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Accuracy of Diffusion Weighted MRI in Prediction of Metastasis to Cervical Lymph Nodes in Oral Cancer Patients at a Tertiary Care Center in Jaipur.

Himanshu Sharma[1], Naima Mannan[2], Usha Jaipal[3], Rajkumar Yadav[4], Raj Govind Sharma[5], Pawan Singhal [6], Vandna Yadav[7].

[1] Post Graduate Student, [2] Professor, [3] Senior Professor & Head, [4] Assistant Professor, [5] Senior Professor & Head, [6] Professor, [7] Assistant Professor.

[1-4] Department of Radiodiagnosis and Modern Imaging, SMS Medical College, RUHS, Jaipur.

[5] Department of Oncosurgery, SMS Medical College, RUHS, Jaipur.

[6] Department of ENT, SMS Medical College, RUHS, Jaipur.

[7] Department of Pathology, SMS Medical College, RUHS, Jaipur.

ABSTRACT:

Aim:- To find out Sensitivity, Specificity, Accuracy, Positive and Negative predictive value of Diffusion weighted MRI in the prediction of metastasis in enlarged cervical lymph nodes in oral cancer patients on the basis of diffusion restriction and ADC values.

Material & methods: 70 patients with biopsy proven oral cancer with enlarged neck nodes were included in this study and underwent clinical and MRI examination. MRI was performed on PHILIPS INGENIA 3 TESLA MRI. Diffusion-weighted MR images were obtained at *b* factors of 0, 500, and 1,000 sec/mm^2. Prediction of metastasis to cervical lymph nodes was done on the basis of diffusion restriction and ADC values. All patients underwent Neck dissection and the final diagnosis was made by histopathology. Statistical analysis was applied to find out the sensitivity, specificity, PPV, NPV and diagnostic accuracy. P-value < 0.05 was taken as significant.

Results: Cervical lymph node metastasis was found in 38 out of 70 cases (54.28%) with the most frequent involvement of level I lymph nodes (52.86%). The mean ADCs value for malignant and benign lymph nodes was 0.87±0.21x10^{-3} mm^2/s and 1.31+/-0.20 x10^{-3} mm^2/s respectively. Sensitivity, specificity, accuracy, PPV and NPV of Diffusion Weighted MRI in predicting cervical lymph nodal metastasis was 97.36%, 90.62%, 94.28%, 92.5% and 96.66% respectively when compared histopathologically.

Conclusion: Benign or malignant cervical lymph nodes can be differentiated on diffusion-weighted imaging of MRI on the basis of diffusion restriction and their ADC values concluding that diffusion imaging could be considered an important supportive tool for detecting malignancy in enlarged cervical lymph nodes.

Keywords: Apparent diffusion coefficient, Diffusion Weighted MRI, Oral Cancer.

INTRODUCTION:

Oral cancer is the 12th most common cancer globally and the 8th most common in developing countries.[1] The incidence of oral cancer in Indian males is 13% of all malignancies and is the third most common cancer in Indian females.[2]

Corresponding author: Rajkumar Yadav

Squamous cell carcinomas accounts for more than 90% of malignant tumors of the oral cavity. Squamous cell carcinoma of lower gingivo buccal complex and tongue are the most common cancer in the Indian sub-continent due to tobacco chewing and alcohol abuse and have been described as Indian oral cancer.[3]

The prognosis of carcinoma of the oral cavity is influenced by variety of factors such as degree of cellular differentiation, size, location, presence of infiltration into the bony tissue, immune response, age, gender, patients, socio economic status and the presence of cervical lymph node metastasis, the latter being considered the most important factor when determining the prognosis.[4-6]

Oral squamous cell carcinoma (OSCC) has loco regional evolution. As it grows, it invades the surrounding tissue and metastasizes to regional neck nodes, but it rarely develops distant metastases. SCC with negative nodes at the time of presentation (N0) has a high risk of harboring occult node metastases evading clinical detection, in the majority of cases. Similarly, a large number of patients who undergo elective neck dissection are found to have no evidence of cervical node metastasis on pathological examination and might have been spared this additional procedure.

The presence of cervical lymph node metastases is the most important prognostic factor for survival.[7-9] Diffusion weighted MRI (DW-MRI) has recently become the main area of interest as recent studies have shown it to be superior in detecting nodal metastasis. Diffusion-weighted MRI analyses intercellular water motion: every change in the water protons movements produces a variation of signal intensity in diffusion-weighted sequences and as a consequence on ADC maps.[10]

This study assessed the accuracy of DW-MRI in the prediction of cervical lymph nodal metastasis in oral cancer patients on the basis of diffusion restriction and ADC values.

MATERIAL AND METHODS

This Hospital based Descriptive type of Observational Study was conducted in the Department of Radio-diagnosis and Modern imaging, ENT, Oncosurgery and Pathology of S.M.S. Medical College, Jaipur from march 2017 to February 2018 after approval from institutional Research Review Board.

Sample size of 70 patients with biopsy proven oral cancer with enlarge neck nodes at or below clinical stage T4a according to TNM staging classification were included in study following appropriate consent.

INCLUSION CRITERIA:-

1. All biopsy proven patients (in patients or out patients) of oral cancer with enlarged neck nodes at or below clinical stage T4a referred to the department of Radio-diagnosis for MRI examination.
2. Both male and female patients.
3. Patients who gave appropriate informed and written consent for MRI, Neck Dissection and Histopathological examination.

EXCLUSION CRITERIA:-

1. Claustrophobic patients.
2. Patients with metallic implants, pacemakers.
3. Patients of oral cancer with clinical staging greater than T4a.
4. Malignancies other than tongue and gingivo-buccal in location.
5. Patients who were not willing to have MRI, Neck Dissection and Histopathological examination.

METHOD OF DATA COLLECTION

- All patients underwent clinical and MRI examination.

MRI PROTOCOL:-

- MRI Machine – PHILIPS INGENIA 3 TESLA MRI.
- Position of Patient – Supine on the MRI table and head coil was applied.
- Routine T1WI (Axial and coronal spin echo T1 W), T2WI (Axial, coronal and sagittal fast spin echo T2 W) ,Short Tau Inversion Recover (STIR) sequences, Axial diffusion-weighted sequence (b factor of 0,500 and 1000 s/mm^2 per

axis) [Fig-1] followed by post contrast axial T1W sequences were taken.

- We measured the signal intensity of the lesion with an electronic cursor to define the region of interest (ROI) in each patient. The ADC value was automatically reconstructed by a standard software imager in the main console. The whole-node ADC value was obtained drawing a region of interest (ROI) covering all the pathologic node in all sections in which it was present.[Fig-2]
- We avoided obvious cystic portions and calcified areas to perform diffusion-weighted MR imaging. We paid special attention to the image distortion caused by susceptibility artefacts and to the severity of chemical shift artefacts and ghosts in the phase-encoding direction.
- Prediction of metastasis to cervical lymph nodes was done on the basis of diffusion restriction and ADC values.
- All patients undergone Neck dissection and the final diagnosis was made by histopathology.
- Statistical analysis was applied to find out the sensitivity, specificity, PPV, NPV and diagnostic accuracy. Chi-square test was used. P-value < 0.05 was taken as significant.

[Fig-1] Axial DWI shows enlarged left cervical lymph node showing hyperintense signal.

[Fig-2] On ADC map corresponding lymph node showing hypo intensity denoting restricted diffusion. Measuring ADC values within region of interest (circle).Malignant metastatic lymph node with mean ADC value of .80x10^{-3} mm^2/sec.

RESULTS

We found that 38 (54.28%) out of 70 patients showed lymph node metastasis to various levels. Out of these 38 patients, 24(63.16%) cases positive for lymph node metastasis had their primary lesion over buccal mucosa, followed by tongue 11 cases(28.95%), followed by gingivo-buccal sulcus 3 cases(7.89%). Most frequent involvement of level I lymph nodes (52.86%) was seen.

A total of 40 patients out of 70 patient shows restricted diffusion on DWI at one or the other cervical levels with the ADCs value ranging from (0.5 to 1.2x10^{-3} mm^2/s) while 30 cases did not show restricted diffusion and there ADCs values ranges from (0.6 to 1.4 x10^{-3} mm^2/s).The mean ADCs value for malignant and benign lymph nodes was 0.87±0.21x10^{-3} mm^2/s and 1.31+/-0.20 x10^{-3} mm^2/s respectively. Cut off value to discriminate between malignant and benign lymph nodes was 1.09 x10^{-3} mm^2/s in the present study.

Sensitivity, specificity, accuracy, PPV and NPV of DWMRI in predicting cervical lymph nodal metastasis was 97.36%, 90.62%, 94.28% ,92.5% and 96.66% respectively when compared histopathologically.[Table1]

Table 1: Binary Classification of cervical lymph node metastasis on MRI versus Histopathology

		Histopathology		
		Positive	Negative	Total
MRI	Positive	37	3	40
	Negative	1	29	30
Total		38	32	70

- Chi-square = 51.388 with 1 degree of freedom; $p<0.05$ (S)
- Odds ratio = 357.667 (CI = 35.331 to 3620.725)

Comment: Statistically significant p value <0.05 is calculated when predicting cervical lymph node metastasis on MRI followed by Histopathological assessment. MRI give false positive results in 3 cases and missed 1 case which was positive for cervical lymph node metastasis.

DISCUSSION

The oral squamous cell carcinoma (OSCC) is one of the rapidly growing oral cancers in the literature of oncology and it is the 6th most common cancer in the world. It is more common in south Asian countries specially India and Sri Lanka. Tobacco and heavy alcohol is the predominant cause of oral cancers. Tobacco alone covers 90% of all oral cancers. The five year survival rate of oral cancer is 68% in early stage and 27% in the late stage.[11]

The detection of cervical nodes metastasis is very important for the prognosis and the treatment of head and neck tumours. Up to today parameters used by conventional imaging techniques are shape, size, extra capsular spread and an abnormal inner architecture. The size is certainly the most used criterion for the diagnosis, whereas the presence of central necrosis is the most reliable sign of malignity.[12] Nevertheless several reports showed that these parameters are not enough to discriminate benign from malignant lesions.[13-14] Diffusion-weighted MR imaging (DWI) analyses intercellular water motion: every change in the water protons movements produces a variation of signal intensity in diffusion-weighted sequences and as a consequence on ADC maps.[15]

Diffusion weighted sequence was done in all patients before administration of contrast. ADCs value was calculated in every enlarged lymph nodes. These lymph nodes were than examined histopathologically. A total of 40 patients out of 70 patient shows restricted diffusion on DWI at one or the other cervical levels with the ADCs value ranging from 0.5 to 1.2($x10^{-3}$ mm^2/s) while 30 cases did not show restricted diffusion and there ADCs values ranges from 0.6 to 1.4 ($x10^{-3}$ mm^2/s).The mean value was calculated for malignant metastatic lymph nodes which came out to be $0.87\pm0.21x10^{-3}$ mm^2/s and for benign lymph nodes was 1.31+/-0.2 $x10^{-3}$ mm^2/s.

Averaging both the mean values, ADC threshold value was calculated. So the suggested cut-off point to discriminate between malignant and benign lymph nodes was 1.09 $x10^{-3}$ mm^2/s in the present study. Approximately similar value of ADCs was also found in study by Anna Perrone et al [16] 1.03 $x10^{-3}$ mm^2/s, J Si et al (2014)[76] 0.887 $x10^{-3}$ mm^2/s. All these studies showed low threshold ADCs value for malignant lymph nodes and higher for benign lymph nodes. However Misa sumi et al [17] showed exactly opposite result in his study ADC significantly greater metastatic lymph nodes (0.410 +/- 0.105 $x10^{-3}$ mm^2/s, $P <$ .01) than in benign lymphadenopathy (0.302 +/- 0.062 $x10^{-3}$ mm^2/s).

In the present study, Sensitivity, specificity and accuracy for detecting cervical lymph nodal metastasis by DWI/ADC values on MRI is 97.36% (80.00-97.00%), 90.62% (83.00-99.00%) and 94.28% and positive and negative predictive value are 92.50% and 96.66% respectively.

38 out of 70 post-operative resected specimen were histopathology positive for lymph nodal metastasis. There was 1 case which was not identified on MRI examination and 3 cases which were false-positive for nodal metastasis on MRI but were histopathologically benign.

Level I was the most involved group for metastasis showing restricted diffusion in 30 cases however postoperative Histopathological findings showed 37 cases out of 70 cases which were positive for metastasis at the same level. This was in accordance with the Jochen A Werneret al[18] who stated that, the dense lymphatic system of the gingiva-buccal complex drains primarily into the submandibular lymph node through 8 to 10 collectors that extend through the buccal muscle. Essig H et al[19] found that incidence of lymph node metastasis in level I was high as compared to other levels of lymph node from carcinoma of the buccal mucosa.

18 cases shows restricted diffusion at level II .On histopathological examination,a total of 23 cases showed level II positive for malignancy. This difference can be explained on the basis of image distortion caused by susceptibility artifacts and to the severity of chemical shift artifacts and ghosts in the phase-encoding direction. Level III and IV were the least involved lymph node. We did not find any case positive for level V in our study.

We found that 38 (54.28%) out of 70 patients showed lymph node metastasis to various levels. Out of these 38 patients, 24(63.16%) cases positive for lymph node metastasis had their primary lesion over buccal mucosa, followed by tongue 11 cases(28.95%), followed by gingivo-buccal sulcus 3 cases(7.89%).

CONCLUSION

Benign or malignant cervical lymph nodes can be differentiated on diffusion-weighted imaging of MRI on the basis of diffusion restriction and their ADC values concluding that diffusion imaging could be considered an important supportive tool for detecting malignancy in enlarged cervical lymph nodes.

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