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9. TRANSORAL ENDOSCOPIC THYROIDECTOMY: A SINGAPOREAN PERSPECTIVE

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10. INCIDENCE, TREATMENT AND OUTCOME OF MALIGNANT PAROTID TUMOURS

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11. UTILIZING DIGITAL METHYLATION PCR FOR DETECTION OF HEAD AND NECK SQUAMOUS CELL CARCINOMA

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12. A NOMOGRAM BASED PROGNOSTIC SCORE THAT IS SUPERIOR TO CONVENTIONAL TNM STAGING IN PREDICTING OUTCOME OF SURGICALLY TREATED T4 BUCCAL MUCOSA CANCER: TIME TO THINK BEYOND TNM

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13. POSTOPERATIVE STAGING OF THE NECK DISSECTION USING EXTRACAPSULAR SPREAD AND LYMPH NODE RATIO AS PROGNOSTIC FACTORS

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1. To study the role of diffusion weighted MRI in predicting response to concurrent chemoradiotherapy or radical radiotherapy in locally advanced laryngeal and hypopharyngeal malignancy as part of the organ preservation protocol

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**Rationale:** Globocan fact sheet reports, approximately 130,000 new laryngeal cases and about 70,000 deaths annually while hypopharyngeal cases are less common. Laryngeal and hypopharyngeal malignancies have been traditionally offered surgery which severely affected the patient’s quality of life (impaired swallowing and speech deficit) as well as social losses due to cosmetic deformity. Organ-preserving approach with concurrent chemoradiotherapy or radical radiotherapy followed by salvage surgery in case of residual or relapse, has now been accepted as a standard of care. However, not all patients respond to the treatment and end up undergoing surgery. Hence if outcome can be predicted at an early stage of treatment using imaging biomarkers like diffusion weighted MRI (dWMRI). The treatment outcome may be improved by using an optimized and tailored treatment strategy.

**Materials and methods:** A total of 19 patients locally advanced laryngeal & hypopharyngeal malignancies, treated with organ preservation intent. They were assessed for treatment response with dWMRI at baseline, first week, fourth week and at first follow up. The ADC values were compared and correlated with treatment response.

**Results:** The pretreatment ADC (ptADC) values were correlated with the treatment response. Based on the results of this study, ptADC could predict treatment response with a sensitivity of 80% and specificity of 62%. It was observed that an abrupt rise from the ptADC to the first week ADC was characteristic of complete response while a gradual rise of ADC was suggestive of partial treatment response. There was correlation between ADC values at different time points and also between ptADC and pretreatment size. However, these observations have to be validated over a larger study population, before it can used in routine clinical practice.

**Conclusions:** The dWMRI with the ADC values allowed early response prediction which correlated with tumour response. The rate of increase in the ADC value is independent of the ptADC and is useful in response prediction. The slow rise or no change in the ADC values may predict partial or no response. Thus early treatment response prediction would help in offering individualised treatment by administering early surgical interventions in case of non responders or offer dose escalation / boost radiotherapy in case of partial treatment response.
2. HDR Interstitial brachytherapy in Recurrent head and neck cancer: An effective Salvage option

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Rationale: High Dose Rate (HDR) Interstitial Brachytherapy has an established role in head and neck malignancies and offers good survival rates, however, there are scant data on improved local control (LC) and treatment-related complications in patients with recurrent head and neck cancers.

Materials and methods: Twenty-Five patients with recurrent H&N cancers were treated with HDR interstitial brachytherapy between January 2010 and December 2016. Primarily, 6 had received EBRT alone, 6 had underwent surgery alone and 13 had both the treatment modalities received. Of these, 75% received radical brachytherapy and 25% received external beam radiation therapy (EBRT) followed by brachytherapy boost. The treatment sites were oral cavity (15/25) and oropharynx (10/25). The median dose was 4.5 Gy twice per day with median total dose with brachytherapy of 40.5Gy in radical and 27Gy for EBRT cases. The EBRT median total was 46Gy. HDR Interstitial Brachytherapy was initiated from next day of implant and after removal of the catheters, the patients were followed up as per the institutional protocol and were assessed for survival outcomes and toxicities.

Results: With a median follow-up of 25 months, 4 local recurrences were observed within first year of follow up after the procedure. The 2-year local control and overall survival outcomes for the entire group were 58.3% and 83.3%, respectively. The 4-year disease free survival was 50% and distant metastases was seen in 33.3% at 5 years. The dosimetric assessment revealed D90 – 4.07Gy, V100 – 90.3%, V150 – 23.7% and V200 – 12.5%. Homogeneity index and Dose Non Uniformity Ratio were 0.71 and 0.37 respectively. Mean interval between the EBRT and Brachytherapy was 16 days. Median implant volume was 85 cc. On toxicity assessment, xerostomia, altered taste and dysphagia was seen as major complications albeit in grade I and II. Grade III toxicity was only 2% and no Grade IV Toxicity was seen. BED and EQD2 of 44Gy and 38Gy respectively were significant in preventing late toxicities and improve the survival outcomes.

Conclusions: The results of HDR Interstitial brachytherapy have shown an acceptable local control and overall survival rates along with tolerable toxicities and morbidity in recurrent H&N cancers. Based on these encouraging results, prospective clinical trials are warranted using HDR Interstitial Brachytherapy.
3. Metastatic Cutaneous Squamous Cell Carcinoma of the Parotid Gland: Prognostic factors and Patterns of Relapses. Results from a Tertiary Australian Institution

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Rationale: To analyse the outcomes of patients with advanced cHNSCC.

To examine the influence of patient, tumour, and treatment factors on loco-regional recurrence.

Materials and methods: We conducted a retrospective review of all patients with cHNSCC and metastatic disease to the parotid gland. Patients were treated with parotidectomy and neck dissection, followed by PORT between 1997 and 2017.

Results: 127 patients were identified. Median follow-up was 22.9 months. 84% were males with median age of 73 (range 39-92). 15% were immunosuppressed (haematological 9%, renal transplant 3%, HIV 2%, rheumatological 1%).

Poor tumour differentiation was seen in 53% and positive margin in 46%. Perineural invasion (PNI) was seen in 36% and lymphovascular invasion (LVSI) in 20%. Cervical lymph nodes were involved in 34%.

Electrons were used in 44%, 3D-conformal Radiation Therapy in 24% and Intensity Modulated Radiation Therapy in 32%. Median RT dose was 60Gy (range 45-70Gy).

The 1, 2, and 5-year disease free survival (DFS) rates were 78%, 70% and 70% respectively. Loco-regional recurrence was seen in 26%. Eleven percent developed metastatic disease (predominately lung, other sites included liver, brain and bone). Median time to recurrence was 9 months (range 2 to 181 months).

Deaths from other causes were classified as lost to follow-up. The overall survival rates at 1, 2 and 5 years were 76%, 67% and 59% respectively.

The parameters that significantly correlated with DFS were positive margin status, PNI, LVSI and involved cervical lymph nodes.

Conclusions: Our data supports that combined modality treatment with surgery and adjuvant radiotherapy provides good loco-regional control in patients with metastatic cHNSCC to the parotid gland.
4. An Algorithm for Primary Closure of Free Fibula Flap Donor Site

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Rationale: Free flap surgery enjoys great success rates these days. An experienced reconstructive surgeon should now be re-directing his attention to minimizing complications not only of the reconstruction but also of the donor site. The free fibula flap is the workhorse flap for bony reconstruction of head and neck defects. Traditionally the donor site of this flap is closed with a skin graft. Closure with a skin graft is not without complication and the cosmetic outcome pales in comparison to a primarily closed donor site. We propose a new algorithm based on our surgical experience that enables the primary closure of the free fibula donor site without undue wound tension.

Materials and methods: Retrospective review of prospectively collected data on 30 patients operated on by two experienced surgeons over 18 months period.

Results: Algorithm:

(1) defects less than 3 cm: primary closure; (2) defects 3 – 6 cm: we propose 3 techniques based on the configuration of available perforators at the donor site – propeller proximal peroneal perforator flap, freestyle propeller myo-cutaneous perforator flap or tear-drop design of the skin paddle; and finally (3) defects more than 6 cm: we raise a chimeric flap consisting of a proximal lateral leg perforator flap for soft tissue coverage combined with a fibula bone flap for the bony reconstruction; the donor site of the proximal lateral leg perforator flap in most instances can be closed primarily.

Conclusions: By adopting this algorithm, we were able to achieve primary closure of more than 90% of our free fibula flap donor sites.
5. **Clinical prognostic factors in patients with local relapse and/or metastatic adenoid cystic carcinoma of the salivary glands**

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**Rationale:** Adenoid cystic carcinoma (ACC) is characterized by a prolonged natural history. Local relapses (LR) are common and distant metastases (lung, liver, bone, brain, etc) can appear during the years in at least 50% of the patients. Not all metastatic sites seem to have the same prognosis, lung metastasis (LM) having a better survival. To confirm these data, we have reviewed our institutional series of patients with metastatic ACC.

**Materials and methods:** Clinical case records of metastatic ACC patients (pts) referred to our Unit since 2008 have been retrospectively analyzed. Follow-up (FU) and overall survival (OS) were measured in years (yrs) from the diagnosis of metastatic disease to death or last follow-up and were estimated with Kaplan Meier method. Survival curves were compared with log-rank test.

**Results:** In a ten-year period (2008-2017), 200 pts (85 men; median age 50 yrs, range 19-76) with relapsed and/or metastatic ACC have been observed with a median FU of 5.9 yrs.

In the overall population 134 pts had only LM, the others (66) had distant visceral disease at different sites (28 liver, 24 bone, 14 other). mOS in pts with only LM and in those with extra-pulmonary disease were 6.9 and 2.6 years, respectively (p<0.0001); mOS in pts with liver metastases was longer than in those with bone disease (3.5 vs 1.5 years, p=0.03). Overall mOS was 5.3 yrs for all series (6.3 yrs in women vs 4.6 yrs in men, p=0.016).

Time to first metastasis was longer in pts with LM than in those with extra-pulmonary disease (3.6 vs 1.9 yrs, p=0.0006).

The first site of relapse was locoregional in 39 pts (group A) and distant in 161 pts, among these 29 had both LR and distant metastases (group B). mOS was 14.9 and 9.8 yrs in group A and B, respectively (p=0.004).

**Conclusions:** In this large and homogeneous single center experience, pts with distant relapse, with or without LR, seem to have a worse prognosis than those with only LR. We confirm that LM is associated to a better outcome; likely a longer time to relapse could underlie an intrinsically indolent disease in pts with LM. As already observed in the scientific literature, a worse OS has been observed in patients with bone and liver metastasis.
Soft tissue metastasis in head and neck carcinomas – an undefined pathological entity

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Rationale: Head and neck cancer patients with advanced disease, especially elderly patients, show contiguously located soft tissue metastasis (cSTM) in the postoperative neck dissection specimens. These specimens contain histopathologically metastatic tissue without evidence of primary lymph node tissue. Currently, for these cases there is no distinct staging according to the UICC/AJCC TNM system.

Materials and methods: A total of 610 consecutive patients with head and neck cancer operated between 01/14-12/16 were analyzed retrospectively. 17 (2.8%) showed cSTM. Histopathological slides were assessed twice by achieved by independent examiners, to differentiate cSTM and metastatic lymph nodes of the neck.

Results: The average follow-up of patients with cSTM was 33.2±9.3 months after diagnosis. Mean age at diagnosis was 65.6±11.7 years (f n=2; 11.8%). Primary tumor subsites were: oral cavity (n=1), oropharynx (n=12), Hypopharynx (n=2), Nasopharynx (n=2), Gl. Parotidea (n=1)). 3 patients (17.6%) showed a distant metastasis at time of primary diagnosis; In Patients with oropharyngeal squamous cell carcinoma six patients (50%) were p16 – positive. Three (17.6%) patients showed a recurrence of disease. Squamous cell carcinoma was detected in 15 (88.2%) patients, further adenocarcinoma (n=1) und undifferentiated carcinoma (n=1) were found.

Conclusions: Currently there is no clear guideline whether cSTM should be staged as regional or distant metastasis, a difference in diagnosis which changes the management of the patient completely. This study exclusively reports on a cohort with STM contiguously located to the primary tumor and results will be compared to current literature.
Role of SAMITAL® in prevention and treatment of chemo-radiotherapy induced oral mucositis in head and neck squamous cell carcinoma patients: a randomized double blind phase 2 clinical trial. A preliminary study

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Rationale: In patients affected by head and neck cancer, the onset of severe oral mucositis is a decisive factor in completing concurrent radio-chemotherapy. Nowadays, few interventions have demonstrated a modest benefit in the prevention or treatment of oral mucositis.

Materials and methods: The primary study aim was to evaluate the role of SAMITAL® in reducing the incidence of grade 3/4 severe mucositis induced by concurrent radio-chemotherapy; secondary aims were to evaluate the tolerability and patient reported quality of life measures. All patients received 60-70 Gy radiation therapy (3D-CRT or IMRT) and induction or concomitant chemotherapy. Patients were randomized to one of two treatment arms, SAMITAL® Granules for Suspension 20 mL (Vaccinium myrtillus extract 40 mg, Macleaya cordata alkaloids 70%, 2.7 mg, and Echinacea angustifolia extract 0.6 mg), four times daily or matching placebo in a 1:1 way using a stratified block randomization scheme by disease site (oropharynx and oral cavity versus other) and type of chemotherapy (induction plus concomitant versus concomitant). All patients were submitted to weekly endoscopic evaluations and the presence of mucositis was measured by the World Health Organization and Oral Assessment Guide scores. In addition, patients’ outcomes were reported by using the Xerostomia Questionnaire, EORTC QLQ-C30 and QLQ-H&N35.

Results: 120 stage III-IV squamous cell carcinoma patients were enrolled between December 2012 and September 2016 in a double blinded, randomized, placebo, controlled phase 2 clinical trial at the Veneto Institute of Oncology, Padua, Italy.

Patients received a median total dose of 66 Gy in both groups (89.7% were treated with IMRT).

Overall, the incidence of severe mucositis was 51.7%, 45.8% in the SAMITAL® and 57.9% in the Placebo arm (OR=0.6 - 95%CI: 0.3; 1.3). The efficacy analysis stratified by randomization factors highlighted a statistically significant reduction in the probability of developing severe mucositis in patients treated with SAMITAL® who did not receive induction therapy (OR=0.3 - 95%CI: 0.1;0.8).

After radiotherapy, patients randomized to SAMITAL® reported a significantly lower xerostomy, coughing and swallowing scores and a better quality of life.

Conclusions: SAMITAL® seems to be able to reduce the incidence of severe mucositis in a well-defined subgroup of patients and an improvement in patients’ quality of life supports this finding.
8. No significant benefit to the addition of docetaxel to cetuximab monotherapy in second line treatment of advanced head and neck squamous cell carcinoma

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**Rationale:** The combination of cetuximab and docetaxel has been used in various protocols mostly in induction therapy with cisplatin as TPE. Some authors have proposed the use of cetuximab and docetaxel in second line treatment of patients not suitable for EXTREME therapy. Our department has been performing this combination therapy on some suitable patients as escalation of cetuximab monotherapy. With the onset of checkpoint inhibitors dominating this treatment phase we wanted to evaluate if the combination therapy showed any benefit in retrospective analysis.

**Materials and methods:** 103 patients were treated between 2010 and 2017 were selected from treatment records. 64 of these had been treated with cetuximab monotherapy, 39 patients with cetuximab and docetaxel.

Cetuximab was administered as 400mg/m² loading dose and 250mg/m² continuation. Docetaxel was administered as 75mg/m² infusion every 3 weeks. Initial staging was after 8 weeks, after that every 3 months. Patients were stratified by age, gender, tnm and hpv grading and whether primary treatment was operative or via chemotherapy and radiation. Haematological side effects, progression free and overall survival were analyzed.

**Results:** Progression free survival was 4.5 and 5.5 months for cetuximab and cetuximab and docetaxel respectively. Overall survival was 9.1 and 8.0 months median (38% and 36% after one year) for cetuximab and cetuximab and docetaxel respectively. Two patients died as a direct result of neutropenia related to docetaxel.

**Conclusions:** In our retrospective analysis we do not see a significant benefit to the inclusion of docetaxel to cetuximab in the second line setting. This is exacerbated by the hematological side effects due to docetaxel.
9. Transoral Endoscopic Thyroidectomy: A Singaporean Perspective

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Rationale: In the last 3 years, there has been an enthusiastic crop of publications endorsing the transoral endoscopic method. Contradictorily, there are also detractors who acknowledge its feasibility but challenge its safety and long-term oncologic outcomes. In the largest national series to date, we explore our early experience with the transoral vestibular approach.

Materials and methods: 33 patients were operated on by 4 head and neck surgeons from 2 institutions within a 2-year period from December 2015. Inclusion criteria were nodules less than 5cm, no previous neck surgery or radiotherapy, absence of suspicious cervical nodes, and patient choice.

Results: All patients were females, mean age of 41 years (range 22-69). We were able to remove thyroid lobes up to 7.3cm (mean 5.33cm), with multiple nodules up to 4.4cm. 8 patients (24.2%) had a pre-operative diagnosis of papillary carcinoma on fine needle aspiration cytology.

As we progressed along our learning curve, the minimum operative time for a hemithyroidectomy was 75 minutes (mean 165mins), which approximated timing for open surgery (mean 101mins). There was no clinical difference in the length of stay (2.7 vs 2.1 days for open). The incidence of hypocalcemia was nil, and no cases of recurrent laryngeal nerve injury. Drains were placed only for patients who underwent total thyroidectomy (n=4).

1 patient experienced submental paraesthesia which resolved at 3 months. There was 1 case of post-operative seroma formation requiring aspiration at 2 weeks, and 1 minor dermal injury from diathermy. There were 2 conversions to open surgery — 1 to facilitate central compartment neck dissection after tracheo-esophageal nodes were found positive for metastatic carcinoma on frozen section, and another after prolonged dissection as planes were fibrotic from thyroiditis.

Conclusions: Transoral endoscopic thyroidectomy is gaining acceptance as a cosmetically superior alternative for definitive treatment of thyroid nodules and micropapillary cancers. However, as technical skills continue to mature, there still exists uncertain benefit for additional procedures such as nodal clearance. In view of the indolent nature of well-differentiated thyroid cancers and its excellent prognosis, demonstrating equivalence in terms of its long-term oncological outcomes may realistically never be achieved in the near future.
Incidence, treatment and outcome of malignant parotid tumours

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**Rationale:** Malignant salivary gland tumours are a rare entity that comprises between 1 and 5% of malignancy of the head and neck. Primary parotid cancers represent between 70 and 80% of all salivary gland cancers. Its wide histological variety and its uncertain evolution pose a challenge when it comes to categorizing them and proposing their treatment.

**Materials and methods:** There are few epidemiological studies of parotid cancer in our country. The aim of this study is to review the cases treated in our department from 2007 to the present, and to evaluate patterns of treatment and survival, making a comparison with the literature. The data collection was carried out through a systematic review of the files of the oral and maxillofacial surgery department of our hospital, evaluating the clinicopathological characteristics of the tumours (histology, growth pattern ...), age of the patient, treatment ...

**Results:** After the analysis of the results, a predilection for the male sex in patients in the sixth decade of life is shown. The superficial lobe is the most frequently affected and the palpable mass is the most frequent presenting symptom. Our patients presented an average evolution prior to the diagnosis of 10 months and the most frequent treatment was surgery, evaluating in an individualized way the need to complete the treatment with a therapeutic or prophylactic lymph node dissection, and in 15% of the cases, hidden cervical metastasis were found. In the follow-up, our series showed a 95% survival rate at the first year, and 87% at the fifth years, with patients with N-positive or high histological grade being the once with higher mortality.

**Conclusions:** In conclusion, these are rare tumours, with diverse histology and uncertain prognosis, the treatment of which is difficult and must be addressed individually. The incidence of malignant parotid tumours increases in elderly patients. The age of the patient, the histological grade of the tumour and the TNM staging are the best predictors of survival.
11. Utilizing digital methylation PCR for detection of Head and Neck Squamous Cell Carcinoma

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Rationale: Promoter methylation of the tumour suppressor genes has been previously observed in the various type of cancers, including Head and Neck Squamous Cell Carcinoma (HNSCC). It is hoped that using the detection of the methylation signature could act as the marker for early detection and diagnosis of HNSCC, which will allow identification of patients at an earlier stage of the disease. Here we evaluate the use digital droplet PCR detection of methylation markers in the early detection of HNSCC.

Materials and methods: Tumour and paired normal tissues were prospectively collected from eligible HNSCC patients, also along with the collection of tissues from non-cancer control subjects. Promoter methylation of reported tumour suppressor genes in HNSCC patient tumour tissues, HNSCC oral rinses, normal control tissues and normal oral rinses were assessed using digital droplet PCR. The data was analysed by Mann-Whitney U test, Student’s t-test comparison of means and ROC analysis of the samples for sensitivity and specificity with MedCalc Statistical Software version 17.6 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2017).

Results: Samples from 55 HNSCC patients and 26 non-cancer subjects were analysed. (Patient age range: 31 yr-92 yr, median: 66 yr; Gender: 39 M, 16 F). Using digital droplet PCR there was significant difference in the methylation density of PAX5 (P<0.001), EDNRB (P<0.001), DCC (P<0.001), MGMT (P<0.007), DAPK (P<0.03) and P16 (P = 0.03) when comparing HNSCC with paired normal tissues. PAX5 (P<0.001), EDNRB (P<0.001), DCC (P<0.001) shown aberrant methylation when compared with control tissues. A further analysis of oral rinses between HNSCC and control patients for PAX5 showed a sensitivity of 89.1% and specificity of 73.1% (PPV: 87.5%, NPV: 76%). EDNRB demonstrated a lower sensitivity of 46.4% and specificity of 92.3% (PPV: 89.7%, NPV: 44.2%) for oral rinses when compared between HNSCC and control patients.

Conclusions: Using digital methylation PCR may provide a sensitive method for the detection of HNSCC, with the usage of the PAX5 methylation detection in oral rinse setting could provide a relative less invasive method for the detection of HNSCC.
12. A nomogram based prognostic score that is superior to conventional TNM staging in predicting outcome of surgically treated T4 buccal mucosa cancer: time to think beyond TNM

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**Rationale:** T4 squamous cell carcinomas of the buccal mucosa are known to have ominous outcome. The TNM consists of the size of the primary tumor (T stage), description of regional Nodal metastasis (N stage), and distant metastasis (M stage). Consequently, clustering of various subsets of TNM categories are clubbed into four stages. But this clustering results in a loss of accuracy because, for example, a patient with a T4N0M0 carcinoma may biologically be very different from a patient with a T1N2M0 carcinoma, whereas but both these tumors are classified as stage IV. The aim of this study was to develop a nomogram for and demonstrate the difference in survival based on prognosticators beyond those covered by the traditional TNM staging system.

**Materials and methods:** Medical records of treatment naïve 205 T4 buccal mucosa cancer patients were analyzed. A nomogram was developed using multivariate cox- regression. The nomogram was validated internally by bootstrapping and externally in an independent validation set of 198 patients. This is one of the largest series of T4 oral cancer patients in the literature.

**Results:** By multivariate logistic regression analysis using the stepdown model reduction method, pathological lymph nodal status, tumor differentiation, perineural invasion and bone involvement were found to be independently associated with OS (p < 0.05). Based on this Cox proportional hazard model, a nomogram was developed to calculate the probability of survival within three years. The nomogram was found to have a c-index of 0.7266 for predicting the three year OS. Based on nomogram, a score was assigned to each patient and they were divided into two groups based on Youden derived cut-off value (13.5). In the training set, the three year survival rate for patients in Group I and Group II was found to be 83.1% and 42.1% respectively (p <0.00). Similarly, in validation set 3- year survival in Group I and Group II was found to be 79.8% and 29.7% 16 respectively (p <0.00). Comparable sensitivity and specificity of nomogram for predicting survival was observed in both validation and training sets.

**Conclusions:** Nomogram is one robust alternative to TNM staging which can be efficiently utilized for both, prognostication of individual patient as well as development of a new score based simple, flexible and comprehensive staging system.
Postoperative staging of the neck dissection using extracapsular spread and lymph node ratio as prognostic factors

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Rationale: The presence of lymph nodes with extracapsular spread (ECS) and the lymph node ratio (LNR) have prognostic capacity in the pathological evaluation of patients with head and neck squamous cell carcinoma (HNSCC) treated with neck dissection. The purpose of this study was to assess the prognostic capacity of the pathological classification of the neck dissection obtained evaluating ECS and LNR together and to compare this classification with the 8th edition of the TNM classification.

Materials and methods: We carried out a retrospective study of 1383 patients with HNSCC treated with a neck dissection between 1985 and 2013. We developed a classification of the patients according to the presence of nodes with ECS and the LNR value with a recursive partitioning analysis (RPA) model.

Results: We obtained a classification tree with four terminal nodes: for patients without ECS (including pN0 patients) the cut-off point for LNR was 1.6%, while for patients with lymph nodes with ECS it was 11.4%. The 5-year cancer-specific survival for patients without ECS and LNR <1.6% was 83.3%; for patients without ECS and LNR ≥1.6% it was 61.5%; for patients with ECS and LNR <11.4% it was 33.7%; and for patients with ECS and LNR ≥11.4% it was 18.5%.

This classification obtained greater differences in survival between stages (better hazard discrimination) and a more homogenous distribution of patients in each stage (better balance between groups) than those obtained when applying the criteria of the 8th edition of the TNM classification.

Conclusions: ECS status and LNR value proved high prognostic capacity in the pathological evaluation of the neck dissection. The combination of ECS and LNR improved the predictive capacity of the 8th edition of the TNM classification.