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Original Research Article

Assessment and to evaluate the eminence of depth of invasion in gingivobuccal sulcus carcinoma with the use of preoperative computed tomography and to compare it with depth of invasion measured histopathologically in the resected primary tumor, with the cervical nodal metastasis

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ABSTRACT

Background: Depth of invasion (DOI) being one of the significant predictors in determining the prognosis of the disease, hence this data is available only post operatively but now with the advance technology we can assess DOI preoperatively. Here in our study, we used contrast enhanced computed tomography scan (CECT) to determine preoperative DOI. This measured data eventually helps the surgeon to plan resection of the oral primary tumor 3 dimensionally with safe margins.
Methods: Prospective study was conducted between 2019 to 2021 with patients diagnosed with Gingivobuccal sulcus (GBS) carcinoma who were subjected for resection with neck dissection procedures. Preoperative CECT scan was performed to evaluate the depth of invasion (DOI). This was then compared with the DOI measured post operatively of resected specimen by histological assessment. A cut-off value for DOI was derived, beyond which nodal metastasis was evident.
Results: Out of 51 patients 40 (78.4%) were male patients and 11 (21.6%) were female. Age ranged from 20 to 70 years. Preoperative DOI measured from CECT scan showed average value of 18.84 mm, with sensitivity of 100% which was highly statistically significant. Histopathological DOI showed average value of 7.26 mm. lowest DOI at which nodal metastasis observed was 3.4mm, so the cut-off value of DOI above which metastasis was probable decided was 3.5mm for this series.
Conclusions: Hence CECT scan showed better sensitivity and specificity in determining early bony invasion in GBS carcinomas. Thus, making DOI a very reliable and predictable prognostic factor in oral GBS carcinoma.

Keywords: Contrast enhanced computed tomography, Depth of invasion, Gingivo buccal sulcus, Lymph node metastasis, Oral squamous cell carcinoma

INTRODUCTION

Squamous cell carcinoma of head and neck region being the 6th most common malignancy throughout the world, has its own peculiarities in the etiology, presentation and its management. Kane et al.[1] in his literature states that approximately 33% of patient being diagnosed with oral malignancies have lymph node involvement in initial

presentation of their disease course and when nodal metastasis occurs, the cure rate of disease gets reduces by 50%. According to AJCC 8th edition classification of TNM staging the T stage of the tumor which now involves the third dimension of the tumor that is depth of invasion (DOI) has been considered important in determining the prognosis of disease effectively.[2] Recent advancement in imaging modalities have given a surgeon a 3-dimensional extent of any tumor in oral cavity to be assessed preoperatively before planning any final surgical treatment. The primary objective of the study was to assess the depth of invasion measured preoperatively by contrast enhanced computed tomography (CECT) scan of gingivo buccal sulcus (GBS) carcinoma in oral cavity and then compared it to the histopathological examination of resected specimen, keeping histological depth of invasion a s gold standard with nodal metastasis.

METHODS

This is a single centre prospective study including 51 patients, reporting to Department of Oral and Maxillofacial Surgery at SDM college of Dental sciences and hospital Dharwad, India from June 2019 to November 2021 who were subjected to surgery for resection of oral primary tumour along with neck dissection and reconstruction procedures with various free and loco regional flaps. Patients included were Biopsy proven cases of squamous cell carcinoma of gingivo buccal sulcus indicated for surgery (Figure 1). patients with age group between 20 years to 70 years and Patients who are fit to undergo surgery.

Patients excluded from the study were previous operated cases and other primary tumours, patients previously treated with neo adjuvant chemotherapy and primary radiation, also cases with recurrence or second primary. All patients were included in the study after obtaining institutional ethical clearance (IRB-2019/P/OS/66) and patient specific consents. A simple random sampling technique was used to calculate the sample size of this study with 95% confidence level and a standard deviation of 0.5 and a confidence interval (Margin of error) of +5% or –5%.

Preoperative DOI evaluation of the lesion using computed tomography

Preoperative CT imaging was performed using 128 multi slice and multi detector SIMENS CT scanner with contrast. Puffed cheek technique was used for the lesion and denta scan was also performed at 1mm sections including coronal, axial and sagittal sections with 3D reconstruction extending from the floor of the maxillary sinus, mandible and including the entire length of neck bilaterally. Post contrast CT scan was done. similarly, 1mm sections were procured in all planes, after recording all the sections pre contrast and post contrast infusion data transferred to the work station, to generate the panoramic and cross-sectional reformatting images by Dent scan software. Tumour depth of invasion was measured from surface of tumour to the deepest point of invasion. Similarly, the values for all patients tabulated for DOI and the neck lymph node metastasis was also analysed pre and post contrast and the lymph node involved for metastasis were tabulated (Figure 2).

Post operative histopathological evaluation of the lesion for DOI

Post operatively the resected specimens were examined for induration from the surrounding normal tissue and fixed in the 10% phosphate buffered formalin and submitted for the histopathological examination for the depth of the invasion. (Considering the 30% tissue shrinkage as the standard after formalin fixation). After which tissues were processed and then mounted in paraffin wax. 4-5 micromillimeter thickness sections were obtained from microtome and were placed on glass slide. Tissues on the slides were stained in the hematoxylin and eosin stain. These sections were then examined in the optical microscope LEICA-DM 400B equipped with measuring device i.e. graticule within the eyepiece. These specimens were then viewed under 1.25X magnification and the vertical distance from the membrane to the deepest part of the tumour invasion was measured. All values obtained for DOI were tabulated and the resected lymph nodes were subjected to histopathological examination and lymph node positive for metastasis were noted and tabulated (figure 3).

Study analysis

The value obtained preoperatively from CECT scans were compared with histopathological DOI of primary lesion after resection. Histopathological measured DOI of tumour was then correlated with cervical lymph node metastasized. All the values obtained were subjected to a suitable statistical analysis.

RESULTS

A total of 51 patients were included in this prospective study of which 40 (78.4%) were male patients and 11 (21.6%) were female patients. Patients age ranged from 20 to 70 years with primary tumour site being only gingivobuccal sulcus. Based on tumour staging maximum number of patients were staged in T4 stage-35 (68.6%), followed by T3 stage-10 (19.6%), T2 stage-5 (9.8%) and T1 stage-1 (1.8%) respectively.

Depth of invasion (DOI) measured preoperatively from computed tomography (CT) scan in these cases ranged from 6 mm to 32 mm with average of 18.84 mm, similarly histopathological DOI measured of resected specimen post operatively of all these patients ranged from 1.3 mm to 16 mm with average of 7.26 mm (Table 1). Comparison of DOI measured preoperatively using MDCT scan of face (1 mm cuts coronal section) and postoperatively measured DOI from Histopathological

assessment of resected specimen (in mm) is done by dependent t test and was noted that it is highly statistically significant with p value of 0.0001 and sensitivity 100.00% (Table 2).

Table 1: comparison of DOI measured preoperatively of gingivobuccal carcinoma of oral cavity using MDCT scan of face (1mm cuts coronal section) and postoperatively measured DOI from histopathological assessment of resected specimen (in mm) by dependent t test.

Methods	Mean	SD	Mean Diff.	SD Diff.	% of difference	T value	P value
CT method	18.84	7.01					
Histological method	7.26	3.57	11.58	7.19	61.46	11.5088	0.0001

*p<0.05

Table 2: Sensitivity and specificity of CT method and Histological method.

Sensitivity	Pr (+D)	100.00%
Specificity	Pr (-~D)	0.00
Positive predictive value	Pr (D+)	82.35
Negative predictive value	Pr (~D-)	0.00
False+rate for true~D	Pr (+~D)	100.00
False-rate for true D	Pr (-D)	0.00
False+rate for classified	Pr (~D+)	17.65
False-rate for classified	Pr (D-)	0.00
Correctly classified		82.35

Table 3: Correlation between the histological measured DOI with the cervical lymph node metastasis (LNM).

DOI	LNM positive	%	LNM negative	%	Total	%
<3.5mm	2	22.22	7	77.78	9	100
>3.5mm	13	30.95	29	69.05	42	100
Total	15	29.41	36	70.59	51	100

Chi-square with Yates's correction=0.0140, p=0.9060.

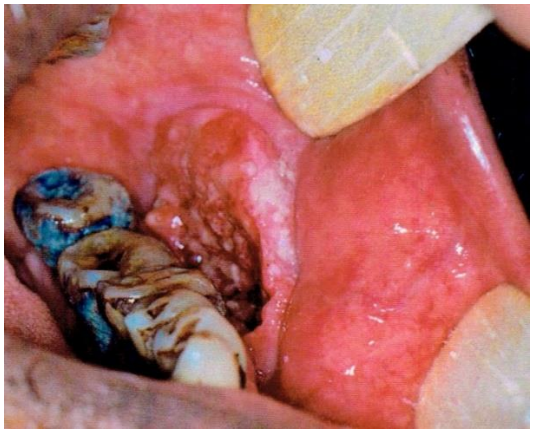

Figure 1: Patient with carcinoma of gingivobuccal sulcus of left side. (Intraoral ulcer proliferative growth noted extending from lower left premolar teeth region to 3rd molar region).

Cervical lymph node metastasis was histologically positive in 15 (29.41%) patients out of 51 patients, therefore there was a significant correlation between the histological assessment of DOI and the occurrence of the cervical lymph node metastasis. In our study the least invasive depth at which the nodal metastasis was seen was 3.4 mm. In the cases were the depth of invasion exceeded 3.5 mm the lymph node metastasis was seen in 13 (30.95%) patients. In cases where DOI was less than or equal to 3.5 mm the incidence of lymph node metastasis was seen in only 2 (22.22%) patients. The critical DOI that separated the Gingivo buccal carcinoma into high risk and low risk category in our study was, therefore 3.5 mm (Table 3). Follow up period of the patient after surgery was ranged from 3 years to 5 years in every case. None of the patients had any evidence of the recurrence locally or at distant sites.

Figure 2: Measurement of depth of invasion of tumour using computed tomography (Coronal 1 mm section) scan.

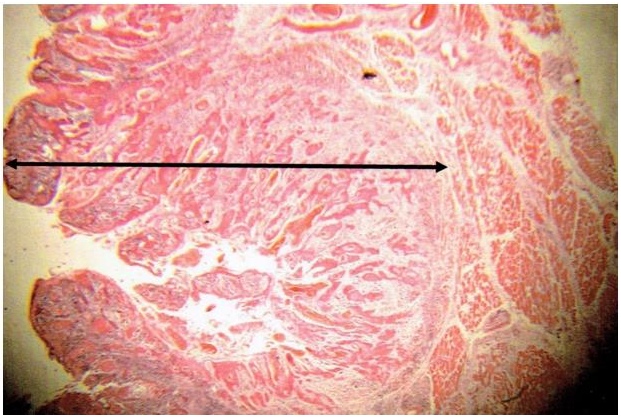

Figure 3: Measurement of depth of invasion of tumour using histopathological examination.

DISCUSSION

Cervical metastasis correlates with the growth type, tumor differentiation and nuclear pleomorphism of the deepest layer, tumor border, infiltrative growth and DOI and among all these the DOI has a powerful predictive value for cervical metastasis.[3] DOI has been shown to be more important than the surface diameter, as a determinant factor for lymph node metastasis and disease related death by various authors.[4-6]

Using 128 multi slice and multi detector SIMENS CT scanner, GBS lesion was scanned at 1 mm sections including coronal, axial and sagittal sections with 3D reconstruction the deepest point of invasion that is DOI was measured, and compared with the DOI measured with microscopic examination of resected specimens post operatively. The CT scan DOI ranged from 6 to 32 mm with average value of 18.84 mm. In the study done by Struckmeier et al, CT scan exhibited 76.85% sensitivity, 82.20% specificity, 47.14% PPV, and 89.67% NPV.[7]

In this study estimation of DOI using the CT scan had a sensitivity of 100% and 0% of negative predictive value, which showed the specificity similar to the negative predictive value with relative coefficient of 0.0001, which was highly statistically significant. Uribe s et al, study shown that CT scan with early invasion to bone especially seen in these gingivo buccal carcinoma has the diagnostic accuracy of 87% in the initial assessment of bone invasion which makes the DOI assessment very accurate in cases of buccal carcinoma with bony invasion which will be difficult with measurement from other scans.[8]

Others authors like Pereira et al, and Nakayama et al, have showed that CT scan has the ability to detect the small cortical erosions usually not detected by other means of examination including clinical and other radiological investigations, the pattern of bone destruction can have impact on the outcome in oral malignancies.[9,10]

In this study, the histological DOI measured ranged from 1.3 to 16 mm with an average value of 7.26 mm. 15 (29.4%) patients showed lymph node involvement, and there was extremely high co-relation, between the DOI measured from histopathological assessment and the cervical lymph node metastasis (p value of 0.9060). The results demonstrated that the patients in this sample could be separated statistically into two groups hence the critical DOI was, therefore 3.5 mm.

Brockhoff et al, found a different cut off values for different subsites carcinoma in the oral cavity.[11] They offered a neck dissection at above 2 mm DOI in tongue tumours, 2-3 mm DOI in floor of mouth tumours and 3-4 mm DOI for the retromolar trigone and alveolus/hard palate tumours. Similar study done by Den Toom et al.[12] The ROC-curve showed an area under the curve of 0.65 with a most optimal cutoff point of 3.4 mm DOI (sensitivity 83% and specificity 47%). Regional metastases were found in 15% of patients with DOI≤3.4 mm. In this study the critical cutoff point was 3.5mm DOI which was also near similar with the by Den Toom et al, study.[12] 9 (17.6%) Patients had DOI less than or equal to 3.5 mm and remaining 42(82.4%) patients showed DOI greater than 3.5 mm, hence the study depicts a very significant direct proportional between DOI and lymph node involvement. Therefore, the strength of the study is that it is prospective study design with 3 to 5-year follow-ups period with no recurrence and mortality rate till date. The limitation of this study is Although greater number of patients were in T4 stage lesions with DOI ranging from 1.3 mm to 16 mm, we suggest further more studies to be done on T1 and T2 lesions to treat early oral malignancies and also to study other histological variants to understand more about the prognosis of disease.

CONCLUSION

The role of important diagnostic tool i.e. is CT scan in preoperative measurement of DOI in gingivo buccal carcinoma apart from giving extension of local invasion it also provides help in preoperative treatment planning regarding the extent of wide resection with safe margins and reconstruction. The study also determines the incidence of cervical lymph node metastasis and need for elective neck dissection from preoperative DOI values. Finding of the study also provides correlation between the DOI with cervical lymph node metastasized and loco regional recurrence which would play a significant role in the prognosis of the disease.

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