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Egyptian Journal of Radiology and Nuclear Medicine (2021) 52:278
https://doi.org/10.1186/s43055-021-00652-5

Egyptian Journal of Radiology and Nuclear Medicine

RESEARCH Open Access

Use of diffusion-weighted imaging and diffusion tensor imaging in assessment of myometrial invasion in patients of endometrial carcinoma and its correlation with histopathological grading (Prospective study)

Mahmoud Abdel-Latif* and Hebatullah Safwat Mosaad

Abstract

Background: Endometrial cancer (EMC) is considered one of the most common gynecological cancers worldwide. In particular, the depth of myometrial invasion and histological grade of endometrial cancers (EMCs) are strong prognostic factors. Diffusion tensor measurements as mean diffusivity (MD) and fractional anisotropy (FA) values could be useful for assessing the depth of tumor invasion and its histological grade. The study aimed to evaluate the role of diffusion-weighted imaging (DWI) and diffusion tensor imaging in the detection of myometrial invasion in cases of endometrial carcinoma and prediction of its grade in vivo.

Results: This study included 50 female patients with pathologically proved endometrial carcinoma**,** and their ages ranged from 38 to 67 years; the mean age was 56.15 years (±8.229 standard deviation "SD"). There was a significant statistical difference regarding the mean values of diffusion tensor fractional anisotropy (DT-FA), diffusion tensor mean diffusivity (DT-MD) and diffusion-weighted apparent diffusion coefficient(DW-ADC) values in differentiating between intact and infiltrated myometrium with (*P* value ≤ 0.001). The accuracy of DT-MD, DT-FA and DWI-ADC was 98%, 90% and 86%, respectively, in the detection of myometrial invasion. There was a statistically significant difference in the mean values of DT-FA, DT-MD and DW-ADC for differentiating endometrioid adenocarcinoma grades with the overall *P* values (˂0.001). The accuracy of DT-FA, DT- MD and DWI-ADC for differentiating grade 3 from grade 1 or 2 endometrioid adenocarcinoma was 94.9%, 84.6% and 74.4%, respectively. For differentiating grade 1 from grade 2 or 3 endometrioid adenocarcinoma, the accuracy of DT-FA, DT-MD and DWI-ADC was 90%, 89.7% and 84.6%, respectively. Mean DT-FA, DT-MD and DW-ADC values were inversely proportional to the degree of pathological grading with r = −0.867, −0.762 and −0.706, respectively.

Conclusion: Diffusion tensor imaging and DWI are helpful in the assessment of myometrial invasion and have a high negative correlation with histopathological grading in patients with endometrial cancer.

Keywords: Diffusion tensor, Endometrial carcinoma, Myometrial invasion, Histopathological grading, ADC value

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Background

Endometrial cancer (EMC) is considered one of the most common gynecological cancers worldwide and its incidence is increasing especially in developed countries. Among endometrial cancer cases, approximately 5 percent are women younger than 40 years of age [1].

The International Federation of Gynecology and Obstetrics (FIGO) stage, lymphovascular invasion, histological subtype and grade, and presence of lymph node metastases are important prognostic indicators in the endometrial cancer (EMC). In particular, the depth of myometrial invasion and histological grade of endometrial cancers (EMCs) are strong prognostic factors. The accurate preoperative assessment of the depth of the tumor invasion and its histologic grade will therefore have a definitive impact on the selection and planning of optimal treatment in patients with endometrial cancer (EMC) [2].

Endometrial cytology and biopsy are considered the mainstays for the diagnosis of endometrial lesions, but the difficulty is encountered in patients with stenosis of the vagina or the cervix, and they may not offer an exact definite diagnosis. In addition, they are still considered to be invasive procedures [3–6].

Hysterectomy is the ordinary treatment used for endometrial cancer resulting in sterilization. Instead, conservative therapy with progestins may be used in young patients who wish to save their fertility, which can only be done if the tumor is well-differentiated grade 1 and the disease is restricted to the endometrium. Therefore, an accurate evaluation of tumor grading is essential for the selection of the appropriate treatment [1].

Conventional magnetic resonance imaging provides adequate morphological information on the uterus, and thanks to technical advances and improvements in magnetic resonance imaging (MRI) software, diffusion-weighted imaging and diffusion tensor imaging (DWI and DTI) have significantly improved the diagnostic value of MRI of the pelvic region as it provides functional information and are therefore considered to be imperceptible [7].

Diffusion-weighted imaging (DWI) is a non-invasive method based on diffusion (Brownian motion) of water molecules in the extracellular space. Diffusion tensor magnetic resonance imaging (DT-MRI) is an extension of diffusion-weighted imaging (DWI), used for characterizing microstructural organization such as density and orientation of fibrous tissue in vivo. It generates parametric maps that help visualize the different aspects of tissue microstructure (mean diffusivity, tissue anisotropy, and dominant fiber orientation) [8].

Diffusion tensor imaging (DTI) is valuable in determining uterine fiber architecture. It is therefore believed that diffusion tensor imaging(DTI) quantitative measurements as mean diffusivity (MD) and fractional anisotropy (FA) values could be useful for assessing the depth of tumor invasion and its histological grade, which are the most important predictive indicators of endometrial cancers (EMCs) [1, 9].

This study aims to evaluate the role of diffusion-weighted imaging (DWI), apparent diffusion coefficient (ADC) value and diffusion tensor imaging (DTI) (mean diffusivity "MD" and fractional anisotropy "FA") in the detection of myometrial invasion in cases of endometrial carcinoma and the prediction of its grade in vivo (Figs. 1, 2, 3, 4, 5, 6, 7, 8).

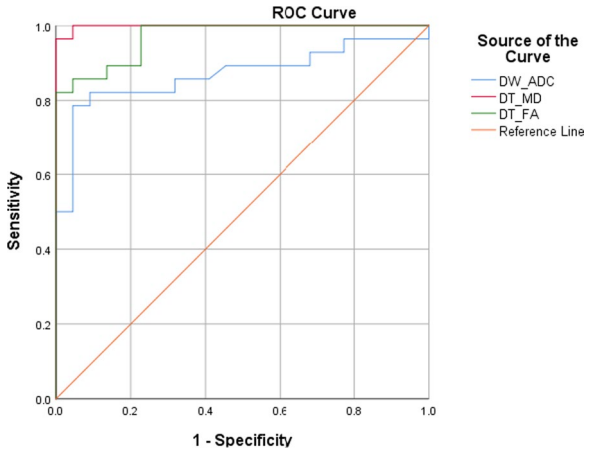

Fig. 1 ROC curve of DT-FA, MD and DW-ADC in differentiating myometrial invasion

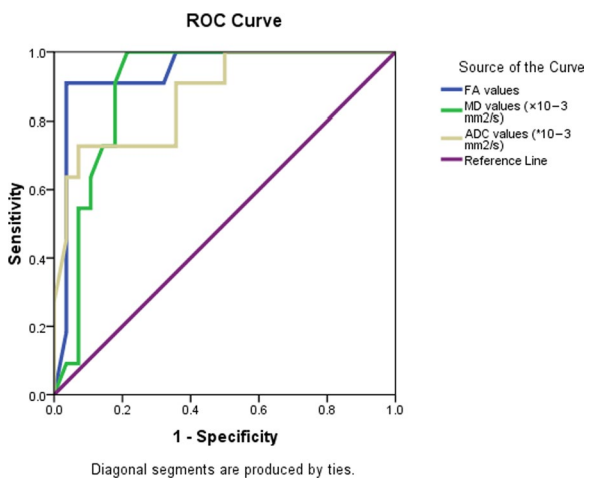

Fig. 2 ROC curve of FA, MD and ADC in differentiating grade 3 from grade 1 and 2 endometrioid adenocarcinoma

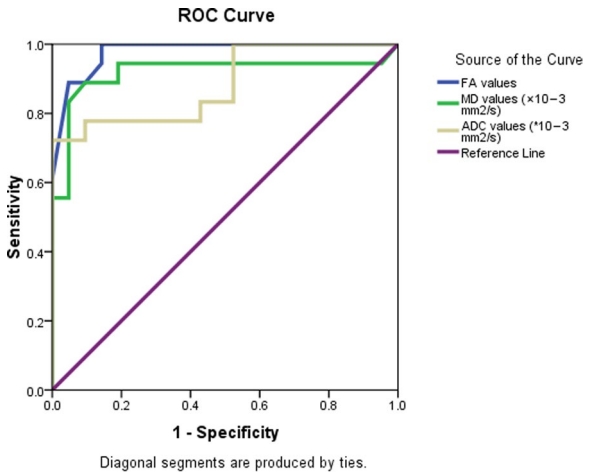

Fig. 3 ROC curve of FA, MD, ADC in differentiating grade 2 from grade 1 and 3 endometrial carcinoma

Methods

This prospective study received approval from the local medical research ethics committee. Informed verbal and written consent had been obtained from each participant in the study or their person of charge. It included 50 consecutive patients with pathological confirmed endometrial cancer (EMC).The inclusion criteria were as follows: (1) Patients with suspected EMC and MRI done as part of the preoperative assessment; (2) Patients with no history of pelvic surgery, radiotherapy, or chemotherapy; (3) Patients with surgery done within 2 weeks after MRI; and (4) patients with confirmed histopathological diagnosis of EMC. The exclusion criteria were as follows: (1) Patients with confirmed uterine malignancies other than EMC; (2) Patients with previous pelvic surgery or had pelvic radio or chemotherapy and patients with general contraindications to MRI study, *e.g., cardiac pacemaker or cochlear implant, metallic foreign body in their eyes and participants with claustrophobia or bad general condition who need life support*; (3) patients with contraindication to contrast administration; and (4) patients with incomplete MRI examinations.

Patients' age ranged from 38 to 67 years; the mean age was 56.15 years. All patients underwent MRI, including diffusion tensor imaging (DTI), as part of the preoperative assessment. The examination was done in the Diagnostic Radiology Department at the MRI unit within the duration from April 2020 to April 2021.

Image acquisition and post-processing

The examination was done using the MR machine (Philips—Ingenia, 1.5 Tesla, Netherland) with maximum amplitude 45 mT/m; gantry aperture 700 mm and 8—channel phased array coils for abdomino-pelvic studies.

Conventional MRI was done using the following sequences*:* Axial T1-wieghted images (T1WI) and axial T2-wieghted images (T2WI) with fat suppression with slice thickness (5 mm "mm"); spacing (1 mm "mm"); field of view (28 cm "cm"); matrix (263×171). Sagittal and coronal fat-suppressed T2-wieghted images (T2WI)with slice thickness (5 mm "mm"); space (1 mm "mm"); field of view (28 to 36 cm "cm"); matrix (256×256).

Diffusion-weighted imaging (DWI) was done using echo-planar imaging with fat suppression in the axial oblique and sagittal planes with: Repetition time "TR" (10,000 ms "ms"); Echo time "TE" (80–100 ms "ms"); slice thickness (5 mm "mm"); inter-slice-space (1 mm "mm"); Field Of View "FOV" (28–40 cm "cm"); matrix (128×128); *b* value 0, 500 and 1000 s per square millimeter "s/mm^2".

Diffusion tensor imaging (DTI) data were obtained in sagittal, axial oblique planes using a spin-echo echo-planar sequence *with b* value of 0 and 800 s/mm^2 with the following parameters: Repetition time "TR" (10,000 ms "ms"); Echo time "TE" (60–80 ms "ms"); slice thickness (3 mm "mm"); spacing (1 mm "mm"); matrix (100×132); voxel size ($1.67 \times 1.67 \times 3.00$ mm "mm"); acquisition time (about 6 min); and Field Of View "FOV" (28×36 square centimeter "cm^2").

Post-processing

All the images were transferred to the magnetic resonance (MR) workstation (Workspace 2.6.3.5, Philips, Netherland).The signal intensity of the endometrial lesions was evaluated on high *b* value images, and the apparent diffusion coefficient (ADC) was obtained from the diffusion-weighted (DW) images. The signal intensity of the lesions was recorded from the diffusion tensor-mean diffusivity [DT-ADC (MD)] and fraction anisotropy (DT-FA) color maps which were automatically generated.

Image analysis

All the MR images, DWI and DT images and maps were revised and evaluated in consensus by 2 radiologists (HSM and MAL) with experience of 5 and 18 years in MR imaging, respectively. Both were blinded to the clinical and pathological results. The cases of disagreement were resolved by discussion and consensus.

Moreover, the inter-observer agreement percentage (%) was measured for the 2 radiologists (both observers) as regard DW-ADC, DT-MD and DT-FA in myometrial invasion and grading of endometrial cancer, to add more reliability of the results.

On DW images, the regions of interest (ROIs) were manually drawn on the tumor region avoiding necrotic or

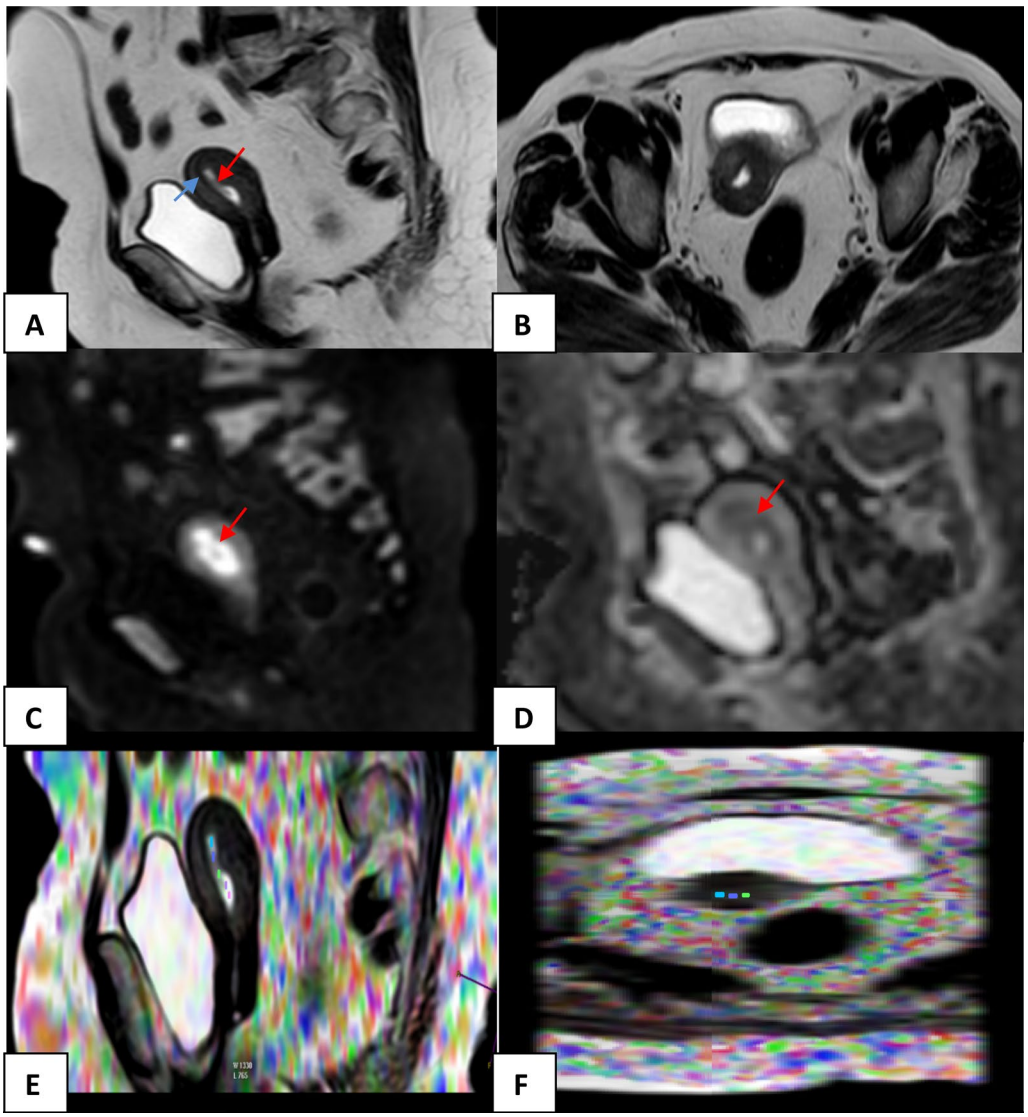

Fig. 4 A 53-year-old postmenopausal female presented by abnormal vaginal bleeding. **A**, **B** *Sagittal and axial T2 WIs* irregular endometrial thickening which is occupied by a soft-tissue mass displaying intermediate SI (red arrow). No visible tumor breaching through the junctional zone (blue arrow). **C** *Sagittal DWI with b value of 1000 s/mm²* high signal intensity of the endometrial soft-tissue mass (red arrow). **D** *Sagittal DW-ADC map image:* low signal intensity of the endometrial soft-tissue mass (red arrow). Mean DW-ADC value = 0.939×10^{-3}mm²/s. **E**, **F** Sagittal and axial DTI map images: values of DT-FA and DT-MD in multiple ROI along the endometrial mass. Mean DT-FA value = 0.401, and mean DT-MD value = 0.962×10^{-3}mm²/s. *Diagnosis* Pathologically proved endometrioid adenocarcinoma G1

cystic parts. In cases of myometrial invasion, additional (ROIs) were placed on the intact myometrium.

The diffusion tensor parameters (DT-MD and DT-FA) were calculated by manually drawing regions of interest (ROIs) with 3–5 (ROIs) were placed on the normal or diseased endometrium in the sagittal plane image and 3 (ROIs) in the axial plane image. In cases of myometrial invasion, an additional two (ROIs) were placed on the infiltrated myometrium and another two (ROIs) on the intact myometrium on a sagittal plane image.

The average values of DW-ADC, DT-FA and DT-MD were then calculated and recorded.

Statistical analysis and data interpretation

This study is a prospective methodological study. The collected data were statistically analyzed by the IBM Statistical Product and Service Solution (IBM SPSS) Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. Qualitative data were described using numbers and percentages. Quantitative data were described

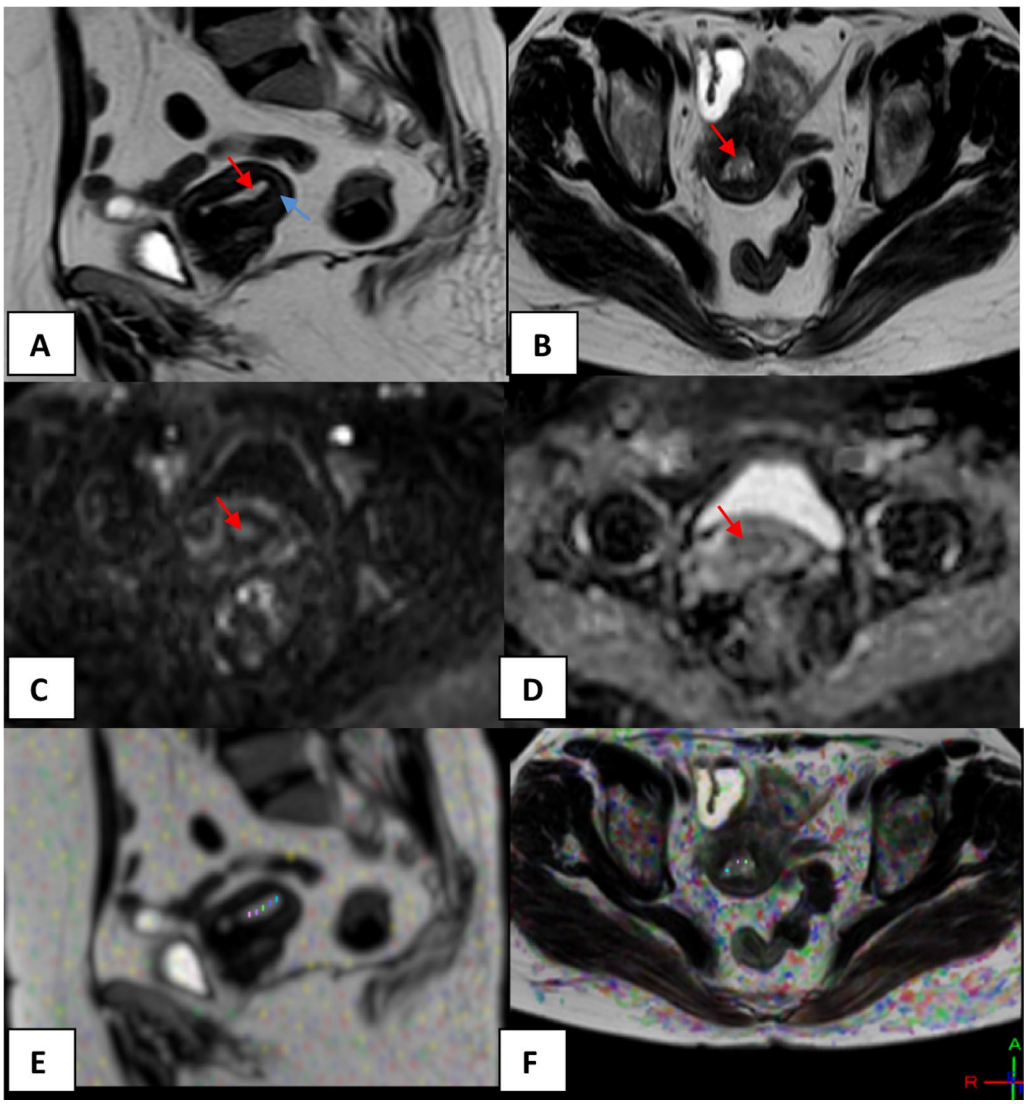

Fig. 5 A 55-year-old postmenopausal female presented by abnormal vaginal bleeding. **A**, **B** *Sagittal and axial T2 WIs* irregular endometrial thickening which is occupied by a soft-tissue mass displaying intermediate SI (red arrow). No visible tumor breaching through the junctional zone (blue arrow). **C** *Axial DWI with b value of 1000 s/mm*^{2} high signal intensity of the endometrial soft-tissue mass (red arrow). **D** *Axial DW-ADC map image* low signal intensity of the endometrial soft-tissue mass (red arrow). Mean DW-ADC value = 0.854×10^{-3}mm^2/s. **E**, **F** *Sagittal and axial DTI map images:* values of DT-FA and DT-ADC (MD) in multiple ROI along the endometrial mass. Mean DT-FA value = 0.264, and mean DT-ADC (MD) value = 0.831×10^{-3}mm^2/s. *Diagnosis* Pathologically proved endometrioid adenocarcinoma G2

using mean and standard deviation (SD) for parametric data after testing normality using the Kolmogorov–Smirnov test. The significance of the obtained results was judged at the (0.05) level.

One Way Analysis Of Variance (ANOVA) test was used to compare more than 2 independent groups with Post Hoc Tukey test to detect pair-wise comparison. The Kappa test was used for the inter-observer agreement percent.

The diagnostic performance of a test or the accuracy of a test to discriminate diseased cases from non-diseased cases is evaluated using receiver operating characteristic (ROC) curve analysis. Sensitivity and specificity were detected from the curve and positive predictive value (PPV), negative predictive value (NPV) and accuracy were calculated through cross-tabulation.

Results

There were 50 female patients in the study, with age range from 38 to 67 years; the mean age was 56.15 years (SD ± 8.229). The most common age group among the studied cases was between 50–59 age group (26 cases

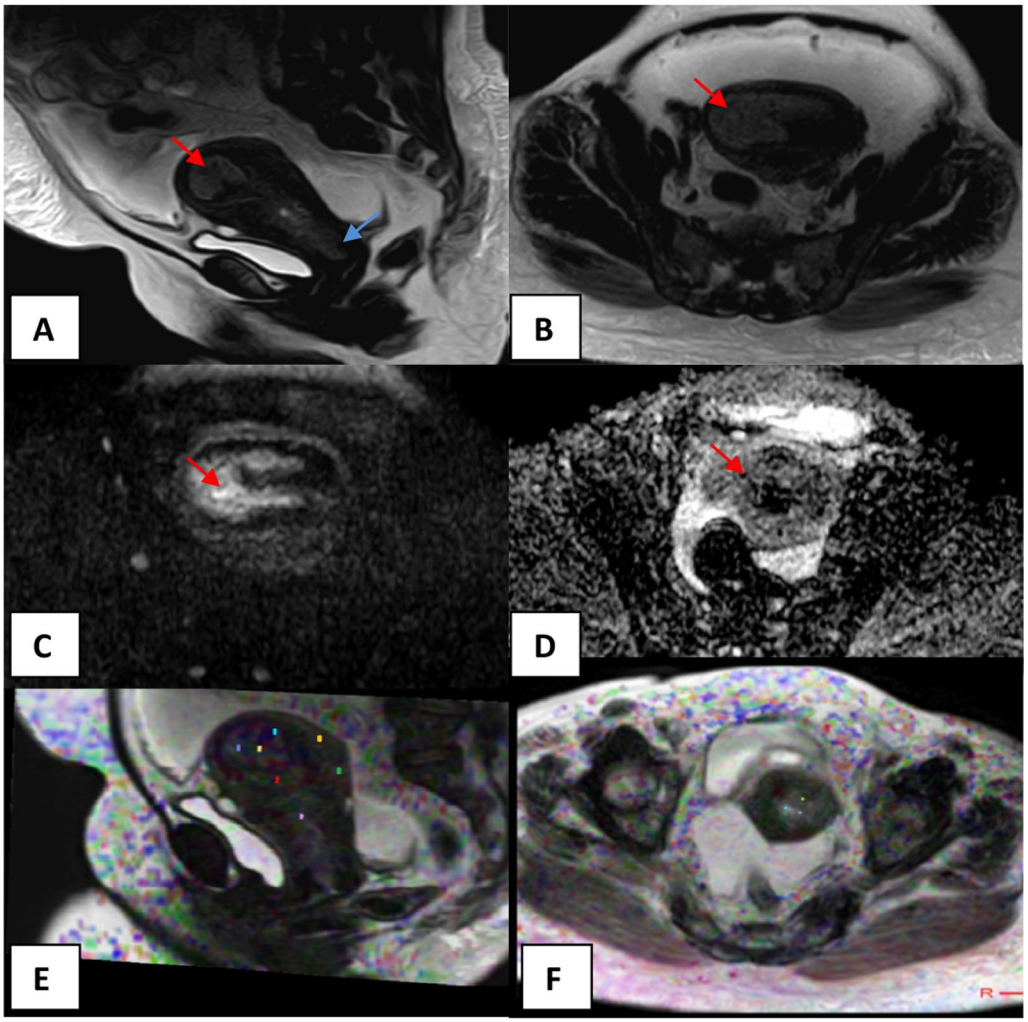

Fig. 6 A 54-year-old postmenopausal female presented by abnormal vaginal bleeding. **A**, **B** *Sagittal and axial T2 WIs* irregular endometrial soft-tissue mass with ill-defined margins displaying intermediate SI (red arrow). The mass distends and fills the endometrial cavity with myometrial thinning. The mass also extends to the cervix (blue arrow). **C** *Axial DWI with b value of 1000 s/mm²* high SI of the endometrial soft-tissue mass (red arrow). **D** *Axial DW-ADC map image* low signal intensity of the endometrial soft-tissue mass(red arrow). Mean DW-ADC value of the mass = 0.839×10^{-3} mm²/s. Mean DW-ADC values at areas of intact and infiltrated myometrium = 1.073 and 0.853×10^{-3} mm²/s, respectively. **E**, **F** *Sagittal and axial DTI map images* values of DT-FA and DT-MD in multiple ROI. Mean DT-FA and DT-MD values of the endometrial mass = 0.240 and 0.711×10^{-3}mm²/s, respectively. Mean DT-FA and DT-MD values at areas of infiltrated myometrium = 0.215 and 0.683×10^{-3}mm²/s, respectively. Mean DT-FA and DT-MD values at areas of intact myometrium = 0.423 and 1.069×10^{-3}mm²/s, respectively. *Diagnosis* Pathologically proved endometrioid adenocarcinomaG3

representing 52% of total cases), and the least common was 40–49 age group (3 cases representing 6% of total cases) (Table 1). All patients had pathologically proved endometrial carcinoma with the most common pathology was endometrioid adenocarcinoma 39 patients (about 78% of total cases), and the least common was clear cell carcinoma, and endometrial stromal sarcoma (each pathology 2 cases representing 4% of total cases) (Table 2).

There was a statistical significant difference between mean values of DT-FA and DT-ADC (MD) of different malignant endometrial tumors with P value = 0.003 and < 0.001, respectively. However, the mean values of DW-ADC for different malignant endometrial lesions show no significant statistical difference (P value was $P = 0.07$) (Table 2).

Table 3 shows that 28 cases of endometrial lesions had positive myometrial infiltration (representing 56% of total cases), and 22 cases had negative myometrial infiltration (representing 44% of total cases). There was a significant statistical difference regarding the mean values of DT-FA, DT-MD and DW-ADC values in differentiating between

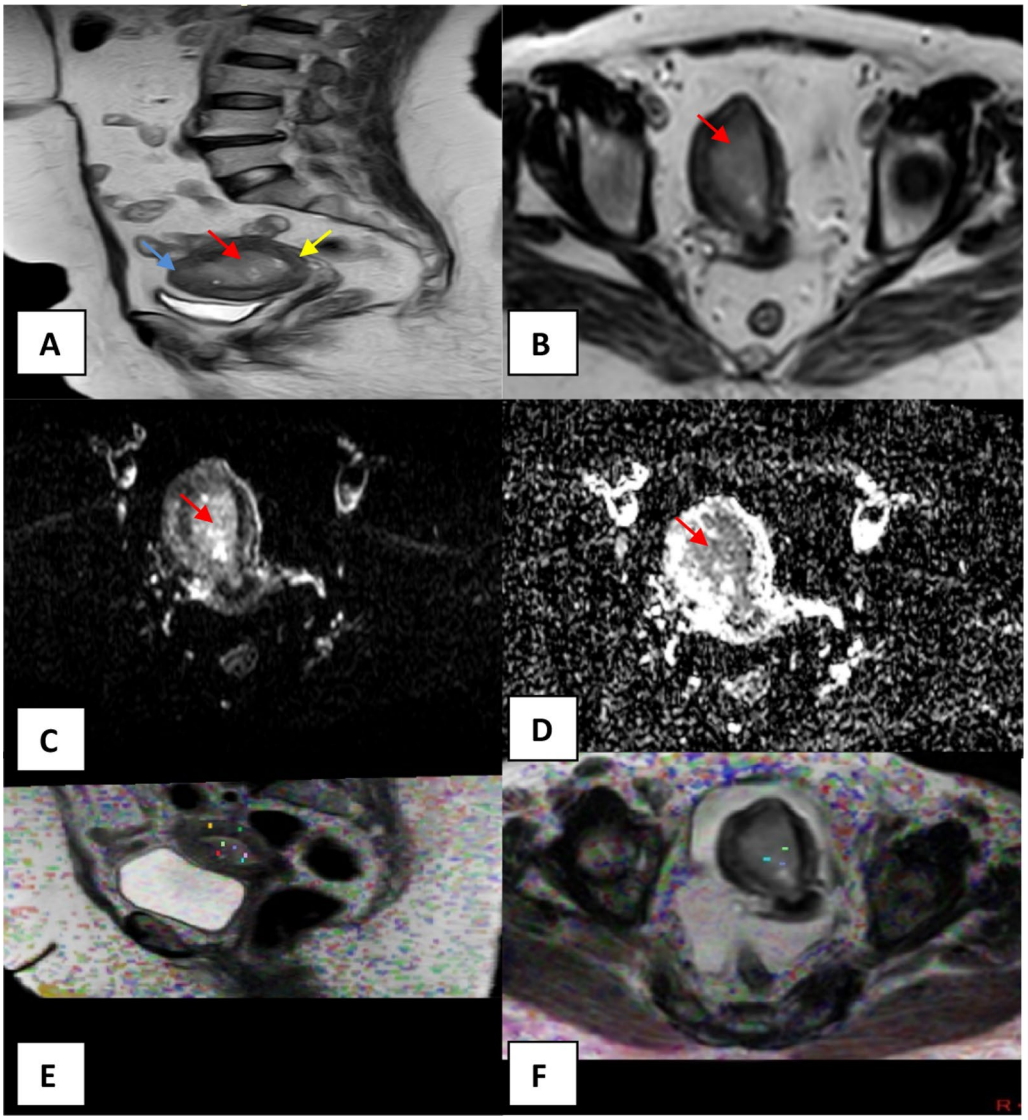

Fig. 7 A 50-year-old postmenopausal female presented by abnormal vaginal bleeding. **A**, **B** *Sagittal and axial T2 WIs* irregular endometrial soft-tissue mass with ill-defined margins displaying intermediate SI (blue arrow). The mass distends and fills the endometrial cavity with myometrial thinning (red arrow). No cervical extension (yellow arrow). **C** *Axial DWI with b value of 1000 s/mm²* high SI of the endometrial soft-tissue mass denoting restricted diffusion (red arrow). **D** *Axial DW-ADC map image* shows low signal intensity of the endometrial soft-tissue mass (red arrow). Mean DW-ADC value of the mass = 0.784×10^{-3}mm²/s. Mean DW-ADC values at areas of intact and infiltrated myometrium = 1.247 and 0.805×10^{-3}mm²/s, respectively. **E**, **F** *Sagittal and axial DTI map images* values of DT-FA and DT-ADC (MD) in multiple ROI. Mean DT-FA and DT-MD values of the endometrial mass = 0.181 and 0.508×10^{-3}mm²/s, respectively. Mean DT-FA and DT-ADC (MD) values at areas of infiltrated myometrium = 0.193 and 0.597×10^{-3}mm²/s, respectively. Mean DT-FA and DT-ADC (MD) values at areas of intact myometrium = 0.517 and 1.367×10^{-3} mm²/s, respectively. *Diagnosis* Pathologically proved endometrial papillary serous carcinoma

intact and infiltrated myometrium with (P value ≤ 0.001) for all parameters (Table 3).

Table 4 shows that: *(a) Using the cutoff DT-FA value* = $(0.320 \times 10^{-3}$ mm²/s) to detect myometrial invasion, the area under curve (AUC) was 0.969. The ROC curve shows that the sensitivity, specificity and accuracy were 85.7%, 95.5% and 90.0%, respectively. P value was ˂0.001. *(b)Using the cutoff DT-ADC (MD) value* = $(0.970 \times 10^{-3}$ mm²/s) to detect myometrial invasion, the area under curve (AUC) was 0.998 with the sensitivity, specificity and accuracy were 96.4%, 100.0% and 98.0%, respectively. P value was ˂0.001. *(c)Using the cutoff DW-ADC value* = $(0.990 \times 10^{-3}$ mm²/s) to detect myometrial infiltration, the area under curve (AUC*)* was

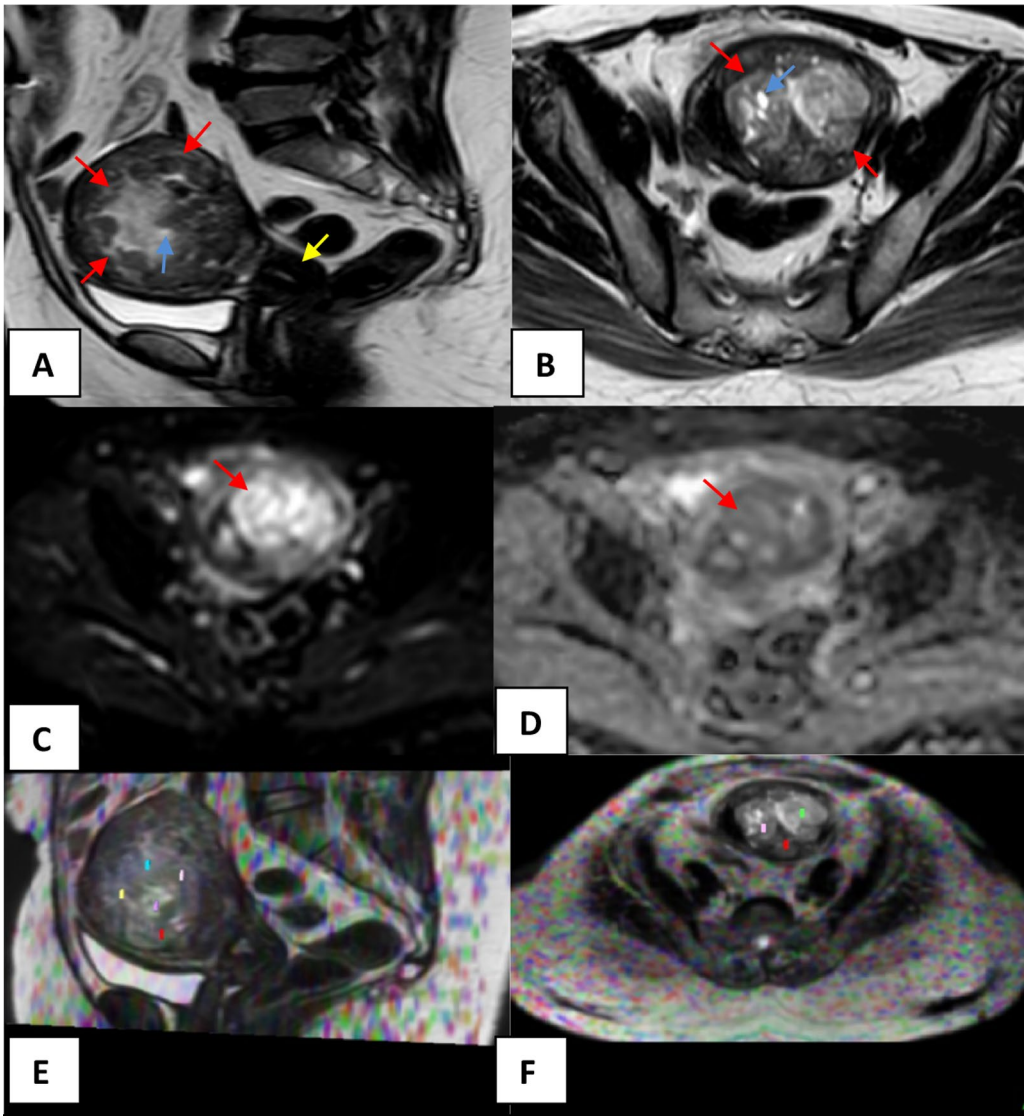

Fig. 8 A 51-year-old postmenopausal female presented by menorrhagia and pelvic pain. **A**, **B** *Sagittal and axial T2 WIs* occupation of the endometrial cavity by a poorly defined large oval-shaped polypoidal soft-tissue mass displaying heterogeneous SI and infiltrating the uterine body (red arrow). The mass has foci of high SI due to necrosis (blue arrow). No cervical extension (red arrow). **C** *Axial DWI with b value of 1000 s/mm²* high SI of the endometrial soft-tissue mass (yellow arrow). **D** *Axial DW-ADC map image* low signal intensity of the endometrial soft-tissue mass (red arrow). Mean DW-ADC value of the mass = 0.898×10^{-3}mm²/s. Mean DW-ADC values at areas of intact and infiltrated myometrium = 1.104 and 0.912×10^{-3}mm²/s, respectively. **E**, **F** *Sagittal and axial DTI map images* values of DT-FA and DT-MD in multiple ROI. Mean DT-FA and DT-MD values of the endometrial mass = 0.143 and 0.415×10^{-3}mm²/s, respectively. Mean DT-FA and DT-MD values at areas of infiltrated myometrium = 0.146 and 0.478×10^{-3}mm²/s, respectively. Mean DT-FA and DT-MD values at areas of intact myometrium = 0.389 and 1.252×10^{-3}mm²/s, respectively. *Diagnosis* Pathologically proved endometrial stromal sarcoma

0.869. The ROC curve shows that the sensitivity, specificity and accuracy were 82.1%, 90.9% and 86.0%, respectively. *P* value was ˂0.001.

Table 5 shows that a statistically significant difference in the mean values of DT-FA, DT-MD and DW-ADC for differentiating endometrioid adenocarcinoma grades with the overall *P* value was ˂ 0.001 for all parameters.

For differentiating grade 3 from grade 1 or 2 endometrioid adenocarcinoma, Table 6 shows that: *(a) Using the cutoff DT-FA value* = 0.236 had AUC = 0.942 with the sensitivity, specificity and accuracy = 90.9%, 96.4% and 94.9%, respectively. *P* value was < 0.001. *(b) Using the cutoff DT-MD value* = 0.825 had AUC = 0.894, the sensitivity, specificity and accuracy = 81.8%, 82.1% and 84.6%, respectively. *P* value was < 0.001. *(c) Using the cutoff*

Table 1 Age distribution and clinical presentation of the studied 50 cases

Age group (years)	No. of patients	Symptoms	No. of patients
30–39	5	Vaginal bleeding	35
40–49	3	Pelvic pain	3
50–59	26	Painful urination	2
60–69	16	Vaginal bleeding + pelvic pain	5
Age range: 38–67 years (mean age = 56.15 years (SD ± 8.229)		Vaginal bleeding + painful urination	5
Total	50		50

DW-ADC value = 0.916 had AUC = 0.894 with the sensitivity, specificity and accuracy were 90.9%, 64.3% and 74.4%, respectively. *P* value was < 0.001.

For differentiating grade 1 from grade 2 or 3 endometrioid adenocarcinoma, Table 6 shows that: *(a) Using the cutoff DT-FA value* = 0.335 had AUC = 0.980 with the sensitivity, specificity and accuracy = 94.4%, 85.7% and 90.0%, respectively. *P* value was < 0.001. *(b) Using the cutoff DT-MD value* = 0.983 had AUC = 0.918 with the sensitivity, specificity and accuracy were 88.9%, 90.5% and 89.7%, respectively. *P* value was < 0.001. *(c) Using the cutoff DW-ADC value* = 0.941 had AUC = 0.884 with the sensitivity, specificity and accuracy were 77.8%, 85.7% and 84.6%, respectively. *P* value was < 0.001.

Tables 5 and 7 show that the highest DT-FA, DT-MD and DW-ADC mean values were detected in endometrioid adenocarcinoma grade 1 (G1) followed by endometrioid adenocarcinoma G2, while the lowest was detected in G3 (*P* value ≤ 0.001), so mean DT-FA, DT-MD and DW-ADC values were inversely proportional to the degree of pathological grading with r = − 0.867, − 0.762 and − 0.706, respectively (Table 7).

The inter-observer correlation coefficient for variability between the two observers in detecting myometrial invasions among the studied cases was 0.96, 0.89 and 1 for DW-ADC, DT-FA and DT-MD, respectively, and in differentiating Grade 3 from Grade 1 or 2 endometrioid adenocarcinoma was 0.92, 1 and 0.91 for DW-ADC, DT-FA and DT-MD, respectively, and in differentiating Grade 2 or 3 from grade 1 endometrioid adenocarcinoma was 0.94, 0.86 and 0.85 for DW-ADC, DT-FA and DT-MD, respectively (*P* value ≤ 0.001 for all) (Table 8).

Table 3 Comparison of DT-FA, MD and DW-ADC in differentiating myometrial invasion

	No myometrial invasion *N* = 22 (44%)	Myometrial invasion *N* = 28 (56%)	Test of significance
DT-FA	0.450 ± 0.07	0.260 ± 0.07	< 0.001*
DT-MD	1.310 ± 0.15	0.650 ± 0.16	< 0.001*
DW-ADC	1.260 ± 0.17	0.870 ± 0.16	< 0.001*

t: Student *t* test, *statistically significant if *P* < 0.05

Parameters described as mean ± SD

Discussion

Diffusion-weighted (DW) MR imaging has a higher diagnostic accuracy in assessing the depth of myometrial invasion and the overall staging of endometrial cancer than dynamic contrast-enhanced (DCE) MR imaging, and this was confirmed by Beddy et al. [10]. Yamada et al. [11, 12] proved that DTI had a role in evaluation of the depth of invasion in esophageal and gastric carcinomas.

Only few articles were published about using DTI parameters in the evaluation of myometrial invasion and grading of endometrial carcinoma. The current study was designed to investigate the role of both DW-ADC and diffusion tensor parameters (mainly DT-FA and DT-MD) in the detection of myometrial infiltration and grading of endometrial carcinoma with the most common malignant pathology were endometrioid adenocarcinoma. Similar findings were detected by Toba et al. [1], Zhang et al. [13] and Yamada et al. [14], as the most common pathology was endometrioid adenocarcinoma.

Table 2 Mean FA, ADC and MD in differentiating endometrial carcinoma pathology

Pathology	Total = 50	DT-FA	DT-MD	DW-ADC
Papillary serous carcinoma	*N* = 4 (8%)	0.187 ± 0.01	0.509 ± 0.04	0.812 ± 0.11
Mixed type adenocarcinoma	*N* = 3 (6%)	0.183 ± 0.012	0.445 ± 0.048	0.767 ± 0.103
Endometrioid adenocarcinoma	*N* = 39 (78%)	0.35 ± 0.13	0.907 ± 0.19	0.935 ± 0.129
Endometrial stromal sarcoma	*N* = 2 (4%)	0.158 ± 0.04	0.445 ± 0.02	0.864 ± 0.053
Clear cell carcinoma	*N* = 2 (4%)	0.18 ± 0.01	0.467 ± 0.034	0.818 ± 0.071
One way ANOVA test		*P* = 0.003*	*P* < 0.001*	*P* = 0.07

Parameters described as mean ± SD

F: One Way ANOVA test, *statistically significant if *P* < 0.05

Table 4 Validity of DT-FA, MD, and DW-ADC in differentiating myometrial invasion

	AUC (95% CI)	*P* value	Cutoff point	Sensitivity%	Specificity%	PPV%	NPV%	Accuracy%
DT-FA	0.969	< 0.001*	0.320	85.7	95.5	96.0	84.0	90.0
DT-MD	0.998	< 0.001*	0.970	96.4	100.0	100.0	95.7	98.0
DW-ADC	0.869	< 0.001*	0.990	82.1	90.9	92.0	80.0	86.0

*Highly significant

AUC area under curve, *CI* confidence interval, *NPV* negative predictive value, *PPV* positive predictive value

Table 5 Comparison of FA, ADC and MD in differentiating endometrioid adenocarcinoma grades

	Grade 1 *N* = 18	Grade 2 *N* = 10	Grade 3 *N* = 11	Test of significance	*P*1	*P*2	*P*3
DT-FA	0.463 ± 0.085	0.296 ± 0.058	0.225 ± 0.042	< 0.001*	< 0.001*	< 0.001*	0.025*
DT-MD	1.042 ± 0.16	0.861 ± 0.12	0.731 ± 0.094	< 0.001*	0.002*	< 0.001*	0.035*
DW-ADC	1.03 ± 0.12	0.892 ± 0.062	0.824 ± 0.072	< 0.001*	0.001*	< 0.001*	0.049*

F = One Way ANOVA test, *P*: probability, *statistically significant if $P < 0.05$

*P*1: difference between grade 1 and grade 2, *P*2: difference between grade 1 and 3, *P*3: difference between grade 2 and 3

Parameters described as mean ± SD

Table 6 Validity of FA, ADC and MD in differentiating endometrial carcinoma grades

	AUC (95% CI)	*P* value	Cutoff point	Sensitivity %	Specificity%	PPV%	NPV%	Accuracy%
Grade 3 from grade 1 or 2 endometrioid adenocarcinoma								
DT-FA	0.942 (0.860–1.0)	< 0.001*	0.236	90.9	96.4	90.9	96.4	94.9
DT-MD	0.894 (0.793–0.99)	< 0.001*	0.825	81.8	82.1	64.3	92.0	84.6
DW-ADC	0.894 (0.793–0.996)	< 0.001*	0.916	90.9	64.3	50.0	94.7	74.4
Grade 2 or 3 from grade 1 endometrioid adenocarcinoma								
DT-FA	0.980 (0.947–1.0)	< 0.001*	0.335	94.4	85.7	85.0	94.7	90.0
DT-MD	0.918 (0.81–1.0)	< 0.001*	0.983	88.9	90.5	88.9	90.5	89.7
DW-ADC	0.884 (0.774–0.99)	< 0.001*	0.941	77.8	85.7	82.4	81.8	84.6

*Highly significant

AUC area under curve, *CI* confidence interval, *NPV* negative predictive value, *PPV* positive predictive value

Tian et al. [15] concluded that diffusion-weighted and diffusion tensor imaging could help in the differentiation of endometrioid adenocarcinoma and serous adenocarcinoma. Also, the results of the current study showed that mean DT-FA and DT-MD values of endometrioid adenocarcinoma (0.35 ± 0.13 and 0.907 ± 0.19, respectively) were more than that of papillary serous carcinoma (0.187 ± 0.01 and 0.509 ± 0.04, respectively).

As accurate diagnosis of *myometrial invasion* is essential in the preoperative assessment of endometrial cancer, Deng et al. [16] reported that diffusion and ADC value could aid in the prediction of deep myometrial invasion. Also, Gil et al. [17] stated that the conjunction of diffusion-weighted imaging with T2WI had better results than the dynamic contrast study and T2WI in the evaluation of myometrial invasion. Similar findings were detected in the current study, and there was a significant statistical difference considering mean DW-ADC values between intact (1.260 ± 0.17) and invaded areas of the myometrium (0.870 ± 0.16) (*P* value ˂0.001).

Table 7 Correlation between DT-FA, MD and DW-ADC and endometrioid adenocarcinoma grades

		Endometrioid adenocarcinoma grade
FA values	*r*	−0.867**
	P value	< 0.001
MD values ($\times 10^{-3}$ mm^2/s)	*r*	−0.762**
	P value	< 0.001
ADC values ($*10^{-3}$ mm^2/s)	*r*	−0.706**
	P value	< 0.001

*Highly significant

In this study, there was a significant statistical difference regarding DT-FA mean values between intact (0.450 ± 0.07) and invaded areas of myometrium (0.260 ± 0.07) (*P* value ≤ 0.001).

Also, there was a significant statistical difference regarding DT-MD mean values between intact (1.310 ± 0.15) and infiltrated regions of myometrium (0.650 ± 0.16) (*P* value ˂0.001).

This is compatible with Zhang et al. [13], who stated that DT-FA mean values showed significant differences between cancerous (0.41) versus non-cancerous areas (0.27) within the superficial myometrium (*P* value ˂ 0.001). Also, they reported that mean DT-MD could distinguish cancerous (1.16) from non-cancerous areas (1.48) within the superficial myometrium (*P* value ˂ 0.001).

Also, Toba et al. [1] and Yamada et al. [14] concluded that DTI might be a useful tool for diagnosing myometrial invasion of uterine endometrial cancer, both ex vivo and in vivo, respectively.

Previous studies by Zhang et al. [13] and Yamada et al. [14] confirmed that the DTI parameters were superior to the ADC in the assessment of myometrial invasion of endometrial carcinoma. This is in agreement with the results of this study, as the accuracy of DT-MD (98.0%) and DT-FA (90.0%) was superior to the accuracy of DW-ADC (86.0%) in the prediction of myometrial infiltration.

*For grading of endometrial carcinoma***,** Nakamura et al. [18], Inoue et al. [19] and Habib et al. [20] reported that DW-ADC may have a value in differentiation of endometrioid adenocarcinoma pathologic grades and the lower ADC value is associated with the higher grade of the tumor.

The results of this study are matching with the previous studies, and there was a significant statistical difference regarding DW-ADC mean values in different endometrioid adenocarcinoma grades (G1 = 1.03 ± 0.12; G2 = 0.892 ± 0.062 and G3 = 0.824 ± 0.072) (*P* value ≤ 0.001).

Table 8 The inter-observer correlation coefficient between both observers as regard DW-ADC, DT-FA and DT-MD in differentiating myometrial invasion and grading of endometrioid adenocarcinoma

	Observer 1	Observer 2	Kappa agreement
+ve myometrial invasion			
DW-ADC	23	24	0.96
DT-FA	26	24	0.89
DT-MD	27	27	1
Grade 3 from grade 1 or 2			
DW-ADC	9	10	0.92
DT-FA	10	10	1
DT-MD	9	8	0.91
Grade 2 or 3 from grade 1			
DW-ADC	16	17	0.94
DT-FA	21	19	0.86
DT-MD	19	16	0.85

Diffusion tensor imaging proved to have a role in grading of breast, renal cancers and brain gliomas [21–26], especially DT-FA parameter which is decreased with a higher grade of the tumor and this is mostly due to packed cells and heterogeneity [22].

Yamada et al. [14] reported that the mean DT-FA and DT-MD values of endometrioid adenocarcinoma G1, G2, and G3 were statistically different with significant (*P* value ≤ 0.001).

Similar findings were detected in the current study: there was a significant statistical difference between DT-FA mean values and the pathological grade of endometrioid adenocarcinoma as G1 = 0.463 ± 0.085, G2 (0.296 ± 0.058) and G3 (0.225 ± 0.042). Also, the mean DT-MD values of endometrioid adenocarcinoma G1 = 1.042 ± 0.16, G2 = 0.861 ± 0.12 and G3 = 0.731 ± 0.094 with significant (*P* value ≤ 0.001).

The results of this study confirmed that there is an inverse correlation between the mean values of DW-ADC, DT-MD and DT-FA; and the pathological grade of endometrioid adenocarcinoma (the higher the grade, the lower the value, and vice versa) (*P* value ≤ 0.001). This is in accordance with Habib et al. [20] with (*P* value = 0.03 for DW-ADC) and in harmony with Yamada et al. [14] who stated that there was a significant inverse correlation between DT-FA and DT-MD values and histo-pathologic grades (*P* value < 0.001).

The analysis of the ROC curve showed that DW-ADC, DT-FA and DT-MD were useful for grading of

endometrioid adenocarcinoma with DT-FA had more accuracy than DT-MD and DW-ADC for differentiation of G3 from G1 or 2 (94.9%) and also differentiation of G1 from G 2 or 3 endometrioid adenocarcinoma (90.0%). This is in agreement with Yamada et al. [14] who stated that DT-FA had the largest area under curve for differentiation of Grade 1 from G2 or 3 and for differentiation of Grade 3 from G1 or G2 endometrioid adenocarcinoma. They added that the use of DTI parameters, especially FA values, is useful for evaluating the degree of aggressiveness of endometrial carcinoma.

Lastly, a preliminary recent study done by Ghosh et al. [27] used the whole tumor histogram texture for defining the ROI to measure the DTI parameters in evaluation of myoinvasion and type of endometrial carcinoma. They assumed that this texture approach will have more reproducibility and make the results more confident than subjective drawing the region of interests (ROIs) and added that more future extensive studies are needed for better results.

Limitation

This study pays attention to endometrioid subtype of endometrial carcinoma and its histopathological grades with small numbers of other subtypes of endometrial cancer.

Also, the relatively small numbers of overall patients participated in the study.

Further studies with a large scale of patients and adding DTI and DWI to conventional pelvic MRI with more standardization of the protocols are recommended in the evaluation of endometrial cancer patients. Also, more detailed inter-observer agreement studies are recommended.

Conclusions

Diffusion tensor parameters and diffusion ADC value are non-invasive measures that can be useful in distinguishing between intact and infiltrated myometrium and help in accurate histopathological grading of endometrial carcinoma (with both DT-MD and DT-FA had more specificity and accuracy than DW-ADC). This is mandatory for planning appropriate treatment and surgery in patients with endometrial cancer. This indicates that diffusion and diffusion tensor imaging can be applied to asses' malignant pelvic pathologies.

Abbreviations

EMC: Endometrial cancer; FA: Fractional anisotropy; MD: Mean diffusivity; DWI: Diffusion-weighted imaging; DTI: Diffusion tensor imaging; SD: Standard deviation; mm: Millimeter; ms: Millisecond; FOV: Field of view; cm: Centimeter; ROI: Region of interest; ROC curve: Receiver operating characteristic curve; PPV: Positive predictive value; NPV: Negative predictive value; AUC: Area under curve; DCE-MR imaging: Dynamic contrast-enhanced-magnetic resonance imaging; no: Number; G1, G2, G3: Grade 1, grade 2, grade 3.

Acknowledgements

To technicians at radiology department who help in examination of patients.

Authors' contributions

MAL contributed to idea of the manuscript, writing of the manuscript, final revision of data, statistical tables and radiological images, and finalization of the research manuscript. HSM contributed to collecting of data, helping in writing of the manuscript, and radiological examination of patients (under supervision). All authors read and approved the final manuscript.

Funding

Not applicable.

Availability of data and materials

Authors can confirm that all relevant data are included in the article and/or its supplementary information files.

Declarations

Ethics approval and consent to participate

This study was approved by the Mansoura Faculty of Medicine—Institutional Research Board (MFM-IRB) and written informed consent to participate was obtained from all patients. Ethics committee reference number (Code No. R.21.03.1248).

Consent for publication

All patients included in this research gave written informed consent to publish the data contained within this study.

Competing interests

The authors declare that they have no competing interests.

Received: 29 July 2021 Accepted: 7 November 2021
Published online: 16 November 2021

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