOS than expected according to pivotal trials, respectively.

Pts with LDH> upper limit normal (ULN), NLR≥6, and regional disease presented worse outcome in terms of OS. In the adjusted MVA, only LDH>ULN and presence of regional disease were associated with worse OS (Table 2). In the univariate analysis LDH>ULN vs ≤ULN was the only prognostic factor for PFS: 1.2 (0.7-NR) vs 3.9 (95% CI 2.1-5.4), p 0.000.

We generated a new score using LDH>ULN and presence of regional disease. Pts with low (0) vs medium (1) vs high score (2) had a mOS of 18.9m (95% CI 13.4-NR) vs 8.5m (95% CI 3.5-10.4) vs 1.8m (95% CI 1.3-2.3), p=0.000.

Conclusion

In our cohort, up to 60% of pts with R/M HNSCC treated within Ph1-CT when alternative SOC was available had improved survival when compared historical data, with moderate G3-4 TRAEs. Both

LDH>ULN and presence of regional disease were independent predictors of poor outcome in the context of Ph1CT.

Table 2. Prognostic factors for OS (univariate and multivariate analysis)

	Univariate analysis			Multivariate analysis		
	HR	95% CI	p value	HR	95% CI	p value
Age ≥65	0.86	0.40- 1.85	0.69			
ECOG≥1	1.67	0.50-5.54	0.40			
Local disease	0.66	0.31-1.41	0.28			
Regional disease	2.27	1.07-4.80	**0.03**	3.66	1.58-8.48	**0.00**
Metastatic disease	1.09	0.48-2.50	0.84			
LDH>ULN	13.20	4.23-41.20	**0.00**	16.14	4.01-64.92	**0.00**
NLR ratio ≥6	3.16	1.37-7.27	**0.01**	2.07	0.78-5.56	0.15
IT pretreated	1.02	0.46- 2.27	0.96			
Previous lines>2	0 .63	0.24-1.68	0.36			
Toxicity G3-4	0.68	0.26-1.83	0.45			

Tabla 1. Cohort characteristics

Variable	
Age: average (range)	61.5 (37 - 9)
Gender: n(%) Male vs Female	 28 (74) vs 10 (26)
Location: n(%) Larynx Oropharynx; VPH-related Oral Cavity Hypopharynx Unknown primary	 12 (31) 11 (29); 2 (18) 8 (21) 6 (16) 1 (3)
ECOG: n (%) 0 vs 1	 5 (13) vs 33 (87)
Disease location: n(%) Local vs Regional vs Distant	 21 (56.8) vs 19 (50.0) vs 26 (70.3)
Previous IT: n (%) Yes vs No	 13 (34) vs 25 (66)
Number of line: n (%) 1 vs 2 vs ≥3	 6 (16) vs 13 (35) vs 18 (49)
LDH value: n(%) ≤ULN vs >ULN	 32 (84) vs 6 (16)
NLR <6 vs ≥6	 29 (76) vs 9 (24)
Type of treatment: Anti-PD1 + other IT combination Anti-PDL1 + other IT combination TLR agonist+ Ox 40 agonist SHP2 inhibitor CD44v6 tirosin kinase receptor inhibitor Parp inhibitor + chemotherapy	 24 (63) 10 (25) 1 (3) 1 (3) 1 (3) 1 (3)
Alternative SOC available: n (%) Yes vs No	 28 (74) vs 10 (26)
Toxicity G3-4: n(%) No vs Yes	 30 (79) vs 8 (21)

PO-282 | Role of the Speech-therapist in the Head and Neck Cancer MDT – A Single-institution Experience

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Key words

Cancer, head and neck, multidisciplinary team, speech therapist

Introduction

Tumors of the head and neck result in serious consequences for patient quality of life and preservation of anatomical structures during treatment does not guarantee preservation of organ function. The most common disorders in patients with head and neck cancer are: breathing, swallowing, voice, and speech disorders, reduced mobility of the orofacial musculature, neck, and shoulders, lymphoedema, and pain. The voice quality and speech can be significantly damaged.

Materials and Methods

In Croatia, 1003 malignant tumors of the head and neck were diagnosed in 2021, with 476 fatal outcomes, and no significant changes in average annual numbers have been observed in the last ten years. The Zagreb Clinical Hospital Center is the largest and main medical institution in Croatia which contains Head and Neck Cancer Multidisciplinary Team (MDT). For a number of years, among others, a speech therapist has been a member of the team. The speech therapist determines an objective and subjective analysis of voice, speech and swallowing for each patient before and after treatment.We have over five hundred presentations per year. These presentations include newly-diagnosed patients with head and neck cancer, patient presentations after completion of surgical treatment or chemotherapy, and presentations of complications.

Results

Our results show the importance of participation of speech therapists in MDT. It is important to assess the functional status before and after the start of treatment. It is important to start rehabilitation as early as possible, and the success of rehabilitation can be demonstrated by objective measurements.

Conclusion

Engagement of a speech therapist is important to prevent and minimize the effects of such functional disorders, and it is also necessary to ensure continuous monitoring in the process of rehabilitation until stabilization. Treatment for head and neck cancer saves lives, and voice, speech, and swallowing rehabilitation provides patients with the opportunity to achieve independence and higher quality of life.

PO-284 | Salvage chemotherapy after immunotherapy in recurrent/metastatic head and neck carcinoma

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Keywords

PDL1, immunotherapy, salvage

Purpose/Objective

AntiPD(L)-1 agents have improved overall survival (OS) in patients (pts) with R/M HNSCC despite modest overall response rates (ORR) and no benefit in progression-free survival (PFS). Enhanced sensitivity to standard-of-care salvage chemotherapy (SCT) at progression might have contributed to these results. The aim of this study was to evaluate the efficacy of SCT in pts with R/M HNSCC after progression on immunotherapy (IT).

Material/methods

Retrospective analysis of R/M HNSCC pts treated with SCT after progression on IT in 2 centres (Institut Català d'Oncologia (ICO) Badalona and ICO-Hospitalet between 2015 and 2022. Clinical data, PDL1 status (positivitiy defined by CPS>1) and ORR were collected. OS, PFS and PFS2 (time from IT initiation to progression on subsequent SCT) were estimated using Kaplan–Meier method. A multivariate Cox regression model and log-rank test were performed to identify predictors of efficacy to SCT in terms of PFS and OS.

Results

A total of 63 pts treated between January 2015 and August 2022, were included. Cohort characteristics are summarised in Table 1.

SCT regimens used were: EXTREME =12 (19.1%); Paclitaxel =34 (54.0%), Paclitaxel+Cetuximab =11 (17.5%), other =6 (9.5%).

ORR to SCT was 48.2% with 8 (14.3%) complete responses. With a median follow up of 14.2 m, PFS and OS were 4.1 m (IC 95% 3.0-5.8) and 9.2 m (IC 95% 6.5-12.3) respectively. PFS2 was 8.6m (IC 95% 6.6–10.5).

Pts with PDL1 positive tumors had improved outcome in terms of ORR: 70.0% vs 17.7% (p 0.003), mPFS 6.1m vs 2.0m (p 0.000), mOS: 16.7m vs 6.1m (p 0.001) and mPFS2: 11.3 m vs 4.4 m (p 0.000). Pts with ECOG 1 vs 2 had improved mOS: 12.3m (7.1-19.0) vs 5.4m (0.3-8.5), with no differences in mPFS or ORR. ORR to SCT was greater in regimens containing cetuximab vs no cetuximab: 70.6% vs 37.8% (p 0.040), with no significant differences in PFS: 6.1m(1.5-9.9) vs 3.8m(2.0-5.1) (p=0.092) or OS: 12.5m(5.6-NR) vs 8.4m(6.1-10.5) (p=0.255).

In the MVA, only PDL1 status significantly impacted on independent prognostic factor for PFS (HR=0.25; IC95% 0.09-0.72; p=0.010) and OS (HR=0.31; IC95% 0.11-0.90; p 0.031) after adjusting by ECOG.

Conclusion

The ORR observed with SCT after immunotherapy was higher than expected regarding the pivotal trials, and is associated with better outcomes in terms of PFS and OS, especially in PDL1 positive pts.

Table 1. Cohort characteristics

Variable	
Age: median (range)	60.6 (24.7 - 78.6)
Sex: n(%)	
Male	48(76.2%)
Female	15 (23.8%)
ECOG: n(%)	
1	39 (81.2%)
2	9 (18.8%)
Tumor location: n(%)	
Oral cavity	21 (33.3%)
Larynx	17 (27.0%)
Oropharynx; VPH-related	16 (25.4%); 8 (50.0%)
Hipopharynx	7 (11.1%)
Nasal cavity	1 (1.6%)
Cervical squamous cell carcinoma with unknown origin	1 (1.6%)
Stage at diagnosis: n(%)	
I	5 (7.9%)
II	2 (3.2%)
III	6 (9.5%)
IVA	27 (42.9%)
IVB	10 (15.9%)
IVC	13 (20.6%)
Status PD-L1: n(%)	
Positive	26 (41.3%)
Negative	17 (27.0%)
Unknown	20 (31.7%)
Number of previous lines before SCT: n(%)	
1	18 (28.6%)
≥2	45 (71.4%)
Previous IT: n(%)	
PD(L)-1 inhibitor alone	31 (49.2%)
PD(L)-1 inhibitor + immunomodulator	22 (34.9%)
PD(L)-1 inhibitor + another checkpoint inhibitor	10 (15.9%)

PO-285 | Free-flap mandibular reconstruction in elderly patients

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(1) University Hospital of Parma

Purpose/Objective

Free flap reconstruction is the first choice to restoring mandibular defects.

Increasing in population life expectancy results in raising numbers of aging patients facing complex reconstructive surgery. Absence of patient morbidity, compliance, quality of life after surgery, are determining factors in the reconstructive choice.

In this study we evaluated our experience with free-flap transfers in older patients, analysing the post-operative reconstructive and systemic complications.

Material/Methods

Between 2000 and 2021, over twenty percent of patients was more than 75 years old at the time of treatment. We classified mandibular defects according to Urken Classification as symphysis defects, body defects, ramus defects and condyle defects or a combination thereof. We included free flap reconstruction using scapula, fibula, iliac crest and ALT or forearm with reconstructive plate.

We considered complications, functional and aesthetic outcomes, dental rehabilitation and quality of life.

Results

Reconstruction with free bone-containing flaps also appears to be the first choice in this type of patient. In our experience low morbidity and quality of vessels of scapula made possible a wider use of this flap.

Fibula flap in our experience contains limitations regarding atherosclerosis and poor patient mobilization in the postoperative period.

No patients undergone to mandible reconstruction with iliac crest flap.

Reconstruction with forearm and reconstructive plate was preferred in lateral defects of mandible or in patient with ASA score >3.

Dental rehabilitation with removable prosthesis or implant was possible in more than 65% of patient.

Conclusion

The results of this study provide evidence that free-tissue transfer may be performed in ageing patients with a high degree of technical success. Symphisis reconstruction using free flap containing bone is mandatory while we can use soft tissue free flap for lateral defect of mandible.

A careful selection of the patients based on comorbidities and general conditions (ASA status) is of primary importance in reducing post-operative complications and to improving the results of surgery.

PO-287 | Preoperative biopsy accuracy for parotid gland tumors

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(1) HOSPITAL CENTRAL DO FUNCHAL

Keywords
Parotid gland; FNA; CNB.

Purpose/Objective

We aimed to evaluate the diagnostic performance of FNA and CNB for the preoperative diagnosis of parotid gland neoplasms.

Material/methods

We retrospectively reviewed the records of 24 patients who underwent parotid surgical excision at Hospital Nélio Mendonça (Funchal) between January 2018 and November 2022. Preoperative biopsy results were categorized as benign, malignant or indeterminate. Indeterminate results were removed from our calculations, these included sufficient cellular content without clear determination of a benign or malignant nature (nondiagnostic) and insufficient cellular content for analysis. Suspicious findings were grouped with those that were clearly malignant. FNA results were reviewed and categorized under the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC). Surgical pathology was grouped as benign or malignant. Sensitivity, specificity, accuracy, and negative predictive value of FNA and CNB for detecting malignant lesions were investigated.

Results

Twenty-four patients met the inclusion criteria, 3 patients were excluded due to unavailable data regarding preoperative biopsy histopathologic results. Fourteen patients (66.7%) were females,

and the median age was 65.8 years. The most common type of surgery performed was superficial parotidectomy. Final histopathology revealed 11 benign lesions (52.4%) and 10 malignant neoplasms (47.6%). Pleomorphic adenoma was the most frequent neoplasm overall. In the majority of patients (95,2%), FNA was the first method chosen for obtaining a specimen for microscopic pathological characterization. Six patients underwent repeat biopsy, usually using a different technique. The cytologic diagnoses changed in 4 of 6 patients (66.7%). According to MSRSGC, 3 FNAs (13%) were classified as nondiagnostic, 2 (8,7%) as nonneoplastic, 1 (4,3%) as atypia of undetermined significance, 8 (34,8%) as benign neoplasm, 4 (17,4%) as salivary gland neoplasm of uncertain malignant potential, and 3 (13,0%) as malignant. We did not find "suspicious for malignancy" cytological reports (category V of the MSRSGC). The sensitivity, specificity, accuracy and negative predictive value of FNA for detecting malignant lesions were 75%, 80%, 77,8% and 80%, respectively, and those of CNB were 66,7%, 100%, 75% and 50%, respectively. The rates of nondiagnostic cytology were 13,0% for FNA and 20,0% for CNB. There were 2 (8,7%) samples with insufficient content for analysis and none for CNB.

Conclusion

In our series of 21 patients, FNA showed lower sensitivity and specificity for detecting malignant neoplasms than previously reported. Conversely, CNB had moderate sensitivity but higher specificity. Despite the small number of patients included, our results show that the decision to choose conservative management should not be based solely on preoperative cytology results.

PO-288 | Descriptive epidemiology of head and neck tumors diagnosed in Algarve, Portugal in 2020-2021

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Keywords

Epidemiology, head and neck tumors, Algarve

Purpose/Objective

The main goal of this study was to perform a descriptive retrospective epidemiologic characterization off all head and neck tumors diagnosed in Algarve's resident population in 2020-2021.

Material/Methods

All patients diagnosed with a head and neck tumor at the Algarve University Hospital Center, between 2020 and 2021 were included (n=183). We have examined the distribution and incidence of all tumors by gender, age, geography, and year. Furthermore, the anatomic location, histology, staging and treatment of all tumors were also characterized.

Results

The average annual incidence rate of all head and neck tumors in Algarve's residents in 2020-2021 is 19.6 per 100.000 population. The average age at the time of the diagnosis is 64.0 years with an associated SD of 11.9. Overall, 78.7% of all tumors occurred in males (144 tumors) and 21.3% in females (39 tumors). Of the total of the 183 head and neck tumors diagnosed in the Algarve region between 2020 and 2021, 93 were diagnosed in 2020 and 90 in 2021. The most frequently reported histology is squamous

cell carcinoma with 90.7% of cases, corresponding to 166 patients. Regarding the anatomic location, tumors of the larynx were the most frequent, accounting for 25% of cases, followed by tumors of the oral cavity with 21% and oropharynx with 19%, respectively. Approximately 75% of the head and neck tumors diagnosed were considered advanced cancers (staged as III or IV) and thus, treated using a combined approach: surgery followed by radiotherapy (19.7%) or radiotherapy and concomitant chemotherapy(38.3%).

Conclusion

Altogether, our descriptive epidemiologic study based on a Portuguese population has unreveal tumor's incidences, patterns and features that could improve our knowledge of this type of tumors. From our knowledge, it is the first time that such a comprehensive study is performed in Portugal.

PO-290 | Arenobufagin induce cell apoptosis by modulating claspin and JNK pathway in NPC cells

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Keywords

Nasopharyngeal carcinoma; Arenobufagin; Claspin

Background

Nasopharyngeal carcinoma (NPC) is a malignant tumor type that begins in nasopharynx, which mostly belongs to non-keratinizing undifferentiated carcinoma in high-rate area, such as Southeast Asia and North Africa. In Taiwan, the Cancer registry annual report for 2019 has indicated that the incidence rate of NPC ranges from 2.02 to 7.48 per 100,000 person-years, which is much higher than worldwide (less than 1 per 100,000 person--years). Although NPC is highly sensitive to radiation, the high incidence of synchronous distant metastasis still causes a poor prognosis for patients with NPC. Therefore, the development of natural compound is needed to supply combination radiation therapy. Arenobufagin is a component of the traditional Chinese medicine 'toad venom' (also known as Chan'su). Toad venom is often used to treat heart disease and liver cancer. Arenobufagin is an inhibitor of the sodium-potassium pump, which has a simulative effect on the heart. Nevertheless, arenobufagin has not been studied to clarify its therapeutic efficacy for nasopharyngeal carcinoma.

Purpose/Objective

Our study aimed to analyze the effect of arenobufagin on nasopharyngeal carcinoma cells, and further explore the target and specific signaling pathways of arenobufagin.

Material/methods

We investigated the apoptosis effect of arenobufagin in NPC cell lines (NPC-039 and NPC-BM) using a cell viability assay, tumorigenic assay, fluorescence assay, and Western blot assay. The protease array, Western blot assay, and protease array were used to further explore the targets and signaling pathway of arenobufagin-induced apoptosis.

Results

The cell viability and tumorigenic ability of NPC cells were inhibited after arenobufagin treatment in a dose-dependent manner. Meanwhile, chromatin condensation, apoptosis double stain and the activation of cleaved caspase-3, -8, and -9, indicated that arenobufagin drives NPC cell death by initiating apoptosis. The downregulation of claspin was detected and the involvement in arenobufagin-induced apoptosis was confirmed using CLSPN--overexpression system. Furthermore, the combination of MAPK inhibitors and arenobufagin demonstrated that arenobufagin induced NPC apoptosis through the suppression of JNK pathway.

Conclusion

Our present study concludes the apoptotic effect of arenobufagin in both NPC-039 and NPC-BM cell lines. Through downregulation of the claspin and JNK pathway, we clarify the underlying mechanism of arenobufagin-regulated apoptosis in NPC cells.

PO-293 | The role of hypoxia in head and neck squamous cell carcinoma pathogenesis

Kamila Ostrowska [(1)]; *Julia Ostapowicz* [(1)]; *Agnieszka Rawluszko-Wieczorek* [(1)]; *Sabina Koczot* [(1)]; *Wiktoria M. Suchorska* [(1)]; *Wojciech Golusinski* [(1)]

(1) Poznan University of Medical Sciences

Key words

Hypoxia; tumor microenvironment; HNSCC

Background

Head and neck squamous cell carcinoma (HNSCC) is one of the most common cancers worldwide and is characterized by poor prognosis and a high mortality rate. The tumor microenvironment (TME) is a critical factor in cancer progression and treatment response. The majority of HNSCCs are solid tumors; thus they are characterized by reduced oxygen concentration. Hypoxia-inducible factors (HIF) are crucial transcription factors that support tumor cells' adaptation to hypoxic conditions by regulating the expression level of more than 100 genes. For instance, vascular endothelial growth factor (VEGF), carbonic anhydrase IX (CA9), and glucose transporter 1 (GLUT1) are upregulated by HIF-α which are responsible for angiogenesis, pH regulation, and metabolism changes in the tumor cells, respectively. HIF-α level is regulated by the prolyl hydroxylases family (PHD1, PHD2, PHD3) by directing HIF to the degradation pathway. In our study, we demonstrated that hypoxia-related genes (*VEGF*, *CA9*, *GLUT1*), as well as *PHDs* genes, significantly differ in cancerous and adjacent unchanged tissue according to HNSCC patients' outcomes.

Purpose

This study aims to evaluate the influence of hypoxia on HNSCC patients' outcomes.

Methods

PHD1, *PHD2*, *PHD3*, *HIF1A, CA9, VEGF,* and *GLUT1* gene expression was evaluated in mRNA and protein levels using quantitative RT-PCR and Western-Blot in primary cancerous and adjacent unchanged tissues from 102 patients with head and neck squamous cell carcinoma.

Results

We have determined the differences in mRNA and protein levels of selected hypoxia-related and PHDs genes in HNSCC patients' cancerous compared to adjacent unchanged tissues. We have correlated these results with patients' clinical data and suggest probable essential factors in HNSCC tumorigenesis.

Conclusion

Hypoxia may significantly impact HNSCC progression. The future perspectives of the study encompass *in vitro* studies to determine the mechanistic role and key regulators of hypoxia-related tumorigenesis in HNSCC.

PO-294 | Investigation of [18F]FDG PET-imaging and hematological parameters in HNSCC patients

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Keywords

HNSCC; positron emission tomography/computed tomography; [18F]FDG

Purpose

Objective of this study was to investigate the[18F]FDG PET- imaging and hematological parameters in head and neck squamous cell carcinoma (HNSCC) patients.

Material and Methods

Retrospective analysis was performed on a group of 106 HNSCC patients in whom [18F]FDG PET/CT was performed to assess severity of the disease. Several PET-derived parameters (SUVmax, SUVmean, TotalSUV, MTV, TLG, TLRmax, TLRmean, TLRTLG, and HI) for primary tumor and lymph node with highest activity were assessed. Additionally, hematological parameters (LEU, LEU%, NEU, NEU%, MON, MON%, PLT, PLT%, NRL, and LMR) were also assessed. Moreover, the same parameters were compared between HPV-positive and HPV-negative patients.

Results

Patients with N3 stage had significantly higher (p<0.001) primary tumor MTV (48.4) and TLG (471.1) values compared with those with N1 stage (12.3 and 69.8, respectively) and N2 stage (15.5 and

80.6, respectively). Lymph node SUVmax and SUVmean values were significantly higher (p=0.022 and p=0.036) in patients with N3 stage (10.6 and 5.7) compared with those with N1 (4.9 and 2.5) and N2 stages (6.4 and 3.7, respectively). Further, TLRTLG value showed significantly higher values (p=0.002) in N3 stage compared with N1 and N2 (14.1 vs. 3.0 and 2.9, respectively). From hematological parameters, only PLT appeared to differ significantly between CUP Syndrome patients and patients with T4 stage of the primary tumor (207.3 vs. 287.3, p = 0.027). When HPV-positive and HPV-negative group was compared significant between--group differences were observed for two of the semiquantitative [18F]FDG PET-imaging parameters, with higher values in the HPV-negative group: primary tumor MTV (22.2 vs 9.65; p=0.023), and TLRmax (3.50 vs 2.46; p=0.05). The HPV-negative group also had a significantly higher NEU count (4.84 vs. 6.04; p=0.04), NEU% (58.2 vs. 66.2; p=0.007), and NRL% (2.69 vs. 3.94; p=0.038).

Conclusion

This study showed that several semiquantitative parameters derived from [18F]FDG PET/CT imaging of the primary tumor as well as few hematological parameters differs in HNSCC patients in terms of N stage as well as in terms of HPV status.

PO-296 | Malignant Tumors of Salivary Glands: a retrospective study

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Keywords

Malignant neoplasms; salivary glands; Parotid Gland

Purpose/Objective

Analyze the series of malignant neoplasms of salivary glands in order to find out the epidemiological characteristics of the different histological types, treatment and evolution.

Material/methods

We performed a descriptive and retrospective study of our series of malignant neoplasms of salivary glands between 2011 and 2022. The variables analyzed were age, gender, tumor location, imaging examination, histological examination, histological type, initial treatment, adjuvant treatment, complications, recurrence and survival.

Results

We obtained a total of 36 patients, 15 (2%) were male and 21 (58%) were female, the average age was 66 years old. Regarding tumor location, the most frequent site was the Parotid Gland with 18 cases (50%) followed by minor salivary glands with 17 cases (47%) and finally the sublingual gland with only 1 case. The most frequent histological type in parotid gland was squamous cell carcinoma metastasis with 6 cases, in minor salivary glands it was cystic adenoid carcinoma with 8 cases. The majority of imaging examination was CT (61%). The histological diagnosis was obtai-

ned through incisional biopsy in 61 % of the cases and cytology in 33%. The initial treatment was surgery in 89%. Facial paralysis was the most frequent complication, it occurred in 11 patients. 12 patients underwent adjuvant treatment with radiotherapy and 5 with QR/RT. Until 2021, 2 patients had relapses. 2-year survival was 95,7% and 5-year survival was 64,3%.

Conclusion

Our results are similar to the literature with a slight prevalence in women and the parotid gland being the most affected site. Contrasting with the literature, the most frequent histological type was cystic adenoid carcinoma.

PO-298 | Single centre toxicity outcomes with concomitant weekly and 3 weekly cisplatin in H&N cancer

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(1) The Newcastle upon Tyne Hospitals NHS Foundation Trust

Keywords

Chemoradiotherapy, cisplatin, toxicity

Purpose

Concomitant cisplatin chemotherapy is well established as a radiosensitizer in the treatment of head and neck squamous cell carcinoma. We aimed to review the toxicity outcomes at our centre for patients receiving concomitant weekly or 3 weekly cisplatin.

Method

A retrospective analysis of 102 patients at our centre who were well enough to receive radical concomitant chemotherapy with cisplatin over a 12 month period. 39 patients had received 3 weekly (100mg/m2) chemotherapy for 2 cycles (capped at 200 mg/cycle) and 63 patients had received weekly (40mg/m2) for 6 cycles (capped at 70 mg/cycle). Data collected included patient demographics, performance status (PS), staging (AJCC 8th), cumulative dose, dose intensity and toxicities.

Results

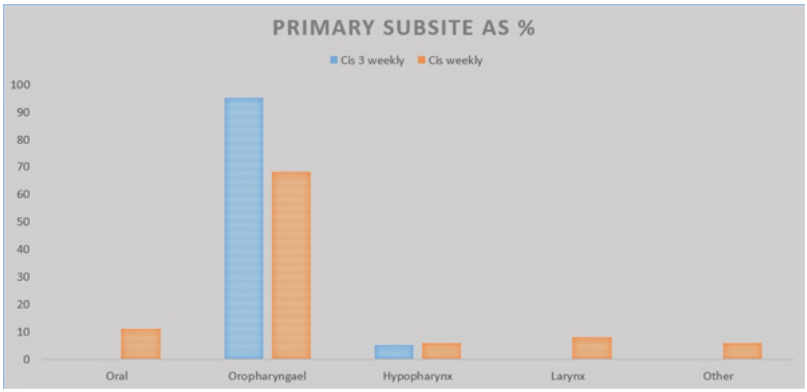
Of the 39 patients included in the 3 weekly cisplatin group, 32 (82%) were performance status 0 compared to 35 (56%) in the weekly group. Median age was 58 (42-68) vs 60 (42-70). Staging was as follows, I (31% vs 13%), II (15% vs 4%, III (41% vs 30%) and IV (13% vs 51%). Most common sub site was oropharynx in both groups (95% vs 68%).

Comparison of the 3 weekly versus weekly regime all grade toxicity included nausea 9 (23%) vs 21 (33%), myelosuppression 10 (26%) vs 15 (24%), ototoxicity 5 (13%) vs 16 (25%), infection 5 (13%) vs 16 (25%), renal dysfunction 0 (0%) vs 7 (11%) and neuropathy 0 (0%) vs 2 (3%). Overall grade 3 (G3) toxicity was 15 (38%) vs 39 (62%) favouring the 3 weekly cisplatin. Further analysis showed G3 nausea (13% vs 13%), fatigue (3% vs 11%), myelosuppression (15% vs 13%) and infection (13% vs 21%).

With regard to 3 weekly versus weekly cohorts, there were 7 (18%) vs 0 (0%) deferrals in the 3 weekly group, predominantly for bone marrow suppression and 7 days in total. However, there were also 7 (18%) vs 61 (60%) of patients having at least one cycle omitted. Median cumulative dose received in the 3 weekly group was 179mg/m2 (out of a planned 200mg/m2) in comparison to 182mg/m2 (out of a planned 240mg/m2), this as a percentage of planned dose is 90% vs 76%.

Conclusion

Both regimes had a similar median cumulative dose of 179mg/m2 (3 weekly) and 182mg/m2 (weekly) although a weekly regimen aims for a higher planned cumulative dose. Only 40% of weekly cisplatin patient managed all 6 cycles of chemotherapy which may be important in HPV negative disease. Furthermore, our data showed grade 3 toxicity of between 38-62%. Our centre has historically used the 3 weekly regimen in favourable HPV positive disease in often younger and fitter patients which may be why the toxicity outcomes are more favourable in this population.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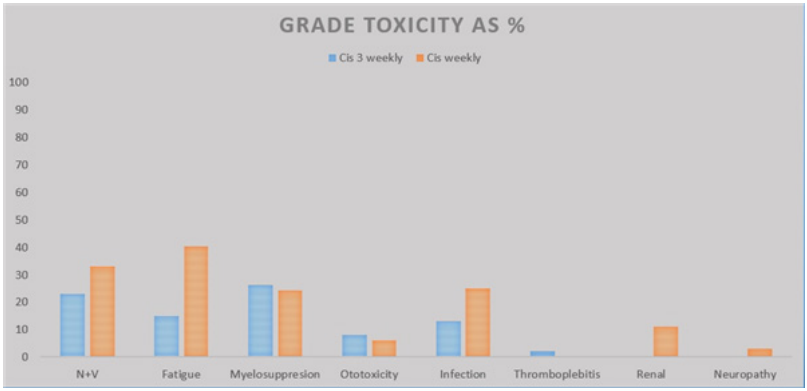
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Myelosuppresion
Ototoxicity
Infection
Thromboplebitis
Renal
Neuropathy

PO-300 | Axitinib for recurrent or metastatic adenoid cystic carcinoma in a real-world setting

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Keywords

Salivary gland cancer, adenoid cystic carcinoma (ACC), axitinb, real-world outcome, next generation sequencing (NGS)

Purpose/Objective

Adenoid cystic carcinoma (ACC) is a rare cancer with no approved systemic therapy in the recurrent/metastatic (r/m) setting. The role of chemotherapy for ACC is limited due to high toxicity and modest efficacy. Recently, the tyrosine kinase inhibitor axitinib demonstrated an improved progression-free survival (PFS) rate compared to observation in a randomized phase II

trial. However, the impact of axitinib in a real-world setting has to be defined.

Material/methods

Patients with r/m ACC treated with axitinib were retrospectively evaluated. Clinical data, treatments, outcomes and toxicitiy were retrieved from the electronic health record. Tumor samples were analyzed by immunohistochemistry (IHC), including expression of hormone receptors (AR, ER, PR), HER-2/neu and PD-L1; and a next generation sequencing (NGS) panel including 38 genes.

Results

A total of 13 patients were included into the study. All patients had radiological confirmed progression before initiation of axitinib. The median age was 57.3 years, with 30.8% of patients ≥65 years. The overall response rate (ORR) was 0% with five patients (38.5%) experiencing tumor shrinkage between 5% and 24%, the disease control rate (DCR) was 92.4%. The median overall survival (OS) was 14.3 month (95% CI 2.9 – 25.78), PFS was 5.13 month (95% CI 0.1 – 15.83). Most common adverse events were fatigue (53.8%), hypertension (38.5%), diarrhea (30.8%) and stomatitis (30.8%). Dose reduction and/or dose interruption was necessary in 46.2%. In two patients an exon 20 mutation of *ARIDA1A* were detected; in one patient a mutation of *PALB2* exon 12 and of *PIK3CA* exon 5, respectively.

Conclusion

Axitinib is an effective and manageable treatment option for ACC in a real-world setting. A more broadly characterization of tumor samples besides a NGS panel covering 38 genes and IHC seems necessary to further improve molecular insight, outcome and clinical decision making in ACC.

PO-301 | The advantages of digitally assisted methods for the aesthetic and functional orbit reconstruction

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(1) University of Medicine and Pharmacy "Grigore T. Popa"

Objectives

Nowadays, one of the most used technologies are using digital assistance such as stereolithography.

The purpose of this study is to evaluate the advantages of using the technology in repairing complex defects which interest the orbital walls.

Material and Methods

The study was performed on a group of 17 patients with orbital defects following tumor pathology.

To reconstruct the defect, using a digital technique, we made preoperatory the stereolithic printed model, and the titanium plates and meshes were preoperatively shaped, these being used intraoperatively in order to reconstruct the defect.

Results

The orbital walls contours were adequately reconstructed with satisfactory restoration of the shape. T

he complexity and duration of the surgery were decreased, and the precision of the reconstruction was greatly increased.

Also, the functionality of the eyeball was restored, postoperatively the patient presented a physiological visual acuity, without visual disturbances.

Conclusion

The use of digital assistance methods as an aid to repairing defects located on the orbit is more efficient, implying shorter surgery time, fewer postoperative complications, and also a lower stress level for the surgeons.

PO-302 | Factors affecting contralateral nodal metastasis in Oral Cavity Squamous Cell Carcinoma.

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Keywords

Oral cancer; tongue carcinoma; gingivobuccal complex cancers; nodal metastasis; neck dissection.

Objectives

To assess various primary tumour (DOI, BGS) and ipsilateral nodal factors (LN Ratio, ENE) associated with contralateral nodal metastases in OCSCC.

Methodology

A prospective cohort study conducted on patients of OCSCC. Contralateral lymph nodes were sampled from patients having biopsy proven OCSCC. Inclusion criteria was kept as tumours crossing the midline, or reaching to within 1cm from the midline, or having depth of invasion (DOI)>10 mm, or gingivobuccal cancers with gross skin involvement; or having a nodal burden of N1 or greater.

Results

A total of 114 cases were analysed, of which 50 (43.9%) were cancers of the tongue, and 57 (50%) were gingivobuccal complex primaries, 2 (1.8%) from the floor of mouth and 5 (4.4%) from the lip. Neck was addressed in 80.7% (n=92/114) with ipsilateral comprehensive neck dissection (CND) along with contralateral selective neck dissection (SND),15.8% (n= 18/114) had bilateral selective

neck dissection, while 3.5% (n=4/114) had bilateral comprehensive neck dissection. 16.7% (n=19/114) had positive nodes on the contralateral side. 14 of these 19 were not detected to have contralateral nodal mets in pre-op assessment (13.2% of all opposite neck N0.) Of them 11 had primary tumour in the tongue, and 8 were from the GBC. This made up 12% (n= 6/50) of all tongue primaries, and 10.5% (n=6/57) of all GBC primaries included in the study. All 11 tongue cases had DOI of 10 mm or greater. 37.5% (n= 3/8) of the GBC primaries had clinically involved skin, which constitutes 7.9% (n=3/38) of all cases which had skin involvement in the pre op workup. Of the involved cases, the mean BG score 3.79, and the mean DOI was 14.15. 32.5% (n=37/114) cases were clinically N0, out of which 21 had received ipsilateral CND for intraoperative reconstruction. 35.1% (n= 40/114) had pathological nodal status of N0 and 64.9% (n=74/114) were N1 or higher, 13 of which were clinically N0. 45.6% (n=52/114) of all nodes had ENE. Significant association was demonstrated with age (p=0.01) and ENE ($p<<0.05$) for contralateral node positivity.

Conclusion

This study tries to shed light on the primary and nodal factors influencing contralateral node positivity, including BG Score and DOI as potential tumour factors for the same, however, there was no statistical significance. Only, age and ENE stand out as significant factors influencing the chances of developing contralateral nodal disease. This suggests that nodal factors have a greater role to play in contralateral spread than primary tumour characteristics. The results of this study are interim results, as further accrual is still ongoing.

PO-306 | How to recognize rare cases of tuberculosis between many head and neck cancer patients?

Marija Pastorcic Grgic [1]; Drago Prgomet [2]; Marko Šutalo [3]; Boris Stubljar [4]; Ljiljana Žmak [5]; Jelena Ostojic [6]; Mirta Zekan Vucetic [7]; Ivana Brnadic [8]; Marko Velimir Grgic [9]

(1) Department of ENT and HNS University Hospital Center Zagreb (2) Department of ENT and HNS University Hospital Center Zagreb School of Medicine Zagreb (3) General County Hospital Požega (4) Division of HNS Department of Surgical Oncology University Hospital for Tumors UHC "Sestre milosrdnice" (5) Croatian Institute for Public Health (6) Special Hospital for Pulmonary Diseases (7) Department for Diagnostic and Interventional Radiogy, University Hospital "Merkur" (8) Department of pathology and cytology University Hospital Centar Zagreb (9) Department of ENT and HNS University Hospital Center "Sestre milosrdnice"

Objective

Head and neck tuberculosis is a form of extrapulmonary tuberculosis. Up to 10 % of patients with tuberculosis can have head and neck manifestations of disease. Neck lymph nodes are the most frequent site of disease in this region. Majority of patients clinically resemble head and neck cancer patients. Delay in diagnosis and treatment is frequent. Multiple biopsies and cytological analyses are performed before correct diagnosis is established and treatment initiated. Unfortunately, some patients are mistreated as head and neck cancer.

Cases

Five different clinical scenarios are presented to show diversity of presentations and resemblance to head and neck cancer. All patients were referred to head and neck cancer surgeon. Delay in diagnosis and treatment initiation was between 6 and 24 months.

Case 1: Male patient with tongue ulcer. After several biopsies negative for cancer, tissue was sent for culture.

Case 2: Female patient with laryngeal lesion. Head and neck CT scan was performed in preparation for microlaryngeal surgery and miliary tuberculosis was recognised in upper parts of lungs.

Case 3: Female patient with multiple unilateral neck nodes. After several fine needle cytological analyses and open biopsy negative for cancer, aspirate of neck node was sent for culture. Diagnosis was established one year after first presentation.

Case 4: Male patient with supraglottic laryngeal lesion and unilateral neck nodes. Microlaryngeal surgery was performed 2 years earlier. After surgery dysphonia progressed and weight loss was noticed. Diagnosis was suspected on chest X-ray. Thorax CT was performed and tuberculosis suspected.

Case 5: Male patient previously treated for T1 laryngeal cancer presented with multiple contralateral lymph nodes. Bovine tuberculosis was diagnosed after fine needle aspiration culture.

In three presented patients diagnosis was established by Mycobacterium culture from fresh specimens obtained by fine needle aspiration or biopsy. In two patients sputum PCR was performed based on suspicious thorax CT finding.

Conclusion

Fresh specimens for Mycobacterium culture should be sent after first finding of granulomatous inflammation in either biopsy or fine needle aspiration cytology. This approach would provide correct diagnosis within 6 weeks for all patients and prevent multiple biopsies or mistreatment.

PO-307 | HER3 expression improves the prognostic stratification of patients with advanced laryngeal SCC.

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Objective

Compared to the other members of human epidermal growth factor family receptors (HER), the role of HER3 has not been well defined in laryngeal cancer. The predictive and prognostic role of HER3 has been the focus of clinical attention but the research findings are contradictory, especially in laryngeal squamous cell carcinoma (LSCC).

Materials and methods

We performed a retrospective analysis of two cohorts of 66 advanced LSCC patients, in which co-expression of HER1, HER2 and HER3 receptors was investigated by semi-quantitative immunohistochemistry. The association of their pattern of expression with survival was evaluated by Kaplan-Meier and Cox's proportional hazard analyses. Multivariable Cox proportional hazards models were developed to predict median 2- and 3-year RFS and 2.5- and 5-year OS. The Akaike information criterion technique and backwards stepwise procedure were used for model selections. The performance of the final Cox models was assessed with respect to calibration and discrimination.

Results

Immunohistochemical labeling for HER1 and HER2 was localized both in the cell membrane and in the cytoplasm, while HER3 labeling was observed both in the cell cytoplasm and in the nucleus. HER3 expression was inversely correlated with HER1 po-

sitivity. The expression patterns of HERs were associated with tumor differentiation. In both cohorts of patients, HER1 expression was associated with reduced relapse-free (RFS) and overall survival (OS). In HER1 positive tumors, the co-expression with nuclear HER3 was associated with better RFS and OS, compared with HER3 negative tumors or tumors expressing HER3 at cytoplasmic level. HER3 expressing tumors had a higher Geminin/MCM7 ratio than HER3 negative ones, regardless of HER1 co-expression. Multivariable analyses identified age at diagnosis, tumor site, HER1, HER3 and age at diagnosis, tumor stage, HER1, HER3, as covariates significantly associated with RFS and OS, respectively. Bootstrapping verified the good fitness of these models for predicting survivals and the optimism-corrected C-indices were 0.76 and 0.77 for RFS and OS, respectively.

Conclusion

Nuclear HER3 expression was strongly associated with favourable prognosis and allows to improve the prognostic stratification of patients with HER1 positive advanced LSCC.

PO-308 | Treatment with ERBITAX in Head and Neck Squamous Cell Carcinoma (HNSCC) post platinum and cetuximab

Juan Jose Serrano [(1)]; *Victor Alia Navarro* [(1)]; *Ana María Barrill Corpa*[(1)]; *Pilar Sotoca Rubio* [(1)]; *Pablo Alvarez Ballesteros* [(1)]; *Jaime Moreno Doval*[(1)]; *Coral García de Quevedo Suero* [(1)]; *Juan Carlos Calvo Pérez* [(1)]; *Patricia Pérez Pérez de Aguado* [(1)]; *Ainara Soria Rivas* [(1)]

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Keywords

ERBITAX, immunotherapy (IO)

Objective

The standard of care (SoC) for first line (1L) treatment of recurrent/metastatic HNSCC before the era of immunotherapy (IO) was the EXTREME schedule. Nevertheless, this scheme is very toxic, which makes difficult its applicability in many patients. In this sense, other less toxic schemes (TEPExtreme, ERBITAX) were designed for unfit patients.

After the 1L, Nivolumab has become the SoC. However, after progression to this, or in patients who have previously received IO there is no SoC. Options include taxanes, cetuximab, capecitabine and methotrexate. It is no clear if maintaning the EGFR blockade with cetuximab after having used it in the 1L provides benefit or not. Our work evaluates the results of patients treated with the ERBITAX scheme (weekly paclitaxel plus cetuximab) in advanced lines.

Material and Methods

We have retrospectively evaluated 18 patients who received platinum (cisplatin or carboplatin) and cetuximab with or without 5-FU as 1L, and after progression, have received the ERBITAX scheme in advanced lines. Between the 1L and the ERBITAX scheme, they may have received other treatments, including IO. We have analyzed the

phenotypic characteristics, toxicity profile, rate of overall response rate (ORR), progression free survival (PFS) and overall survival (OS). Attempts have been also made to find differences between those patients who have received prior IO and those who did not.

Results

Median age was 58.5 years (range 50-89), with 83% of men. Characteristics are summarized in table 1.

The ORR was 44%, with 3 complete responses (17%). None stabilization was observed. Median PFS was 4.9 months (95% Confidence Interval (CI) 3.1-7.7) and median OS was 8.5 months (95% CI 4.6-14.3). The OS was clearly better in those patients who achieved response: 15.8 Vs 6.9 months (Hazard ratio (HR) 0.20, 95% CI 0.05-0.82, p=0.025), figure 1.

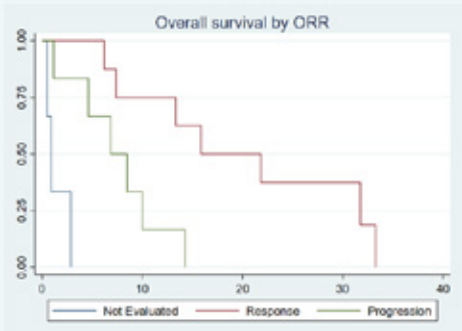
There was a trend benefit for those patients whom had previously used IO. Median PFS was 6.3 Vs. 4.3 month (HR of 0.59 (95% CI 0.19-1.89, p=0.377) and median OS was 13.3 Vs. 8.5 months (HR 0.77, 95% CI 0.27-2.18, p=0.627).

Conclusions

As we said, there is no SoC after 1L treatment in HNSCC, especially after IO. ERBITAX scheme was firstly used at 1L as alternative for unfit patients, with an ORR of 54% (22% of CR) and a median PFS and OS of 4.2 and 8.1 months, respectively. Due to the scarcity of options after 1L (before IO arrival), some authors had used this combination in advanced lines, despite lack of clinical trials.

A retrospective study compared paclitaxel alone Vs. ERBITAX in patient progressing EXTREME scheme. Their results, after propensity score matching, shows a better PFS and OS in the group of ERBITAX: 2.8 Vs. 2.4 months (HR 0.704 95% CI 0.498-0.994, p=0.046) and 5.4 Vs. 4.1 months (HR 0.675, 95% CI 0.463-0.984, p=0.041). Other studies had studied the role of ERBITAX after IO, with ORR of 53.3% and median PFS and OS was 6.2 and 8.4 months, respectively.

Our results show similar results to ERBITAX study in 1L and better than those shown in the other retrospective studies. This allows us to continue supporting the use of ERBITAX in advanced lines, even after the use of prior cetuximab and/or IO. This leaves the chance to considering a sequence of EXTREME, Nivolumab and ERBITAX in those patients who are not candidates for IO in 1L (because of CPS<1), or the use of ERBITAX in second line after IO.



Characteristics	
Age (years)	58.5 (50 – 89)
Male	15 (83%)
Smoke history	12 (67%)
Alcohol history	6 (33%)
Localization	
- Oral Cavity	10 (56%)
- Oropharyngeal	2 (11%)
- Hypopharyngeal	2 (11%)
- Larynx	3 (17%)
Treatment of primary	
- Surgery only	5 (28%)
- Chemoradiotherapy (QRT)	2 (11%)
- Surgery -> radiotherapy	5 (28%)
- Surgery -> (QRT)	6 (33%)
1L scheme	
- Cisplatin + Cetuximab	6 (33%)
- Carboplatin + Cetuximab	7 (39%)
- Cisplatin + 5-FU + Cetuximab	4 (22%)
- Carboplatin + 5-FU + Cetuximab	1 (6%)
Line of ERBITAX	
- 2nd line	9 (50%)
- 3rd line	7 (39%)
- 4th line	2 (11%)
Previous IO	7 (39%)
≤ 3 metastatic sites	14 (78%)
Toxicity grade 3-5	6 (33%)

PO-309 | Therapy with Cetuximab in Laryngeal Carcinoma: May HER1 Be Useful in the Bioselection of Patients?

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Keywords

Radiotherapy, cetuximab, upfront surgery, HER1 expression, laryngeal cancer.

Purpose/Objective

The aim of the study was to evaluate survival in patients with advanced glottic laryngeal squamous cell carcinoma treated by bioradiotherapy (BioRT) with cetuximab and eventual salvage surgery (group A, n = 66) or upfront surgery (total laryngectomy or near-total laryngectomy) with or without postoperative radiotherapy (PORT) (group B, n = 66).

Material/methods

The predictive role of HER1 expression in the bioselection of tumors was evaluated. Relapse-free (RFS), metastasis-free (MFS), overall (OS) survivals, salvageability, and rates of larynx preservation were analyzed. The two groups were balanced by propensity score method on their baseline characteristics.

Results

No significant differences in RFS and OS were found, while MFS results were significantly higher in group A (p = 0.04). Group A showed a 22% reduction in the probability of nodal metastasis (p = 0.0023), mostly in tumors with higher HER1 expression. The salvageability with TL at 3 years was 54% after prior BioRT and 18% after prior upfront NTL (p < 0.05). BioRT with cetuximab showed

a reduction in the risk of lymph node relapse, particularly in the case of HER1 positive tumors, and it allowed to achieve a higher rate of functional larynx preservation and a higher salvageability compared with upfront surgery.

Conclusion

HER1 analysis could be clinically useful in the bioselection of tumors that may benefit from BioRT with cetuximab, particularly in those with neck node metastatic propensity.

PO-311 | Radiosurgery in the treatment of oligometastatic disease from head and neck cancer. Is there a role?

Catarina Martins Silva [1]; Marina Amorim [1]; Osvaldo Carvalhosa [1]; Sara Simões [1]; Sofia Ramos [1]; Guilherme Campos [2]; Carlos Fardilha [2]; Carla Seixas [2]; Pedro Vieira [2]; Adelina Costa [2]; Paulo Costa [2]

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Keyword

Radiosurgery; oligometastatic disease.

Purpose/Objective

Major efforts have been made to define the oligometastatic setting. To date, oligometastatic disease (OMD) is defined as 1-5 metastatic lesions, that could be safely treatable. For head and neck cancer (HNC) limited data are available. The recent accessibility of advanced radiosurgical techniques has therefore improved treatment options for these cases. We aimed to evaluate the role of radiosurgery in the approach of OMD from HNC patients.

Material/methods

15 patients (3 female and 12 male) diagnosed with oligometastatic HNC were evaluated, for a total of 20 metastasis. Five cases were previously treated with systemic therapy. Patients were treated between 2015 and 2021 at our Department, with a total dose that ranged from 24–34Gy delivered in 1-5 fractions. Main endpoints were local control and toxicity, which was evaluated according to the CTCAE version 5.0.

Results

Median age was 65 years (range 39-94). The most common primary site was the oropharynx (9 cases) followed by the tongue (4), buccal mucosa (1) and ethmoid (1). Metastatic sites treated with

radiosurgery were mostly the lung (40%) and bone (26.7%) and the other locations were mediastinum, supraclavicular lymph node and brain. The treatment was well tolerated by all patients, with acute lung toxicity grade 1 (pneumonitis) in 2 cases and there were no cases of late toxicity reported. The median follow-up was 18 months and the median OS was 32,2 months (range 6-42). The local control rate was 80% at 1 year.

Conclusion

There are limited data available regarding the management of oligometastatic HNC patients, and no consensus guidelines are available. The attractive therapeutic profile of radiosurgery is reflected by a high tumor control and a low toxicity and the repeatability of the treatments for recurrent metastases. Radical local treatment in oligometastatic HNC shows promising outcomes in several reports, and needs to be further pursued, identifying the optimal candidates for this approach that should be considered for selection in future prospective trials.

PO-313 | Nasopharynx carcinoma: predictive factors of survival outcomes – RWD real world data

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Keywords

Nasopharyngeal carcinoma

Objective

Nasopharyngeal carcinoma is a head and neck cancer with unique and unusual particularities, leading to a separate approach from all the other head and neck cancers. Treatment approach depends on the stage, and essentially consists in radiotherapy and/or chemotherapy. The introduction of the Intensity-Modulated Radiotherapy in the management of this carcinoma brought satisfactory results.

The aim of this study is to perform a statistical analysis of the population with a nasopharyngeal carcinoma in this institution, from a non-endemic country, in terms of demographic and clinical characteristics and their possible relation with the outcome.

Methods

Clinical data retrospective analysis of patients with the diagnosis of a nasopharyngeal carcinoma between December 2019 and January 2008, in a tertiary Centre. Clinical characteristics considered: ECOG performance status (PS), alcohol and tobacco habits, sexual transmitted diseases, co-morbidities, tumour localization, histological differentiation, stage, LDH and albumin serum levels, nutritional status (PG-SGA), initial treatment and chemotherapy with or without platinum. The collected data from clinical patients file was analysed using SPSS® Statistics v27.

Results

26 patients with the nasopharyngeal carcinoma. Median age of 59yrs-old at the diagnosis [35-87], 88.8% male. >50% had a history of smoking tobacco. > 50% of alcoholism. The nutritional status, evaluated by PG-SGA, was A in 42,3%. The large majority (84,6%) was diagnosed on stage III-IV.

Serum LDH was normal in 65,4%, with the remaining with a CT-CAE grade 1 elevation. The serum albumin was normal in almost all cases, only 2 had a lower level (CTCAE grade 1).

The initial management was performed with radical intent in ~90% of the cases.

All of study population had radiotherapy (RT) included in the treatment protocol, with IMRT technique.

Chemoradiotherapy (CT/RT) followed by chemotherapy (CT) was the initial management in 53,9% of the cases. The large majority had a platinum-based CT.

A complete response rate was achieved in near 50%.

Of the patients who died, cancer was the cause of dead in 30,8% of patients.

The median followup was 47 months [3-166]. Median progression free survival (PFS) was 27 months (IC 95%: 0-56.3) and media PFS was 62 months (IC 95%: 36.8-87.2) and median overall survival (OS) was 48 months (IC 95: 42.47-51.52).

In the univariate and multivariate statistical analysis, no correlation was identified with any of the variables in study with PFS or OS.

Conclusion

Is identified in literature the association with some clinical features and survival. CT/RT followed by adjuvant/palliative CT treatment regimen is described with better survival, compared to other treatment modalities.

None of the variables in our study was identified to be correlated with outcomes. Sample size is the possible main cause.

As it is a rare disease in our geographic area (non-endemic), in our study period, our hospital had a relatively small sample, being the main limitation of this study.

Beside the literature report of serum LDH as a prognostic factor in locally advanced disease, in our study with a high number of locally advanced cases, that was not identified.

Due to the high number of cases with an advanced stage at diagnosis, with the main treatment approach performed in those cases the known as more efficient, it was not possible to demonstrated statistically that superiority in this retrospective study.

PO-314 | Accuracy of fine-needle aspiration and core needle biopsy in the diagnosis of salivary gland tumors

Andrea Sánchez García [(1)]; *Cristina Vázquez López* [(1)]; *José Rigoberto Zepeda Morales* [(1)]; *Dionisio Alberto Guillamón Fernández* [(1)]; *Francisco Antonio Chiquero Ortiz* [(1)]; *Jose Luis Vargas Fernández* [(1)]

(1) Other

Keywords

Salivary tumor, fine needle aspiration, core neelde biopsy.

Purpose/Objective

The aim of this study is to analyze the accuracy of ultrasound-guided fine needle aspiration (US-FNA) and core needle biopsy (US-CNB) in the diagnosis of major salivary gland tumors.

Material/methods

A retrospective study was designed, including patients with diagnosis of major salivary gland tumor following surgical excision between 2017 and 2022 in a single center (n=58). The variables included in the study were age, sex, tumor location, history of previous anatomopathological analysis, preoperative cytological or histological result, type of surgical intervention and final anatomopathological diagnosis. In order to analyze diagnostic accuracy of US-FNA and US-CNB, we excluded all cases without previous anatomopathological analysis previous to the surgery or anatomopathological analysis without ultrasound guide (n=46). The results of FNA or CNB were classified as benign, malignant, indeterminate, or insufficient sample. We evaluated the sensitivity, specificity, negative predictive value, and positive predictive value of the tests. A correlation between histologic subtypes by initial US-FNA or US-CNB and the final histologic result has also been established. Statistical analysis was performed in SPSS 29.

Results

A total of 58 patients were included in the study (29 mens) with a mean age of 59 years (+/-16 years) whose ages ranged from 18 to 82 years. The most frequent location of the tumors was the parotid gland (93%). Malignancy was identified in 14.8% of the parotid gland tumors and in 33.3% of the submaxillary gland tumors. The most frequent benign diagnosis was pleomorphic adenoma (37.9%) followed by Whartin's tumor (36.2%); the most frequent malignant tumors were mucoepidermoid carcinoma and squamous cell carcinoma. Of the 58 patients initially included, 46 underwent preoperative anatomopathological study guided by ultrasound (US-FNA or US-CNB). 33 patients underwent US-FNA (71.7%) and 13 underwent US-CNB (28.3%). Diagnostic accuracy was determined for US-FNA and US-CNB respectively; in terms of sensitivity 75% and 75.5%; specificity 92.5% and 85.7%; positive predictive value 60% and 75% and negative predictive value 96% and 85.7%.

Conclusion

Fine needle aspiration and Core needle biopsy are accurate in the diagnosis of salivary gland tumors, especially to exclude malignancy. The results obtained are consistent with those published in the literature, with high values for specificity and negative predictive value and lower values for sensitivity and positive predictive value.

PO-315 | Induction chemotherapy in oral cavity cancer: the experience of a Cancer Reference Center

José Carlos Pereira [1]; Cláudia Araújo [1]; Rita Canotilho [1]; Cláudia Vieira [1]; Ana Rolo [2]; Maria Leitão [1]; José Dinis [1]; Jorge Guimarães [1]; Joaquim Abreu de Sousa [1]

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Keywords

Induction chemotherapy, oral cavity, squamous cell carcinoma

Background

Surgical excision is the mainstay of treatment for oral cavity cancers. Locoregionally advanced oral cavity squamous cell carcinoma (OCSCC) have a poor survival outcome and surgical treatment in this setting usually implies severe mutilation and organ dysfunction. Induction chemotherapy (IC) is proved to be beneficial in these patients by reducing tumor size and allowing definitive surgery with preservation of organ function. Real-world data is needed to estimate the efficacy and toxicities of this approach.

Purpose/Objective

To evaluate the experience of our institution with induction chemotherapy (IC) in the treatment of locoregionally advanced OCSCC.

Material and Methods

A retrospective analysis of all patients with locoregionally advanced OCSCC, who received IC at our institution between August 2010 and March 2022. All patients received a three drug regimen – docetaxel, cisplatin and fluorouracil (TPF). A clinical and radiological reassessment was performed after the first cycles of treatment. The patients were then planned for either definitive treatment with surgery or chemoradiation (CRT) or palliative care.

Results

107 patients were included in the study, with a median age of 54 years. 85% were male gender and 74.7% were heavy smokers. Tongue (41.1%) and floor of the mouth (35.5%) were the most common locations and almost all patients (96.2%) were stage IV at diagnosis. A median of 4 cycles of chemotherapy with TPF were performed. Clinically relevant toxicities (Grade 3/4) were registered in 29 patients (27.1%). After the first cycles of TPF, a clinical and radiological complete response was observed in 10 patients (9.3%). 50% of these patients were treated with surgery and the other 50% were treated with CRT. A partial response was achieved in 75.7% (81) of the patients and, of those, 57 (70.3%) were submitted to surgery. The rate of complete pathological response was 24.7 % (20). The median overall survival (OS) was 27 months, with 2-year OS of 44% and 5-year OS of 28%. The 5-year DFS was 41%. There was no difference in OS or DFS according to curative intention treatment (surgery or CRT). But in the surgery subgroup patients, those with pCR (pathological complete response) had a statistical significative improvement in OS and DFS.

Conclusion

85% of the patients in our series were responders to TPF. This study shows no survival difference between those submitted to surgery or CRT with curative intent after IC. However, the high proportion of operated patients with pCR (24.7%) had a significantly better OS and DFS. Further studies are needed to evaluate the benefit of this treatment concerning the postoperative functional outcomes and overall survival. Questions regarding which subset of patients would be responders need also to be answered.

PO-316 | Multiple Paragangliomas of the Head and Neck: A Systematic Review

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Keywords

Multiple paragangliomas, glomus tumours

Purpose/Objective

Paragangliomas are usually benign, slowly growing neoplasms that arise from extra-adrenal paraganglionic tissue originated from neural crest cells. Head and neck paragangliomas, also known as glomus tumours, derive from the parasympathetic paraganglia of the skull base and neck. They are located in four primary sites: the carotid bifurcation (carotid paragangliomas), the jugular bulb (jugular paragangliomas), the tympanic plexus (tympanic paragangliomas) and the vagal ganglia (vagal paragangliomas). Given their rarity, their incidence is difficult to be evaluated. It is estimated that they represent approximately 1% of all head and neck tumours, whereas a genetic predisposition is also identified. Treatment options depend on the tumours' and patients' characteristics, hence they are most of the times personalized, with the surgical excision being the mainstay of therapy. The aim of this study is to systematically review the best available evidence regarding the prevalence, diagnosis and management of multiple paragangliomas of the head and neck region.

Material/methods

This was a systematic review of the current literature concerning multiple paragangliomas of the head and neck, which was conduc-

ted according to the PRISMA Protocol. An electronic search of the English-language literature was performed through Pubmed/Medline, Scopus and Embase databases. The risk of bias was estimated by using the Joanna Briggs Institute Critical Appraisal Checklist.

Results

Forty-three studies, with 160 patients (57% females, age range: 12-63 years) and 371 glomus tumours in total, were included in the systematic review. Among these patients, 77% had a positive family history of paragangliomas. The number of head and neck paragangliomas ranged from 2 to 5 and presented either simultaneously (74.8%) or asynchronously (25.2%). In 57.5% of the patients, glomus tumours were encountered bilaterally. As far as the tumours' location is concerned, 179 carotid, 63 jugular, 50 vagal and 38 tympanic paragangliomas were encountered. In the majority of the cases (79%) the paraganglioma was initially presented as a palpable neck mass, whereas the clinical presentation included, also, other symptoms such as dysphagia, tinnitus, hearing loss and facial paralysis. Surgical excision was chosen for 62% of the patients, and radiotherapy or surveillance was preferred in the most complex cases. A recurrence was mentioned in 13 patients and the overall survival was estimated as high as 78%.

Conclusion

In patients with head and neck paragangliomas diagnostic imaging should always involve surveillance of the whole head and neck to detect possible synchronous asymptomatic multicentric tumors, especially in patients with a known relevant family history. As multiple paragangliomas may develop many years after the presentation of the first tumor, regular follow-up of these patients is required. Management of multiple head and neck paragangliomas should take into account the general condition of the patients, the size and tumours' location, the cranial nerves' function and possible synchronous tumors.

PO-317 | Adenoid cystic carcinoma of the head and neck: a retrospective review

Daniel Pedregal-Mallo [1]; *Fernando López* [2]; *Juan Pablo Rodrigo* [2]; *Andrés Coca* [1]; *José Luis Llorente* [3]

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Keywords

Adenoid cystic carcinoma; Salivary glands; Sinonasal tumors

Objective/Purpose

Adenoid Cystic Carcinoma (AdCC) is a rare tumor, with a yearly incidence of 3-4.5 cases per million, accounting for about 1% of head and neck malignancies. It is the most common tumor of the minor salivary glands, also one of the most common cancers of the major salivary glands, and can involve lacrimal and ceruminous glands, the nasal and paranasal sinuses, trachea, and larynx. The aim of this study was to describe our long-term outcomes in the management of AdCC of the head and neck.

Material and Methods

We performed a retrospective study of patients with AdCC of the head and neck surgically treated in the Department of Otorhinolaryngology – Head and Neck Surgery of a tertiary hospital, and referral center for the treatment of these tumors, between 1993 and 2017.

Results

We collected 42 patients with AdCC of the head and neck, 22 males and 20 females, with a mean age of 52 years (21 – 79). Most frequent location of primary tumor were sinonasal cavity (15), parotid gland (12), and minor salivary glands of oral cavity and pharynx (11). In 7 patients neck dissection was performed, fin-

ding lymph node metastases in 3 of them. The most frequent site of distant metastases was the lung. Perineural invasion was present in 55% of tumors. The majority of patients underwent surgery with adjuvant radiotherapy, but 24% of patients were previously treated in other centers with chemo/radiotherapy. Recurrence occurred in 38% of patients, with a mean time to relapse of disease of 56 months. Disease-free survival rates were significantly higher in the group of patients treated with surgery and adjuvant radiotherapy.

Conclusion

Considering the low incidence of this kind of tumor, patients with AdCC of the head and neck should be referred to centers with multidisciplinary teams and experience in the management of this disease to offer the best treatment option.

PO-319 | Surgical treatment of head and neck paragangliomas: 15 years experience of a Cancer Reference Center

Mariana Esteves Marques [1]; *José Carlos Pereira* [1]; *Rita Canotilho* [1]; *Cláudia Araújo* [1]; *José Oliveira Silva* [1]; *Paula Ferreira Pinto* [1]; *Catarina Baía* [1]; *Manuel Jácome* [1]; *Jorge Guimarães* [1]; *Joaquim Abreu de Sousa*[1]

(1) INSTITUTO PORTUGUÊS DE ONCOLOGIA PORTO

Keywords

Paraganglioma; Carotid Body Tumor; Vagus nerve

Purpose

Paragangliomas (PGs) are rare neuroendocrine tumors of extra-adrenal origin, derived from the neural crest originating in sympathetic or parasympathetic paraganglia. Parasympathetic PGs originate from non-chromaffin cells and are located predominantly in the head and neck region, namely in the bifurcation of the common carotid artery (carotid body tumor), in the jugular foramen, in the middle ear and in the cervical portion of the vagus nerve. Most are non-functioning. Head and neck PGs are rare tumors, with a global incidence of 1/300,000 individuals per year, and may be sporadic or appear in the context of a familial syndrome.

Objective

The authors' objective is to describe the experience of a Portuguese Cancer Reference Center with cases of head and neck PGs surgically approached by Surgical Oncology.

Material/Methods

We retrospectively investigated the demographic, clinicopathological and radiological data of patients diagnosed with PG of the head and neck, who were surgically treated at our center, under the care of Surgical Oncology, between 2006 and 2021.

Results

23 patients diagnosed with head and neck PG were surgically treated, one of them with bilateral tumor. Sixteen (69.6%) of the patients were female. The median age at diagnosis was 50 years (29-78). Seventeen carotid body tumors and 7 PG of the cervical vagus nerve were operated. The median diameter of the tumors was 3,6cm. None of the patients had synchronous extracervical PGs.

In 3 patients (13%), the PGs diagnosed were producers of catecholamines. Nineteen patients (82.6%) were symptomatic at the time of diagnosis, with the most common chief complaint being the perception of a new palpable neck mass. Six (26%) patients had SDHB gene mutation. In 2 cases, angioembolization was performed in the preoperative period. Eight patients (34.7%) had postoperative morbidity, and in 3 of these patients it was not possible to preserve the vagus nerve intraoperatively. One patient died after surgery. All 22 other patients are alive and during the follow-up, 3 (13%) patients had disease recurrence, 1 having been reoperated, with surgical cure achieved. None of the patients had distant metastases in this period.

Discussion / Conclusion

Surgery is the definitive treatment in patients with cervical PGs. As it is a rare neoplasm it is important to concentrate the treatment of this disease in differentiated reference centers, with dedicated teams, so that the PGs are treated with the minimum of complications and the best associated oncological outcome.

PO-320 | The treatment of the patients with oropharyngeal cancer with the use of Da Vinci Xi system.

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(1) Poznan University of Medical Sciences

Keywords

TORS, oropgaryngeal cancers, margins.

Purpose/Objective

Radiochemotherapy is still the first line treatment for most oropharyngeal cancer patients. TORS may be a valuable surgical alternative for patients with early-stage oropharyngeal cancer, allowing to avoid adjuvant treatment completely or limit it only to radiotherapy. Our goal was to evaluate the results of surgical treatment of patients with oropharyngeal cancer using the Da Vinci system.

Material/methods

There were 91 patients with oropharyngeal cancer who had TORS using the Da Vinci Xi system (Intuitive Surgical, Inc., Sunnyvale, CA) in the period from March 2019 to September 2202 in the Department of Head and Neck Surgery of Poznan University of Medical Sciences.

Results

Out of 91 operations performed 76 were partial pharyngectomies (72 with neck dissection) and 15 resections of the base of the tongue tumor (3 with neck dissection). In the postoperative pathological report the margins of the removed tumor were assessed. In 26 (28,5%) patients, margins were negative. In 42 (46,1%) margins were close and in 23 (25,2%) margins were positive. Postoperative complications were reported in 10 patients (10.9%). 77 (84,6%) patients were qualified for adjuvant treatment by the decision of the MDT.

Conclusion

TORS is an effective , safe and minimally invasive method of treating cancers of the head of the neck. Our results were similar to the data available in the literature.

PO-321 | PTHrP and its receptor in locally advanced laryngeal cancer, as predictors of relapse and survival

Stefano Settimi [(1)]; *Dario Antonio Mele* [(1)]; *Eugenio De Corso* [(1)]; *Marco Corbò* [(1)]; *Alessandro Cantiani* [(1)]; *Franco Oreste Ranelletti* [(1)]; *Giovanni Almadori* [(1)]

(1) Università Cattolica del Sacro Cuore, Rome

Background

Parathyroid hormone-related peptide (PTHrP) overexpression and poor patient outcome have been reported for many human tumors, but no studies are available in laryngeal cancer.

Methods

We conducted a retrospective exploratory study on PTHrP and parathyroid hormone-related peptide receptor type 1 (PTH1R) expressions in primary locally advanced laryngeal squamous cell carcinomas (LALSCC) of 66 patients treated with bioradiotherapy with cetuximab.

Results

PTHrP/PTH1R expression in LALSCC was associated with tumor grade and histology. Poorly differentiated tumors, with worse prognosis, expressed PTHrP at nuclear level and were PTH1R negative. PTHrP and PTH1R were expressed, at cytoplasmic level, in normal larynx epithelium and more differentiated laryngeal cancer cells, suggesting an autocrine/paracrine role of PTHrP in squamous cell differentiation as well as a paracrine role, PTH1R-dependent, of PTHrP in well differentiated tumors with good prognosis.

HER1 and nuclear PTHrP were expressed in poorly differentiated tumors, consistently with the known up-regulation of PTHrP gene by HER1 signaling.

Conclusions

Our results suggest that in LALSCC nuclear PTHrP and absence of PTH1R expression could be useful in predicting response and/or resistance to cetuximab in combined therapies, contributing to an aggressive behaviour of tumor cells downstream to HER1.

PO-323 | The impact of frailty in oral cancer surgical patients - a prospective study

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Keywords

Frailty, oral cancer, head and neck cancer, quality of life

Purpose/Objective

Oral cancer and its treatment can affect essential functions such as breathing and swallowing, as well have a profound impact on aesthetic appearance, thus interfering with the patient's quality of life. The complexity of the disease, as well as it's preferential targeting of an aging and population with many comorbidities and less social support, requires specific treatment for each patient. Frailty is a complex geriatric syndrome, independent of age characterized by high vulnerability to stressing factors and diminished adaptation capacity.

Several studies suggest an association between frailty and a higher frequency of adverse effects in surgical cancer patients, namely mortality, morbidity and increased length of stay. Our objective is to define the impact of frailty in oral cancer surgical patients, specially focus in elderly patients

Material/methods

A literature review was undertaken in the PubMed/MEDLINE and Science Direct databases concerning frailty, oral cancer and quality of life (QoL). A prospective study was performed from june 2021 to june 2022.

Patients with oral cancer with more than 65 years proposed for primary surgical treatment were included, and comprehensi-

ve assessments of quality of life (EORTC HN 35), frailty (G8, The Modified 5-Item Frailty Index, Clinical Frailty scale) were asked at baseline and 12-month post-operative visits. Tumor location and staging, surgical and medical complications, time of staying and the need of readmission as well as the need of adjuvant treatments were accessed.

Results

This study included 40 patients, with an average age of 75 years old (65 to 98), and a distribution of 20 males and 20 females. According to the literature review frailty was classified as mFi ≥2 and it was present in 55% of the patients (n=22). Comparing non frail and frail patients, frail patients had longer length of stay, more medical and surgical complications, including need of intensive care unit (n=2). In general, 30% (n=12) of the patients had surgical complications classified as Clavien-Dindo ≥II, but only 4 patients required surgical intervention, three of them frail. Six patients died during the first year of follow-up, all of them with mFi ≥1.

Conclusion

Although additional study with prospective analysis are needed, frailty should be considered on oncological therapeutic decisions as well as in the prognostic factor of geriatric oral cancer patients. Adding frailty pre-operative assessments into clinical practice may be an important source to anticipate outcomes and lead to optimal care.

PO-324 | Observation or neck dissection for sentinel node positive in cutaneous head & neck melanoma?

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Keywords

Positive sentinel node biopsy, neck node dissection, head and neck cutaneous melanoma

Purpose/Objective

According to recent studies, CLND has been associated with improved disease-free survival, but not in melanoma-specific mortality. Therefore, watchfull waiting may be an acceptable alternative. However, the representation of melanoma of the head and neck (CHNM) in these publications is small. Our objective is to evaluate the prognostic value of neck dissection and whether there is a factor correlated with the presence of metastases in non-sentinel lymph nodes (NSLN).

Material/Methods

Retrospective study on patients with CHNM submitted to excision of the primary tumor or widening of surgical margin and positive SLNB, treated in a portuguese oncology center between April 2010 and April 2021.

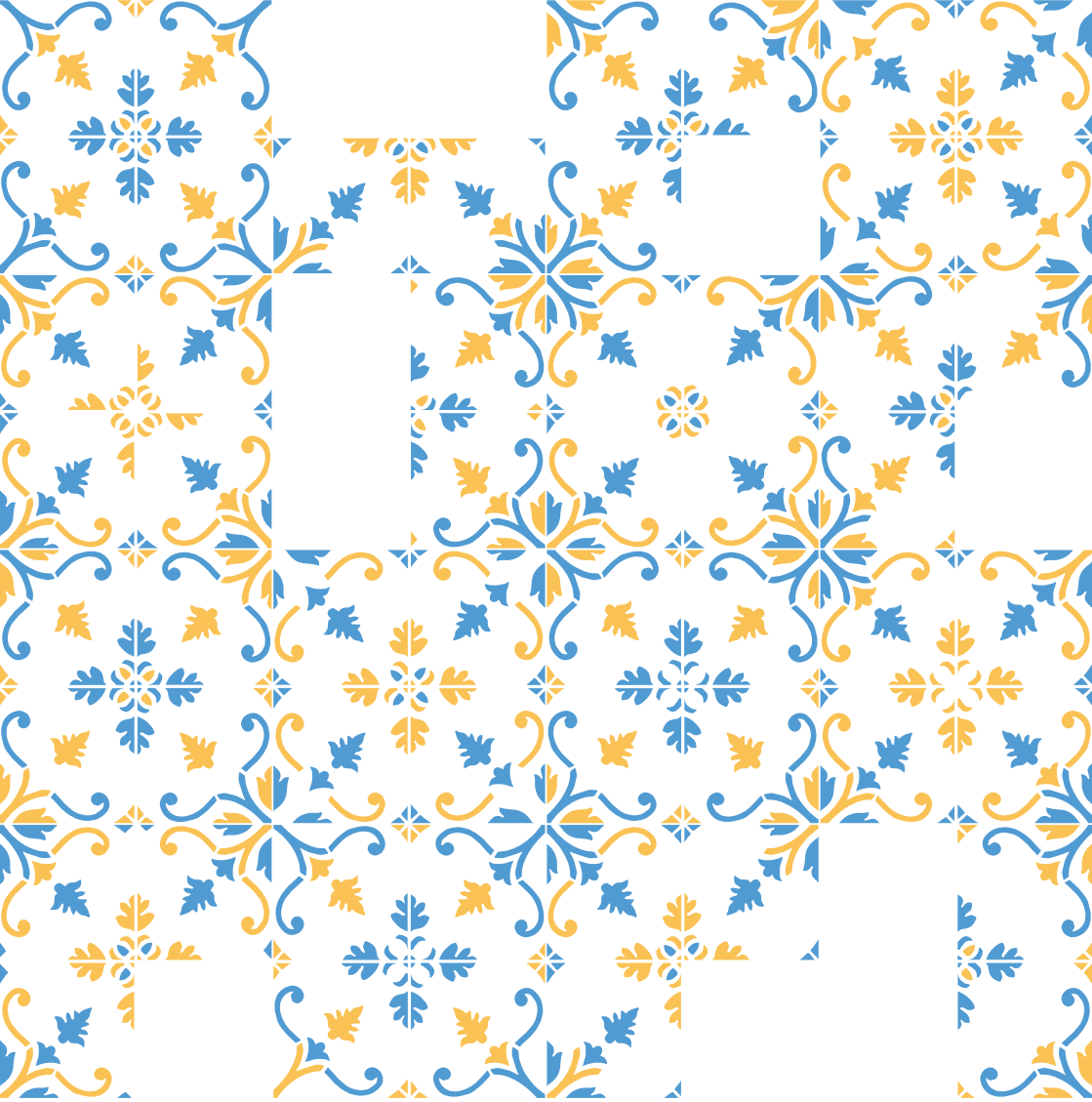
Results

Fifteen patients were included: 12 men (80%) / 3 women (20%); median age 68 (min - 43-max -84) years. The primary tumor had a median breslow depth of 3.8± 6,30 mm and eight (53.3%) of them had ulceration. Median follow-up was 36 months (95% CI 11-49 months). Ninety-three patients did not undergo complete

lymph node dissection after positive sentinel lymph node(SLN). Five (35.3%) had at least one positive non-sentinel lymph node. There was no difference in the two years of overall survival between the group with negative NSLN and positive NSLN (77.8 ± 13.9% vs 60.00 ± 21.9 p= 0.511). The risk of recurrence and distant metastasis after positive SLN was significantly higher (100 vs 55,5%, p = 0.035) in the positive NSLN's group. There was no statistically significant correlation between positivity in non sentinel lymph nodes and the primary tumor´s clinical and histopathological characteristics [histological type (p=0.202), localization (p=0.186), breslow depth (p=0.268), ulceration, (p=0.649), number of mitoses (p=0.084), regression (p=0.700), satelitosis (p=0.870)]. There's also no statistically significant correlation between positivity in non sentinel lymph nodes and histopathological characteristics of the positive SLN [number of positive SLN (p=0.956), proportion of positive NLS (p=0.377), maximum tumor deposit size (p=0.819), extracapsular extension (p=0.343)].

Conclusion

According to the recent studies, active surveillance with ultrasound in CHNM could be an acceptable alternative. There isn't any characteristic in this cohort more correlated with non sentinel lymph node positivity.



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