

Original Research

Preoperative Evaluation of 3D-MRI on the Depth of Myometrial Invasion of Endometrial Carcinoma: 3D Study of Endometrial Carcinoma

Jiaxin Fu¹, Yuhui Cui², Liqun Xu¹, Ping Shen¹, Xilong Liu², Chunlin Chen^{1,*}, Ping Liu^{1,*}

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Abstract

Background: To evaluate the preoperative diagnostic efficacy of 3D-MRI for the depth of myometrial invasion of endometrial carcinoma. **Methods**: A total of 116 patients with endometrial carcinoma who had undergone pelvic MRI before surgery were included. Mimics 21.0 (Materialize Co., Belgium) software was used to reconstruct three-dimensional MRI models (3D-MRI). The tumor volume and surface area, uterine volume and surface area were measured, and the tumor volume ratio was calculated. TVR (Tumor Volume Ratio) = tumor volume/uterine volume, TAR (Tumor Area Ratio) = tumor surface area/uterine surface area. Postoperative pathology was used as the gold standard to compare the accuracy, sensitivity, specificity, negative predictive value, and positive predictive value of conventional MRI and 3D-MRI in preoperative assessment of endometrial carcinoma myometrial invasion. **Results**: The accuracy and specificity of 3D-MRI in the diagnosis of deep myometrial invasion were better than conventional MRI (p < 0.05). There was no statistically significant difference in tumor volume or surface area between stage IA and stage IB (p > 0.05), while TVR and TAR showed significant statistical differences (8.05 \pm 0.66 vs. 19.12 \pm 3.20, p < 0.01; 21.38 \pm 1.04 vs. 35.15 \pm 3.42, p < 0.01). Further analysis, the area under the ROC curve of TVR is 0.738, p < 0.01, and the best cut-off value is 13.59%; the area under the ROC curve of TAR is 0.770, p < 0.01, and the best cut-off value is 27.41%. **Conclusions**: Preoperative 3D-MRI can effectively assess the myometrial invasion of endometrial carcinoma.

Keywords: endometrial carcinoma; 3D-MRI; preoperative; tumor volume; tumor surface

1. Introduction

Endometrial carcinoma is one of the three major malignant tumors in women, accounting for 20%–30% of malignant tumors in the female reproductive tract. In recent years, the incidence rate has been increasing worldwide, mostly in women over 50 years old, and the peak age of onset is 50 to 59 years old [1]. Early stage patients have a better prognosis, with a 5-year survival rate of more than 95%, compared with 17% for stage IV patients [2].

Preoperative accurate staging of endometrial carcinoma is very important for surgical decision and prognosis. The high-risk factors related to prognosis mainly include: pathological type, histological grade, deep myometrial invasion, vascular space invasion, cervical interstitial invasion, lymphatic metastasis, and extrauterine metastasis. Among them, the depth of myometrial invasion is included in the FIGO 2009 staging. The staging standard is divided into IA stage and IB stage according to the depth of tumor invasion. MRI has become an important imaging method for preoperative evaluation due to its high resolution of soft tissues. However, the accuracy of conventional T2W1 for the depth of invasion is still controversial. Some studies believe that the accuracy is 70–80%, and other study is 55– 77% [3]. For postmenopausal women, the uterine atrophy, the obscuration of the junction zone, and the thinning of the

myometrium layer also make it difficult to evaluate. When the cancer is small, located in the corner of the uterus, or combined with special factors such as uterine fibroids, the value of conventional MRI for judging myometrial invasion is limited. Moreover, a single layer of a two-dimensional MRI image cannot fully reflect the relationship between the lesion and the myometrium layer, because the scan is only a section in a certain direction, and the largest or smallest diameter of the lesion and the uterus may not be synchronized at the same layer.

In recent years, domestic and foreign scholars have tried to further improve the accuracy of preoperative staging through various new imaging methods such as DWI, DCE-MRI, FLASH-3D [4–6]. However, the above-mentioned studies require injection of contrast agents. Some patients are unacceptable, sensitive to contrast agents, expensive, and scan time increased significantly. 3D-MRI uses software to reconstruct conventional MRI image data into three-dimensional visualization models of tumors and uterus, simulating the real three-dimensional structure of space, and combining two-dimensional images on the basis of the three-dimensional model to determine myometrial invasion. Currently research in endometrial carcinoma is limited.

¹Department of Obstetrics and Gynecology, Nanfang Hospital, Southern Medical University, 510515 Guangzhou, Guangdong, China

²Department of Radiology, Nanfang Hospital, Southern Medical University, 510515 Guangzhou, Guangdong, China

^{*}Correspondence: ccl1@smu.edu.cn (Chunlin Chen); lp2@smu.edu.cn (Ping Liu)

Therefore, our study intends to perform preoperative visualization of endometrial carcinoma with three-dimensional reconstruction based on conventional MRI data, to measure the volume and surface area of the tumor and uterus, and to explore the value of 3D-MRI in the preoperative diagnosis of myometrial invasion in early endometrial carcinoma.

2. Materials and Methods

2.1 Subjects

This study retrospectively included a total of 222 endometrial carcinoma patients confirmed by histology in our hospital from January 1, 2011 to December 30, 2020, and excluded complicated uterine fibroids with diameter ≥ 2 cm, FIGO 2009 ≥stage II, and other malignancies. 116 cases were eventually included. All patients underwent pelvic MRI scans within 2 weeks before surgery. This study was approved by the Ethics Committee of Nanfang Hospital of Southern Medical University, and the ethics number is [2013] Review (032). All patients obtained informed consent. All patients underwent surgical treatment of endometrial carcinoma in our hospital (according to FIGO 2009) and had complete clinical data, including patient general information, preoperative examination results, surgical records, postoperative pathology, and postoperative diagnosis and treatment plans.

2.2 MRI Imaging

Scans were performed on a 3.0-Tesla MRI scanner (Philips, Achieva 3.0T TX) using an abdominal coil. The examiner took a supine position, with the median sagittal plane perpendicular to the bed surface, holding the head with both hands, and stretching the legs together. First, routine coronal, sagittal and transverse scans were performed, and then fast spin echo sequence T2-weighted imaging (T2WI-TSE) axial thin-slice scans were performed. The parameters were as follows: TR/TE, 4920/85 ms; NSA, 2; flip angle, 90; FOV, 280 mm \times 359 mm \times 262 mm; matrix, 324 \times 343; slice thickness, 3.0 mm; slice gap, 0.5 mm; voxel, 0.8 mm \times 1.0 mm \times 3.0 mm. All image acquisitions are performed by uniformly trained technicians from the Medical Imaging Center. All 2D image data are exported and saved in DICOM 3.0 format.

2.3 Image Analysis and 3D-MRI Construction

Import the DICOM format MRI data into Mimics 21.0 (Materialize Co., Belgium) software, and outline ROI area of the images at all levels, including the uterus and lesions, and reconstruct a complete three-dimensional model. Obtain the volume and surface area of the tumor and the uterus, and calculate: TVR = tumor volume/uterine volume, TAR = tumor surface area/uterine surface area. Considering that we only analyze myometrial invasion of endometrial carcinoma, the cervix is not counted.

Two senior imaging physicians and one obstetrician and gynecologist jointly made the evaluation. If the binding zone is visible and the endometrial surface is smooth and continuous, then there is no myometrial invasion. If the junction zone between the inner membrane and the myometrium layer is irregular or incomplete, the myometrium layer is considered to have been invasion. If the signal intensity of the tumor at the T2W1 level is greater than half, it is considered to be a deep myometrial invasion [7]. 3D-MRI's transparency, contrast, rotation, measurement and other functions, combined with two-dimensional images, to make evaluations together as shown in Figs. 1,2.

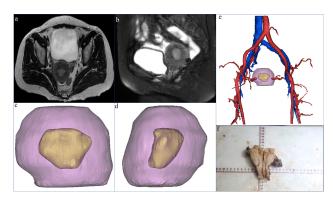


Fig. 1. A 53-year-old female patient, preoperative MRI showed both axial (a) and sagittal (b) deep myometrial invasion. The picture (c,d,e), pink purple represents the uterus, yellow represents the lesion, red represents the arterial blood vessel, and blue represents the venous blood vessel. 3D-MRI indicated superficial myometrial invasion, and showed the three-dimensional positional relationship between the lesion and the uterus and blood vessels. The uterine volume was 84462.09 mm³, the tumor volume was 8086.48 mm³, the TVR was 9.57%. The uterine surface area was 10479.32 mm², the tumor surface area was 2354.46 mm², and the TAR was 22.4%. Postoperative pathology proved to be poorly differentiated endometrioid adenocarcinoma, and superficial myometrial invasion (f).

2.4 Statistical Analysis

SPSS 23.0 software (version 23.0, USA) was used for statistical analysis. Quantitative data are expressed as the mean \pm standard deviation (x \pm s) and categorized as percentages (%), categorical variables were compared using the χ^2 test, the independent-samples T-test was used to compare between different groups. Compare the accuracy, sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) of conventional MRI and 3D-MRI. p values of <0.05 were considered statistically significant.



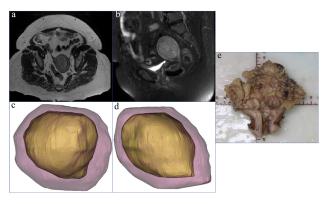


Fig. 2. A 53-year-old female patient, preoperative MRI showed both axial (a) and sagittal (b) deep myometrial invasion. 3D-MRI showed deep myometrial invasion (c,d). The uterine volume was 113623.07 mm³, the tumor volume was 50742.01 mm³, the TVR was 44.66%. The uterine surface area was 12287.16 mm², the tumor surface area was 7231.83 mm², and the TAR was 58.86%. Postoperative pathologically confirmed uterine middle-poorly differentiated endometrioid carcinoma, invading deep myometrium (e).

3. Results

3.1 Patient-Based Analysis

A total of 116 patients were identified in the analysis (Fig. 3). The characteristics of general cases are shown in Table 1. 93 cases were in stage IA and 23 cases were in stage IB. The mean age of the patients was 53.90 ± 9.03 years. Among these patients, 54 (46.6%) were premenopausal and 62 (53.4%) were postmenopausal. Histopathology subtype revealed that 94.0% of tumours were endometrioid adenocarcinoma, 1.7% showed clear cell carcinoma, 0.9% showed clear cell carcinoma, and 3.4% showed mixed carcinoma. 46.5% neoplasms were classified as grade 1, 37.1% as grade 2 and 20.4% as grade 30.

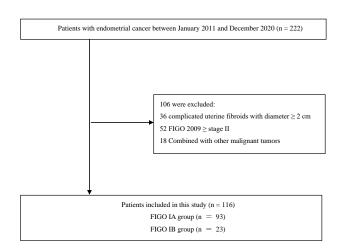


Fig. 3. Flow diagram.



Table 1. General characteristics of patients with endometrial carcinoma.

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General characteristics	Mean \pm SD or n (%)		
Age, years (mean \pm SD)	53.90 ± 9.03		
High risk factors			
Hypertension	33 (28.4)		
Diabetes	9 (0.7)		
BMI	25.04 ± 3.95		
Menopausal status			
Not menopausal	54 (46.6)		
Menopausal	62 (53.4)		
FIGO stage			
IA	93 (80.2)		
IB	23 (19.8)		
Histologic subtype			
Endometrioid adenocarcinoma	109 (94.0)		
Serous carcinoma	2 (1.7)		
Clear cell carcinoma	1 (0.9)		
Mixed carcinoma	4 (3.4)		
Pathological grade			
1	54 (46.5)		
2	43 (37.1)		
3	19 (16.4)		

BMI, Body Mass Index.

3.2 Analysis of the Diagnostic Results of Conventional MRI and 3D-MRI

Taking the postoperative pathological results as the gold standard, comparing the evaluation results of conventional MRI and 3D-MRI, the results showed that the accuracy and specificity of 3D-MRI in diagnosing deep myometrial invasion were better than conventional MRI (p < 0.05), and there is no significant difference in sensitivity, PPV, NPV (p > 0.05). In the diagnosis of myometrial invasion, 3D-MRI is more accurate (Table 2).

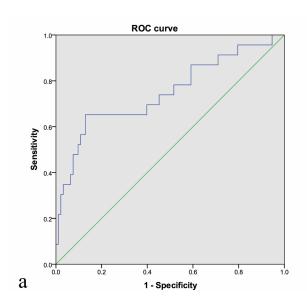
3.3 3D Parameter Analysis

The tumor volume, uterine volume, tumor surface area, and uterine surface area were measured by 3D-MRI, calculated TVR and TAR. The results showed (Table 3) that there was no statistically significant difference in tumor volume or tumor surface area between stage IA and stage IB (p > 0.05), while TVR and TAR both showed significant statistical differences (8.05 ± 0.66 vs. 19.12 ± 3.20 , p < 0.01; 21.38 ± 1.04 vs. 35.15 ± 3.42 , p < 0.01). Further analysis, the area under the ROC curve of TVR is AUC = 0.738 (Fig. 4a), p < 0.01, and the Youden's index is calculated to obtain the best cut-off value of TVR = 13.59%. The area under the ROC curve of TAR is AUC = 0.770 (Fig. 4b), p < 0.01, and the Youden's index is calculated to obtain the best cut-off value of TAR = 27.41%.

Table 2. MRI, 3D-MRI diagnosis results of endometrial carcinoma myometrial invasion.

	TP (n)	TN (n)	FP (n)	FN (n)	Accuracy (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
MRI	17	78	15	6	81.9	73.9	83.8	53.1	92.8
3DMRI	20	87	6	3	92.2	86.9	93.5	76.9	96.6

TP, True positive; TN, True negative; FP, False positive; FN, False negative; PPV, positive predictive value; NPV, negative predictive value.



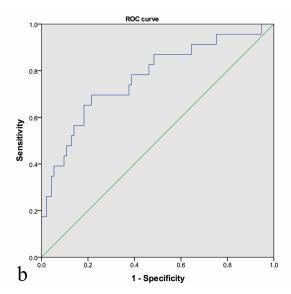


Fig. 4. ROC curve of TVR (a) and TAR (b). The picture a showed the area under the ROC curve of TVR was 0.738, and the Youden's index was 13.59%. The picture b showed the area under the ROC curve of TAR is 0.770, and the Youden's index is 27.41%.

Table 3. Analysis of three-dimensional parameters on the depth of myometrial invasion of endometrial carcinoma.

	IA (n = 93)	IB (n = 23)	p value
Tumor volume (mm ³)	10111.87 ± 1709.59	37532.96 ± 18573.34	0.158
TVR (%)	8.05 ± 0.66	19.12 ± 3.20	0.002
Tumor surface area (mm ²)	2895.49 ± 288.47	5503.00 ± 1415.05	0.084
TAR (%)	21.38 ± 1.04	35.15 ± 3.42	0.001

TVR, Tumor Volume Ratio = tumor volume/uterine volume; TAR, Tumor Area Ratio = tumor surface area/uterine surface area.

4. Discussion

The study reconstruct three-dimensional, visualized three-dimensional models on the basis of conventional MRI, simulate the real three-dimensional structure of space, and combine two-dimensional images on the basis of the three-dimensional model to evaluate tumor invasion. The results confirmed that the accuracy and specificity of 3D-MRI in the diagnosis of early endometrial cancer myometrial invasion is better than conventional MRI (p < 0.05). Next, the study analyzed the parameters measured by 3D-MRI, including tumor volume and surface area, uterine volume and surface area, TVR, and TAR. The results showed that there was no difference in pure tumor volume or tumor surface area between stage IA and stage IB. Statistically significant (p > 0.05), while TVR and TAR both showed significant statistical differences (8.05 \pm 0.66 vs. 19.12 \pm 3.20, p < 0.01; 21.38 \pm 1.04 vs. 35.15 \pm 3.42, p <

0.01). Further analysis, the area under the ROC curve of TVR AUC = 0.738, p < 0.01, and the best cut-off value is 13.59%. The area under the ROC curve of TAR is AUC = 0.770, p < 0.01, and the best cut-off value is 27.41%. As far as the author knows, this study is the first to use 3D-MRI to evaluate preoperative staging. Some scholars use third-party software to construct a three-dimensional model of the uterus and tumor, but the model fails to visualize the anatomical position relationship, and then Cannot evaluate better and more accurately [8].

The depth of myometrial invasion of endometrial cancer has always been the focus of clinicians, and it is also an important factor in determining FIGO staging and prognosis. For young patients who want to preserve fertility, no myometrium invasion and, at most, a superficial myometrial invasion [9]. Studies have shown that on conventional MRI sequences [10], when the largest tumor diameter is



greater than 2 cm, the probability of deep myometrial invasion increases by 10.04 times (95% CI 3.34–30.17, p < 0.001). It is considered that the preoperative MRI shows the largest tumor diameter may be a prognostic indicator of deep myometrial invasion in patients with endometrial carcinoma. However, it is obviously not enough to only consider the diameter of the tumor. For patients with a larger uterus, even if the tumor is large in diameter, it may still be limited to the superficial myometrium.

There are also scholars who had used the new imaging technology to study this problem. Liu, Reyes-Pérez and other scholars calculated the apparent diffusion coefficient (ADC) of diffusion-weighted imaging (DWI), and they all believed that the ADC value was related to the tumor histological grade and the depth of myometrium invasion [11,12]. Yamada found that diffusion tensor imaging (DTI) is useful for evaluating the depth of tumor invasion and histological grading in EMC patients. The results of the study showed that the FA map of all patients clearly identified the junction area as a high FA area (0.864 \pm 0.037), which was significantly different from the endometrium and outer myometrium layer (0.251 \pm 0.030 and 0.471 \pm 0.091, p < 0.001) [13]. The AD image has the best effect on tumor-uterine imaging. The AD value of EMCs (0.977 $\pm 0.120 \times 10^{-3}$ mm²/s) is significantly lower than other layers of the normal uterine wall (2.166 \pm 0.408, 2.010 \pm $0.289, 2.655) \pm 0.203 \times 10^{-3} \text{ mm}^2/\text{s}); p < 0.001).$ The EMCs and the normal uterine wall are clearly demarcated, and the DTI map and histopathological data show that the depth of tumor invasion is the same. The FA value was significantly negatively correlated (r = -0.818; p < 0.001, endometrioid adenocarcinoma with histological grades 1, 2, and 3. Zhang found that three-dimensional magnetic resonance elastography (MRE) can be measured, the tumor stiffness may help predict the tumor grade, FIGO stage, and myometrium invasion of endometrial carcinoma [14]. The results indicate that the tumor stiffness of patients with deep myometrial invasion of endometrial cancer (n = 6) was significantly higher than that of superficial myometrium Infiltrators (n = 9) (3.68 +/- 0.59 kPa vs. 2.61 +/- 0.72 kPa, p = 0.009). Using 3.04 kPa hardness as a cut-off value to distinguish between deep and superficial myometrial invasion has a sensitivity of 100% and a specificity of 77.8%. Li used FLASH-3D to perform preoperative staging on 48 patients with endometrial cancer, and the results showed that the sensitivity, specificity, and accuracy of deep myometrial invasion were 84%, 90%, and 88%, respectively, compared with postoperative pathological results, the difference was not statistically significant (p > 0.05) [6]. Guo, Y et al. [4] found that compared with T2-weighted magnetic resonance imaging (T2WI), T2-weighted magnetic resonance imaging and DWI, the diagnostic accuracy of T2WI-DWI for myometrium invasion was significantly improved (77.6% vs. 94.8%). Enhanced magnetic resonance imaging (DCE-MRI) has also been used as a new method in gynecological

malignancies. Fasmer believe that DCE-MRI is a valuable supplement to traditional MRI, which can provide preoperative predictions [15]. However, the above-mentioned studies need to be imaged by injection of contrast agents, which needs to consider patient compliance, drug sensitivity, and the synchronization and advancement of imaging equipment.It is difficult for many local hospitals to achieve this level.

Similar to our study, Yan discussed the application value of TAR in predicting the deep myometrial invasion and tumor grading of stage I endometrioid adenocarcinoma [16]. This study measured the maximum tumor diameter in three orthogonal planes. Obtain the tumor volume and area, and the results show that TVR and TAR values can be used to distinguish deep and superficial myometrial invasion (p = 0.000). However, the study calculated the volume and area under the assumption that the tumor is a spherical shape. This is obviously inconsistent with the real situation. Whether it is a uterus or a tumor, it is often presented in an irregular three-dimensional shape. The study measured volume obviously exceeds the real tumor volume.

Therefore, in our research, we reconstruct a threedimensional model close to the real state after ROI outline, and calculate the volume by voxel measurement on the software. The result is more accurate and can reflect the myometrial invasion. The depth of tumor invasion and anatomical structure changes can also be intuitively judged by adjusting the blurred 3D model.

Our research has the following limitations. First, there is a certain degree of subjectivity in the delineation of the tumor ROI area, even for experienced radiologists, there are certain errors; second, the use of software requires a time curve. This requires a process for the popular use of older doctors, but skilled users generally only need 5–10 minutes.

5. Conclusions

In conclusion, preoperative 3D-MRI can effectively assess the myometrial invasion of early endometrial carcinoma. The best cut-off value is 13.59%, and the best cut-off value of TAR is 27.41%.

Abbreviations

TVR, Tumor Volume Ratio; TAR, Tumor Area Ratio; 3D, Three-dimensional; MRI, Magnetic resonance imaging; FIGO, International Federation of Gynecology and Obstetrics.

Author Contributions

CC and PL conceptualized, designed the research study. JF performed the research. JF, YC, LX, PS and XL collected data and analyzed the data. JF wrote, reviewed the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.



Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Nanfang Hospital of Southern Medical University, and the ethics number is [2013] Review (032).

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Conflict of Interest

The authors declare no conflict of interest.

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