Original Article

Correlations between dynamic-enhanced magnetic resonance imaging quantitative parameters and postoperative recurrence or metastasis and clinicopathological features in breast cancer patients—a retrospective cohort study

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Background: Few related studies focused on the correlations between the quantitative parameters of dynamic-enhanced magnetic resonance imaging (MRI) and the clinical pathological characteristics of patients with invasive breast cancer have been conducted to date. This study sought to explore the value of quantitative parameters of dynamic-enhanced MRI in predicting postoperative recurrence or metastasis in breast cancer patients and their correlations with clinical pathological features, so as to provide clinicians with understanding of MRI in breast cancer.

Methods: From January 2016 to June 2017, 214 invasive breast cancer patients admitted to Affiliated Kunshan Hospital of Jiangsu University were retrospectively enrolled in this study. Dynamic-enhanced MRI was performed to analyze the relationship between quantitative parameters of dynamic-enhanced MRI and recurrence or metastasis, and analyze their correlations with clinical pathological features in patients with invasive breast cancer.

Results: The apparent diffusion coefficient and peak time had certain diagnostic value for postoperative recurrence or metastasis in breast cancer patients, and the areas under the curve were 0.821 [95% confidence interval (CI): 0.732–0.911; P<0.001] and 0.691 (95% CI: 0.609–0.774; P<0.001), respectively. An apparent diffusion coefficient $<0.78\times10^{-3}$ mm^2/s, a peak time <167.50 s, tumor staging (T staging) ≥2, vascular tumor thrombus, and positive lymph nodes were risk factors for postoperative recurrence or metastasis in breast cancer patients (odds ratio: 19.768, 95% CI: 2.577–151.619, P=0.004; 5.708, 95% CI: 1.088–29.947, P=0.039; 122.474, 95% CI: 5.334–2,812.360, P=0.003; 28.304, 95% CI: 1.372–583.914, P=0.030; 314.407, 95% CI: 10.617–9,310.547, P=0.001), and high estrogen receptor (ER) expression was a protective factor for postoperative recurrence or metastasis in breast cancer patients (odds ratio: 0.056, 95% CI: 0.004–0.795, P=0.033). The apparent diffusion coefficient was related to the site of onset, T staging, vascular tumor thrombus, and positive lymph nodes in breast cancer patients (P<0.05). Peak time was related to a high nuclear-associated antigen Ki-67 index, high ER expression, and high progesterone receptor (PR) expression in breast cancer patients (P<0.05).

Conclusions: The quantitative parameters of MRI were associated with clinical pathological characteristics and recurrence or metastasis in breast cancer after surgery.

Keywords: Dynamic-enhanced magnetic resonance imaging (dynamic-enhanced MRI); invasive breast cancer; apparent diffusion coefficient (ADC); peak time

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Introduction

The Breast cancer is the most common malignancy in women, and its incidence has increased in recent years (1). For breast cancer patients diagnosed for the first time, the current international breast cancer treatment guidelines recommend a dynamic-enhanced magnetic resonance imaging (MRI) examination to determine whether there is lymph node metastasis, evaluate tumor staging (T staging), clarify the scope of tumor invasion, etc., to help clinicians develop individualized treatment plans. MRI has an irreplaceable role in diagnosing and guiding the chemotherapy of invasive breast cancer (2-4).

In addition to the many qualitative indicators, there are quantitative indicators of MRI, including the apparent diffusion coefficient (ADC), and peak time. These quantitative indicators also play an important role for breast cancer patients. When the cell density of malignant tumors in patients is high, the diffusion movement of water molecules is limited, and the value of the ADC decreases; thus, the ADC can be used to distinguish between breast cancer and benign tumors and has better sensitivity and specificity than an ultrasound (5). The peak time is related to the microvascular and extravascular space in breast cancer patients, and angiogenesis is the basis for the rapid growth, infiltration, and metastasis of malignant tumors (6,7).

In a study focused on prostate cancer, it was found that the ADC and peak time may be potential biomarkers of early radiation response (8). Thus, we speculated that the ADC and peak time may have a certain relationship with the prognosis and clinical pathological characteristics of breast cancer patients and may have certain value in predicting the prognosis of breast cancer patients. However, as to date, no relevant studies appeared to have been conducted, we designed this study. We present the following article in accordance with the STARD reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-22-400/rc).

Methods

General information

From January 2016 to June 2017, 214 invasive breast cancer patients treated at the Affiliated Kunshan Hospital of Jiangsu University were retrospectively and continuously enrolled in this study. To be eligible for inclusion in this study, patients had to meet the following inclusion criteria: (I) have been diagnosed with invasive breast cancer; (II) have received this diagnosis of breast cancer for the first time; (III) be aged ≥18 years; and (IV) have complete information. Patients were excluded from the study if they met any of the following exclusion criteria: (I) had carcinoma *in situ* or benign mass; (II) had received special treatment, such as radiotherapy or chemotherapy; (III) had not undergone a breast enhancement MRI examination at the Affiliated Kunshan Hospital of Jiangsu University; (IV) had inflammatory breast cancer or lactating breast cancer; (V) had stage IV breast cancer; and/or (VI) failed to follow up. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Affiliated Kunshan Hospital of Jiangsu University (No. 20210092). Individual consent for this retrospective analysis was waived.

Observation indicators

The observation indicators were as follows: (I) general information: age, onset site, family history, and menopause; (II) MRI characteristics: ADC and peak time; and (III) pathological characteristics: maximum tumor diameter, estrogen receptor (ER) expression, progesterone receptor (PR) expression, nuclear-associated antigen Ki-67 index (%), human epidermal growth factor receptor 2 (HER-2) expression, a positive rate of axillary lymph nodes, subclavian lymph node metastasis, T staging, pathological type, histological grade, vascular tumor thrombus, and the 5-year recurrence or metastasis rate.

Examination methods

All the patients underwent dynamic-enhanced MRI within 72 h of preoperative surgery using the Philips Lntera 1.5T Achieva Nova Dual MR (Philips, Holland) with gadopentetate dimeglumine as the contrast medium (intravenously administered, concentration: 0.2 mmol/kg, speed: 2.5 mL/s).

Detection methods

The following detection methods were used: (I) ER: an expression level ≥10% indicated high expression; (II) PR: an expression level ≥10% indicated high expression; (III) Ki-67: an index >14% indicated high expression; (IV) HER2: intraoperative breast cancer tissue was taken from patients, immunohistochemical staining was performed, and the HER2 protein expression level was defined as (–),

(1+), (2+), or (3+) according to the staining ratio and color intensity of HER2 protein expression level on the cell membrane. If the HER2 protein expression was (3+) or (2+) and fluorescence in situ hybridization (FISH) tests showed that the HER2 gene was amplified, HER2 was positive, or otherwise defined as negative; (V) positive axillary lymph node metastasis or subclavian lymph node metastasis: the presence of axillary lymph node metastasis or subclavian lymph node metastasis was determined according to the postoperative pathological results; (VI) vascular tumor thrombus: a immunohistochemical method using a ×20 microscopic was employed to detect whether vascular tumor thrombus was formed or not; and (VII) recurrence or metastasis: patients were followed-up for 5 years after surgery through clinical visit and cellphone to determine if they suffered from recurrence or metastasis.

Statistical analysis

The data analysis of this study was completed using SPSS 26.0, and a P value <0.05 (two-sided) indicated a statistically significant difference. The continuous measurement data of the 2 groups are expressed as the mean ± standard deviation, and the independent sample *t*-test was used to analyze differences between the 2 groups. The count data are represented as the n (%), and the chi-square test was used to analyze differences between the 2 groups. The diagnostic value of the ADC and peak time on postoperative recurrence or metastasis in breast cancer patients was analyzed using receiver operating characteristic (ROC) curves. The risk factors for postoperative recurrence or metastasis in breast cancer patients were explored by a multifactorial logistics regression analysis.

Results

Clinical pathological features of patients with postoperative recurrence or metastasis of breast cancer

Compared to patients without recurrence or metastasis, the ADC of patients with recurrence or metastasis was lower [$(0.79\pm0.25)\times10^{-3}$ *vs.* $(0.99\pm0.19)\times10^{-3}$ mm^2/s; P<0.001], the peak time was significantly reduced (156.92±25.08 *vs.* 178.56±31.10 s; P<0.001), and the maximum tumor diameter was significantly increased (2.79±1.94 *vs.* 1.91±0.88 cm; P<0.001). Compared to patients without recurrence or metastasis, the proportion of patients with a T staging ≥2, HER-2 positive, a high Ki-67 index, vascular tumor thrombus, and lymph node metastasis increased significantly, and the proportion of patients with high ER and PR expression was reduced in patients with recurrence or metastasis (P<0.05; see *Table 1*).

Diagnostic value of ADC and peak time for postoperative recurrence or metastasis in breast cancer patients

The ADC and peak time had certain diagnostic value for postoperative recurrence or metastasis in breast cancer patients, and the areas under the curve were 0.821 [95% confidence interval (CI): 0.732–0.911; P<0.001] and 0.691 (95% CI: 0.609–0.774; P<0.001), respectively (see *Figure 1* and *Table 2*).

Risk factors for the recurrence or metastasis of breast cancer after surgery

An ADC $<0.78\times10^{-3}$ mm^2/s, a peak time <167.50 s, T staging ≥2, vascular tumor thrombus and positive lymph nodes were risk factors for postoperative recurrence in breast cancer patients, and high ER expression was a protective factor for postoperative recurrence or metastasis in breast cancer patients (P<0.05; see *Table 3*).

Association of ADC with clinical pathological features of breast cancer patients

We found that ADC was associated with the site of onset, T staging, vascular tumor thrombus, and lymph node metastasis in breast cancer patients (P<0.05; see *Table 4*).

Correlation between peak time and clinical pathological characteristics of breast cancer patients

Peak time was related to a high Ki-67 index, high ER expression, and high PR expression (P<0.05; see *Table 5*).

Discussion

Currently, dynamic-enhanced MRI is widely used in the diagnosis of breast cancer to develop individualized treatment plans (9-11). We found that the correlations between the ADC and peak time, and postoperative recurrence or metastasis and the clinical pathological features of breast cancer patients were examined, and it was found that the decreased ADC and peak time were risk factors for postoperative recurrence or metastasis in breast

Table 1 Clinical pathological features of patients with postoperative recurrence or metastasis of breast cancer

Variables	Recurrence or metastasis (n=39)	No recurrence or metastasis (n=175)	t/χ^2 value	P value
Apparent diffusion coefficient ($\times10^{-3}$ mm^2/s)	0.79±0.25	0.99±0.19	5.625	<0.001
Peak time (s)	156.92±25.08	178.56±31.10	4.058	<0.001
Age <40 years	8 (20.51)	29 (16.57)	0.346	0.556
Site of onset			0.319	0.572
Left	19 (48.72)	94 (53.71)		
Right	20 (51.28)	81 (46.29)		
Family history	1 (2.56)	3 (1.71)	0.126	0.723
Menopause	15 (38.46)	80 (45.71)	0.680	0.410
The largest diameter of the tumor (cm)	2.79±1.94	1.91±0.88	4.347	<0.001
T staging			19.964	<0.001
T1	12 (30.77)	121 (69.14)		
≥T2	27 (69.23)	54 (30.86)		
Positive HER-2	19 (48.72)	17 (9.71)	34.674	<0.001
High Ki-67	31 (79.49)	66 (37.71)	22.457	<0.001
High ER	9 (23.08)	148 (84.57)	61.718	<0.001
High PR	13 (33.33)	145 (82.86)	40.485	<0.001
Vascular tumor thrombus	9 (23.08)	10 (5.71)	11.884	0.001
Breast cancer type			1.774	0.183
Non-special types	37 (94.87)	153 (87.43)		
Special types	2 (5.13)	22 (12.57)		
Lymph node metastasis			55.499	<0.001
Yes	33 (84.62)	39 (22.29)		
No	6 (15.38)	136 (77.71)		
Subclavian lymph nodes metastasis			0.681	0.409
Yes	1 (2.56)	0 (0.00)		
No	38 (97.44)	175 (100.00)		
Histological grading			1.760	0.185
Grade II	29 (74.36)	146 (83.43)		
Grade III	10 (25.64)	29 (16.57)		

Data are expressed as n (%) or mean ± standard deviation. HER-2, human epidermal growth factor receptor 2; ER, estrogen receptor; PR, progesterone receptor.

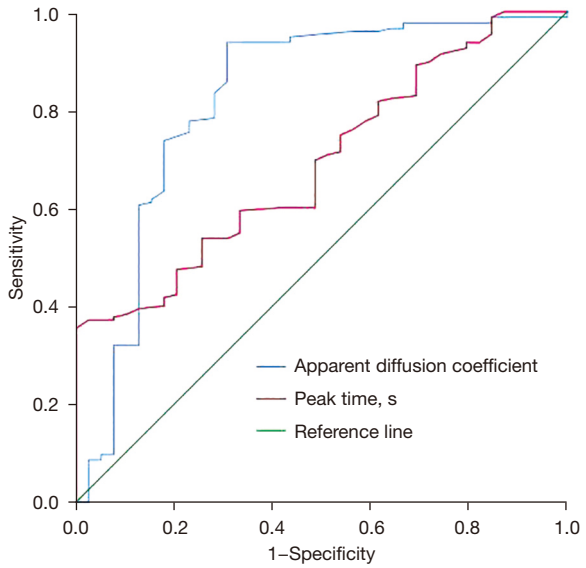

Figure 1 Diagnostic value of apparent diffusion coefficient and peak time for postoperative recurrence or metastasis in breast cancer patients.

cancer patients and were related to the patients' clinical pathological features.

The tissues of malignant tumors got a higher cell density; therefore, the tissue gaps are reduced, which in turn results in limitation of free movement of water molecules. So, the ADC decreases. Normal or benign tumor tissues have low cell density. Previous studies have confirmed that the ADC has a high sensitivity and specificity for the differential diagnosis of benign and malignant mammary tumors (12-15). In recent years, studies have also explored the relationship between ADC and the prognosis of breast cancer patients, and shown that ADCs are related to histological grading, the Ki-67 index, tumor size, molecular subtypes, and axillary lymph node metastasis; thus, the ADC appears to be related to the heterogeneity of breast cancer (16,17), which was supported by the findings of our study. Our study showed that the ADC was related to the site of onset, T staging, vascular tumor thrombus, and lymph node metastasis, and that tumor density tends to be higher in

Table 2 Diagnostic value of apparent diffusion coefficients and peak time for postoperative recurrence or metastasis in breast cancer patients

Variables	Area under the curve	P value	95% confidence interval		Optimal diagnostic cut-offs	Sensitivity	Specificity
			Lower bound	Upper bound			
Apparent diffusion coefficient value	0.821	<0.001	0.732	0.911	0.78	0.937	0.692
Peak time(s)	0.691	<0.001	0.609	0.774	167.5	0.594	0.667

Table 3 Risk factors for postoperative breast cancer recurrence or metastasis

Variables	B	S.E.	Wald	P value	Exp (B)	95% confidence interval
Apparent diffusion coefficient <0.78 ($\times 10^{-3}$ mm^2/s)	2.984	1.039	8.241	0.004	19.768	2.577–151.619
Peak time <167.50 s	1.742	0.846	4.242	0.039	5.708	1.088–29.947
T staging ≥2	4.808	1.599	9.042	0.003	122.474	5.334–2,812.360
High ER	–2.891	1.358	4.531	0.033	0.056	0.004–0.795
High PR	–3.016	1.656	3.316	0.069	0.049	0.002–1.259
Vascular tumor thrombus	3.343	1.544	4.686	0.030	28.304	1.372–583.914
Positive lymph nodes	5.751	1.729	11.066	0.001	314.407	10.617–9,310.547
Constant	–18.839	5.341	12.442	<0.001	–	–

S.E., standard error; ER, estrogen receptor; PR, progesterone receptor.

Table 4 Correlations between apparent diffusion coefficients and clinicopathological features in breast cancer patients

Variables	Apparent diffusion coefficient ($\times10^{-3}$ mm^2/s)	*t* value	P value
Age (years)		1.325	0.187
<40 (n=37)	0.99±0.25		
≥40 (n=177)	0.94±0.21		
Site of onset		2.014	0.045
Left side (n=113)	0.98±0.21		
Right (n=101)	0.92±0.22		
Family history		0.965	0.336
Yes (n=4)	0.85±0.12		
No (n=210)	0.95±0.22		
Menopause		1.367	0.173
Yes (n=95)	0.93±0.23		
No (n=119)	0.97±0.21		
T staging		2.287	0.023
T1 (n=133)	0.98±0.21		
≥ T2 (n=81)	0.91±0.21		
Positive HER-2		1.746	0.082
Yes (n=36)	0.89±0.26		
No (n=178)	0.96±0.21		
High Ki-67		1.887	0.061
Yes (n=97)	0.92±0.22		
No (n=117)	0.98±0.21		
High ER		1.240	0.217
Yes (n=157)	0.96±0.19		
No (n=57)	0.92±0.27		
High PR		1.195	0.233
Yes (n=158)	0.96±0.21		
No (n=56)	0.92±0.25		
Vascular tumor thrombus		2.125	0.035
Yes (n=19)	0.85±0.20		
No (n=195)	0.96±0.22		
Breast cancer type		0.287	0.774
Non-special types (n=190)	0.95±0.21		
Special types (n=24)	0.94±0.25		
Lymph node metastasis		3.262	0.001
Yes (n=72)	0.88±0.24		
No (n=142)	0.98±0.20		
Histological grading		0.004	0.997
Grade II (n=175)	0.95±0.22		
Grade III (n=39)	0.95±0.20		

Data are expressed as mean ± standard deviation. HER-2, human epidermal growth factor receptor 2; ER, estrogen receptor; PR, progesterone receptor.

Table 5 Correlations between peak time and clinicopathological features in breast cancer patients

Variables	Peak time (s)	*t* value	P value
Age (years)		1.109	0.269
<40 (n=37)	179.78±27.16		
≥40 (n=177)	173.54±31.93		
Site of onset		1.025	0.307
Left side (n=113)	176.68±31.23		
Right (n=101)	172.31±31.12		
Family history		0.686	0.493
Yes (n=4)	164.00±43.44		
No (n=210)	174.82±31.01		
Menopause		1.177	0.240
Yes (n=95)	171.81±31.42		
No (n=119)	176.86±30.95		
T staging		1.099	0.273
T1 (n=133)	176.44±30.55		
≥ T2 (n=81)	171.62±32.17		
Positive HER-2		0.663	0.508
Yes (n=36)	171.47±30.64		
No (n=178)	175.25±31.34		
High Ki-67		2.217	0.028
Yes (n=97)	169.47±30.23		
No (n=117)	178.88±31.45		
High ER		2.854	0.005
Yes (n=157)	178.22±31.25		
No (n=57)	164.68±29.02		
High PR		2.078	0.039
Yes (n=158)	177.23±31.35		
No (n=56)	167.23±29.76		
Vascular tumor thrombus		1.186	0.237
Yes (n=19)	166.53±26.57		
No (n=195)	175.41±31.55		
Breast cancer type		1.321	0.188
Non-special types (n=190)	175.62±31.65		
Special types (n=24)	166.71±26.52		
Lymph node metastasis		0.613	0.540
Yes (n=72)	172.78±31.10		
No (n=142)	175.55±31.30		
Histological grading		0.074	0.941
Grade II (n=175)	174.69±32.10		
Grade III (n=39)	174.28±27.06		

Data are expressed as mean ± standard deviation. HER-2, human epidermal growth factor receptor 2; ER, estrogen receptor; PR, progesterone receptor.

patients with high T staging, vascular tumor thrombus, and lymph node metastasis, which results in a reduced ADC. In addition, we found that the ADC had high value in predicting postoperative recurrence or metastasis in breast cancer patients, and a reduction in the ADC was a risk factor for postoperative recurrence or metastasis.

Peak time refers to the time required for the breast cancer tissue signal intensity to reach its peak; the shorter the time, the richer the neovascularization in the tumor body. Our study showed that a decrease in peak time was a risk factor for postoperative recurrence or metastasis in breast cancer, which indicated that patients with more angiogenesis in breast cancer tumors were more likely to suffer from recurrence or metastasis after surgery. Previous studies have also confirmed that angiogenesis is a risk factor for postoperative recurrence or metastasis in breast cancer patients (18-20). A further analysis showed that peak time was more lowly expressed in high Ki-67 patients and more highly expressed in high ER and PR patients. As a high Ki-67 index is a risk factor for a poor prognosis in patients (21), while high ER and PR expression levels are protective factors for a poor prognosis (22-24), we indirectly illustrated that peak time is associated with patient prognosis.

Limitations

This study had a number of limitations. First, it was a retrospective clinical study. Second, it failed to further measure cell density and angiogenesis in breast cancer tissue.

Conclusions

The peak time and even more notably, the ADC have good value in predicting the recurrence or metastasis of breast cancer after surgery, and are related to the clinical pathological characteristics of breast cancer patients.

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Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-22-400/rc

Data Sharing Statement: Available at https://gs.amegroups.com/article/view/10.21037/gs-22-400/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-22-400/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Affiliated Kunshan Hospital of Jiangsu University (No. 20210092). Individual consent for this retrospective analysis was waived.

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