Original Article

Assessment of Relationship between Tumour Thickness and Nodal Metastasis in Head and Neck Squamous Cell Carcinoma

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The present study was undertaken to assess the relationship between tumour thickness and nodal metastasis in head and neck squamous cell carcinoma, with an idea in mind to improvise the treatment for these cancer further. In our study, 40 patients with proven head and neck squamous cell cancer and requiring surgery as primary mode of treatment were included in study. All patients underwent neck dissection along with surgical treatment for the primary tumour. Specimen of neck dissection was sent for histopathological examination. The pathologist examined the tumour thickness and lymph node metastasis. Statistical Package for the Social Sciences (SPSS) 17.0 used and categorical variables are presented as absolute numbers and percentage and were compared using Chi-squared test or Fisher's exact test as appropriate. P value <0.05 was considered statistically significant. In our study of 40 patients, a significant correlation between pathological lymph node metastasis and tumour thickness with p value is of 0.001. Out of 19 oral cancer patients and 21 laryngeal cancer patients, a significant correlation was found between pathological lymph node metastasis and tumour thickness with a 'p' value of 0.023 and 0.02 respectively. Cut-off value for tumour thickness was kept at 7mm.

Tumour thickness gives an accurate estimate of tumour load and it could guide in adjuvant treatment for regional lymph nodes. Elective neck dissection can be avoided in patients with limited tumour thickness but close postoperative follow up is required.

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Key words : Tumour thickness, Nodal metastasis, Elective neck dissection.

Head and Neck Squamous Cell Carcinoma (HNSCC) is the sixth most common cancer worldwide. The annual incidence of head and neck cancers worldwide is more than 5,50,000 cases with around 3,00,000 deaths each year[1]. Overall 57.5% of head and neck squamous cell carcinoma occur in Asia, especially, India where it is the most common cancer[2]. In India, HNSCC accounts for 30% of all cancers[3].

HNSCC includes epithelial cancers arising in the mucosa of the upper aero-digestive tract which include the oral cavity, oropharynx, hypopharynx and larynx. These cancers are strongly associated with certain environmental and lifestyle risk factors like smoking, tobacco chewing, alcohol and also related to several strains of human papilloma virus (HPV 16, 18)[4].

Tumour thickness is a parameter that indicates aggressiveness of a tumour. It is defined as tumour mass that reveals the vertical growth capacity of the tumour.

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Tumour cells with a greater malignant potential are prone to break through these protective barriers and invade vertically. Horizontal spread, on the other hand, occurs in superficial lesions that are under the control of body resistance[5,6]. Accurate prediction of histological tumour thickness may influence management regarding surgical access, planned margins, use of reconstruction and elective neck dissection.

Tumour thickness has been shown to be one of the most important and reliable factor in predicting regional node involvement in oral cavity cancers[7]. It is now widely accepted that thickness is more accurate predictor of sub-clinical nodal metastasis, local recurrence and survival than tumour size[6].Tumour thickness can be measured pre-operatively by intraoral ultrasonography, high resolution CT or MRI. It can be measured post-operatively from the specimen or by frozen section intraoperatively.

Regional lymph node metastasis is a well-known prognostic indicator in many types of solid cancer, including HNSCC[8]. Lymph node metastasis negatively influences the overall survival and increases the likelihood of distant metastases.

Elective neck dissection gives an important pathologic information on the status of lymph node metastasis and

helps to determine need for chemo-radiation. It also clears pathologically undetectable cancer cells lodged in the lymphatics between the primary tumour and the echelon lymph nodes. Shunting of lymph with opening up of abnormal channels occurs when more extensive surgery and radiotherapy is undertaken. Hence, it is important to assess tumour thickness with nodal metastasis, so that a proper treatment plan can be made according to the thickness of tumour to avoid morbidity and more extensive procedures to the patient.

In present study, we aim to assess the relationship of tumour thickness in head and neck squamous cell carcinoma to lymph node metastasis.

MATERIALS AND METHODS

This study was conducted in Department of Otorhinolaryngology, Head and Neck Surgery, Safdarjung Hospital and National Institute of Pathology, New Delhi in 18 months of study period from October 2013 to March 2015.

A cross sectional study of 40 patients attending Outpatient Department of Otorhinolaryngology with proven head and neck squamous cell cancer and requiring surgery as primary mode of treatment were included in the study. Patients were divided into two groups of laryngeal cancer and oral cancer. Patients included were of any age group and both sexes.

A detailed relevant history was taken followed by a thorough general physical and otorhinolaryngological examination. Neck of patients was thoroughly examined for any palpable lymph nodes. Complete assessment of site, size and extent of primary tumour was done to properly stage the tumour. Patients were taken for haematological investigations, chest x-ray and ultrasound abdomen was done for patients to rule out any metastasis in lungs and abdomen. After clinical examinations all the patients were sent for ultrasound neck, contrast enhanced computed tomography-base of skull to thoracic inlet. Biopsy was taken from site of primary tumour in every patient for histopathological confirmation, degree of differentiation, and histological grading of malignancy.

All patients under study underwent neck dissection along with surgical treatment for the primary tumour. Specimen of neck dissection was sent for histopathological examination. The pathologist examined the tumour thickness and lymph node metastasis. The pathologist was blindfolded about the report of clinical examination and contrast enhanced computed tomography.

Statistical Analysis :

Statistical testing was conducted with the statistical package SPSS 17.0. Categorical variables are presented as absolute numbers and percentage and were compared using Chi-squared test or Fisher's exact test as appropriate. P value <0.05 was considered statistically significant.

RESULTS

In our study group, patients ranged from 26-70 years of age with majority of patients in age group of 51-70 (58%). The mean age of patients was 53.3 years (Table 1).

There were 21 patients of laryngeal cancer (52.5%) and 19 patients of oral cancer (47.5%). Out of 19 laryngeal cancer patients, 12 (30%) patients had supraglottic cancer, 2(5%) patients had glottic cancer, 4(10%) patients had transglottic cancer and 3(7.5%) patients had hypopharyngeal cancer. Out of 19 oral cancer patients, 10(25%) patients had buccal mucosa cancer and 9(22.5%) patients had tongue cancer. In our study, the most common site for primary tumour was supraglottis ie, 30% (Table 2).

Table 1	
Age group (years)	No of patients (Percentage)
10-30	2 (5%)
31-50	15 (37.5%)
51-70	23 (57.5%)

In our study group of 40 patients, 13 patients (32.5%) had tumour thickness $\leq$7mm and 27 patients (77.5%) had tumour thickness of >7mm. Of total 19 oral cancer patients, 9 patients (47.4%) had tumour thickness $\leq$7mm, 10 patients (52.6%) had tumour thickness of >7mm. Of total 21 laryngeal cancer patients, 4 patients (19%) had tumour thickness $\leq$7mm, 17 patients (81%) had tumour thickness of >7mm (Table 3).

Table 2	
Primary site	No of patients (Percentage)
Oral	19 (47.5%)
Larynx	21 (52.5%)
Total	40 (100%)

We have compiled pathological lymph node metastasis into 2 groups as positive (N+) and negative (N-). Out of 40 patients, there were 22 patients (55%) in N+ group and 18 patients (45%) in N- group. Among 22 patients of N+ group, 2 patients (9.1%) were having tumour thickness $\leq$7mm and 20 patients (90.9%) were having tumour thickness >7mm. Among 18 patients of N- group, 11 patients (61.1%) were having tumour thickness $\leq$7mm, 7 patients (38.9%) were having tumour thickness >7mm. Association of tumour thickness with pathological lymph node metastasis in head and neck cancers were statistically significant (p<0.001).

Table 3			
Site	Tumour thickness	Tumour thickness >7mm	Total
Oral	9 (47.4%)	10 (52.6%)	19
Larynx	4 (19%)	17 (81%)	21

There were no cases of N+ among laryngeal cancer patients with tumour thickness less than 7mm. The result was similarly statistically significant for both oral and laryngeal cancers separately (Table 4).

DISCUSSION

Head and neck squamous cell cancers themselves represent a fairly heterogeneous group of cancers with

Table 4			
Pathological Ln Metastasis	Tumour Thickness		P-value
	≤7mm Frequency (%)	>7mm Frequency (%)	
Overall :			
Negative	11 (84.6%)	7 (25.9%)	
Positive	2 (15.4%)	20 (74.1%)	<0.001
Total	13 (100.0%)	27 (100.0%)	
Oral :			
Negative	7 (77.8%)	2 (20.0%)	
Positive	2 (22.2%)	8 (80.0%)	0.023
Total	9 (100.0%)	10 (100.0%)	
Larynx :			
Negative	4 (100.0%)	5 (29.4%)	
Positive	0 (0%)	12 (70.6%)	0.02
Total	4 (100.0%)	17 (100.0%)	

different demands for preservation of cosmetic and functional needs as dictated by their anatomical sites, unequal response to treatment protocols, and variable prognosis. In the last decade, studies have provided increased insight in the molecular and genetic changes that are responsible for the development of cancer and the biologic behaviour of cancer cells.

Tumour thickness is a relatively new prognostic factor that has been investigated for head and neck cancers. TNM classification does not represent the real tumour load but integrated classification, which includes use of tumour thickness, can be used to overcome the well-known lack of consistency in the choice of treatment which can eventually improve overall survival. Tumour thickness adds another dimension to the staging system. Although several studies[5,10,11] have considered tumour thickness and tumour depth synonymous, they are different and should be distinguished. The tumour thickness refers to the thickness of the entire tumour mass, whereas the tumour depth is the extent of tumour growth into the tissue beneath the epithelial surface.

Nodal disease demonstrates a major problem in deteriorating survival and highlights the importance of accurate diagnosis and therapeutic control[12]. The anatomical characteristics and biological behaviour of the primary tumour are the main determinants of the cervical nodal status.

In the present study of 40 patients, majority of them ranged between 51-70 years (57.5%) & the mean age of patients was found to be 53.3 years and there was marked male preponderance with male female ratio of 9:1.

In our study of 40 patients, a significant correlation between pathological lymph node metastasis and tumour thickness with p value of 0.001. Various studies[13-15] in literature reported a significant correlation between pathological lymph node metastasis and tumour thickness & have shown that elective neck dissection should be done if tumour thickness is more than cut-off value, even in clinically N0 patients.

Out of 19 oral cancer patients and 21 laryngeal cancer patients, a significant correlation was found between pathological lymph node metastasis and tumour thickness with a 'p' value of 0.023 and 0.02 respectively. Hu et al[13] evaluated 223 patients with oral tongue squamous cell carcinoma and showed a significant correlation between pathological lymph node metastasis and tumour thickness. Melchers et al[14] evaluated 212 oral cancer patients and Ganly et al[15] evaluated 164 oral cancer patients and reported a significant correlation between pathological lymph node metastasis and tumour thickness. Yilmaz et al[16] reported a significant correlation between pathological lymph node metastasis and tumour thickness among 111 laryngeal cancer patients. Ye et al[17] evaluated 127 patients with supraglottic and hypopharyngeal cancer and found that tumour depth provides additional information in an effort to predict nodal status.

The results of our study were in accordance with previous studies. However, there were few limitations in our study. Multiple tumour thickness cut-offs could have been taken to get an accurate idea of nodal metastasis at particular cut-off. But, in previous studies, cut-off point varied greatly and our sample size was limited which suggests the need for a larger prospective study to get more accurate results.

CONCLUSION

In our study, it was found that tumour thickness >7mm lead to significant increase in nodal metastasis. Tumour thickness, 3rd dimension of tumour, has a significant impact on nodal metastasis in Head and Neck Squamous Cell Carcinoma as it gives an accurate estimate of tumour load and it could guide in adjuvant treatment for regional lymph nodes. Elective neck dissection can be avoided in patients with limited tumour thickness but close postoperative follow up is required. Further studies with larger sample size are required to understand the intricate mechanism of nodal metastasis and its relation with tumour thickness which leads to more rational treatment in HNSCC.

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