A retrospective review of lip squamous cell carcinoma characteristics as predictors of nodal spread

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**Introduction**

This is a research highlight of an article published in the *Journal Of Laryngology & Otology* on 25 August 2015 titled “Squamous cell carcinoma of the lip: depth of invasion, local recurrence and regional metastases. Experience of a rural multidisciplinary head and neck unit”[1].

The research was undertaken after observing a number of patients presenting with cervical nodal metastatic disease after having T1/T2 tumours excised from their lip.

Nodal spread or distant metastatic spread is the main risk factors affecting long-term survival. Presence of nodal spread of SCC lowers the survival to approximately 50%[3].

The article aims to review what factors increase the risk of a patients lip SCC tumour developing cervical nodal metastasis so that these factors can be considered when determining the need for neck dissection or post-operative radiotherapy.

Prior to undertaking the analysis, literature review on the subject revealed that tumour depth of invasion likely has a significant role in determining risk of nodal metastasis in these patients[2, 5, 6]. This and other factors were reviewed
including overall tumour size which is the current sole factor utilised in the current staging system (American Joint Committee on Cancer Tumour-Node-Metastasis staging ‘TNM’ system).

Studies have highlighted a varied approach to recommending neck treatment in the setting of lip SCC & a clinically disease free neck. Onerci et al. suggest that the risk of nodal spread for tumors greater than 5 mm is sufficient to undergo suprahyoid neck dissection [2]. Najim et al. found tumors with a thickness of greater than 4 mm had a three-fold increased risk of nodal spread, and therefore required close follow up or prophylactic neck dissection [7]. Based on TNM staging, many studies have suggested close clinical follow up or elective neck dissection for T2a tumors (larger than 3 cm) whilst others advise surgery in the setting of known nodal spread only [7,8,9].

Our hypothesis prior to the study was that increased maximal tumor thickness is a risk factor for nodal spread in patients who otherwise have early stage disease (T1 or T2). Furthermore we looked at patients distance to treatment center to assess whether patient distance to care would affect their likelihood for more advanced disease.

The concern over distance to treatment center reviewed in this article stem from the wide catchment area of the treating hospitals service district (over 77 388km²). This causes strain on patients presenting for care due to cost of travel, distance from home, burden of travel & time off. Whether these burdens affected patients clinically & causing later stage disease presentation was of interest.

Materials and methods

A retrospective chart review from 2005 until 2013 was undertaken in Toowoomba General Hospital looking at all Lip SCC’s excised.

The focus of the review was finding key information on; tumor depth (distance from surface to maximal invasive depth of tumor), initial staging, presence of perineural invasion, tumor differentiation, maximal tumor size (largest size of the tumor in any dimension), smoking status (current or ex-smokers being any patient with >100 cigarettes or >1 pack year), treatment undertaken, location at the time of diagnosis and signs of recurrence [1].

The patient data was statistically analyzed initially with the Kolmogorov-Smirnov test of normality to determine normally distributed data variables & then parametric statistics used for those variables; alternatively, non-parametric statistics were used. The choice of parametric or non-parametric statistical hypothesis testing techniques to address the research questions was made in a similar manner [1].

Results

Data from 68 patients with SCC of the lip was collated from the years 2005 to 2013 [1].

- 12 had evidence of lymphatic spread
- 3 at the time of initial diagnosis/ treatment, 9 diagnosed during follow up
- Mean time of 11 months (SD ± 3.2 months) following initial excision of SCC for detection of nodal disease.
- 1 case of nodal metastasis to an intra-parotid node from upper lip

Test of normality

A Kolmogorov-Smirnov test of normality was applied to the continuous variables however, except for age, the variables could not be assumed from a normally distributed population within 0.001 significance therefore non-parametric analysis was used for the analysis of tumor size, tumor thickness and distance from the treatment center.

Demographic and clinical characteristics

- Average age 61.09 years (SD = 16.43 years range 17 - 89).
- Male 56: Female 12
- Smokers or ex- smokers (n = 37, 54.41 per cent).
- Median tumor size was 8.65 mm (IQR = 11.72 mm)
- Median tumor thickness was 3.68 mm (IQR = 4.00 mm).

Staging

- T1 = 56 (83.5 per cent) T1N0 for all T1 patients
- T2 = 8 (11.76 per cent) T2N0 for all T2 patients
- T3 = 1 (1.47 per cent) T3N2c for all T3 patients
- T4 = 3 (4.41 per cent) T4aN2, T4N0 and T4N1.

Tumor differentiation
Perineural invasion was absent in most patients (n = 59, 86.76 per cent) and the majority of patients lived very close to the treatment center (median ≈ 0km, IQR = 139 km).

Hypotheses testing

Tumor size, tumor thickness & distance from the treatment center data were compared to identify a statistically significant difference between patients with and without nodal metastasis. The Mann-Whitney U test confirmed that the median tumor size (U (68) = 163.50, p = 0.005), median tumor thickness (U (68)=103.50, p<0.001) and median distance from the treatment center (U (68) = 199.00, p = 0.018) were significantly greater for patients with nodal metastasis compared to the patients without nodal metastasis.

The chi-square test of independence found no association between smoking status and nodal metastasis. The relation between these variables was not significant (chi-square=0.114; n=68; p=0.735).

The mean tumor thickness in the patients with nodal spread was 8.3mm (SD=3.19 from 3.5 - 20mm) & without nodal spread was 3.72 mm (SD = 1.69 0.5 - 15mm. Using the Mann-Whitney U test, the difference in mean tumor thickness was found to be statistically significant (U (68) = 572, p = 0.001).

Discussion

Squamous cell carcinoma of the lip, with early detection carries a five-year survival rate between 85 and 95 per cent, which drops significantly when metastasis is present [10]. Acknowledging & identifying the at risk patients more likely to develop loco-regional or distant metastatic spread is therefore vital.

When nodal disease is not present on clinical review, a more varied approach seems to be undertaken. For the N0 neck, there is no consensus regarding management; multiple studies have attempted to formulate criteria for prophylactic neck dissection.

This study suggests that factors such as tumor thickness have a predictive role in identifying at risk patients as does current staging practices. This is consistent with the available literature. Onerci et al. indicated that prophylactic neck dissection should be considered for tumors all tumors [2]. Najim et al. found that the risk of lymphatic metastasis was significantly increased for tumors over 4 mm thick [7]. Vanderlei et al. focused on current TNM staging, and suggested that tumors larger than 3 cm in their greatest dimension also be considered for prophylactic neck dissection [8].

This analysis suggests that tumor depth of invasion, overall tumor size and distance from treatment center may be helpful in predicting which patients have tumors that are at higher risk of nodal spread; these patients should receive closer review or be considered for further treatment. Larger prospective studies are needed in this area.

Increased attention to regional healthcare, particularly from specialist departments is also suggested as a way to improve outcomes for patients presenting from rural healthcare.

Conflicting interests

The authors have declared that no conflict of interests exist.

References


