Am J Transl Res 2021;13(11):12228-12234
www.ajtr.org /ISSN:1943-8141/AJTR0127874

Original Article

Analysis of quantitative and semi-quantitative parameters of DCE-MRI in differential diagnosis of benign and malignant cervical tumors

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Received December 8, 2020; Accepted June 28, 2021; Epub November 15, 2021; Published November 30, 2021

Abstract: Objective: To explore and analyze the value of quantitative and semi-quantitative parameters of dynamic contrast enhanced-magnetic resonance imaging (DCE-MRI) in the differential diagnosis of benign and malignant cervical tumors. Methods: A total of 51 patients with cervical tumor who were treated in our hospital from April 2017 to October 2019 were recruited as the research subjects. All patients underwent conventional MRI plain scan and DCE-MRI examination. With histopathological results as the gold standard, the participants were classified into a malignant tumor group (n = 36) and a benign tumor group (n = 15) on the basis of the nature of the cervical tumor. The difference of quantitative and semi-quantitative parameters of DCE-MRI between the two groups was compared, and the specificity, sensitivity, negative and positive predictive values of quantitative and semi-quantitative parameters in differentiating benign from malignant cervical tumors were analyzed to evaluate the value of quantitative and semi-quantitative parameters of DCE-MRI in the differential diagnosis of benign and malignant cervical tumors. Results: The quantitative parameters Kep, Ktrans and Ve of DCE-MRI in the malignant-tumor-group were critically higher than that in the benign tumor group ($P<0.05$). When distinguishing between the benign and malignant cervical tumors, the specificity and sensitivity of kep, Ktrans and Ve were higher in the differential diagnosis of malignant cervical tumors than in the benign cervical tumors. The peak of the malignant tumor group was remarkably earlier than that of the benign tumor group, and SI60% of the malignant tumor group was dramatically higher than that of benign tumor group ($P<0.05$). In addition, compared with benign cervical tumors, the semi-quantitative parameters of DCE-MR TTP and SI60% were more sensitive to malignant cervical tumors. Conclusion: The quantitative and semi-quantitative parameters of DCE-MRI have high value in differentiating benign and malignant cervical tumors. When adopting conventional MRI to diagnose oncologic cervical tumors, the differential diagnosis of quantitative and semi-quantitative parameters of DCE-MRI has demonstrated a high clinical value by avoiding unnecessary radical surgeries.

Keywords: Magnetic resonance imaging, dynamic contrast enhanced-magnetic resonance imaging, quantitative parameters, semi-quantitative parameters, cervical tumors, value of differential diagnosis

Introduction

Cervical tumors are malignant tumors that commonly occur in the female reproductive system and it has a high incidence rate (ranking second to breast cancer). It has been revealed through investigation that the incidence rate of cervical tumors has been increasing annually and has become one of the top malignant tumors that seriously threaten women's health and life [1]. The early clinical diagnosis and treatment of cervical tumors is a key factor in reducing the mortality, improving prognosis and the patients' quality of life. Currently, the first choice for clinical diagnosis of suspected cervical lesions is transabdominal ultrasound or transvaginal ultrasound [2]. Most cervical lesions can be diagnosed by transabdominal sonography and transvaginal sonography due to their typical benign or malignant features. While for a few benign or malignant tumors without typical characteristics, diagnostic experience of the sonographer is relied on to figure out the nature of the lesions; otherwise CT, MRI and other imaging devices are adopted for further diagnosis. However, the CT imaging has

lower contrast than MRI with surrounding soft tissue even after using a contrast medium, along with the disadvantages of having higher ionizing radiation and the increased risk of adverse reactions due to the use of the iodine contrast medium; as such, it cannot be adopted as a superior inspection method for repeated imaging or screening for premenopausal females [3, 4]. Magnetic resonance imaging (MRI) has gradually turned into the superior inspection method for the diagnosis of complex imaging of atypical tumors due to its advantages of having good tissue contrast, non-invasiveness, and multiple functional imaging. Among which, quantitatively or semi-quantitatively analysis of blood perfusion in tissues can be conducted through the hemodynamic parameters obtained under non-invasive operation to differentiate the benign and malignant lesions of cervical tumors [5, 6]. By comparing the differences between quantitative and semi-quantitative parameters of DCE-MRI in benign and malignant tumors, this research evaluated its differential diagnostic value for benign and malignant cervical tumors, aiming to provide imaging references for differential diagnosis of benign and malignant cervical tumors in the clinic.

Data and methods

General materials

A total of 51 patients hospitalized for cervical tumors from April 2017 to October 2019 were selected as research subjects. Taking histopathological results as the key criterion, the participants were classified into a malignant tumor group and a benign tumor group based on the nature of the cervical tumor. There were 36 cases in the malignant tumor group, with an average age of (50.63±5.28) years; and 15 cases in the benign tumor group with an average age of (51.34±6.12) years. No significant difference in age was found between the two groups (P>0.05). The study obtained approval from the ethics committee of the principal investigating hospital.

Inclusive and exclusive criteria

The inclusive criteria: (1) The patients included in this study had not received anti-tumor treatment such as surgery or radiotherapy/chemotherapy before undergoing MRI; (2) The complete scan images of patients were obtained after routine MRI and DCE-MRI pelvic examination, and all data were well preserved and image quality met the requirement of diagnosis; (3) No metal implants in the patient; (4) The tumor diameter ≥3 mm; (5) All patients involved in the study voluntarily signed the informed consent.

The exclusive criteria: (1) Patients with asthma and/or claustrophobia, or with MRI contraindications such as being sensitive to the contrast medium; (2) Patients without histopathological results; (3) The tumor was purely cystic; (4) Patients with poor quality of scanning image; (5) Patients with other malignant tumors in the reproductive system.

Methods

Conventional MRI scanning: A 3.0T magnetic resonance imaging system was adopted as the diagnostic instrument. All patients were not in their menstrual period. The patients drank about 500 ml of water 1 h before the examination to make sure their bladders were full. They were then placed in a supine position and instructed to breathe calmly before scanning. A 32-channel phased array coil and an abdominal band were used to reduce the artifacts caused by respiratory movements during the scan. For obese patients, a saturation band can be placed in front to eliminate the artifacts caused by the subcutaneous fat. The scanning range was from the upper edge of the patella to the position of bilateral femoral neck.

DCE-MRI: Before performing the dynamic enhancement scan, we corrected the inspection sequence of the cross-sectional area interpolator with T1WI, TR 4.94 ms, TE 1.63 ms, matrix 142×192, layer interval at 0.76 mm, layer thickness at 3.8 mm, reversal angle by 2° and 5°, and 8 times on average. Dynamic enhancement scanning was then performed by TR 4.56 ms, TE 1.68 ms, matrix 142×192, layer interval: 0.74 mm, layer thickness: 3.8 mm. A total of 40 times were collected, with collection time of 5 minutes and 34 seconds. After the first scan, an injection of Gd-DTPA contrast medium was injected through the patient's indewelling needle in the vein with a high-pressure syringe. The injection was quickly completed in 6 s at a rate of 2.5 ml/s, and 2-40 scans of continuous dynamic enhanced scanning was

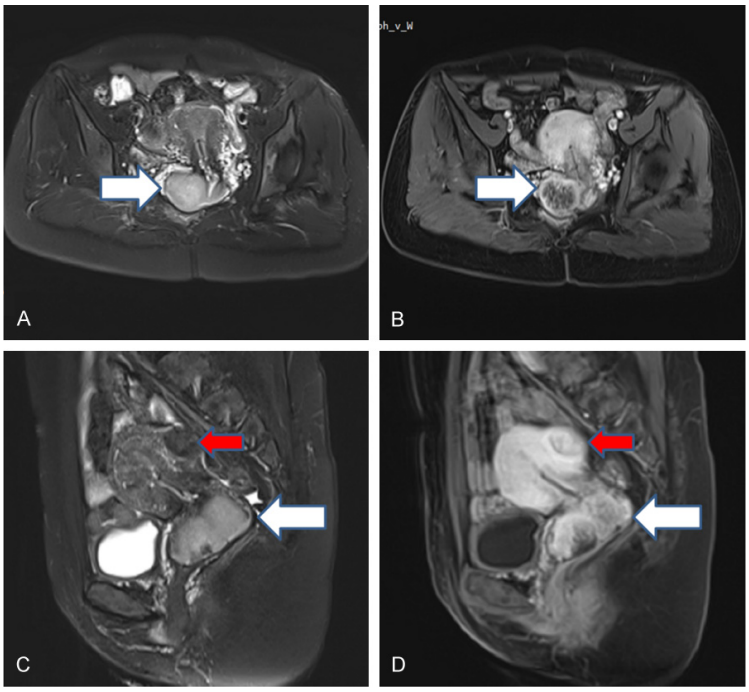

Figure 1. MR image of a 46-year-old patient with cervical squamous cell carcinoma. A. T2 fat suppression sequence (axial position) shows a high signal mass (white arrow) on the right side of the posterior lip of the cervix. B. T1WI enhanced sequence (axial view) shows that the cervical mass is obviously unevenly enhanced, with the main edge enhancement. C. T2 fat suppression sequence (sagittal position) shows a high signal mass on the posterior lip of the cervix, uneven signal in the lower posterior part (white arrow), and a smaller and slightly lower confounding signal nodule on the posterior wall of the uterus. The posterior pathology showed uterine fibroids (red arrow). D. T1WI enhancement sequence (sagittal view) showed obvious uneven enhancement of cervical mass (white arrow), and uneven and obvious enhancement of posterior wall fibroids (red arrow).

performed after 20 s. The scan range included all solid tumor lesions as much as possible.

Image analysis and data processing

Quantitative parameters: The patients' DCE-MRI images were transferred to 3.0T MRI system workstation and measured by two experienced senior radiologists in our hospital. Analysis was carried out by Siemens Tissue 4D software package for Data processing, the three largest tumor layers were selected and the ROI was outlined to automatically generate equal quantitative parameters of rate constant (Kep), volumetric transfer constant (Ktrans) and extravascular extracellular space volume ratio (Ve). When selecting the ROI, we avoided the edge of the lesions, bleeding, necrosis, cystic degeneration and sites containing large vessels in the tumor as much as possible. The quantitative parameter data was the average value after 3 times of drawing.

Semi-quantitative parameters: The obtained data was transmitted to Siemens workstation and processed by two experienced radiologists in our hospital with Mean Curve software. The abnormally enhanced soft tissue area was selected as the focus area to display the maximum enhancement amplitude and time of the lesion, and semi-quantitative parameters were automatically obtained according to the TIC curve: time-to-peak (TTP), maximum strengthening rate of 60 s (SI60%) = (the maximum signal intensity value of the lesion after enhanced scanning for 60 s, SIpost60s - signal strength value before enhanced scanning SIpre).

Statistical methods

SPSS19.0 statistical data software was adopted for statistical analysis. The difference between quantitative and semi-quantitative parameters of DCE-MRI in benign and malignant cervical tumors were determined by Mann-Whitney U. Statistical significance was accepted at $P< 0.05$. Quantitative and semi-quantitative parameters were analyzed in the specificity, sensitivity, negative and positive predictive value of the benign and malignant cervical tumors.

Results

Pathological results

There were 36 cases with malignant tumors among the 51 patients, including 32 cases of squamous cell carcinoma, 3 cases of adenocarcinoma, and 1 case of papillary carcinoma. There were 15 cases with benign tumors, including 9 cases of intramuscular myoma, 4 cases of intermuscular fibroids, and 2 cases of subserous myoma of the uterus. The in-

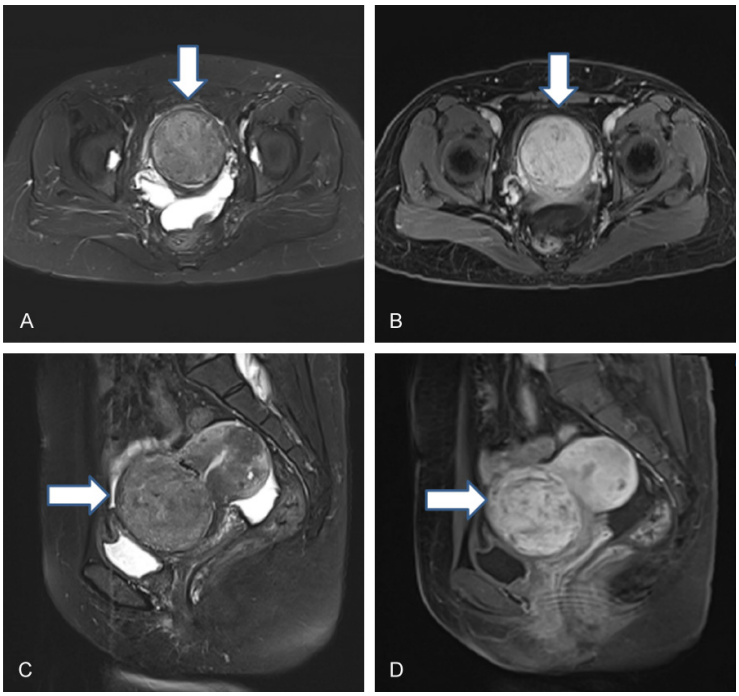

Figure 2. MR images of a 47 year old patient with leiomyoma of the anterior cervical lip (A). T2 fat suppression sequence (axial) showed slightly high signal mass in the middle of anterior lip of cervix with uneven signal (white arrow). (B) T1WI enhanced sequence (axial) showed that the cervical mass with significantly heterogeneous enhancement. (C) T2 fat suppression sequence (sagittal) showed a slightly hyper-intense mass in the anterior lip of the cervix with compression and displacement of surrounding structures (white arrow). (D) T1WI enhanced sequence (sagittal) showed obvious heterogeneous enhancement of cervical mass (white arrow).

Table 1. Comparison of DCE-MRI quantitative parameters between the two groups of patients

Group	Kep (min)	Ktrans (min)	Ve
Malignant tumor group (n = 36)	0.65±0.14	0.38±0.12	0.79±0.38
Benign tumor group (n = 15)	0.23±0.11	0.17±0.05	0.38±0.13
t	10.3437	6.5153	4.0601
P	<0.0001	<0.0001	0.0002

spection results of a 46-year-old patient with cervical squamous cell carcinoma and a 47-year-old patient with cervical intramuscular myoma are respectively shown in **Figures 1** and **2**.

Comparison of DCE-MRI quantitative parameters between the two groups

The malignant tumor group had DCE-MRI quantitative parameters Kep, Ktrans and Ve that were critically higher than that in the benign tumor group, and the difference was statistically significant (P<0.05). See **Table 1**.

The prediction of DCE-MR parameters in specificity, sensitivity, and negative/positive predictive values of the benign and malignant cervical tumors

DCE-MR quantitative parameters Kep, Ktrans and Ve had high specificity and sensitivity for malignant uterine tumors when identifying the nature of the cervical tumors. See **Table 2**.

Comparison of DCE-MRI semi-quantitative parameters between the two groups of patients

The time-to-peak (TTP) of the malignant tumor group was notably earlier than that of the benign tumor group, and SI60% in the malignant-group was remarkably higher than that in the benign-group (P<0.05). The difference was statistically significant (P<0.05). See **Table 3**.

The prediction of DCE-MR semi-parameters in specificity, sensitivity, and negative/positive predictive values of the benign and malignant cervical tumors

DCE-MR semi-quantitative parameters TTP and SI60% had high specificity and sensitivity to malignant uterine tumors when identifying the nature of the cervical tumors. See **Table 4**.

Discussion

The treatment of cervical tumors is tightly close to its nature and it is very important to accurately evaluate the nature of the tumor. Currently, the preferred method of clinical diagnosis for suspected cervical lesions is transabdominal sonography or transvaginal sonography, which are widely adopted in clinical practice due to their moderate price, high time efficiency and the characteristic of excluding most malignant cervical tumors. However, this app-

Table 2. The prediction of DCE-MR parameters in specificity, sensitivity and negative and positive predictive values of benign and malignant cervical tumors

Parameter	Inspection Result	Pathologic Result		Specificity (%)	Sensitivity (%)	Negative prediction value (%)	Positive predict value (%)
		Malignant	Benign				
Kep value	Malignant	31	1	93.33	86.11	73.68	96.88
	Benign	5	14				
Ktrans value	Malignant	32	0	100.00	88.89	78.95	-
	Benign	4	15				
Ve value	Malignant	29	1	93.33	80.56	66.67	96.67
	Benign	7	14				

Table 3. Comparison of DCE-MRI semi-quantitative parameters between the two groups of patients

Group	TTP (s)	SI60%
Malignant tumor group (n = 36)	74.82±19.34	122.45±19.37
Benign tumor group (n = 15)	138.24±34.76	66.34±36.49
t	8.3392	7.1700
P	<0.0001	<0.0001

roach has the disadvantages of highly relying on the technical level of the diagnostic operator, or requiring CT, MRI and other imaging for further diagnosis [7, 8]. At present, MRI is widely considered as an important examination technique to accurately determine the nature of cervical tumors due to its high resolution of soft tissue, clear display of anatomical structures, and the function of distinguishing the types of tumor tissues according to the characteristics of signal intensity. It suggests a malignant cervical tumor if there is an enhanced solid soft tissue component in the lesion. However, it cannot be determined by MRI for nature of all types of cervical tumors, especially for the complex cystic and solid cervical tumors [9, 10]. When performing routine MRI examinations, the diagnosticians may have limitation in knowledge of images and experience of morphological diagnosis of disease which will affect the diagnosis results of plain scanning and conventional enhanced examination, with a lack of objective quantitative indicators, thus influencing the selection for clinical treatment [11, 12]. DCE-MRI is a functional examination technique that can describe physiological changes and pathological morphology in a non-invasive manner. DCE-MRI mainly conducts rapid imaging of tissues, and obtains images of contrast medium before and after entering tissues via MRI acquisition technology, and obtained quantitative and semi-quantitative parameters to objectively reflect the pathological characteristics of the lesions [13, 14].

The quantitative parameters of DCE-MRI are permeability parameters derived from complex pharmacokinetic models, which include rate constant (Kep), volume transfer constant (Ktrans) and extracellular space volume ratio (VE). Kep refers to the rate constant of the contrast medium returning from the patient's extracellular space to intravascular space. Studies have suggested that it may leads to incompleteness and leakage of vascular endothelial cells due to the excessive growth of micro-vessels in tumor tissues. Therefore, a higher Kep value indicates the more leakage of contrast medium [15, 16]. Ktrans, the rate constant of the contrast medium from patients' blood vessels that crosses the endothelial cells into the extracellular spaces, is an important indicator that reflects the surface permeability of blood vessels and the integrity of blood vessel cells. It can also reflect whether the capillary permeability in the tumor cells of the body has changed. A higher value indicates a faster metabolism and a higher probability of malignancy. Ve reflects the necrosis degree of cells in the region of interest [17]. In this study, the DCE-MRI quantitative parameters Kep, Ktrans and Ve of the malignant tumor group were significantly higher than those of the benign tumor group ($P<0.05$), which was consistent with most other studies [18-20]. The quantitative parameters of DCE-MR Kep, Ktrans and Ve in the study had high specificity and sensitivity in malignant cervical tumors, indicating that quantitative parameters of DCE-MR have high value in the differential diagnosis of the nature of tumors.

Table 4. The prediction of DCE-MR semi-parameters in the specificity, sensitivity and negative and positive predictive value of benign and malignant cervical tumors

Parameter	Inspection Result	Pathological Result		Specificity (%)	Sensitivity (%)	Negative Prediction Value (%)	Positive Prediction Value (%)
		Malignant	Benign				
TTP	Malignant	35	5	66.67	97.22	90.91	87.50
	Benign	1	10				
SI60%	Malignant	34	4	73.33	94.44	84.42	89.47
	Benign	2	11				

The semi-quantitative parameters of DCE-MRI can be calculated according to the time-signal curve through workstation software. This study mainly adopts time-to-peak (TTP) and SI60% (maximum strengthening rate of 60 s) as the semi-quantitative parameters of DCE-MRI. The results showed that the TTP in the malignant tumor group was significantly earlier than that of benign tumor group ($P<0.05$), indicating the higher vascular permeability in malignant cervical tumors than in benign tumors. When passing through vascular endothelial cells of malignant tumors, the speed of contrast medium is significantly accelerated, thus the TTP of malignant tumors is significantly earlier than that of benign tumors. The SI60% in the malignant tumor group was significantly higher than that in the benign tumor group ($P<0.05$), indicating that the perfusion of the malignant tumor increased dramatically compared with that of the benign tumor group, and the concentration of the contrast medium in the blood vessels also increased significantly. The semi-quantitative parameters of DCE-MR TTP and SI60% are more sensitive to malignant uterine tumors when distinguishing the nature of tumors. This suggested that the quantitative parameters of DCE-MR have a high differential diagnosis value in benign and malignant cervical tumors [21].

However, due to the relatively small sample size included in this study, the research results may be biased, and the sample size needs to be further expanded to obtain more reliable clinical research results and provide a basis for guiding clinical work.

In conclusion, quantitative and semi-quantitative parameters of DCE-MRI have high diagnostic value in benign and malignant cervical tumors. When used in the diagnosis of cervical tumors by undiagnosed conventional MRI results, the differential diagnosis of DCE-MRI quantitative and semi-quantitative parameters can avoid unnecessary radical surgery, thus has high clinical value.

Disclosure of conflict of interest

None.

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