Original Article

Tumor Size and Its Relation to Cervical Lymph Node Metastasis and Its Significance as a Prognostic Indicator for Oral Squamous Cell Carcinomas

Abstract

Context: Oral cancer is the sixth most common cause of cancer-related deaths worldwide. In the Indian scenario, oral cancer is the second most common cancer. The presence of metastatic cervical lymphadenopathy is of particular importance as with every single nodal metastasis, survival of the patient is reduced by one half. Thus, regional metastasis is one of the most important factors in the prognosis and treatment planning of patients with head and neck squamous cell carcinomas. The inaccuracies in clinical examination have been well documented and the diagnostic imaging modalities have been shown to have superior diagnostic accuracy in detecting occult nodal metastasis Considering the numerous uncertainties regarding the progression, management and outcome of oral cancers, an attempt was made to detect the role of tumor size as a predictive indicator for lymph node metastasis using magnetic resonance imaging (MRI). **Aim of the Study:** The aims of the present study was to evaluate tumor size and its relation to cervical lymph node metastasis and its significance as a prognostic indicator for oral squamous cell carcinomas (OSCCs); and to identify and evaluate inaccuracies of the clinical diagnostic criteria with the help of magnetic resonance imaging (MRI). **Materials and Methods:** A total number of 27 patients (12 oral cancer-alveolus, 8 oral cancer-tongue, 7 oral cancer-buccal mucosa) attending as out-patients were included in the study. The patients clinically diagnosed and histopathologically proven to have oral squamous cell carcinoma were examined and were evaluated for the tumour size and lymph node status with the help of MRI. **Statistical Analysis Used:** Values of sensitivity, specificity, positive and negative predictive values and accuracy were calculated. Paired *t*-test was performed for evaluating size of the tumor and lymph node recorded on clinical and imaging findings. **Results:** 40% cases were found to be true positive for detecting metastasis using clinical diagnostic criteria whereas 55% cases were found to be true positive for detecting metastasis using imaging criteria. The paired *t*-test value for the difference in tumor size between clinical and imaging staging was statistically significant ($P < 0.01$). The paired *t*-test value for the difference in lymph node size between clinical and imaging staging was, also, found to be statistically significant ($P < 0.01$). Overall specificity of 100%, sensitivity of 75%, positive predictive value 72%, negative predictive value 100% and accuracy of 85% were noticed for imaging staging. **Conclusion:** Detection of tumor size and lymph node metastasis was found to be higher on MRI than that by clinical staging alone. The present study, also, proved that clinical diagnostic criteria alone are less accurate for detecting metastatic lymphadenopathy. MRI, thus, can be safely made a recommendation in all head and neck malignancies for preoperative diagnostic imaging procedures in order to get extremely useful information regarding treatment planning and prognosis in such patients presenting with oral carcinomas.

Keywords: *Cervical lymph node metastasis, oral squamous cell carcinomas, prognostic indicator, tumor size*

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Introduction

Oral cancer is the sixth most common cause of cancer-related deaths worldwide.[1] In the Indian scenario, oral cancer is the second most common cancer.[2] The presence of metastatic cervical lymphadenopathy is of particular importance as with every single nodal metastasis, survival of the patient is reduced by one half.[3] Thus, regional metastasis is one of the most important factors in the prognosis and treatment planning of patients with head and neck squamous cell carcinomas.[4-6] The inaccuracies in clinical examination have been well documented[7] and the diagnostic imaging modalities have been shown to have superior diagnostic accuracy in detecting occult nodal metastasis.[8-11] Most commonly

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used tumour, node and metastasis (TNM) classification system fails to define the exact size and measurements of the tumor including diameter, length, width, area, volume and tumor thickness[12] and the clinical issues related to it.[13,14] The appropriate management of the oral carcinomas requires a good understanding of the factors affecting incidence, patterns and prognostic implications of the nodal metastasis.[6] Identification of such prognostic factors could constitute one of the important keys not only to predict tumor extent but, also, to reduce the mortality, morbidity, recurrences and most importantly, the cost of the treatment associated with oral cancers. The prognosis for patients with oral cancers that is treated early is much better because cure can be achieved with less complex and lesser aggressive measures than that which are necessary for the advanced lesions. A number of studies have identified that among all the dimensions of tumor size studied, tumor thickness is found to be the only significant factor for the prediction of nodal metastasis, local recurrence and survival in patients with oral squamous cell carcinomas (OSCCs).[15-22] Several such studies have been conducted on postoperative resected specimens while some have been conducted preoperatively using biopsy tissues. Further complicating this situation is that tumor size involving different areas has been found to affect lymph node levels and thereby, survival in a varied manner.[4,5] Hence, an accurate preoperative assessment of the tumor size is essential in optimizing the treatment algorithm.[23] Cervical lymph node metastasis has been investigated with a number of imaging modalities, however, tumor size related to the level of cervical lymph node metastasis and its prognostic implications using specialized imaging modalities like magnetic resonance imaging (MRI) preoperatively needs more elaboration. MRI is a powerful tool for cross-sectional analysis of the head and neck anatomy and pathology. This is especially true with regards to the oro-pharyngeal neoplasms where soft tissue spread, nodal disease, peri-neural invasions and osseous involvement significantly alter the therapy and prognosis.[23] Furthermore, MRI is, also, preferred for being a nonionizing specialized imaging modality.[23,24] Considering the numerous uncertainties regarding the progression, management and outcome of oral cancers, an attempt was made to detect the role of tumor size as a predictive indicator for lymph node metastasis using MRI. The objectives of the present study were to evaluate the tumor size and its relation to cervical lymph node metastasis and its significance as a prognostic indicator for oral squamous cell carcinomas (OSCCs) and to identify and evaluate inaccuracies of the clinical diagnostic criteria with the help of MRI.

Materials and Methods

Study Population: A total number of 27 patients (12 oral cancer-alveolus, 8 oral cancer-tongue, 7 oral cancer-buccal mucosa [Figure 1]) attending as out patients in the Department of Oral Medicine and Radiology were included in the study in the span from September 2007 to June 2009. The patients clinically diagnosed and histopathologically

Figure 1: Carcinomatous ulcer in relation to right buccal mucosa

proven to have OSCC were examined and were evaluated for the tumour size and lymph node status with the help of MRI [Figure 2]. The protocol of the present study was approved by the Research and Ethics Committee of the Institute. A written, informed consent was taken from all the patients who participated in the study. The patients were selected based on the following inclusion and exclusion criteria.

Inclusion criteria

- Individuals with clinical evidence and histopathologically proven as OSCC
- Patients willing to give consent regarding the conduct of the study alone were included.

Exclusion criteria

1. Individuals with any known systemic diseases
2. Individuals who have undergone previous radiotherapy, surgery or, chemotherapy
3. Individuals with contraindications to MRI
   - Cardiac pacemaker
   - Cochlear prostheses
   - Ocular implants/ocular metallic foreign body
   - Magnetic dental implants etc.
4. Patients with contraindication to gadolinium based magnetic resonance (MR) contrast agent.

Study design

This prospective clinical and imaging study was done in the Department of Oral Medicine and Radiology. A total number of 27 patients underwent clinical and MR examination. The said patients were divided into 3 groups as follows:

- Group I included patients with oral cancer-alveolus
- Group II included patients with oral cancer-tongue
- Group III included patients with oral cancer-buccal mucosa.

All the patients were subjected to routine blood investigations, fine needle aspiration cytology (FNAC) of the ipsilateral submandibular lymph node (Level I) and

other investigations were done followed by biopsy of the oral lesion to confirm the diagnosis.

Armamentarium for clinical examination

- Mouth mirror and Explore [Figure 3]
- Tongue depressor
- Examination gloves
- Gauze pieces.

Methodology

Clinical examination

A thorough clinical examination was performed and the details were recorded in a specially devised proforma. Complete lymph node examination was carried-out [Figure 4].

Magnetic resonance imaging examination

Armamentarium for MRI Examination - MRI was performed on 1.5 Tesla Magnetom Avanto systems (Siemens, Germany) [Figure 5]. All patients were asked to fast for 6 h prior to the MR examination.

The following sequences were obtained:

1. Axial T1-weighted spin-echo images from the face and neck region involving maxilla, mandible and neck region. Localizer was widened in cases of larger fields (TR/TE: 400–640 ms/10–14 ms; slice thickness: 4–7 mm; gap: 1–2 mm; field of view: 24–38 cm; NEX: 1–2; matrix: 256 × 192–256).
2. Axial T2-weighted fast spin-echo images of the face and neck (TR/TE: 4000–6000 ms/90–110 ms; echo-train length: 8; slice thickness: 4–7 mm; gap: 1–2 mm; field of view: 24–38 cm; NEX: 2; matrix: 512 × 256).
3. Sagittal T2-weighted fast spin-echo images from cantho-meatal line to supra-clavicular level (TR/TE: 4000–6000 ms/90–110 ms; echo-train length: 8; slice thickness: 4–7 mm; gap: 1–2 mm; field of view: 24–32 cm, NEX: 2; matrix: 512 × 256).
4. Unenhanced and enhanced fat-suppressed T1-weighted images in the coronal as well as best plane to visualize the lesion (TR/TE: 126 ms/2.47 ms; flip angle: 70°; slice thickness: 4–7 mm; gap: 1–2 mm; field of view 30–36 cm; NEX: 2–4; matrix: 256 × 192–256; spectral fat suppression).

Contrast-enhanced images were obtained after intravenous injection of 0.1 mmol/kg body weight of gadobenate dimeglumine (Multihance; Bracco, Milan, Italy). Postcontrast images were obtained in at least two planes. Additional sequences were taken in some patients as per the requirement while doing the procedure. The following parameters were studied with MRI [Figure 6].

1. Tumor size
   - Length
   - Width
   - Thickness
2. Lymph node
   - Size
   - Number
   - Grouping/confluence of lymph node.
   - Associated changes.

MRI parameters were analyzed by expert radiologists unaware of the findings of clinical examination. Tumor size

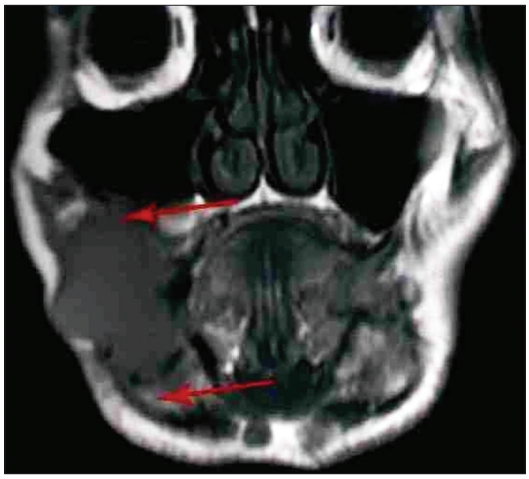


Figure 2: MRI image (coronal view) in same patient

Figure 3: Armamentarium used for clinical examination

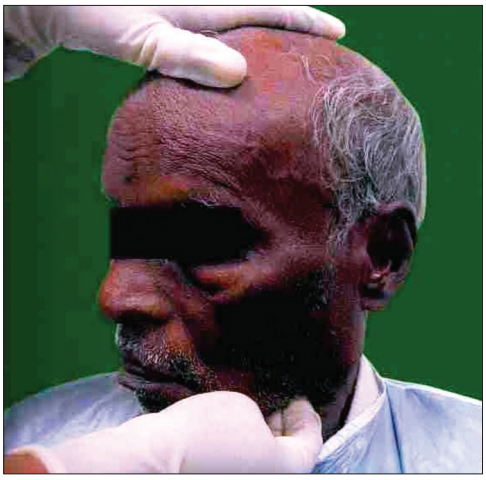


Figure 4: Lymph nodal examination being carried-out in a patient

in all the three dimensions [Figure 7] were studied for its relation with lymph node metastasis and hence, for giving more information about tumor staging. For measuring tumor thickness, a horizontal line joining the two tumor-mucosa junctions was drawn as a reference line. The tumor thickness was, then, measured by drawing perpendicular lines from the said reference line to the point of maximal tumor projection and invasion as seen on MRI images and then, calculated the greatest determined tumor thickness by adding these two parameters [Figure 8]. There is a lot of heterogeneity regarding imaging criteria of malignant lymphadenopathy in the literature. In the present study, diagnosis of the lymph node metastasis was made based on the following imaging criteria on MR imaging: size >8 mm, round shape. Size criterion was taken as standard and diagnostic reliability of all other criteria were calculated for predicting lymph node metastasis [Figure 9]. Out of the 27 patients included, 3 patients did not cooperate for the examination giving blurred and poor quality images and were, thus, excluded. Finally, 24 patients [11 oral cancer-alveolus, 6 oral cancer-tongue and 7 oral cancer-buccal mucosa] fulfilling the inclusion and exclusion criteria were included in the study. All the 24 patients were studied for tumor size, lymph node metastasis and grouping [Figure 10] and peri-neural spread [Figures 11 and 12] using MR imaging.

Statistical analysis used

For tumor size and lymph node metastasis, decision was made based on clinical examination adjuncted with MR images. For assessing the relationship between tumor thickness and lymph node metastasis for Level I lymph node and for all lymph node levels separately, diagnostic reliability for lymph node metastasis in relation to tumor thickness was calculated. Values of sensitivity, specificity, positive and negative predictive values and accuracy were calculated. Clinical diagnostic criteria for metastasis like hard and fixed lymph node and imaging criteria were assessed. Tumor size and lymph node size upon clinical examination and imaging findings were evaluated. Paired *t*-test was performed for evaluating size of the tumor and lymph node recorded on clinical and imaging findings.

Figure 5: MRI equipment

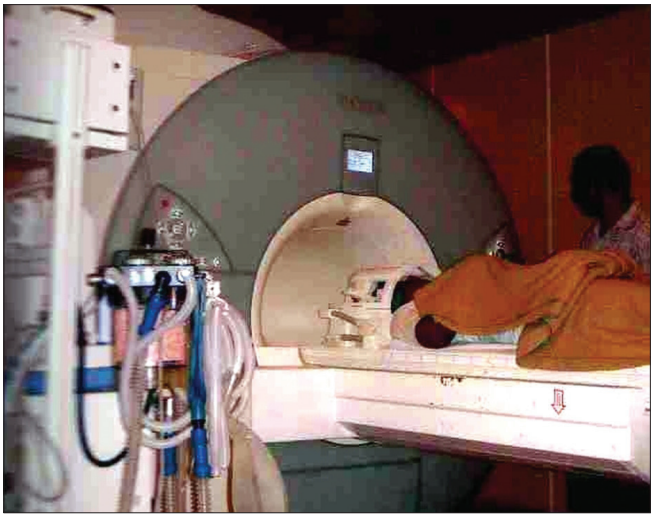


Figure 6: MR scan in progress in a patient

Figure 7: Tumor size on MRI image (axial view)

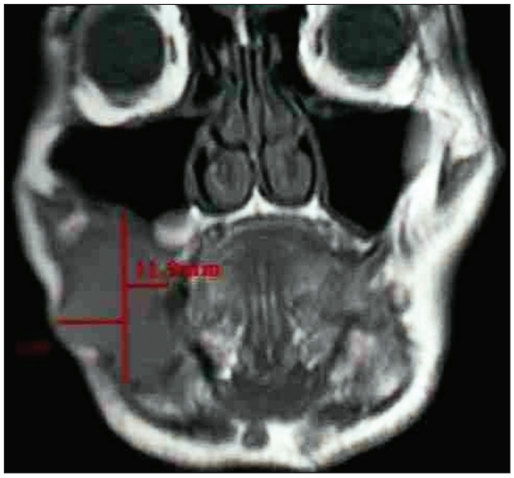


Figure 8: Tumor thickness on MRI image (coronal view);

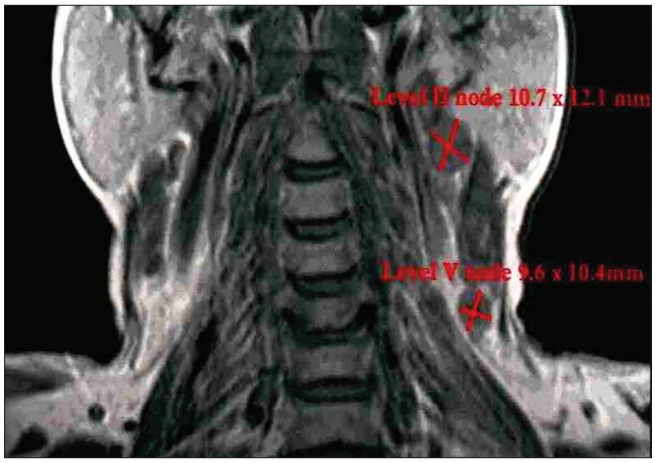
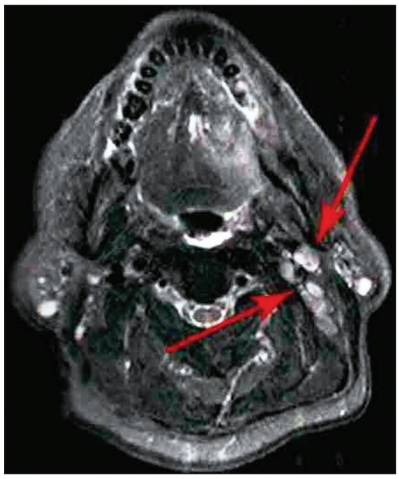


Figure 9: Lymph node size on MRI image (coronal view)



Figuer 10: Lymph node grouping on MRI image (axial view)

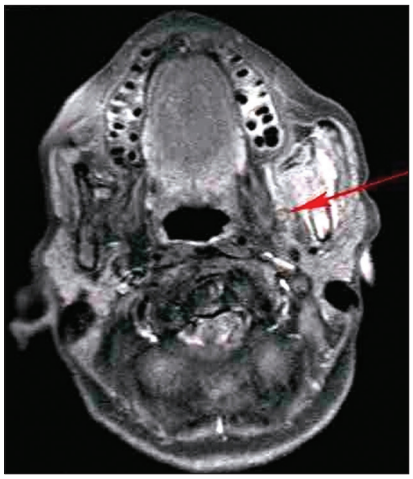


Figure 11: Peri-neural spread on MRI image (axial view)

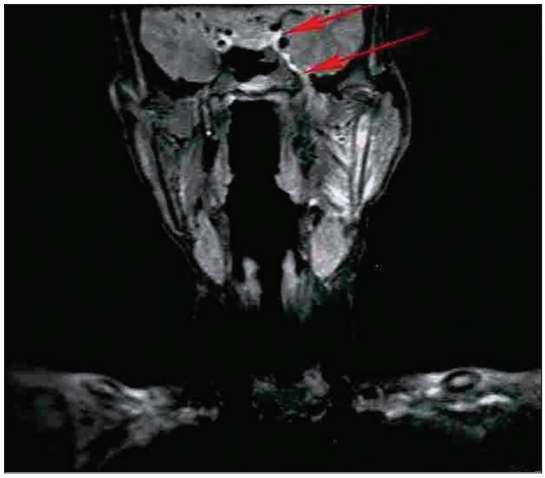


Figure 12: Peri-neural spread on MRI image (coronal view)

Eventually, the overall sensitivity, specificity and accuracy of the imaging were analyzed.

Results

The age of the patients in the study ranged from 37-84 years with a mean age of 60 years. The distribution of the cases with various cancers by age was done in three categories for upto 50 years, 51-65 years and above 65 years [Table 1]. There were 15 male and 9 female patients. [Table 1]. The study comprised of 11 patients with alveolo-buccal complex cancer; 6 cases involving the tongue and 7 cases with cancer of buccal mucosa [Table 2]. There were 15 cases of well-differentiated squamous cell carcinoma, 7 cases of moderately differentiated carcinoma and 2 cases of poorly differentiated carcinoma [Table 3]. Out of the 24 patients having palpable lymph nodes, 20 lymph nodes were positive for FNAC confirming metastatic spread [Table 4]. On clinical examination, one case was T1N1M0, 2 were T2N0M0, 14 were T2N1M0, 7 were T3N1M0 and 2 cases were T4N1M0. Similarly, after staging was done based on imaging criteria, 2 cases were T1N1M0, 1 was T2N0M0, 9 were from each T2N1M0 and T3N1M0 and 3 cases were T4N1M0 [Table 5 and Graph 1]. Tumor size (T-staging) was studied on clinical and imaging staging. Imaging staging was found to have higher value for most

Table 1: Distribution of cases by personal characters

Personal characteristics	*n*	Total (%)
Age (years)		
Up to 50	6	25.0
51-65	10	41.7
Above 65	8	33.3
Sex		
Male	15	62.5
Female	9	37.5
Total	24	100.0

Table 2: Distribution of cases by site

Site distribution	*n*	Total (%)
Alveolus	11	45.8
Tongue	6	25.0
Buccal mucosa	7	29.2
Total	24	100

of the cases as compared to the size of the same tumor reported clinically. On MR examination, 5 cases got upgraded from T2 to T3, 2 patients from T3 to T4 while only one patient was downgraded from T2 to T1 after MR examination. On imaging the lymph nodes, 5 cases got upgraded from N0 to N1 while 1 case was upgraded from N2a to N2b as noticed on MR images. Also, the nodal involvement was found to be more when higher T-staging was noticed on MR images [Table 5]. Tumor thickness noticed in the present study population varied from 1.4 to 5.6 cm. Table 6 shows the relationship between tumor thickness and lymph node metastasis for Level I lymph nodes [Graph 2]. Positive cases for lymph node metastasis were more when tumor thickness was >3 cm (8/9 positive cases) and 2-3 cm (3/10 positive cases) as compared to number of positive cases with tumor thickness of upto 2 cm (2/6 positive cases). Therefore, three cut-off thickness levels (2 cm, 3 cm and 4 cm) were chosen to calculate the diagnostic reliability for lymph node metastasis in relation to tumor thickness values in terms of sensitivity, specificity, positive and negative predictive values and accuracy [Table 6 and Graph 2]. Tables 6 and 7 show the relationship between cut-off tumor thickness of 2 cm, 3 cm and 4 cm and lymph node metastasis for Level I lymph nodes. When a cut-off thickness of 2 cm was taken, the values of specificity, sensitivity, positive and negative predictive values and accuracy were 66.6, 15.4, 42.1, 33.3 and 40% respectively [Table 7 and Graph 3] while when a cut-off thickness of 3 cm was taken into consideration, the values of specificity, sensitivity, positive and negative predictive values and accuracy were 41.7, 23.1, 33.3, 30 and 32% respectively [Table 7 and Graph 3]. On analyzing the data with a cut-off thickness of 4 cm, the values of specificity, sensitivity, positive and negative predictive values and accuracy were 91.7, 61.5, 68.7, 88.9 and 76% respectively [Table 7 and Graph 3]. The diagnostic accuracy for the detection of lymph node metastasis in relation to tumor thickness of 2 cm, 3 cm and 4 cm was reported to the extent of 40%, 32% and 76% respectively [Table 7 and Graph 3]. Table 8 shows the relationship between tumor thickness and lymph node metastasis for all levels of lymph nodes. On analyzing the data, it was evident that lymph node metastasis was positive for 3/11 cases with a tumor thickness of upto 2 cm while when tumor thickness was 2-3 cm, 8/19 cases were found to be positive. In case of tumor thickness >3 cm, 13/16 cases were found to be positive for lymph node metastasis [Table 8 and Graph 4]. On analyzing data with a cut-off thickness of 2 cm, the values of specificity, sensitivity, positive and

Table 3: Distribution of cases by tumor differentiation

Status	*n*	Total (%)
Poor	2	8.3
Moderate	7	29.2
Well	15	62.5
Total	24	100.0

Table 4: Distribution of cases by fine needle aspiration cytology positive lymph nodes

FNAC	*n* (%)
Positive	20 (83.33)
Negative	4 (16.67)
Total	24 (100.0)

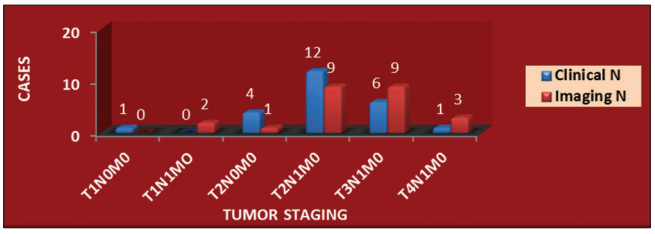
FNAC: Fine needle aspiration cytology

Table 5: Distribution of cases by clinical and imaging staging

Staging	Clinical, *n* (%)	Imaging, *n* (%)
T1N1M0	1 (4.2)	2 (8.3)
T2N0M0	2 (8.3)	1 (4.2)
T2N1M0	14 (58.3)	9 (37.5)
T3N1M0	7 (29.2)	9 (37.5)
T4N1M0	-	3 (12.5)
Total	24 (100.0)	24 (100.0)

Table 6: Relationship between tumor thickness and lymph node metastasis for Level I lymph nodes

Tumor thickness (cm)	Lymph node metastasis		Total (suction)
	Negative	Positive	
Up to 2	4	2	6
2.0-3	7	3	10
>3	1	8	9
Total	12	13	25



Graph 1: Distribution of cases by clinical and imaging staging

Table 7: Diagnostic reliability of different cut off thickness in relation to lymph node metastasis for Level I lymph nodes

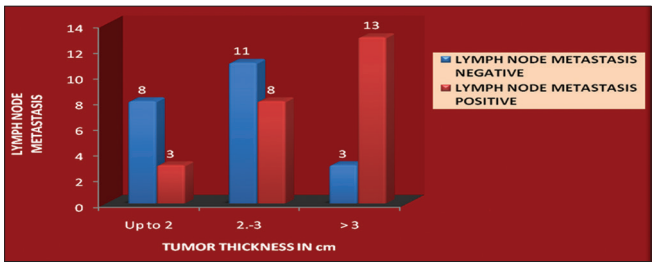
Tumor thickness (cm)	Specificity (%)	Sensitivity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
2	66.67	15.38	42.11	33.33	40
3	41.67	23.08	33.33	30	32
4	91.67	61.54	68.75	88.89	76

negative predictive values and accuracy of 63.6, 12.5, 40, 27.3 and 37% respectively were reported [Table 9 and Graph 5] When a cut-off thickness of 3 cm was taken into consideration, the values of specificity, sensitivity, positive and negative predictive values and accuracy were 50, 33.3, 40.7, 42.1and 41.3% respectively [Table 9 and Graph 5]. Taking cut-off thickness of 4 cm, the values of specificity, sensitivity, positive and negative predictive values and accuracy were found to be 86.4, 54.2, 63.3, 81.3 and 69.6% respectively [Table 9 and Graph 5]. When all the lymph node levels were studied for calculating the diagnostic reliability of lymph node metastasis in relation to tumor thickness 2 cm, 3 cm and 4 cm, the values of accuracy were 37, 41.3 and 69.6% respectively [Table 9 and Graph 5]. In the present study, size criterion was taken as standard and diagnostic reliability of all other criteria were calculated for predicting the lymph node metastasis. Table 10 shows the relationship between lymph node number and metastasis for Level I lymph nodes. It was evident from the results of the present study that when only one lymph node was enlarged, 8/17 cases were positive for lymph node metastasis, 5/7 cases were positive when two lymph nodes were enlarged. Surprisingly, no node was positive for lymph node metastasis when 4 lymph nodes were enlarged. Table 11 shows the diagnostic reliability for lymph node metastasis in relation to lymph node number, grouping and associated changes for Level I lymph nodes. The values of specificity, sensitivity, positive and negative predictive value and accuracy were 75, 38.5, 53, 62.5 and 56% respectively for number of lymph nodes for predicting Level I lymph node metastasis [Graph 6]. The values of specificity, sensitivity, positive and negative predictive value and accuracy were 83.3, 30.8, 52.6, 66.7 and 56% respectively for the grouping of lymph nodes for predicting Level I lymph node metastasis [Table 11 and Graph 6]. The values of specificity, sensitivity, positive and negative predictive value and accuracy were 100, 7.7, 50, 100 and 52% respectively for associated changes of lymph nodes for predicting Level I lymph node metastasis. [Table 11 and Graph 6] Table 12 shows the relationship between lymph node number and metastasis for all levels of lymph nodes. The values of specificity, sensitivity and accuracy were found to be 77.3, 45.9 and 60.8% respectively [Graph 7]. The diagnostic accuracy for the detection of lymph node metastasis in relation to lymph node grouping was to the extent of 56% for all levels of lymph nodes [Table 12 and Graph 7]. A specificity of 100.00% and sensitivity of 4.2% was noticed with an accuracy ratio of 50.00% was noticed when diagnostic reliability for lymph node metastasis in relation to lymph node associated changes in all levels of lymph nodes was evaluated [Table 12 and Graph 7].

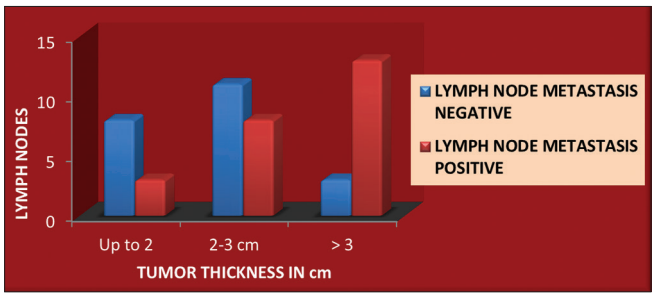
Clinical Diagnostic Criteria vs. Imaging Criteria: 40% cases were found to be true positive for detecting metastasis

Table 8: Relationship between tumor thickness and lymph node metastasis for all levels of lymph nodes

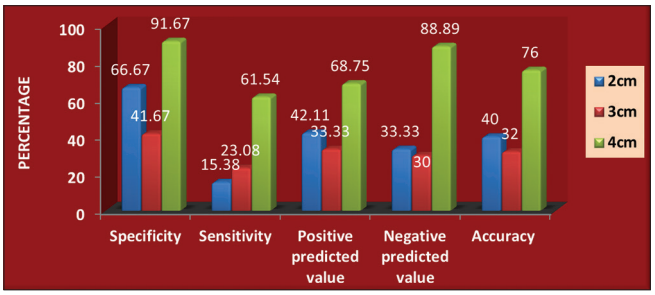
Thickness (cm)	Lymph node metastasis		Total
	Negative	Positive	
Up to 2	8	3	11
2-3	11	8	19
>3	3	13	16
Total	22	24	46



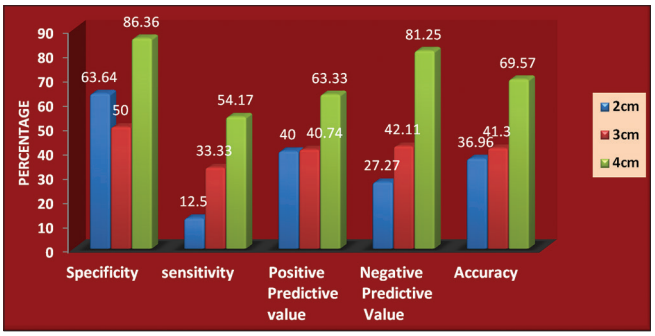
Graph 2: Relationship between tumor and lymph node metastasis for level 1 lymph nodes



Graph 4: Relationship between tumor thickness and lymph node metastasis for all levels of lymph nodes



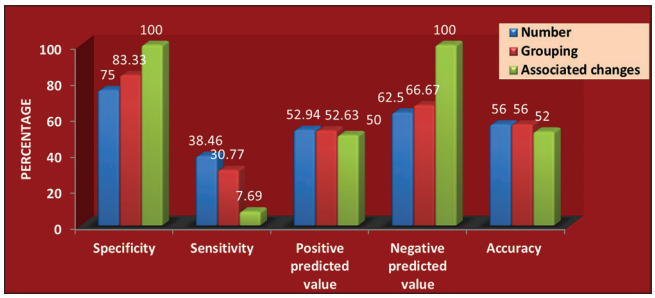
Graph 3: Diagnostic reliabilities of different cutoff tumor thickness for level 1 lymph nodes



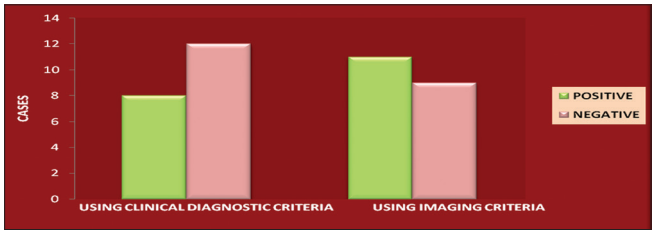
Graph 5: Diagnostic reliabilities of different cutoff tumor thicknesses for all levels of lymph nodes

Table 9: Diagnostic reliability of different cut off thickness in relation to lymph node metastasis for all levels of lymph nodes

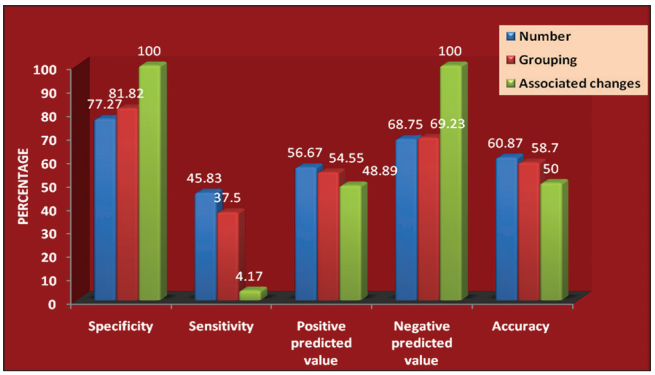
Tumor thickness (cm)	Specificity (%)	Sensitivity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
2	63.64	12.5	40	27.27	36.96
3	50	33.33	40.74	42.11	41.3
4	86.36	54.17	63.33	81.25	69.57



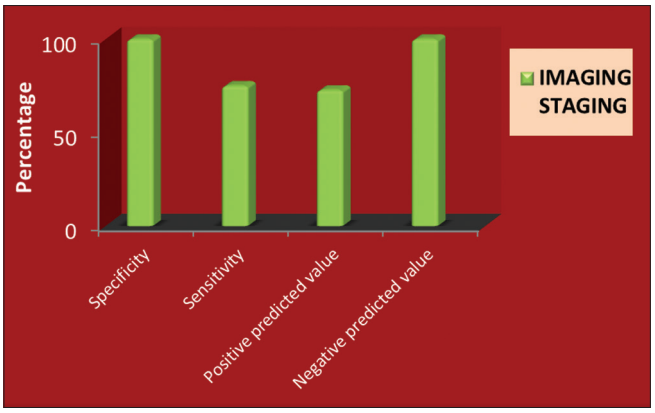
Graph 6: Diagnostic reliabilities of imaging criteria for level 1 lymph nodes



Graph 8: Cases by clinical diagnostic criteria and imaging criteria



Graph 7: Diagnostic reliabilities of images criteria for all levels of lymph nodes



Graph 9: Overall diagnostic reliability of imaging staging

using clinical diagnostic criteria while 55% cases were found to be true positive for detecting metastasis using imaging criteria [Table 13 and Graph 8]. The tumor size identified by imaging (mean = 4.04 mm and 3.08 mm for length and width respectively) was significantly higher than that assessed by clinical staging (mean = 2.94 mm and 2.47 mm for length and width respectively) with the corresponding paired '*t*' test value for the difference in tumor size between imaging and clinical staging statistically significant ($P < 0.01$) [Table 14]. Similarly, the size of lymph nodes identified by imaging (mean = 11.45 mm) was found to be significantly higher than that palpated clinically (mean = 8.00 mm) with the corresponding results being statistically significant ($P < 0.01$) [Table 15]. The overall specificity, sensitivity and positive and negative predictive values as observed on imaging were found to be 100%, 75%, 72.73% and 100% respectively while the overall accuracy was noticed at 85% [Table 16 and Graph 9].

Discussion

Early detection of malignancy is a continuing goal. Unfortunately, patients are most often identified only after the development of symptoms at advanced stages of the disease process. In a large clinical trial in India by Ramadas K *et al*.,[25] thorough head and neck examinations have been shown to result in early identification of oral squamous cell carcinomas (OSCCs) and translate into improved survival compared to the select control group. Som PM *et al*.[14] stated that clinical examination is an inaccurate technique to stage cancer and diagnostic imaging is superior to clinical staging in the detection of malignancy as well as malignant lymphadenopathy. Size, staging and lymph node metastasis are important determinants of prognosis as well as survival for oral carcinoma.[4] As described by the previous researchers also,[4,19] the presence of lymph node metastasis in the neck of the patients with cancers of head and neck region is an important prognostic determinant in staging cancers and in treatment planning for such patients. Furthermore, the survival rate is positively affected by treatment of the neck upon presentation of the cancer[26] as this can prevent late neck disease due to persistent growth of occult metastases. By detecting clinically occult lymphadenopathy, magnetic resonance imaging (MRI) helps in an accurate assessment

of malignant lymphadenopathy.[8-10,27] Amongst all the tumor parameters including the tumor size, tumor thickness has been found to be a significant factor that has a significant predictive value for sub-clinical nodal metastasis, local recurrence and survival.[17-19,21,22] In a study conducted by O-charoenrat P *et al*.,[18] the tumor thickness of primary tumor was found to have a strong predictive value for occult cervical metastasis and poor outcomes in patients with oral squamous cell carcinoma (OSCC). Despite higher incidence and also, the higher mortality rates reported from India,[2,28] no study describing diagnostic accuracy of important prognostic factors like tumor thickness related to lymph node metastasis using modern imaging techniques and inaccuracies of clinical examination has been documented so far to the best of our knowledge. Although computed tomography (CT) remains the most widely used imaging modality for head and neck examination, it delivers a very high dose of radiation to the patients.[24,29] Ultrasonography (USG), on the other hand, is a highly operator dependent imaging modality.[18] Magnetic resonance imaging (MRI) is a safer and new procedure for the evaluation of oral cancer and lymphadenopathy and its excellent soft tissue resolution can give better results.[24,29] MRI has been found to provide good visualization of oral cancer and is the imaging technique of choice for studying head and neck tumors.[30] It provides better resolution of detailed soft tissue architecture than either CT or, USG, especially, in 3D visualization of the soft-tissue lesions.

Table 10: Relationship between lymph node number and metastasis

Number of lymph nodes enlarged	Lymph node metastasis		Total
	Negative	Positive	
1	17	13	30
2	4	7	11
3	0	1	1
4	1	1	2
5	0	1	1
6	0	1	1
Total	22	24	46

MR imaging, also, assists in the visualization of nodal metastasis.[29,31-33] Though MR imaging is costly,[4] its use for accurate pre-operative evaluation of tumor size and metastatic lymphadenopathy can significantly decrease the morbidity as well as mortality of the cases.[33] Use of MRI, in the head and neck region, is, also, supported by the facts that oro-facial tissues have variable amount of fat in different regions and tumor extent can be clearly seen on MR images by fat suppression techniques. Moreover, MR imaging is free from metal streak artifacts caused due to dental restorations as seen on CT images.[29] The major limitations of MR imaging include its restricted availability and difficulty in performing MRI scan in claustrophobic, old and uncooperative patients. MR imaging is, also, contraindicated in patients with pacemakers and vascular clips. The detection of lymph node metastasis in OSCC cases by specialized imaging modality like MRI is of particular interest because of its potential application as a diagnostic tool to predict lymph node metastasis and hence, the prognosis of the patients.[29,33] Bipat *et al*.[34] after reviewing 57 high quality studies concluded that the sensitivity of MR imaging was higher (60%) as compared to CT (43%) for detecting metastatic lymph nodal involvements. Based on the findings of the previous studies in this regard and also, MR imaging being a non-ionizing modality with higher resolution of soft tissues, MR imaging was preferred in the present study. In the present study, tumor size i.e. T staging of the carcinomas and lymph node involvement as seen on imaging was higher for most of the cases as compared to the T staging documented on clinical examination. Only one case was downgraded from T2 to T1 after MR examination the probable reason for which could be that the largest tumor dimension got obscured within 4-7 mm slice thickness used for MR image acquisition. Also, nodal involvement was found to be more when seen on MR images as compared to the clinical staging. Five cases i.e. 20.83% were upgraded from N0 to N1 and one case (4.17%) was upgraded from N2a to N2b as noticed on MR images. Thus, it is evident from the present study that whenever tumor size was larger, more nodal metastasis was noticed. The overall diagnostic

Table 11: Diagnostic reliability of different imaging criteria for predicting lymph node metastasis for Level I lymph nodes

Lymph node	Specificity (%)	Sensitivity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
Number	75	38.46	52.94	62.5	56
Grouping	83.33	30.77	52.63	66.67	56
Associated changes	100	7.69	50	100	52

Table 12: Diagnostic reliability of different imaging criteria for predicting lymph node metastasis for all levels of lymph nodes

Lymph node	Specificity (%)	Sensitivity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
Number	77.27	45.83	56.67	68.75	60.87
Grouping	81.82	37.5	54.55	69.23	58.7
Associated changes	100	4.17	48.89	100	50

Table 13: Clinical diagnostic criteria and imaging criteria

Using clinical diagnostic criteria	Using imaging criteria
Negative	Positive
Negative	Negative
Positive	Negative
Negative	Negative
Positive	Positive
Positive	Positive
Negative	Positive
Positive	Negative
Negative	Negative
Positive	Positive
Positive	Positive
Negative	Negative
Negative	Positive
Negative	Negative
Negative	Negative
Negative	Negative
Negative	Positive
Negative	Positive
Positive	Positive
Positive	Positive

Table 14: Tumor size (mm) between clinical and imaging staging

Staging	*n*	Mean	SD	Mean difference	*t*	*P*
Tumor length						
Clinical	24	2.94	1.18	−1.10	−7.22	0.00
Imaging	24	4.04	1.71			
Tumor width						
Clinical	24	2.47	0.97	−0.61	−3.38	0.00
Imaging	24	3.08	1.53			

P<0.01. SD: Standard deviation

accuracy of MR imaging for lymph node involvement in the present study was reported to be remarkable with a specificity and negative predictive value of 100% and an accuracy of 85%. In the present study, the values of specificity, sensitivity and positive predictive value were remarkably higher when a tumor thickness cut-off of 4 cm was taken as compared to 2 cm or 3 cm cut-off values. In India, patients are not well-aware of the health problems, particularly, oral health and report to oral physicians only after the size of the tumor has increased significantly. Hence, the cut-off value for which higher lymph node metastasis was noticed was higher in the present study as compared to other studies reported in the literature. Hayashi T *et al*.[35] reported an accuracy of 75% with a cut-off value of 5 mm tumor thickness for subsequent lymph node metastasis when using CT. In the present study, a diagnostic accuracy of 76% was achieved with a cut-off value of 4 cm tumor thickness for subsequent lymph node metastasis when using MRI. Diagnostic accuracy reported by Hayashi T *et al*.[35] using CT and the present study study

Table 15: Lymph node size (mm) between clinical and imaging staging

Staging	*n*	Mean	SD	Mean difference	*t*	*P*
Clinical	20	8.00	5.48	−3.45	4.21	0.0005
Imaging	20	11.45	7.22			

P<0.01. SD: Standard deviation

Table 16: Overall diagnostic reliability of magnetic resonance imaging staging for lymph node metastasis

Clinical staging	Imaging staging		Total (cut-off)
	Negative	Positive	
Negative	8	3	11
Positive	0	9	9
Total (metastasis)	8	12	20
True positive		9	
True negative		8	
False positive		0	
False negative		3	
Specificity		100.00	
Sensitivity		75.00	
Positive predictive value (%)		72.73	
Positive predictive value (%)		100.00	
Accuracy		85.00	

using MRI are comparable, however, disadvantages of CT have to be kept in mind. Significantly increased risk of cervical metastasis has been noticed with a thickness >5 mm for oral cavity and oro-pharyngeal carcinomas by Fukano H *et al*.[16] and O-charoenrat P *et al*.[18] Furthermore, poor survival and consideration of elective neck treatment was proposed by Brown B *et al*.[15] and Urist MM *et al*.[20] for tumor thickness of >2 mm for carcinomas of the tongue and for a thickness of 6 mm for carcinomas of buccal mucosa respectively. It is true that tumor deposits within a node are only microscopic and detection of metastasis by CT or, MR imaging is impossible at microscopic level, but when metastases are large enough to be detected by CT or, MRI, criteria are necessary to stage the disease properly.[33] There are no clear recommendations regarding size criterion and different values have been studied.[36-42] The present study took size criteria of 8 mm as standard for predicting lymph node metatstasis and analyzed the accuracy of other imaging criteria. Number of lymph nodes involved was not studied as imaging criterion before, however, literature review reveals worse prognosis when more number of lymph nodes are involved.[43] The present study was able to achieve an accuracy of 56-60% using scales of single and multiple lymph node involvement. In the present study, it was found that imaging criterion of grouping of lymph nodes gave superior specificity to an extent of 81-83%. This finding was contradictory to the previous study by van den Brekel MW *et al*.[42] who stated that the grouping criterion did not increase the specificity for the detection of lymph node metastasis. Recently, the prediction of peri-neural spread along the nerve till base of

skull has been described by Hanna E *et al*.[44] using CT and MRI. They reported a sensitivity of 100% and a specificity of 85% using MRI and a sensitivity and specificity of 88% and 89%, respectively using CT. However, in the present study, a sensitivity of 4.17-7.79% and a specificity of 100% using peri-neural spread as imaging criterion on MR imaging was reported. The low value of sensitivity could be attributed to the fact that only one case in the present study was found to have associated changes with lymph node metastasis in the form of peri-neural spread on MR imaging. Clinical examination remains the worldwide standard and the first step for the initial screening and evaluation of oral carcinomas; however, it fails to define the exact tumor extent and nodal metastasis. Surface size is the main verifiable clinical parameter available before treatment because nodal spread estimates are so often erroneous[45] and biopsies often do not reflect the whole tumor histology.[13,46] Size is used by all clinicians for staging and is usually expressed as the measurement of greatest surface diameter. If clinicians measure thickness or, total volume before treatment, it can only be a rough estimate and these estimates are not mentioned in the official TNM manual.[47,48] In patients with head and neck carcinoma, the prognosis is usually obtained based on TNM classification which is based on clinical criteria[49] and is highly useful, especially, to assess the essential features of cancers such as local extension, regional dissemination and distant metastasis.[50] However, this classification lacks a clear idea about the aggressiveness of tumor and inflammatory versus metastatic node enlargements. Clinical impression of node metastasis on first examination is often overestimated by 30% or, more of the examiners45 because of regional inflammatory reaction to a metastatic node and/or, overzealous examination as reported by Moore C *et al*.[13] However, histopathological examination which is the gold standard can be done post-operatively only. Probably, a study correlating MR imaging and histologic tumor thickness in the assessment of oral carcinoma gives a more clear view about this aspect. One such study done by Lam P *et al*.[19] in oral tongue carcinomas stated that the radiologic tumor thickness as measured on contrast-enhanced MRI images had significant correlation with histologic tumor thickness. Oral cancers may have different behaviors in different areas of oral mucosa. Thus, traditional TNM clinical staging fails to predict exact prognosis also. It has, also, been reported previously that when dealing with primary tumors, advanced cases with infiltration of adjacent structures are hardly assessed on clinical examination.[51,52] The percentage of accuracy was found to be still higher when CT and MR imaging are used for classification and staging of neoplasias[51] as compared to TNM clinical staging alone. In the present study, only 8/20 i.e. 40% cases were found to be true positive for detecting metastasis using clinical diagnostic criteria. On the other hand, 11/20 i.e. 55% cases were found to be true positive for detecting lymph node metastasis using the imaging criteria. Thus, imaging criteria were found to be more accurate than the clinical diagnostic criteria with 9 false negative lymph nodes. This might, also, be because none of the available imaging criteria for lymph node metastasis are standardized till date. It is interesting to report that few cases in the present study, particularly, tongue and buccal mucosa showed involvement of Level III and IV lymph nodes on MR imaging but were clinically occult (N0), thereby, emphasizing the significance of MR imaging in providing useful information regarding the treatment planning in such cases and highlighting the significance of the option of consideration of the neck for treatment in such cases. By detecting some otherwise clinically occult lymphadenopathy, MR imaging may have increased sensitivity for detecting positive nodes and consequently, may decrease the risk of occult metastasis to below 20%.[53] The assessment of tumor size and lymph node metastasis by MR imaging before surgery can evaluate whether the patients with clinically N0 neck are having nodal involvement. This useful information forms an important part of decision making as treatment strategies for N0 and N1 or, N2 necks differ distinctly. For clinically N positive cases, MR imaging provides more accurate assessment of lymph node metastasis which helps in the treatment planning necessary to improve local and nodal control. The comparatively lower sensitivity and specificity reported in the present study might be attributed to the reason that cases involving three different regions of oral cavity were included which might have different patterns of nodal metastasis. But clinicians are especially interested in the "accuracy" of modern imaging techniques for staging of the cancer cases rather than the sensitivity and specificity in terms of nodal metastasis.[53] Sample population was taken at random in the present study and because of less number of cases involving different regions; analysis was carried-out for all the cases together. Furthermore, carcinoma of alveolus does not spread to the lymph nodes as rapidly as tongue and buccal mucosa.[4,5,18,35] The present study, also, showed the application of pre-operative MR imaging assessment of tumor thickness in oral cancers and that this, in turn, might translate into better prediction of lymph node metastasis and hence, prognosis and optimal treatment planning. The major limitations encountered in the present study included the relatively small number of cases for different sites of involvement as well as different sites of involvement and enhancement of the adjacent inflamed and edematous soft tissues on MR imaging, especially, on T2-weighted, spin-echo images.[19,23] Despite these drawbacks, pre-operative MR imaging assessment for oral cancers in the present study provided extremely useful information regarding the prognosis and treatment of the cases affected by practically incurable carcinomas. Based on the findings of the present study, it is highly recommended that whenever tumor size, particularly a tumor thickness of >4 cm for oral carcinomas is noticed on MR imaging, higher lymph node metastasis could be

predicted accurately which, in turn, has a significant impact on the prognosis.

Conclusion

Cervical lymph node metastasis has been investigated with a number of imaging modalities, however, tumor size related to the level of cervical lymph node metastasis using MRI needs more elaboration. With this in mind, the prime objective of the present study was to evaluate tumor size as a predictive indicator for the detection of lymph node metastasis in oral carcinoma and to further validate its role as a prognostic indicator. In the present study, clinical and MRI findings of 24 histopathologically proven cases of oral carcinoma were analyzed and studied for relation of tumor size with cervical lymph node metastasis. The clinical diagnostic criteria and imaging criteria were, also, evaluated. It is evident from the results of the present study that MRI is a reliable imaging method to assess tumor size. Detection of tumor size and lymph node metastasis was found to be higher on MRI than that by clinical staging alone. It was noticed that whenever the tumor size was larger on MR images, more nodal metastasis was noticed. Tumor size, particularly, tumor thickness measured on MRI can be used as a predictive indicator for cervical lymph node metastasis. In the present study, diagnostic accuracy of the tumor thickness for the detection of Level I lymph nodes as well as for all levels of lymph nodes was found to be higher i.e., 76% when 4 cm tumor thickness was taken as a cut-off value as compared to 2 cm and 3 cm. It could, thus, be concluded from the results of the present study that whenever larger tumor size, particularly tumor thickness of >4 cm for oral carcinoma, is noticed on MRI, higher lymph node metastasis can be predicted accurately. Different imaging criteria for detecting metastatic lymphadenopathy e.g., number, grouping/confluence and associated changes have almost equal accuracy and can be used for detecting lymph node metastasis accurately. This high value of accuracy obtained using MRI obviates the need for CT which is at present the most widely used modality for head and neck imaging. By using MRI instead of CT, high dose of radiation exposure delivered to the patient by CT can be avoided as MRI is a nonionizing based imaging modality. The present study, also, validated that clinically occult lymphadenopathy can be detected with the help of MRI. From the present study, it could, also, be inferred that the overall diagnostic accuracy of MRI for lymph node detection is remarkable i.e., specificity of 100% and accuracy of 85% was achieved in the present study. The present study, also, proved that clinical diagnostic criteria alone are less accurate for detecting metastatic lymphadenopathy. As good decisions increase the chances of better outcome, the better decision making done regarding treatment of oral carcinomas will help to decrease not only the mortality but, also, the morbidity in patients. Though, there are numerous modalities available for imaging of oral cancers, it is necessary for the clinicians to use a modality which is safer and accurate. MRI is very useful for preoperative evaluation in patients presenting with oral cancers, however, it might not provide equally useful information postsurgery and/or, radiotherapy when the anatomical planes are disturbed posttreatment. In such cases, FDG-PET may be used to get necessary information regarding residual/recurrent malignant and metastatic foci and associated lymphadenopathy.[54] MR imaging, thus, can be safely made a recommendation in all head and neck malignancies for pre-operative diagnostic imaging procedures in order to get extremely useful information regarding treatment planning and prognosis in such patients presenting with oral carcinomas. In future, newer technologies applied to MRI including functional MRI,[26] MRI micro-imaging[40] etc. might give more advanced outcomes with higher diagnostic and predictive accuracies and help in improving survival of cancer patients.

To conclude cancer is a word, not a "sentence" and Accurate diagnosis is not the end, it is just the beginning of practice-John Diamond and Martin H Fischer.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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