

ORIGINAL ARTICLE

Research on the correlation between ultrasonographic features of breast cancer and expressions of ER, CD34 and p53

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Summary

Purpose: To investigate the expressions of estrogen receptor (ER), highly glycosylated type I transmembrane glycoprotein (CD34) and p53 in breast cancer tissue and analyze their correlation with color Doppler ultrasonographic features.

Methods: 86 patients who were admitted to our hospital with confirmed breast cancer diagnosis from January 2016 to December 2016 were selected. The expressions of ER, CD34 and p53 in cancer tissue and corresponding cancer-adjacent normal tissue were detected by immunohistochemical staining, and the color Doppler ultrasonographic features of patients were observed and analysed by Spearman correlation test.

Results: The positive rates of ER, CD34 and p53 expressions in cancer tissue of the case group were 46.5, 50 and 52.3%, respectively, significantly higher than 1.7% of the control group ($p < 0.05$). The expressions of ER, CD34 and p53 in the cancer tissue of case group were correlated with the existence of calcification, spicule sign and lymph node

metastasis detected by Doppler ultrasound ($p < 0.05$), but not associated with tumor diameter and morphology ($p > 0.05$). Spearman correlation test indicated positive correlation between expressions of ER and CD34 in cancer tissue of the case group ($r = 0.703$, $p < 0.05$); ER expression was positively associated with p53 expression ($r = 0.716$, $p < 0.05$) and CD34 expression was positively related to p53 expression ($r = 0.684$, $p < 0.05$).

Conclusions: The expressions of ER, CD34 and p53 have significant roles in the occurrence and development of breast cancer. There is a certain correlation between expressions of ER, CD34 and p53 of breast cancer and color Doppler ultrasonographic features. The expression levels of ER, CD34 and p53 in breast cancer tissue can be evaluated by color Doppler ultrasonographic features, which is conducive to assessing the prognosis of these patients.

Key words: breast cancer, color Doppler ultrasound, estrogen receptor, ultrasonographic features

Introduction

Breast cancer is a common malignant tumor of women and presents difficulties in early diagnosis due to its insidious onset. Part of breast cancer cases are in advanced stage when they are definitely diagnosed, and the prognosis is not ideal [1]. In recent years, the methods of diagnosing breast cancer have been evolved continuously [2-4] and among them, color Doppler ultrasound and other imaging technologies have become common diagnostic methods [5]. With the development of gene technology, ER, CD34, p53 and other related cancer

factors for the diagnosis of malignant tumors have become increasingly used. Whether there is any correlation between color Doppler ultrasonographic features of breast cancer and ER, CD34, p53 and other related cancer factors is a key point of this study. Based on this, this study was designed to investigate the expressions of ER, CD34 and p53 in breast cancer tissue and analyze their correlation with color Doppler ultrasonographic features of breast cancer, so as to provide a valuable reference for the diagnosis and treatment of this disease.

Methods

General data

A total of 86 patients who were admitted to our hospital with confirmed breast cancer diagnosis from January 2016 to December 2016 were selected as the case group, and all of them were women. The patient age ranged from 31 to 68 years (mean 61.2±2.5). There were 51 cases with lymph node metastasis and 35 cases without. Tumor diameter was <2 cm in 42 patients and ≥2 cm in 44. Forty five patients had left breast disease and in 44 the disease was confined to the right breast. The diagnosis of breast cancer was established by pathological examination after the operation [6]. Additionally, 60 cases with cancer-adjacent normal breast tissue (5 cm away from cancer tissue) composed the normal control group. This group included women aged from 32 to 67 years (mean 60.8±1.7).

The expressions of ER, CD34 and p53 in the case and control groups were detected by the immunohistochemical streptavidin-peroxidase (SP) method according to the instructions of EnVision kit of rabbit anti-human ER antibody, rabbit anti-human CD34 antibody and rabbit anti-human p53 antibody (purchased from Shanghai Tocan Bio-technology Co., Ltd., Shanghai, China), and the results of staining were assessed.

The patients were examined by color Doppler ultrasound device (Philips Co,Ltd, Amsterdam, The Netherlands) before operation. The films were read by two highly qualified clinicians engaged in ultrasound diagnosis, who analyzed tumor diameter, spicule sign, lymph node metastasis and other ultrasonic imaging characteristics of patients, and the results taken were correlated to pathological features and analyzed.

Evaluation criteria

Semi-quantitative scoring combined with Berry classification method was utilized [6]: positive expressions of ER, CD34 and p53 displayed cytoplasmic staining; the product of staining degree score and the score of percentage of positive cells in the observed cells was evaluated as follows: 0-3 points: (-), 4-5 points: (+), 6-7 points: (++) , 8 or above: (+++); ≤3 points (-), >3 points (+).

Statistics

SPSS20.0 (IBM, USA, New York, USA) statistical software package was used for statistical analyses. The chi-square test was used for the comparison of positive rates between groups, and t-test was used for intergroup comparison. Spearman correlation test was utilized for correlation analysis. A p value <0.05 was considered as statistically significant.

Results

Expressions of ER, CD34 and p53 in breast cancer tissue

The positive expression of ER, CD34 and p53 was located in the cytoplasm, showing brown-yellow granules as shown in Figure 1 (A-F). The positive rate of ER expression in cancer tissue of the case group was 46.5%, significantly higher than 1.7% of the control group (p<0.05) (Table 1). The positive rate of CD34 expression in cancer tissue of the case group was 50%, significantly higher than 1.7% of the control group (p<0.05) (Table 2).

Table 1. Expression of ER in cancer tissue and cancer-adjacent normal tissue

Group	n	+	++	+++	Positive rate (%)	-
Case group	86	10	17	13	46.5	46
Control group	60	1	0	0	1.7	59
p					<0.05	

Table 2. Expression of CD34 in cancer tissue and cancer-adjacent normal tissue

Group	n	+	++	+++	Positive rate (%)	-
Case group	86	10	17	13	46.5	46
Control group	60	1	0	0	1.7	59
p					<0.05	

Table 3. Expression of p53 in cancer tissue and cancer-adjacent normal tissue

Group	n	+	++	+++	Positive rate (%)	-
Case group	86	14	18	13	52.3	41
Control group	60	1	0	0	1.7	59
p					<0.05	

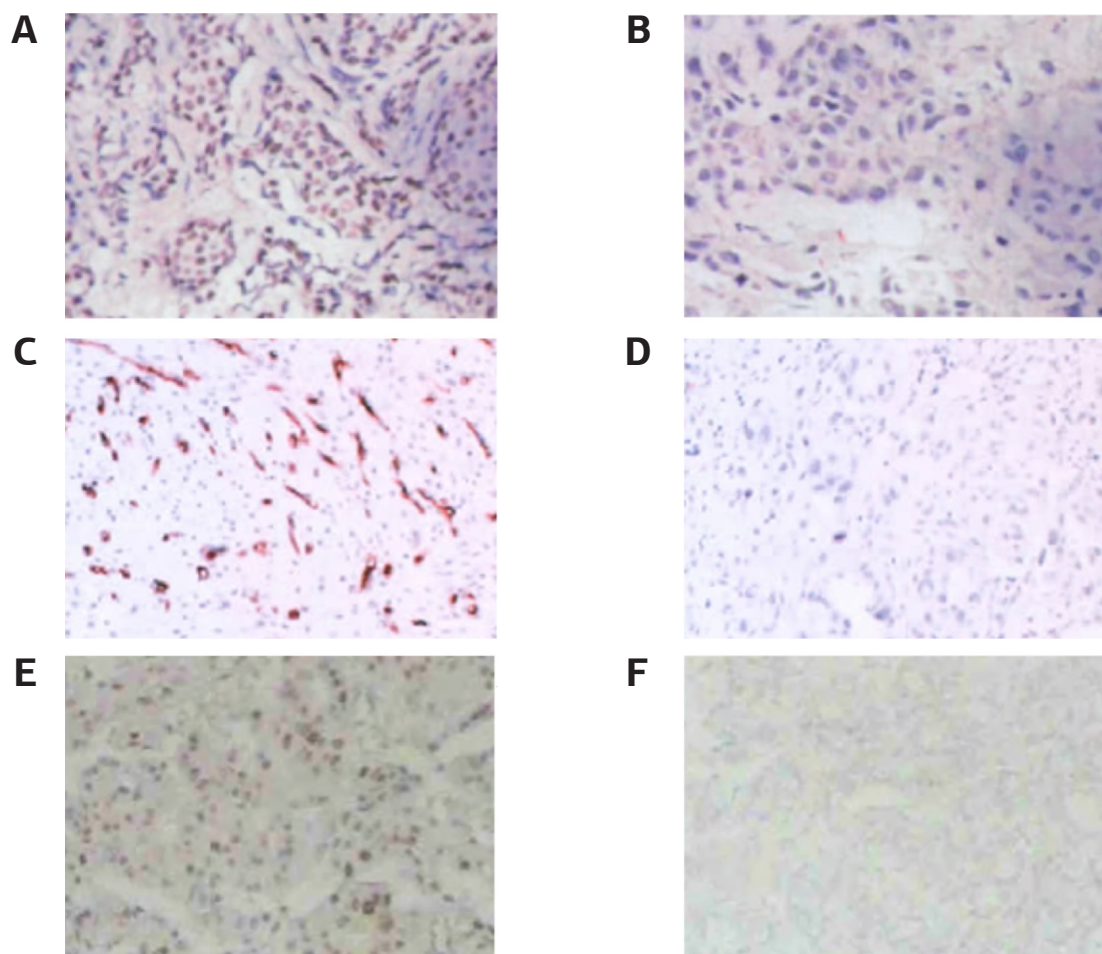


Figure 1. **A:** Expressions of ER: Positive expression of ER in cancer tissue (magnification 200×); **B:** Negative expression of ER in cancer adjacent tissue (magnification 200×). **C:** Expressions of CD34: Positive expression of CD34 in cancer tissue (magnification 200×); **D:** Negative expression of CD34 in cancer-adjacent tissue (magnification 200×). **E:** Expressions of p53: Positive expression of p53 in cancer tissue (magnification 200×). **F:** Negative expression of p53 in cancer-adjacent tissue (magnification 200×).

Table 4. Relationship between ultrasonographic features of breast cancer and expressions of ER, CD34 and p53

Ultrasonographic features	n	ER positive cases (n=40)	p	CD34 positive cases (n=43)	p	P53 positive cases (n=45)	p
Tumor diameter, cm			>0.05		>0.05		>0.05
<2	42	20		22		23	
≥2	44	20		21		22	
Tumor morphology			>0.05		>0.05		>0.05
Irregular	47	21		22		22	
Lobulated + analogous round	39	19		21		23	
Calcification			<0.05		<0.05		<0.05
Yes	54	25		27		30	
No	32	15		16		15	
Spicule sign			<0.05		<0.05		<0.05
Yes	50	27		28		31	
No	36	13		15		14	
Lymph node metastasis			<0.05		<0.05		<0.05
Yes	51	30		29		33	
No	35	10		14		12	

The positive rate of p53 expression in cancer tissue of the case group was 52.3%, significantly higher than 1.7% of the control group ($p < 0.05$) (Table 3).

Color Doppler ultrasonographic features in the case group

Among the 86 patients of the case group, there were 42 cases with tumor diameter $< 2\text{cm}$ and 44 cases with lump $\geq 2\text{cm}$; there were 50 cases with spicules at the margin of the lump and 47 cases with lump that was irregular, 32 cases with lobulated mass and 7 cases being round. There were also 54 cases with calcification and 51 cases with lymph node metastasis, which are shown in Figure 2.

Relationship between ultrasonographic features of breast cancer and expressions of ER, CD34 and p53

The expressions of ER, CD34 and p53 in the cancer tissue of the case group were significantly correlated with the existence of calcification, spicule sign and lymph node metastasis ($p < 0.05$), but not associated with tumor diameter and morphology ($p > 0.05$) (Table 4).

Correlations among ER, CD34 and p53

Spearman correlation analysis showed that there was a positive correlation between expressions of ER and CD34 in cancer tissue of the case

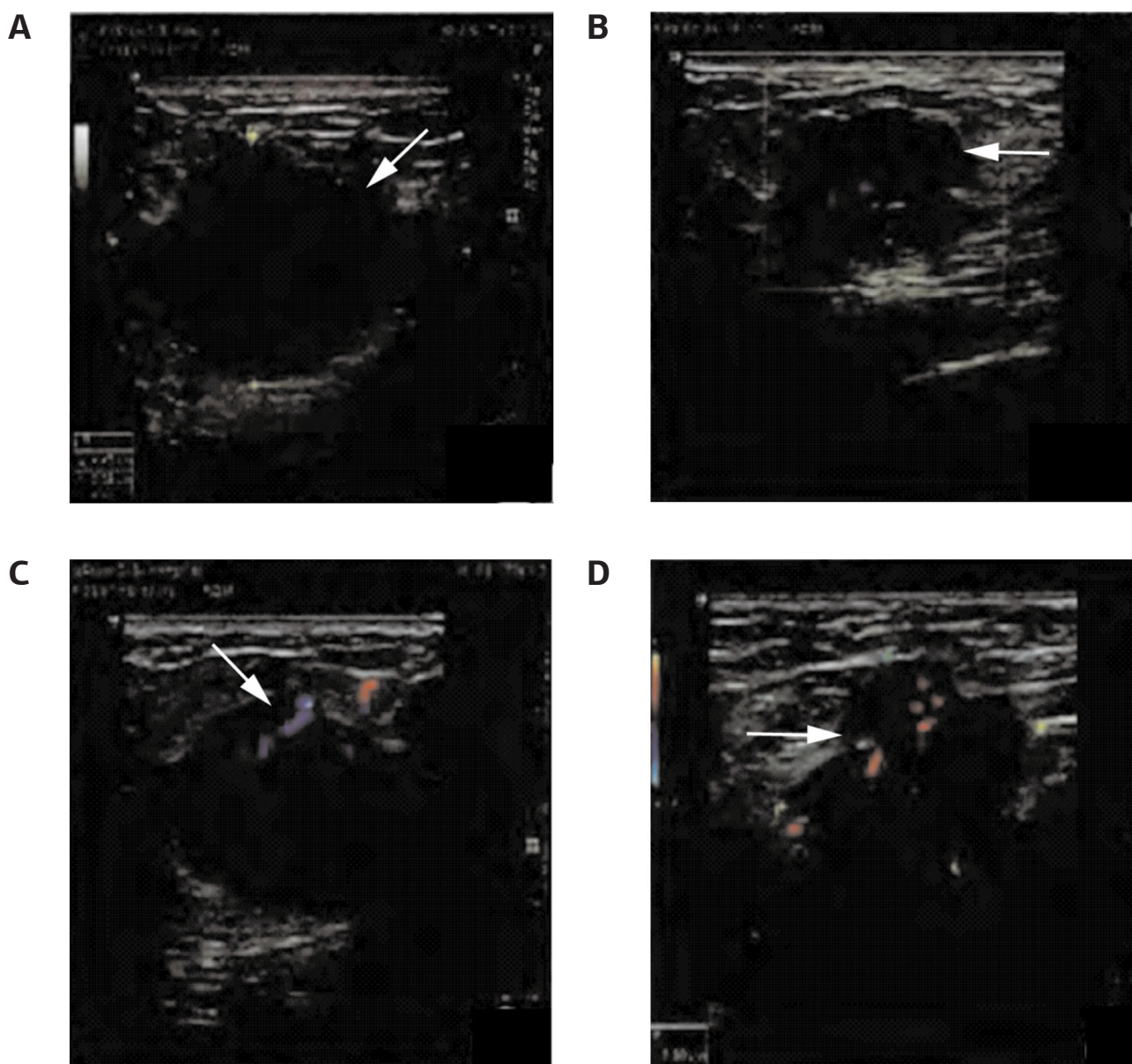


Figure 2. Color Doppler ultrasonographic features. **A:** Patient aged 57 years, with breast cancer 4.3cm x 2.4cm, the morphology of which is irregular. **B:** Patient aged 42 years, with irregular morphology of breast tumor and multiple calcifications inside. **C:** Patient aged 57 years, with irregular morphology of breast tumor and abundant blood flow signal. **D:** Patient aged 55 years, with axillary lymph node metastasis. Arrows show the breast tumors.

group ($r=0.703$, $p<0.05$) (Figure 3A); ER expression was positively associated with p53 expression ($r=0.716$, $p<0.05$) (Figure 3B); CD34 expression was positively correlated to p53 expression ($r=0.684$, $p<0.05$) (Figure 3C).

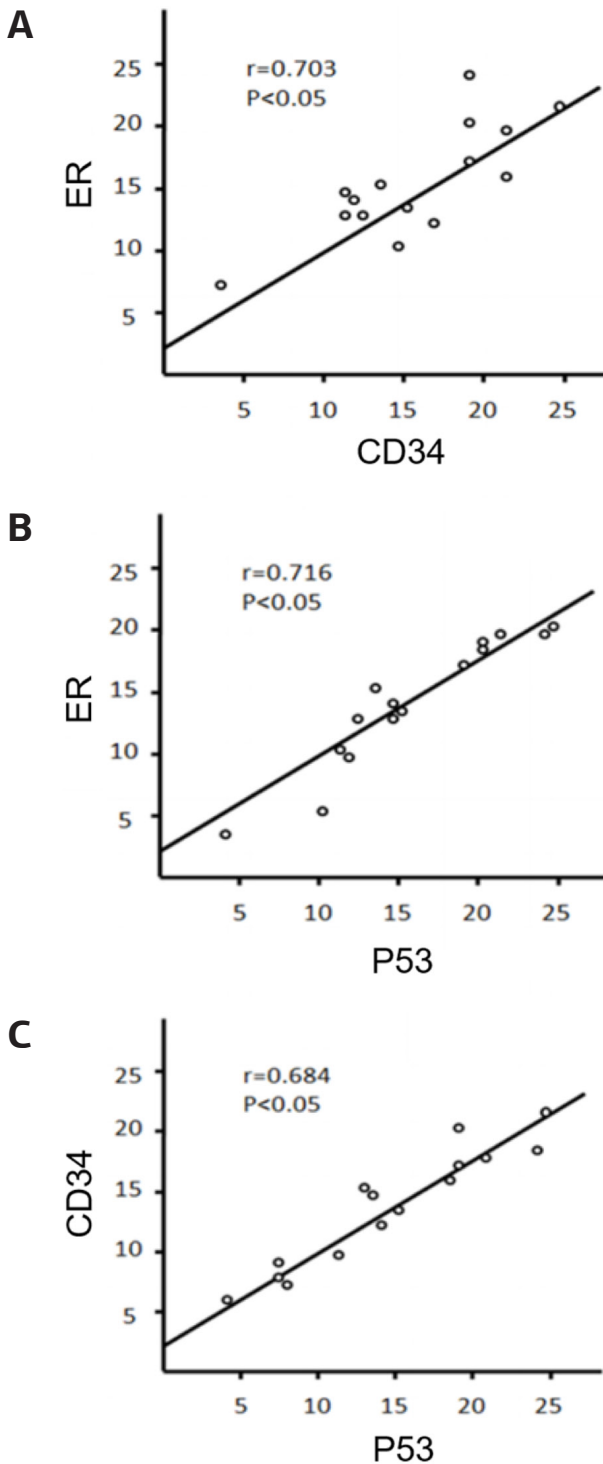


Figure 3. Correlation between expressions of ER, CD34 and p53. **A:** Positive correlation between expressions of ER and CD34 ($r=0.703$, $p<0.05$). **B:** Positive correlation between expressions of ER and p53 ($r=0.716$, $p<0.05$). **C:** Positive correlation between expressions of CD34 and p53 ($r=0.684$, $p<0.05$).

Discussion

The pathogenesis of breast cancer is quite complex, and some biological factors are involved in the occurrence and development of this disease [7-9]. The histopathological changes induced by abnormal expression of biological factors can be reflected by color Doppler ultrasonography to some extent [10]. There are few studies on color Doppler ultrasonography and biological factors of the breast cancer at present. In recent years, with the continuous advancements in molecular biology, pathological biological factors have attracted the attention of researchers worldwide [11-13].

ER is one of the most common steroid hormone receptors and authors have confirmed that the degree of ER expression is closely associated with treatment and prognosis of patients with breast cancer [14]. Related data revealed that CD34 is abnormally expressed in gastric cancer, liver cancer and many other tumors, which can promote tumor vascular endothelial cell proliferation, thus promoting tumor cell invasion and metastasis [15,16]. p53 is a tumor suppressor, but this gene can be found as wild type and mutated type. The repair level of DNA is enhanced by the wild type, promoting inhibition of proliferation of tumor cells, but the mutated type, losing the normal role of tumor suppression, will induce tumor promotion [17-20].

The results of this study indicated that the positive rates of ER, CD34 and p53 expressions in cancer tissue of the case group were 46.5, 50 and 52.3%, respectively, which were significantly higher than 1.7% of the control group ($p<0.05$). The expressions of ER, CD34 and p53 in cancer tissue of the case group were correlated with the existence of calcification, spicule sign and lymph node metastasis ($p<0.05$), but not associated with tumor diameter and morphology ($p>0.05$). Based on this, it can be speculated that the infiltration of breast cancer with existence of calcification, spicule sign, lymph node metastasis and other ultrasonographic features is more intense, the grade of lesions is higher, and the clinical prognosis is not ideal. Spearman correlation test indicated that there was a positive correlation between the expressions of ER and CD34 in cancer tissue of the case group ($r=0.703$, $p<0.05$), ER expression was positively associated with p53 expression ($r=0.716$, $p<0.05$), CD34 expression was positively related to p53 expression ($r=0.684$, $p<0.05$), further demonstrating the relationships among ER, CD34 and p53. The results convincingly showed that the expressions of ER, CD34 and p53 are correlated with the occurrence and development of breast cancer, and

the mechanism may be that neovascularization in breast cancer tissue is promoted by ER, CD34 and p53 via inducing proliferation of breast cancer cells, inhibiting apoptosis and other pathways, thus paving the way for the occurrence, evolution and metastasis of breast cancer.

In summary, the expressions of ER, CD34 and p53 are of great importance in the occurrence and development of breast cancer. There is a certain correlation between the expressions of ER, CD34

and p53 of breast cancer and color Doppler ultrasonographic features. The expression levels of these biomarkers in breast cancer can be evaluated by color Doppler ultrasonographic features, which are conducive to assessing the prognosis of these patients.

Conflict of interests

The authors declare no conflict of interests.

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