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ORIGINAL ARTICLE

Retrospective Study

Correlation of magnetic resonance imaging quantitative parameters and apparent diffusion coefficient value with pathological breast cancer

Zhe Wang, Guan-Ying Ren, Qian Yin, Qian Wang

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Abstract

BACKGROUND

China ranks 120th worldwide for the incidence of breast cancer and 163rd for mortality. Early screening, diagnosis, and timely determination of the optimal treatment plan can help ensure clinical efficacy and prognosis.

AIM

To investigate the relationship between quantitative magnetic resonance imaging parameters, apparent diffusion coefficient value, pathological immunohistochemical status, and patient prognosis.

METHODS

A total of 108 patients with breast cancer (breast cancer group) and 110 patients with benign breast tumors (benign group) confirmed by pathological examination at our Hospital from September 2013 to August 2016 were selected. All patients had undergone preoperative magnetic resonance imaging (MRI) examinations, and the quantitative parameters of MRI and apparent diffusion coefficient (ADC) values for the two groups were compared. The MRI quantitative parameters and ADC values of patients with different estrogen receptor (ER), progesterone receptor, and human epidermal growth factor receptor-2 expression were statistically analyzed. The relationship between the quantitative parameters of MRI and ADC values and patient recurrence was analyzed using receiver operating curves.

RESULTS

The measured values of the quantitative parameters of MRI- Ktrans, Kep, and Ve in the breast cancer group were higher than those in the benign group; the ADC value in the breast cancer group was lower than that in the benign group, and the difference was statistically significant ($P < 0.05$). The Ktrans, Ve, and ADC values in patients with ER-positive breast cancer were significantly lower than those in patients with negative ER expression ($P < 0.05$). After 5 years of follow-up, 22 patients with breast cancer experienced postoperative recurrence. The Kep, Ve, and ADC values of the recurrence group were significantly lower than those of the non-recurrence group, and the difference was statistically significant ($P < 0.05$).

CONCLUSION

MRI quantitative parameters and ADC are related to the expression of breast cancer-related immunological receptor factors and have certain clinical value in assessing postoperative recurrence in patients.

Key Words: Magnetic resonance; Apparent diffusion coefficient; Breast cancer; Immunohistochemistry; Prognosis

Core Tip: The high sensitivity and repeatability of magnetic resonance imaging make it more widely used in disease screening and treatment. Its advantages in soft tissue resolution and radiation make it more meaningful for lesions that cannot be clarified by clinical and ultrasound techniques in breast examination. Especially, diffusion weighted imaging has more advantages in cell structure and cell membrane integrity.

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INTRODUCTION

Breast cancer is one of the most common malignant tumors in women worldwide[1], and disease staging at the time of diagnosis is crucial for the prognosis of patients[2]. Studies have also found that different prognostic factors, such as human epidermal growth factor receptor-2 (HER-2); progesterone receptor (PR); estrogen receptor (ER); and cell proliferation antigen marker (Ki-67) also affect the treatment and prognosis of breast cancer[3,4]. The advantages that magnetic resonance imaging (MRI) has over the resolution and radiation of soft tissue make it extremely useful for lesions that cannot be clarified by clinical or ultrasonic breast examination techniques. In particular, diffusion-weighted imaging (DWI) has advantages in terms of cell structure and cell membrane integrity. Various influencing factors have different effects on the diagnosis and prognosis of the disease, and various quantitative parameters have different correlations with prognostic factors and cancer classification. Therefore, this study explored the relationship between MRI quantitative parameters and apparent diffusion coefficient (ADC) values of different prognostic factors in patients with breast cancer and benign breast tumors confirmed by pathological examination to provide clinical value for evaluating postoperative recurrence.

MATERIALS AND METHODS

General information

A total of 108 patients with breast cancer (breast cancer group) and 110 patients with benign breast tumors (benign group) confirmed by pathological examination in our hospital from September 2013 to August 2016 were selected.

The inclusion criteria were set according to the diagnostic criteria of the "National Comprehensive Cancer Network Breast Cancer Clinical Practice Guidelines 2010, First Edition". Patients aged 19–65 years, diagnosed with breast cancer and benign breast tumors, underwent surgical treatment in our hospital. The tumors were confirmed by postoperative pathological examination. Patients also underwent X-ray mammography, MRI examination, ultrasound examination, and complete

examination data before surgery. All patients were followed up for > 5 years. Exclusion criteria included: (1) Patients with recurrent breast cancer after surgery; (2) Patients with malignant tumors in other parts of the body, which had metastasized to the breast; (3) Patients who received preoperative chemoradiotherapy; (4) Patients who failed to receive postoperative follow-up; and (5) Patients with a lack of imaging data. This study was approved by the Medical Ethics Committee.

Immunohistochemistry detection

The American Society for Clinical Oncology[5] has defined the invasive positive tumor nucleus < 1% as PR and ER negative, and vice versa. HER-2 expression scores of 0 and + were negative, 3+ was positive, and 2+ were further analyzed by Fluorescent *in situ* Hybridization (FISH). If FISH was positive, gene amplification was performed; otherwise, the results were negative.

MRI examination

The patients were asked to take the prone position, put their arms on the side of their heads, and the positioning line was aligned with the patient's nipple. The conventional examination was performed using 3.0T MRI (Siemens Skyra, Germany), followed by DWI scanning. The transverse T2-weighted image parameters were: TR/TE, 4270/66 ms, layer thickness, 4.0 mm; layer spacing, 4.8 mm; fOV, 34 cm × 34 cm; and number of incentives, 2. The T1-weighted image parameters were: TR/TE, 6.02/2.43 ms; layer thickness, 1.2 mm; fOV, 34 cm × 34 cm; and number of incentives, 2. The DWI parameters were: TR/TE, 8070/82 ms; layer spacing, 6 mm; layer thickness, 4.0 mm; fOV, 34 cm × 34 cm; and number of incentives, 2; matrix, 10.2 cm × 19.2 cm. The two b values were: 0 s/mm^2 and 800 s/mm^2. The 4D tissue processing software was used to correct the artifacts first and then input the T1 map image data to fit the image to obtain the quantitative T1 value. Transfusions such as the internal thoracic artery, obtain function, select ROI (obvious lesion area), and avoid necrotic area were combined with T1 value, using Tolfs model to measure Ve, Ktrans, Kep, select ROI, and to calculate the average.

Statistical analysis

In this study, the measurement indexes such as Ktrans, Kep, Ve, and ADC values were assessed whether they were normally distributed, and they were all in line with an approximately normal or normal distribution, which was represented by mean ± SD. A *t*-test was used to compare the two groups of data. The discrete data were expressed as percentages, and the comparison was performed using the χ^2 test. The receiver operating characteristic (ROC curve) was drawn to analyze the value of each index in predicting postoperative recurrence. The professional SPSS 21.0 software (IBM Corp., Armonk, NY, USA) was used for data processing, with a test level $\alpha = 0.05$.

RESULTS

Comparison of patient characteristics

The age, body mass index, distribution of affected side, comorbidities, and menopausal status were compared between the breast cancer and benign tumor groups, and the difference was not statistically significant ($P > 0.05$, Table 1).

Comparison of MRI parameters and ADC values of the two patient groups

The Ktrans, Kep, and Ve values of the breast cancer group were higher than those of the benign group. The values of Ktrans, Kep and Ve in the breast cancer group were higher than those in the benign group, and the ADC value in the breast cancer group was lower than that in the benign group; the difference was statistically significant ($P < 0.05$) (Table 2).

Comparison of MRI parameters and ADC values of breast cancer patients with different immunostaining and histochemical results

The values of Ktrans, Ve, and ADC in patients with ER positive breast cancer were significantly lower than those in patients with negative expression, and the difference was statistically significant ($P < 0.05$). The Kep value of patients with breast cancer with PR-positive expression was significantly lower than that of patients with negative expression, and the difference was statistically significant ($P < 0.05$). The Kep value of HER-2 positive breast cancer patients was higher than that of negative breast cancer patients, and the difference was statistically significant ($P < 0.05$). The Ve value of HER-2 positive breast cancer patients was significantly lower than that of HER-2 negative breast cancer patients, and the Kep value was significantly higher than that of HER-2 negative breast cancer patients; the difference was statistically significant ($P < 0.05$, Table 3).

Comparison of MRI parameters and ADC values in breast cancer patients with different prognoses

After 5 years of follow-up, a total of 22 patients with breast cancer had postoperative recurrence. The measured values of Kep, Ve and ADC in the recurrence group were significantly lower than those in the

Table 1 Comparison of general information of the two groups of patients, *n* (%)

Factor	Breast cancer group (*n* = 108)	Benign group (*n* = 110)	t/χ^2	*P* value
Age (mean ± SD, yr)	46.1 ± 7.0	47.5 ± 8.4	-1.336	0.183
Body mass index (mean ± SD, kg/m^2)	24.6 ± 2.5	24.3 ± 2.6	0.868	0.386
Affected side distribution			0.902	0.342
Left side	58 (53.7)	52 (48.15)		
Right	50 (46.3)	58 (53.7)		
Hypertension			0.618	0.432
Yes	11 (10.19)	15 (13.89)		
No	97 (89.81)	95 (87.96)		
Diabetes			2.062	0.151
Yes	6 (5.56)	12 (11.11)		
No	102 (94.44)	98 (90.74)		
Hyperlipidemia			2.221	0.136
Yes	17 (15.74)	10 (9.26)		
No	91 (84.26)	100 (92.59)		
Menopause			0.930	0.335
Yes	18 (16.67)	24 (22.22)		
No	90 (83.33)	86 (79.63)		

Table 2 Comparison of magnetic resonance imaging parameters and apparent diffusion coefficient values between the two groups (mean ± SD)

Groups	Ktrans (min^{-1})	Kep (min^{-1})	Ve	ADC (× 10^{-3} mm^2/s)
Breast cancer group (*n* = 108)	0.481 ± 0.113	0.577 ± 0.120	0.764 ± 0.170	0.741 ± 0.184
Benign group (*n* = 110)	0.264 ± 0.096	0.408 ± 0.113	0.528 ± 0.150	1.109 ± 0.241
t value	15.290	10.707	10.874	-12.655
P value	0.000	0.000	0.000	0.000

ADC: Apparent diffusion coefficient.

non-recurrence group. The difference between the two groups was statistically significant ($P < 0.05$, Table 4).

MRI parameters and ADC values for predicting patient recurrence

The ROC curve was drawn using the Kep, Ve, and ADC values. The results showed that the area under the curve (AUC) value of the Kep, Ve, and ADC values for predicting postoperative recurrence were 0.599, 0.572, and 0.739, respectively. The AUC value of Kep + Ve + ADC value for predicting postoperative recurrence was 0.858 (Table 5, Figure 1).

DISCUSSION

Angiogenesis, or the formation of new blood vessels, is essential for the occurrence and development of breast cancer. Vascular endothelial growth factor, which encourages angiogenesis, is released during hypoxic stress, resulting in increased capillary osmotic pressure. This allows small molecules to quickly pass through the vascular wall (along with any contrast agent) into the tissue gap, resulting in a shortened T1 value. At this time, early lesions can be significantly enhanced[6,7].

The high sensitivity and repeatability of MRI make it more widely used in disease screening and treatment determination[8]. There are two methods for the quantitative and semi-quantitative analysis of breast diseases. In particular, quantitative analysis has important value for identifying benign and

Table 3 Comparison of magnetic resonance imaging parameters and apparent diffusion coefficient values in breast cancer patients with different immunostaining and histochemical results (mean ± SD)

Express the situation	*n*	Ktrans (min^{-1})	Kep (min^{-1})	Ve	ADC (× 10^{-3} mm^2/s)
ER					
Positive	74	0.462 ± 0.105	0.563 ± 0.112	0.740 ± 0.166	0.713 ± 0.170
Feminine	34	0.522 ± 0.100	0.607 ± 0.109	0.816 ± 0.154	0.802 ± 0.168
t value		-2.698	-1.912	-2.259	-2.536
P value		0.008	0.059	0.026	0.013
PR					
Positive	62	0.468 ± 0.108	0.542 ± 0.115	0.751 ± 0.165	0.721 ± 0.180
Feminine	46	0.499 ± 0.111	0.624 ± 0.116	0.782 ± 0.158	0.768 ± 0.178
t value		-1.458	-3.651	-0.983	-1.348
P value		0.148	0.000	0.328	0.180
HER-2					
Positive	34	0.461 ± 0.107	0.621 ± 0.116	0.713 ± 0.166	0.719 ± 0.181
Feminine	74	0.490 ± 0.110	0.557 ± 0.109	0.787 ± 0.162	0.751 ± 0.178
t value		-1.283	2.777	-2.188	-0.863
P value		0.202	0.006	0.031	0.390

ADC: Apparent diffusion coefficient; ER: Estrogen receptor; PR: Progesterone receptor; HER-2: Human epidermal growth factor receptor-2.

Table 4 Comparison of magnetic resonance imaging parameters and apparent diffusion coefficient values in breast cancer patients with different prognosis (mean ± SD)

Recurrence	*n*	Ktrans (min^{-1})	Kep (min^{-1})	Ve	ADC (× 10^{-3} mm^2/s)
Relapse	22	0.457 ± 0.111	0.528 ± 0.109	0.698 ± 0.155	0.663 ± 0.181
No recurrence	86	0.487 ± 0.107	0.590 ± 0.112	0.781 ± 0.165	0.761 ± 0.176
t value		-1.165	-2.329	-2.130	-2.317
P value		0.247	0.022	0.035	0.022

ADC: Apparent diffusion coefficient.

Table 5 The value of magnetic resonance imaging parameters and apparent diffusion coefficient values in predicting patient recurrence

Index	Critical value	AUC	Sensitivity (%)	Specificity (%)	Missed diagnosis rate (%)	Misdiagnosis rate (%)
Kep (min^{-1})	0.561	0.599	65.19	55.40	34.81	44.60
Ve	0.725	0.527	58.04	51.06	41.96	48.94
ADC (×10^{-3} mm^2/s)	0.718	0.739	71.57	61.09	28.43	38.91
ADC + Kep + Ve	-	0.858	83.67	77.18	16.33	22.82

ADC: Apparent diffusion coefficient; AUC: Area under the curve.

malignant tumors, prognosis, and evaluation of chemotherapy effects. However, due to research limitations, the current MRI experiments mainly focus on semi-quantitative parameters[9,10]. The research on quantitative parameters is relatively small, and the research results of various studies are different[10]. In this study, quantitative MRI parameters and ADC values of different prognostic factors in patients with breast cancer or benign breast tumors confirmed by pathological examination were compared, and the MRI quantitative parameters and ADC values of patients with different expressions

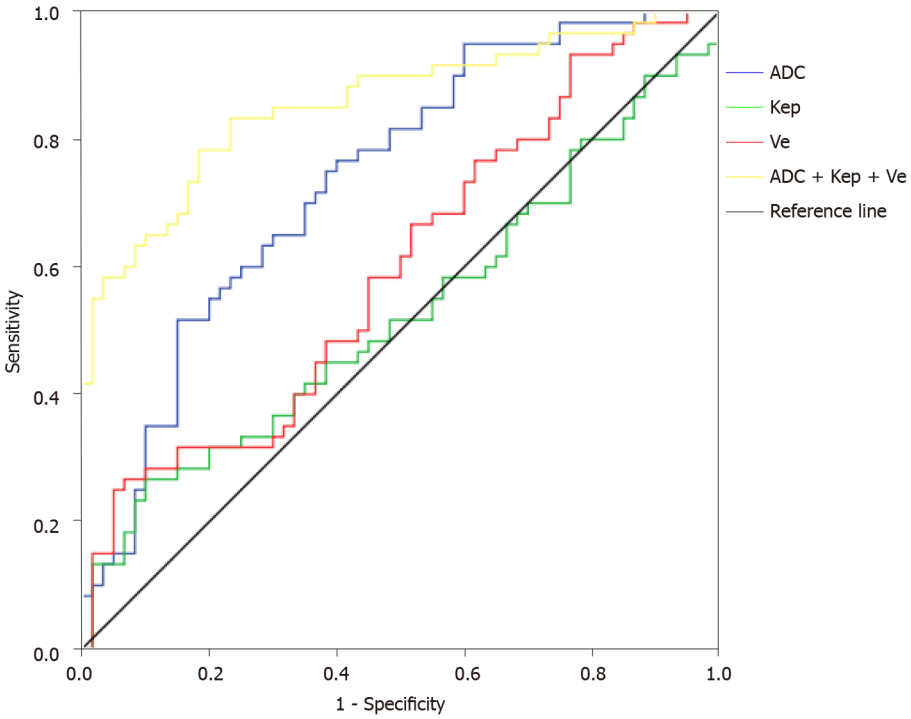

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Figure 1 The receiver operating characteristic curve of Kep, Ve, apparent diffusion coefficient measurement value predicting patient recurrence. ADC: Apparent diffusion coefficient.

of ER, PR, and HER-2 were statistically analyzed. The relationship between the quantitative parameters of MRI and ADC values and the recurrence of patients was analyzed using the ROC curve, with the aim of providing a reference for clinical diagnosis and treatment.

The results showed that the measured values of Ktrans, Kep, and Ve of the breast cancer group were higher than those of the benign group, while the ADC value was lower than that of the benign group, which was consistent with the results of Martincich *et al*[11]. In this study, the Ktrans, Ve, and ADC values of patients with ER-positive breast cancer were significantly lower than those of patients with ER-negative breast cancer. The Kep values of patients with HER-2 positive breast cancer were significantly higher than that of patients with HER-2 negative breast cancer[12]. In contrast, the Ve values of patients with HER-2 positive breast cancer were significantly higher than that of patients with HER-2 negative breast cancer. The Kep value of patients with PR-positive breast cancer was significantly lower than that of patients with negative expression, consistent with Lee *et al*[13]. In contrast to previous experiments, we found that after 5 years of follow-up, the Kep, Ve, and ADC values of patients in the recurrence group were significantly lower than those of patients without recurrence. The ROC curve results showed that the AUC values of Kep, Ve, and ADC values for predicting postoperative recurrence were 0.599, 0.572, and 0.739, respectively. The AUC value of the Kep + Ve + ADC value for predicting postoperative recurrence was 0.858. The reason for this may be that the sample size was not large enough, resulting in a decrease in the estimation accuracy of the data. In addition, the influence of blood flow factors, such as hypertension, was not considered.

The sensitivity of patients with breast cancer with PR and ER-positive expression to endocrine therapy was significantly higher than that of patients with negative expression, and their survival rate was also higher, therefore the prognosis was relatively better[14-16]. HER-2, as a growth factor receptor with tyrosine kinase activity, is less expressed in normal tissues, and its expression can be used as an important indicator of breast cancer and prognosis in the clinical setting[17,18]. Ki-67, a nuclear antigen, can effectively mark cell proliferation. In this study, when the expression of Ki-67 was higher, the possibility of tumor recurrence was greater. Previous studies have found that Ki-67 is inversely proportional to the ADC value, and AUC can more intuitively compare the predictive value of other parameters[19,20]; in other words, when the expression of Ki-67 is higher, the ADC value is lower, which also has a certain effect on our prediction of recurrence.

CONCLUSION

In summary, this study shows a correlation between MRI quantitative parameters, ADC, and the expression of immune receptor factors related to breast cancer. Therefore, the prognosis of patients can

be evaluated by detecting Kep, Ve, and ADC values, which have clinical significance.

ARTICLE HIGHLIGHTS

Research background

It has been reported that the 5-year survival rate of patients with breast cancer in stage I is 100% but is only 20% in stage IV; with the evolution of the disease, the total survival period gradually decreases.

Research motivation

This study analyzed the magnetic resonance imaging (MRI) quantitative parameters and apparent diffusion coefficient (ADC) values of patients with different estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER-2) expression.

Research objectives

This study aimed to investigate the relationship between quantitative MRI parameters.

Research methods

A total of 108 patients with breast cancer and 110 patients with benign breast tumors confirmed by pathological examination were selected. All patients had undergone preoperative MRI examinations, and the MRI quantitative parameters and ADC values of patients with different ER, PR, and HER-2 expression were statistically analyzed.

Research results

The measured values of the quantitative parameters of MRI- Ktrans, Kep, and Ve in the breast cancer group were higher than those in the benign group.

Research conclusions

MRI quantitative parameters and ADC are related to the expression of breast.

Research perspectives

This study explored the relationship between MRI quantitative parameters and ADC values of different prognostic factors in patients with breast cancer and benign breast tumors confirmed by pathological examination to provide clinical value for evaluating postoperative recurrence.

FOOTNOTES

Author contributions: Wang Z and Ren GY contributed equally to this study, and should be considered as co-first authors; Wang Z and Ren GY design the experiment; Wang Z drafted the manuscript; Wang Z, Ren GY, Yin Q, and Wang Q collected the data; Yin Q and Wang Q analysed and interpreted data; Wang Z and Ren GY revised the manuscript.

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