Original Research Article

ROLE OF DIFFUSION-WEIGHTED IMAGING FOR PREDICTION OF PELVIC LYMPH NODAL METASTASIS IN GYNAECOLOGICAL MALIGNANCIES

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ABSTRACT

Background: To evaluate diagnostic accuracy of diffusion-weighted imaging in detection of metastatic lymph nodes in gynecological malignancies.

Material and Methods: Thirty patients with gynecological cancer who underwent MRI and histopathological examination were included. The pelvic lymph nodes were grouped into six regions. The morphology and apparent diffusion coefficient (ADC) value of lymph nodes were measured including short axis diameter (SAD) and long axis diameter (LAD), ADC max, ADC mean and ADC min. Categorical variables were taken as mean frequency to compare the differences of all criteria between Metastatic Lymph Nodes (MLNs) and non- MLNs. Correlation of quantitative ADC values with histopathological examination result were done to obtain cut off ADC value by ROC curve. Sensitivity, specificity and diagnostic accuracy of DWI were evaluated.

Results: The SAD of MLN was significantly greater than that of non- MLN (p=0.001). The differences in LAD between MLN and non- MLN was also significant. The ADC max and ADC mean value of MLN were significantly lower ($p<0.05$) while ADC min value of MLN was insignificantly lower than those of non-MLN ($p>0.05$). ADC max had the highest AUC 0.879 with 75% sensitivity and 85.7% specificity.

Conclusion: MRI with DWI had potential in diagnosing normal- sized pelvic lymph nodes metastases in patients with gynaecological cancer. The SAD and ADC values of lymph nodes were moderately valuable for detection of normal- sized MLNs as sole indices.

Key Words: Onco-imaging, ADC value, metastatic lymph nodes.

INTRODUCTION

While diagnosing and planning the course of therapy for patients with gynaecological malignancies, imaging is an essential diagnostic tool. Computed tomography (CT) or magnetic resonance imaging (MRI) has taken the lead in diagnostic imaging, even though ultrasonography (US) is still the preferred method for the initial evaluation of gynaecological imaging due to its accessibility, affordability, and relative noninvasiveness.[1]

Two significant gynaecological cancers that impact women's health globally are endometrial cancer and uterine cervical cancers. The European Society of Urogenital Radiology (ESUR), in accordance with the guidelines of the International Federation of Gynaecology and Obstetrics (FIGO), acknowledges the critical role that imaging, particularly MRI, plays in endometrial and cervical cancer. Diffusion weighted imaging (DWI) has shown to be an invaluable tool for the diagnosis of cancer as well as for disease staging, therapy planning, response to treatment monitoring, and long-term recurrence surveillance.[2]

For patients with malignancy, accurate and noninvasive pre-operative evaluation of the tumor's size, shape and lymphovascular involvement is essential. Knowing the disease's stage and lymph node involvement prior to therapy helps predict prognosis and choose the right management and treatment approach. In order to increase patient survival and quality of life as well as to decide financial resources allocated to disease management, this assessment is crucial. For the purpose of determining the scope of radiotherapy, whether it is necessary based on the stage of cancer and to enable the classification of patients into low, intermediate and high-risk groups, it is desirable that the cancer progress and any lymph node involvement be detected. In this sense, determining the kind of pelvic lesions and locating metastatic lymph nodes depend heavily on MRI with an exceptional soft-tissue resolution. The utility and precision of MRI have been enhanced by significant technological advancements in DWI.[3]

The three-dimensional microscopic movement of water molecules inside and outside of biological compartments may be seen using DWI. With the use of DWI, one can see how variations in tissue cellularity, cell membrane integrity, and fluid viscosity might affect water mobility. The signal strength produced on DWI increases with increasing water flow restriction. By calculating the degree of diffusion using various b-values, the apparent diffusion coefficient (ADC) can offer a quantitative evaluation; restricted diffusion is represented by low signal intensity on an ADC map. Because of the increased cellularity, the flow of water molecules is usually limited inside the tumour microenvironment.[4]

The DWI method provides a comprehensive evaluation of the staging of gynaecological tumours by giving molecular tissue diffusion and perhaps detecting local metastasis in tumours.[3]

In addition to helping diagnose cancer, diffusion-weighted imaging has also shown to be a valuable tool for staging the illness, designing treatments, monitoring the effectiveness of those treatments and doing long-term recurrence surveillance.[5]

Patients with nodal metastases have far poorer survival rates than those without such metastases, making the degree of lymph node (LN) metastasis a key prognostic indicator. Surgical lymph node examination is considered the gold standard for identifying lymph node metastases; nevertheless, this method has a higher risk of both acute and chronic patient complications, in addition to increased diagnostic time and cost. Thus, having a non-invasive technique that can accurately identify lymph node metastases would be advantageous.[6]

By using DWI instead of contrast-enhanced imaging, scan time and contrast costs can be decreased. It was hypothesized that DWI, as opposed to contrast-enhanced imaging, provides superior sensitivity and specificity for assessing metastatic lymph nodes.[7]

Aim

Role of diffusion-weighted imaging for prediction of pelvic lymph nodal metastasis in gynaecological malignancies.

Objective

To evaluate diagnostic accuracy of diffusion-weighted imaging in detection of metastatic lymph nodes in gynaecological malignancies.

MATERIALS AND METHODS

This study is a cross sectional study conducted in the Department of Radiodiagnosis in a tertiary care hospital in northern India with sample size of 30 and includes patients with gynaecological malignancy who presented to the Department of Radiology for MRI pelvis from July 2021 to June 2023.

Inclusion Criteria: Patients with pre-operative MRI pelvis for gynaecological malignancies, patients with no therapy prior to MRI (chemotherapy/radiotherapy), patients with MRI to surgery duration less than or equal to 1 month and patients having histopathological examination available.

Exclusion Criteria: Patients with non-primary pelvic malignancy, patients with no measurable lymph node on MRI and patients with concurrent malignancies.

Prior written consent after a proper explanation of the procedure was obtained from the patients. The patients were examined using the pelvic coil in a 1.5T MRI machine (Siemens Magnetom Avanto). Axial TSE T1W, Axial FS TSE T2W, Sagittal TSE T2W, Coronal FS TSE T1W, DWI with corresponding ADC mapping done at b-value of 0, 400, and 800 sec/mm2 were taken.

Study plan- The pelvic lymph nodes were grouped into six regions: bilateral obturator chains, external iliac and internal iliac on conventional axial T2W and DWI sequences. The MRI images were analyzed without knowing the histological findings. Radiologist chose all visible lymph nodes on axial T2W images, then recorded the location and size of the lymph node. The short axis diameter (SAD) and long axis diameter (LAD) of selected nodes were measured. Accordingly, the hyperintense nodes in each region on DW images ($b = 800\ s\ mm^{-2}$) were identified and correlated with T2W images and then the ADC values of these nodes were measured. The regions of interest (ROI) were manually drawn on ADC map by referring to T2W and DWI ($b = 800\ s\ mm^{-2}$). ROI of 20+/- 10 mm2/s was carefully placed around the center of a node avoiding the margin and adjacent vessels. The ADC max value, ADC mean value and ADC min value were calculated by the software. The findings were compared with the histopathological examination.[8] [Figure 1]

Statistical Analysis: Categorical variables were taken as mean frequency. Correlation of quantitative ADC values with histopathological examination result were done to obtain cut off ADC value by ROC curve. Sensitivity, specificity and diagnostic accuracy of DWI were evaluated.

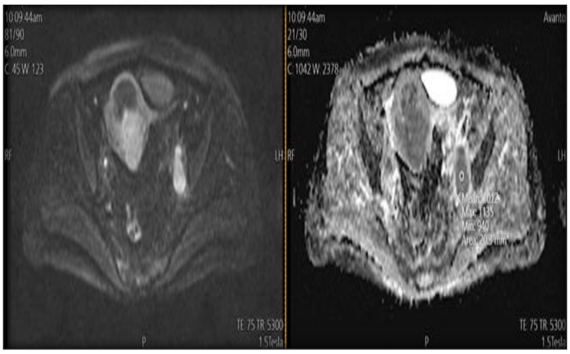

Figure 1: Obturator lymph node on left side showing diffusion restriction with ADC mean, ADC max and ADC min values on ADC image

RESULTS

The patients in the study population ranged in age from 42 to 79 years, with 6 being less than 50 and 24 being older than 50. Based on the results of the MRI, 3 individuals had ovarian tumour, 15 had cervical cancer and 12 had endometrial cancer. 7 individuals had metastases to the pelvic lymph nodes as determined by the histological analysis of all patients. The prevalence of pelvic lymph node metastasis was as follows: obturator (n = 3); external iliac (n = 6) and internal iliac (n = 2).

For metastatic lymph nodes (MLN), the mean SAD (± standard deviation) was 4.26 ± 3.38 mm, whereas for non-metastasizing lymph nodes (Non-MLN), it was 1.25 ± 1.15 mm. The SAD of MLN was significantly greater than that of non- MLN (p=0.001). The differences in LAD between MLN and non- MLN was also significant and it was 5.77 ± 3.53 mm for MLN and 1.79 ± 1.94 mm for Non-MLN respectively. [Table 1]

The difference of ADC based criteria between MLN and non-MLN: the ADC max value, ADC mean value, ADC min value of MLN was (862.86±134.79), (735.86±151.0) and (677.0±185.74) respectively and those of non-MLN were (1090.50±180.39), (907.75±119.92) and (748.88±128.59), respectively. The ADC max and ADC mean value of MLN were significantly lower (p<0.05) while ADC min value of MLN was insignificantly lower than those of non-MLN (p>0.05). [Table 2]

Table 3 and figure 2 summarize the area under the curve (AUC) and the optimal cut off of ADC- based criteria (ADC max value, ADC mean value, ADC min value) of lymph nodes for distinguishing MLN from non-MLN. Using 836.50 mm as the cut off, the sensitivity and specificity of ADC mean for selection of MLNs from non- MLNs were 81.3%and 71.4%, respectively. Using 944.0 as the ADC max cut-off value, the sensitivity and specificity were 75.0% and 85.7% respectively. [Table 3]

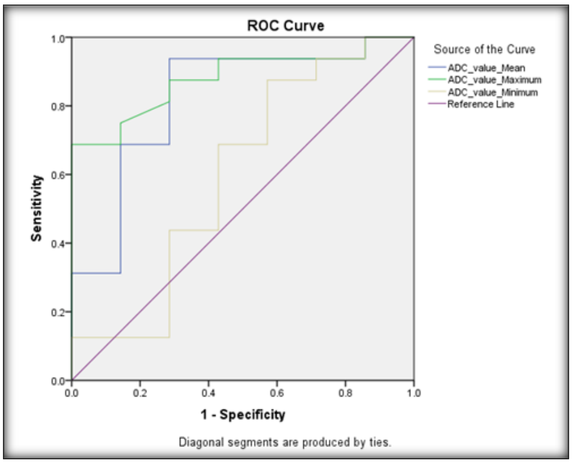

Figure 2: The receiver operating characteristic (ROC) curve for ADC values of lymph nodes to differentiate MLN from non- MLN

Table 1: Mean short axis diameter and long axis diameter of MLN and Non-MLN

	MLNs (n=7)	non- MLNs (n=23)	p-value
LAD	5.77±3.53	1.79±1.94	0.001
SAD	4.26±3.38	1.25±1.15	0.001

Table 2: ADC max, ADC mean and ADC min values of MLN and non- MLN

	MLNs (n=7)	non- MLNs (n=23)	p-value
ADC value Maximum	862.86±134.79	1090.50±180.39	0.007
ADC value Mean	735.86±151.0	907.75±119.92	0.008
ADC value Minimum	677.0±185.74	748.88±128.59	0.293

Table 3: Diagnostic performances of ADC-based criteria for detecting metastatic lymph nodes

Calculated value	ADC value mean	ADC value maximum	ADC value minimum
Cut off	836.50	944	619
AUC	0.821	0.879	0.598
Sensitivity	81.3%	75.0%	87.5%
Specificity	71.4%	85.7%	42.9%
Diagnostic accuracy	82.1%	87.9%	59.8%

DISCUSSION

Patients who were subject to be diagnosed as early-stage cancer, accurate detection of MLN is especially important. Because these individuals will receive two completely different therapies depending on the state of their lymph nodes.

These factors make it preferable to use a non-invasive, precise technique like MRI to identify lymph node metastases. Traditionally, lymph node size was the only factor used to estimate lymph node metastasis, with a lymph node with a SAD of less than 10 mm being classified as benign. However, Benedetti's research showed that in 225 cervical cancer patients who underwent radical hysterectomy and pelvic lymphadenectomy, the SAD of more than 80% of the metastatic nodes was less than 10 mm.[9] Furthermore, according to Song J et al., 42.4% of MRI-recognizable lymph nodes with a SAD of 5 to 10 mm were metastatic.[10] If the lymph nodes' status is determined by applying the 10 mm threshold, there is a greater chance of a missed diagnosis. Our research also revealed that lymph nodes with a short axis diameter of less than 10 mm had to be taken into account when assessing metastasis. The SAD results from this study indicated that while morphological criteria are useful in certain situations, they are not reliable indicators for MLN identification.

According to certain studies, there was no significant difference in the ADC values of MLN and non-MLN with normal sizes. Maybe there was a probability of partial volume effects when measuring ADC values of sub centimeter nodes.[11,12] Thus, ROIs were drawn manually in this study on every section of a node in order to reduce the impact of other tissues.

ADC min values of MLN were insignificantly lower than those of non-MLN ($p>0.05$), however ADC max and ADC mean values of MLN were significantly lower ($p<0.05$). The findings were consistent with other earlier correlational studies that found that DWI was more accurate than conventional MRI at diagnosing MLN from non-MLN. The degree of tissue cellularity is directly proportional to the restriction in water molecule diffusion. Malignant tumour cells differ from benign tissue cells in that they grow more quickly and in greater quantities, causing the intracellular structure to become disorganised and the extracellular spaces to decrease. Because malignant tumour cells have a greater nucleus/cytoplasm ratio, the intracellular spaces reduce.[13,14] Ultimately, ADC values of MLN decreased as a result of the restrictions of both intracellular and extracellular water molecules movement which were caused by the above histopathological changes. The study's outcomes using ADC-based criteria aligned with the findings of the previously mentioned studies. The ADC mean had the sensitivity 81.3% and the specificity 71.4% for distinguishing MLNs from non- MLNs, the sensitivity of ADC max and ADC min was 75.0 and 87.5%, respectively and specificity was 85.7% and 42.9% respectively.

Regardless of the quantity of tumour cells and the degree of malignant dissemination, a lymph node's characteristics are dependent on the infiltration of tumour cells. Determining MLN that only had localised infiltration of malignant tumour cells is therefore crucial. The ADC max can be an important criterion to facilitate the selection of the MLNs timely. In line with the previously mentioned viewpoints, the ROC curve showed that, when compared to other independent criteria, ADC max had the best AUC and specificity in separating MLN from non-MLN.[13,14,15]

We acknowledge that our study has certain limitations. Initially, a single centre had a rather limited patient population. Thus, more studies using a bigger sample size have to be conducted in order to corroborate the findings of the current investigation. Lastly, despite the fact that the existence of para-aortic lymph node metastases is a significant prognostic factor, the scanning range limitation prevented this from being examined in our research. Our findings will be improved by additional research that takes the occurrence of para-aortic lymph node metastases into account.

CONCLUSION

In conclusion, DWI is a useful and advanced quantitative tool for differentiating between metastatic and benign lymph nodes in patients with gynaecological cancers. The SAD and ADC values of lymph nodes were moderately valuable for detection of normal- sized MLNs as sole indices.

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