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Diffusion Weighted MR Imaging (DWI) and ADC Values in Endometrial Carcinoma

Imrana Masroor, Muhammad Zeeshan, Shaista Afzal, Nadeem Ahmad and Gulnaz Shafqat

ABSTRACT

Objective: To determine the sensitivity of MR imaging utilizing diffusion weighted imaging (DWI) in detection of endometrial cancer and to compare the Apparent Diffusion Coefficient (ADC) values of malignant and normal endometrium.

Study Design: Cross-sectional analytical study.

Place and Duration of Study: Radiology Department, Aga Khan University Hospital Karachi, from January 2007 to December 2009.

Methodology: Patients were defined as undergoing MRI for suspected endometrial malignancy, and the controls were female subjects who underwent MRI examination for indications other than endometrial malignancy. Studied variables included the signal characteristics of the endometrium and ADC values. The sensitivity of DWI for the detection of endometrial carcinoma was calculated using histopathology as the gold standard, and the ADC values of the endometrium in patients and controls were recorded. The mean ADC values were compared using two-sided t-test with significance at $p < 0.05$ at 95% confidence interval.

Results: Out of 52 patients, 10 had hyperintense, 40 had hypointense and 2 had isointense endometrium on T2 weighted imaging. On DWI, 42 patients had hyperintense and 10 patients had hypointense endometrium. In comparison, 40 controls had hypointense endometrium on DWI and 12 had hyperintense endometrium. The mean ADC value for abnormal endometrium was $0.730 \pm 0.215 \times 10^{-3} \text{ mm}^2/\text{sec}$ and of normal endometrium was $1.265 \pm 0.305 \times 10^{-3} \text{ mm}^2/\text{sec}$ ($p < 0.001$). The sensitivity for detection of endometrial carcinoma on DWI was 77.77%. False positive cases were found to be due to secretory and hyperplastic endometrium. False negative findings were found in a few cases of adenocarcinoma, endometrioid carcinoma and clear cell sarcoma.

Conclusion: In patients with suspected endometrial carcinoma, MRI examination utilizing DWI was a sensitive tool in detecting endometrial cancers with significantly lower ADC values for carcinoma in general. Physiological and histopathological variants may be responsible for a few false results.

Key words: Diffusion weighted imaging (DWI). Apparent diffusion coefficient (ADC). Endometrial cancer. Hypointense endometrium. MRI.

INTRODUCTION

Endometrial cancer is the most common gynaecological malignancy of developed countries.¹ In Pakistan no separate data regarding the prevalence of endometrial carcinoma is available, however, according to the Karachi Cancer Registry statistics, cancers of female genital tract i.e. cervix, ovary and uterine body encompass 13.1% of the total cancers in the females.²

The prognosis of endometrial cancer is dependent on a number of factors i.e. the sub-type and grade on histology, stage of tumour at diagnosis (including depth of myometrial invasion) and lymph node metastasis. Most of the patients with endometrial cancer present with vaginal bleeding and the diagnosis is made by endometrial biopsy. But pre-operative staging is very

important in planning proper surgical procedure and ascertaining whether to perform lymph node sampling. Patients with lymph nodes metastasis have a significantly higher recurrence rate and a lower 5-years survival rate than the patients without lymph node involvement by disease.³

MRI is an excellent imaging method to evaluate the local stage of endometrial cancer. Endometrial cancer is seen as thickened endometrium on T2-weighted images. The signal intensity may range from high to low; at times it may be impossible to differentiate from normal endometrium or adjacent myometrium on conventional MRI.⁴

Diffusion-weighted imaging (DWI) is a recent new imaging technique which depicts tissue characteristics based on diffusion motion of water molecules. Diffusion weighted MR imaging visualizes a random microscopic motion of molecules and that is how it provides a tissue contrast different from that of conventional T1 and T2 weighted images. Initially the usefulness of this technique was established in central nervous system, and now DW imaging is the most accurate modality for

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diagnosing acute brain infarction.^{5,6} The technique is applied to the abdominal organs and is known to depict malignant tumours with high sensitivity.⁷⁻¹² DWI can also provide values of apparent diffusion coefficient (ADC) of tissues under investigation. The ADC value of tissue is influenced by nuclear-to-cytoplasmic ratio (NCR) and cellular density.^{7,13-16} It is known that the ADC values of malignant neoplasm are lower than those of normal tissues and benign lesion in the breast, the liver, the pancreas, the kidneys, the bladder, the prostate and the uterine cervix.¹⁷⁻²² In highly cellular tissues such as cancers, relatively little extracellular space is available leading to restricted motion of water molecules, causing decreased ADC values which was the rationale of this study.

This study was conducted to determine the sensitivity of DWI for the diagnosis of endometrial cancer and to determine the difference in ADC values of endometrial cancer verses normal endometrium.

METHODOLOGY

It was a cross-sectional analytical study, conducted at the Radiology Department of The Aga Khan University Hospital. Convenience sampling was used and all adult female patients, who underwent MR examination of pelvis with suspicion of endometrial cancer and which later had surgery and histopathology, were included in the study. The study period was from January 2007 to December 2009. Fifty two patients with complete medical records were included in the study. Another group of 52 adult females, who underwent MR examination of pelvis for clinical suspicion of carcinoma cervix or ovary, or uterine fibroid, and had normal endometrium at surgery and histopathology, were taken as controls for comparison of the ADC value and signal characteristics of the normal endometrium. Patients with incomplete medical records were excluded.

The MR pelvis was performed on 1.5 Tesla Siemens machine, both pre- and postcontrast images were obtained. The sequences included axial, coronal, and sagittal, T2 weighted and fat suppressed T1 post contrast images. In addition DW imaging in axial plane was done at b-value of 50, 400 and 800 sec/mm². ADC images were obtained. The ADC value was calculated at b-value of 800 of both the normal and abnormal endometrium by taking region of interest (ROI).

All MR images were reviewed by two radiologists. If there was a difference in opinion, it was resolved by taking unbiased opinion from a third radiologist. The abnormal endometrium was defined as either hypointense, isointense or hyperintense signal within endometrial cavity as compared to normal endometrium on T2 weighted images. Patients who had high signal intensity endometrium on DWI and low signal intensity on ADC images were taken as diffusion positive and

patients who had high or low signal on DWI and high signal on ADC images were taken as diffusion negative. True positives were patients who had diffusion positive endometrium and on histopathologically proved to have endometrial malignancy. True negative were those patients who had endometrium which was negative on both diffusion imaging and histopathology. False positive patients had diffusion positive endometrium but the histopathology reported benign findings. False negative were defined as patients who were diffusion negative but histopathology reported them as endometrial malignancy.

Statistical analysis was done on SPSS 16. The statistical difference between normal and abnormal endometrial ADC values was calculated by two-sided student t-test; p-value of < 0.05 was considered statistically significant with confidence interval of 95%.

RESULTS

The mean age of patients with diagnosed endometrial cancer was 58 ± 13 years whereas the 52 controls had mean age of 48 ± 16 years. All patients with endometrial carcinoma had presented with postmenopausal bleeding. The controls presented with different complaints like progressive abdominal fullness and distention, or menorrhagia, etc.

Out of the 52 patients with clinical suspicion of endometrial carcinoma, 10 had hyperintense, 40 had hypointense and 2 had isointense endometrium on T2 weighted imaging. Thirty seven patients had endometrium which was diffusion positive being hyperintense on DW images and low on ADC images (Figures 1 and 2) and diffusion negative in 15 patients.

Among 52 patients the distribution of true positive, false negative, false positive and true negative is given in Table I. The sensitivity of DW magnetic resonance

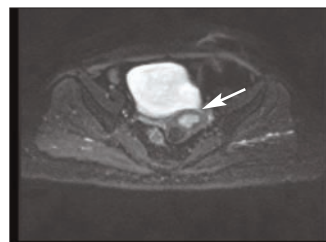


Figure 1: Axial diffusion weighted image showing hyperintense endometrium (arrow).

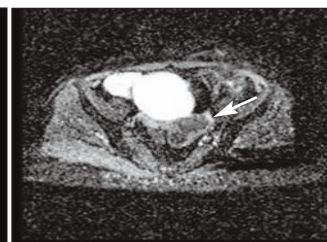


Figure 2: Axial ADC image showing hypointense endometrium (arrow).

Table I: Accuracy of diffusion weighted imaging.

| | Values |
|---------------------------|--------|
| True positive | n = 35 |
| True negative | n = 5 |
| False positive | n = 02 |
| False negative | n = 10 |
| Sensitivity | 77.77% |
| Specificity | 71% |
| Positive predictive value | 94.6% |
| Negative predictive value | 33.33% |

imaging for detection of endometrial carcinoma was 77.77%. The specificity, positive and negative predictive value was 71%, 94.60% and 33.33% respectively.

Among 52 patients reported on MR examination with endometrial malignancy, all patients had histopathological proven diagnosis. Among true positives 26 had adenocarcinoma and 9 had endometrioid type malignancy they were positive on DWI. Eight patients had adenocarcinoma, and 2 had endometrioid carcinoma and clear cell sarcoma respectively; they were negative on DWI and were taken as false negatives.

Five patients were diffusion negative; histopathology showed benign pathologies like endometrial polyps, complex hyperplasia so they were taken as true negatives. The two false positive cases were reported on histopathology as non-secretory endometrium and complex endometrial hyperplasia respectively.

Among the controls, 45 patients had endometrium which was hyperintense on T2 weighted and diffusion weighted images.

The mean ADC value for abnormal endometrium was $0.730 \pm 0.215 \times 10^{-3} \text{ mm}^2/\text{sec}$ and of normal endometrium was $1.265 \pm 0.305 \times 10^{-3} \text{ mm}^2/\text{sec}$ ($p < 0.001$), at b-value of 800 sec/mm².

DISCUSSION

MRI examination is a useful modality for staging and evaluation of pelvic malignancy in general and uterine malignancy in particular. The previously reported local studies have only described the role in staging; this is the first local study regarding the improvisation of routine MR imaging in the diagnosis of endometrial malignancy with possible fallacies. Furthermore the calculations of specificity and positive and negative predictive values is an outstanding feature not reported previously even in international studies.

In this study, 37 patients and 45 controls showed increased signal intensity on DWI images at b-value of 800 sec/mm². Out of 37 patients 35 had endometrial malignancy on histopathology. This is in slight contrast to a study conducted by Tamai *et al.* in which 18 patient had surgically proven endometrial cancer, and 12 female patients had histopathologically proven normal endometrium.²³ They concluded that all endometrial cancers appeared hyperintense on DW images. DW imaging is helpful in detection and demonstration of endometrial cancer, although it is difficult to differentiate between normal and cancerous tissue only on the basis of increased signal intensity of endometrium on DW images.

This study is also in slight contrast to a study conducted by Wang *et al.* In his study all endometrial carcinoma and normal endometrium showed high signal intensity on

DW images, however, all endometrial polyps and hyperplasias showed a relatively lower or intermediate signal intensity compared to the spared outer myometrium.²⁴

The reason for the increased signal intensity of normal endometrium is not completely known.²³ The T2 shine-through effect is not a cause as hyperintense fluid in bowel or bladder on T2-weighted images do not show high signal on DW images at a b-value of 1000 sec/mm².

This difference between this study and other studies may be due to the fact that we obtained diffusion images at a b-value of 800 sec/mm², where as the others obtained the images at a b value of 1000 sec/mm².^{23,24}

The sensitivity of diffusion weighted imaging for detection of endometrial cancer in this study was 77.77% as compared to 96% in a study conducted by Inada *et al.* the high sensitivity in his study can be attributed to the small sample size of only 23 patients.²⁵

The specificity and positive and negative predictive values of this study cannot be compared with local or international literature because of the non-availability of these values in other studies.

The ADC value of normal endometrium is much higher than that of cancerous endometrium. The difference was statistically significant, having a p-value of < 0.0001 . Comparable results are described by Inada *et al.*²⁵ They recorded the ADC values for 23 patients with surgically proven endometrial cancer, and of normal endometrium in 31 healthy volunteers (14 with leiomyomas and adenomyosis in 10 patients). They concluded that the mean ADC value of endometrial cancer was significantly lower, than that of normal endometrium, leiomyomas and adenomyosis. Their results are comparable to this study.

In another study conducted by Shen *et al.* similar findings were described, and the mean ADC of endometrial carcinoma of 24 cases was $0.864 \times 10^{-3} \text{ mm}^2/\text{sec}$ and that of benign endometrial lesion (including endometrial hyperplasia of 4 cases and endometrial polyps of 3 cases) was $1.277 \times 10^{-3} \text{ mm}^2/\text{sec}$. The difference between the two groups was significant.²⁶

In published literature, a decreased ADC values for malignant tumours has been reported for various organs.²⁷

The exact mechanism is under investigation, some investigators suggest that decreased ADC value is related to increased cellular density in malignant tissues. In highly cellular tissues such as malignant tumours, relatively reduced extracellular space may restrict the movement of water molecules leading to reduced ADC values.²³

Furthermore the degree of signal intensity on DW images may be different between normal and abnormal

endometrium, subjective assessment is always difficult because the signal intensity on MRI is not the absolute value and the visual assessment of signal may be affected by the adjustment of window level and width. On the other hand, the ADC value calculated from DW images can provide quantitative analysis of microscopic water diffusibility in the tissue under analysis. In this study, the ADC value of cancerous endometrium was statistically lower than of normal endometrium without any overlap. The results suggest that the measurement of ADC value has a potential capability to differentiate between normal and cancerous tissue in the endometrium.

There were a few limitations of this study. The first was that the controls were not strictly age-matched and included some pre-menopausal ladies as well while the cases were all postmenopausal. This was due to logistic and cost issues and could not be overcome. However, the large sample size was an attempt to reduce the chances of error.

While taking ADC values of controls that underwent MR examination for indications such as fibroid or ovarian carcinoma and had surgically proven normal endometrium, the phase of the menstrual cycle was not taken in consideration. This is important as ADC values may vary, depending on phase of menstrual cycle in pre-menopausal patients in the control group. A larger series of randomly controlled subjects with matching of age and menstrual phase; and also the malignant vs. benign pathologies must also be contemplated for accurate comparison.

CONCLUSION

DW imaging is a sensitive tool in detection of endometrial cancer. Malignant endometrium appear hyperintense on DW imaging in majority of patients with fallacies induced by the secretory/hyperplastic/histologic variants of the malignancy but the ADC value of endometrial cancer is significantly lower than that of normal endometrium. Therefore, the measurement of ADC value has a potential role in differentiating normal from cancerous endometrium.

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