Importance: The majority of patients with oral cavity squamous cell cancer (OCSCC) present at an early stage (I and II). Treatment and prognosis have not changed significantly over recent decades. Although patient and tumor prognostic features have been analyzed extensively, there is a dearth of population level data examining how variations in treatment factors impact survival.

Objectives: Analyze treatment variables associated with survival in early stage (I and II) oral cavity squamous cell carcinoma using population level data.

Patients and methods: Patients diagnosed with stage I or II OCSCC between 2003 and 2006 and treated with surgery were identified in the National Cancer Data Base (NCDB). This database captures approximately 70% of incident cases of cancer in the United States. Univariate and multivariate analyses of overall survival based on patient, disease, and treatment characteristics were conducted.

Results: 6,830 early-stage OCSCC patients who underwent surgery were identified. Overall survival at 5-years was 69.7%. Treatment variables associated with improved survival in multivariate analysis included elective neck dissection (HR 0.86; 95% CI 0.77-0.95), negative surgical margins (HR 0.79; 95% CI 0.68-0.93), treatment at an academic/research facility (HR 0.86; 95% CI 0.78-0.94), no insurance through Medicare (HR 1.37, 95% CI 1.20-1.56) or Medicaid (HR 2.01, 95% CI 1.65-2.45), and no treatment with radiation therapy (HR 1.30; 95% CI 1.15-1.47). Clinical characteristics including stage II disease (HR 1.57, p < 0.0005), intermediate tumor grade (HR 1.29, p < 0.0005), high tumor grade (HR 1.59, p < 0.0005), and disease of the floor of mouth (HR 1.56, p < 0.0005) were associated with decreased survival.

Conclusion: Treatment variables have significant associations with prognosis in early stage OCSCC. Survival variations between insurance carriers and treating facility types suggest differences in quality of care. Survival disadvantage associated with receiving radiation and not undergoing elective neck dissection may be due to selection bias and under-staging. Identifying underlying causes of survival differences associated with treatment variation may enable sharing of best practices and system based approaches to improve outcomes.
SUBCLASSIFICATION OF PERINEURAL INVASION IN ORAL SQUAMOUS CELL CARCINOMA: PROGNOSTIC IMPLICATIONS

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Background:

Perineural invasion (PNI) is an important negative predictors for outcome in patients with oral tumour. PNI is often reported as a homogenous entity, when tumour cells are noted within the perineural space, disregarding on whether it is a small nerve or large nerve; or whether only one nerve or multiple nerves are involved.

Aim:

We attempt to subclassify patients with histologic PNI to better stratify the adverse risks amongst patients with oral tumour.

Method:

Clinicopathological data of patients with oral tumour were obtained from a prospectively collected database (1995-2012) at a single institution. The pathology was re-reviewed by a senior pathologist (RG) for tumor differentiation, tumor depth, patterns of invasion (POI), PNI, lymphovascular invasion (LVI), bone invasion and margin status.

The patterns PNI are assessed and classified into (a)uni vs multifocal, (b) the size of the involved nerve (<=1mm vs >1mm), (c) the location of the involved nerve (at the advancing edge of the tumor front vs those >0.1mm away).

Statistical analyses included Chi-square test, Kaplan-Meier method, Cox regression

Results:

372 patients were identified with 93 patients (25%) having PNI, with median follow up of 1.6 years. Patients with multifocal PNI have worse prognosis compared to unifocal PNI, with 5 year disease specific survival (DSS) of 65% vs 85% (p=0.035) and 5 year local control of 74% vs 91% (p=0.016). The regional and distant control is similar between the two groups (p= 0.472 and p= 0.513 respectively).

Tumour involvement in nerve >1mm predicts worse local control compared to nerve <=1mm (5 year local control 57% vs 86%, p=0.028). No difference is noted in DSS (p=0.426), regional control (p=0.725) or distant control (p=0.495).

The location of the PNI whether it is at the edge of tumour or away from the tumour does not seemed to influence local control (p=0.916), DSS (p=0.425), regional control (p=0.198) or distant control (p=0.239).

Conclusion:
The data from this well characterised cohort indicate that presence of multifocal PNI is a significant predictor of DSS and local failure. The size of the involved nerve >1mm is also a significant predictor of local failure. While pathology reports may comment on multifocality of PNI, the size of the nerve is rarely measured. Objective inclusion of these parameters in reports would be useful to facilitate larger multicenter studies.
SIGNIFICANCE OF DEPTH OF INVASION IN SQUAMOUS CELL CARCINOMA OF BUCCAL MUCOSA
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Objective

1. To study if the depth of primary site invasion has an impact on neck node metastasis in buccal mucosal squamous cell carcinoma.

2. A comparison of the impact of depth of invasion in buccal carcinoma versus tongue carcinoma on nodal metastases.

Method and material

This is a retrospective study involving 130 consecutive patients of primary buccal and tongue squamous cell carcinoma who underwent surgery from January 2011 to October 2013. There were 72 buccal and 58 tongue carcinoma patients. All previously treated tumours and histopathology other than squamous cell carcinoma were excluded from the study.

Patients were divided into two categories for each of the two primary subsites-

1. Tumors with depth of invasion of 4mm or less (shallow invasion)

2. Tumors with depth of invasion of more than 4 mm (deep invasion)

Results

In buccal mucosal carcinoma, no patient out of 15 patients with a shallow depth of invasion demonstrated lymph node metastasis. Twenty-nine out of 57 patients with depth of invasion exceeding 4 mm presented with lymph node metastasis i.e. more than 50%. Results were compared with chi square test. Depth of invasion proved to be a statistically significant criterion in predicting neck nodal metastasis (p value < 0.05) in patients with buccal carcinoma.

When compared with squamous cell carcinoma of tongue, depth of invasion of the primary tumor in buccal mucosal squamous cell carcinoma correlated better with predicting presence or absence of neck metastases.

Conclusion

Depth of invasion is significant criteria for predicting neck node metastases in buccal mucosal squamous cell carcinoma.
A NEW CLASSIFICATION OF GINGIVAL SQUAMOUS CELL CARCINOMA (SCC)
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A unique group of gingival squamous cell carcinoma (SCC) patients who underwent dental extraction before diagnosis of malignancy has been overlooked. Gingival SCC probably mimicked ordinary dental disease initially, and therefore, the affected tooth was extracted by a primary clinician. In this unique group of patients, they may present with asymptomatic clinical features, exhibit distinctive mechanisms of bony invasion, and have worse treatment outcomes than those of non-extraction patients. Thus, a more sophisticated classification system is needed to gain a more comprehensive understanding of gingival SCC. We propose a new classification of gingival SCC based on dental status, as follows: dentate (type I), edentulous (type II) and dental extraction (type III). The aim of this study was to clarify the clinical implications of cases of recent dental extractions with a view to establishing a new classification of gingival SCC. Among 181 gingival SCC patients, those with type I and type II comprised 26% and 30%, respectively. Fifty-five patients (30%) were classified as type III and showed a high probability of bony invasion (80%), but a low 5-year survival rate (48%) than the other non-extraction groups. Consistent with previous studies, we found that our type III patients who previously underwent dental extraction tended to show more advanced malignancy which was characterized by an asymptomatic clinical presentation with earlier bony invasion through unhealthy periodontal ligament and that the tumor was likely growing from the inner epithelium of gingiva. Our proposed classification by dental status could be helpful in identifying a unique group of gingival squamous cell carcinoma (SCC) patients who present with more advanced disease status.
**S092 USE OF HOPKIN'S TELESCOPIC EXAMINATION AS AN OPD TOOL TO CLINICALLY EVALUATE AND RECORD ORAL CAVITY LESIONS: OUR EXPERIENCE IN EARLY DETECTION ESPECIALLY IN PATIENTS WITH LIMITED MOUTH OPENING FOR 2000 PATIENTS AND PILOT SCREENING PROJECT**

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**Aim:**

To use magnified view and reach of a slender telescope to document and evaluate oral cavity premalignant and malignant lesions, especially for patients with restricted mouth opening. Role of screening is very vital in high risk group.

**Material and Methods:**

A Ninety degree Hopkin's telescope is used to evaluate and document oral cavity examination in our Out Patients Department (OPD). The data of first 2000 patients was analysed. Difficult to reach areas, where mouth opening was severely restricted were the significant subset. 1394 Patients approached in OPD for primary diagnosis at our tertiary cancer care center. Second set of patients were the ones in follow up after treatment in form of Surgery, Chemotherapy or Radiotherapy, or combination (n=606). Telescope guided biopsies were also taken in 56 patients. Serial recordings were compared objectively in premalignant, treatment evaluation and close watch groups. A pilot project was done to screen a high risk group (n=127) of local community, out of which premalignant lesions were identified in 32 patients. Early malignancy was identified in 2 patients, who required surgeries subsequently.

**Discussions:**

Lip and Oral cavity cancers are leading cancers in India (Globocan 2012). Restricted moth opening due to Submucous fibrosis is very common in Indian patients. This is usually following prolonged insult with tobacco and/or Areca nut use. The pliability of buccal mucosa is restricted. Discolouration also masks subtle changes which are not visible with naked eyes. Many patients have near zero mouth opening. It is very difficult to evaluate, document and biopsy the lesions due to inability to access, vast area and diversity of premalignant lesions and subject variations. Slender Outpatient examination telescope was found useful tool in this. It was able to go in oral cavity and record with good illumination and magnification, which was an objective record for future comparison also. Telescope guided biopsies were also taken in outpatients from difficult to reach areas like floor mouth, retromolar triagone, which otherwise may have required under anaesthesia procedures.

**Conclusion:**

Hopkin's telescopic examination is a useful tool to evaluate and record oral cavity lesions, especially in patients with restricted mouth openings. It is a useful tool for screening high risk group, giving definite advantage of objective evaluation and recording of the lesion. It can also prevent cancer by detecting pre-malignant lesions effectively.
SQUAMOUS CELL CARCINOMA OF THE ORAL TONGUE: HISTOPATHOLOGIC MARKERS ASSOCIATED WITH OUTCOME

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Statement of Problem: Cancer of the head and neck is among the top ten malignancies with squamous cell carcinoma (SCC) of the oral cavity / oropharynx representing the vast majority. Despite current advances in treatment, the five year disease free survival remains largely unchanged over the last several decades. Advanced stage tumors (III/IV) are treated with multi-modality therapy while early tumors (stage I/II) are treated for the most part with single modality treatment. Treatment based on the TNM staging system unfortunately carries a 25-37% rate of recurrence in this later group of patients, emphasizing the need for additional information on tumor characteristics. The identification of histopathologic markers indicative of tumor aggressiveness has been suggested to assist to identify more aggressive cancers that would benefit from adjunct treatment while sparing others the unnecessary side effects associated with chemo/radiotherapy.

Materials/Methods: Patient records with the diagnosis of oral tongue SCC treated with surgery at the University of Illinois at Chicago between January 1995 and January 2005 were reviewed. 41 patients fit the established criteria for inclusion. Only cases with available histopathologic slides were reviewed and re-examined to assess for the following histologic findings: degree of lymphocytic host response, perineural invasion, worst pattern of invasion, predominant pattern of invasion, keratinization, eosinophilia, foreign body reaction, vascular/lymphatic invasion, and multi focal carcinoma in-situ. We then utilized a histologic risk model for head and neck SCC previously reported by Brandwein-Gensler (BG) to assess its efficacy in our subset of patients.

Conclusion: The examination of histologic slides for multiple reported predictors of negative prognosis resulted in several conclusions. First, the risk assessment model reported by (BG) did not predict outcome in our subset of patients. This may be due to inclusion of all head and neck SCC sites in their study while our focus was on the oral tongue. In addition, few predictors of negative outcome previously employed for risk stratification proved to be significant in our population while others did not correlate with poor prognosis. In conclusion, patients with oral tongue SCC with specific histopathologic markers indicative of aggressiveness may have poor outcome and thus require more aggressive treatment regiments. We believe that examination of SCC from each subsite of the head and neck for those histopathologic predictors of negative outcome could provide a better understanding of this disease behavior and variability in response to treatment.

References:


ANALYSIS OF THE SURGICAL MARGINS WITH FLUORESCENCE SPECTROSCOPY IN VIVO IN PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY

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Background: Oral cancer is a public health problem with high prevalence in the population. Local tumor control is best achieved by complete surgical resection with adequate margins. A disease-free surgical margin correlates with a lower rate of local recurrence and a higher rate of disease-free survival. Fluorescence spectroscopy is a noninvasive diagnostic tool that can aid in real-time cancer detection. The technique, which evaluates the biochemical composition and structure of tissue fluorescence, is relatively simple, fast and accurate.

Objectives: This study aimed to compare oral squamous cell carcinoma lesions to surgical margins and the mucosa of healthy volunteers by fluorescence spectroscopy.

Patients and methods: The sample consisted of 56 individuals, 28 with oral squamous cell carcinoma and 28 healthy volunteers with normal oral mucosa. Thirty six cases (64.3%) were male and the mean age was 60.9 years old. The spectra were classified and compared to histopathology to determine fluorescence efficiency for diagnostic discrimination of tumors. In the analysis of the other cases we observed discrimination between normal mucosa, injury and margins.

Results: Global survival of patients with T1-T2 and T3-T4 stage tumors after two-year follow-up was 91% and 78%, respectively, and specific disease-free survival after two years was 91.7% for T1-T2 and 66% for T3-T4 stages. In addition, individuals with lymph node metastasis had 44.5% of specific disease-free survival after two years (p = 0.008). Of the 28 cases, six (21.4%) cases had recurrence within two years, three (10.7%) cases had local recurrence specifically in the primary site, and the other three cases were in regional lymph nodes or distant metastasis. In all three cases of local recurrence, fluorescence had previously identified spectra that were similar to the primary tumor. The recurrent cases had grade II OSCC and free surgical margins of tumor in the primary surgery.

Conclusions: In situ analysis of oral mucosa showed the potential of fluorescence spectroscopy as a diagnostic tool that can aid in discrimination of altered mucosa and normal mucosa during the surgical procedure.
Background: India has one of the highest incidence of oral cancer, with 75,000 to 80,000 new cases diagnosed per year. It is one of the common fatal cancers in our country. Several factors like tobacco and tobacco related products, alcohol, genetic predisposition and hormonal factors are suspected as possible causative factors. Recent data have now attributed a subset of head and neck cancer to human papilloma virus (HPV).

Aims and Objectives: Prevalence of high risk HPV in oral cancer and its subsites and its relation to various demographic, clinical and pathological parameters and influence of HPV status on outcome.

Material and Methods: 250 patients with oral cancers undergoing treatment in department of surgical oncology, KGMU, Lucknow, India were included in this study. Epidemiological, clinical profile, treatment given, pathological parameters and follow up were recorded. Assessment of high risk HPV status was done by real time PCR.

Result: Overall HPV prevalence in oral cavity cancers was 22/250 (8.8%). HPV was found in 10.5%, 9.1% and 8.1% cancers of the tongue, lower alveolus and buccal mucosa respectively. Median age for HPV positive tumors was 52.5 years. Although recurrence was more common with HPV positive status, they also had a better survival.

Conclusion: Our results showed lower prevalence of high risk HPV positivity than other Indian as well as western studies. Recurrence was more common in patients with HPV positive tumors. They also had better survival than patients with HPV negative tumors.
Background: Lymph Node Density (LND) was previously reported to be a valuable prognostic indicator in oral cavity squamous cell carcinoma. This study validates prognostic value of LND in squamous cell carcinoma (SCC) of the tongue.

Material & Methods: A retrospective review of 106 patients with SCC of the tongue who underwent curative surgery and neck dissection from 2006 to 2010 was conducted. LND is defined as the ratio of positive lymph nodes to total lymph nodes removed. A LND value of 0.06 was used as the cut-off based on previous published literature. Patients were divided into 3 distinct LND groups: A) LND = 0 B) LND < 0.06 C) LND > 0.06. Overall survival (OS), disease-free survival (DFS) and loco-regional recurrence (LRR) rates for each group were calculated using the Kaplan Meier method and compared. Multivariate analysis was further performed using the Cox's proportional hazards model.

Results: Median age of patients is 62 years (23 - 94) with 56% male and 44% female. The distribution of Stage I to IV disease in the study cohort was 26.3%, 27.4%, 18.9% and 27.4% respectively. 41.9% of patients underwent selective neck dissection while the rest had radical/modified radical neck dissection. 43% of the cohort had nodal positive disease. Five-year OS and DFS rates were significantly different between the three groups: OS- 79.0%, 58.2% and 47.4% (p = 0.04) and DFS- 78.9%, 52.9% and 47.7% (p = 0.03) for groups A, B and C respectively. Furthermore, the impact of LND on OS and DFS remained significant on multivariate analysis (p=0.022 and p=0.004). In addition to LND, T staging and tumour invasion depth remained significant predictors of OS (p=<0.001 and p=0.03) and DFS (p=<0.001 and p=0.027) on multivariate analysis. However, nodal stage was not (p=0.73 and p=0.93).

Conclusion: LND is a strong prognostic indicator for disease recurrence and survival in tongue cancer. Multivariate analyses shows that it may be superior to the conventional N staging of the TNM classification, suggesting that future editions of TNM staging may require refinements to lymph node staging strategies.