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Detection and Clinical Significance of Peripheral Blood CTC, CA125, CA153, and CEA Levels in Patients with Ductal Carcinoma in situ

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Abstract: *Objective:* To explore the detection and clinical significance of peripheral blood CTC, CA125, CA153, and CEA levels in patients with DCIS. *Methods:* 210 patients who received surgical treatment for breast cancer in our hospital from January 2019 to December 2022 were selected as the research subjects. According to the postoperative pathology, 100 cases were divided into breast cancer and 110 benign breast tumor groups. One hundred ten healthy patients undergoing physical examination during the same period were selected as the control group. CA153, CA125, and CEA levels were observed in the three groups. *Results:* The levels of CA153, CA125, and CEA in the breast cancer group were significantly higher than those in the benign breast tumor group and the control group ($P < 0.05$); the levels of CA153, CA125, and CEA in the benign breast tumor group were all higher than those in the control group, but the differences were not statistically significant; among the three tumor markers, CA153 has the highest sensitivity at 39.00%, CA125 has the second highest sensitivity at 18.00%, and CEA has the lowest sensitivity at 17.00%; The sensitivity of the two joint tests of CA153+CA125, CA153+CEA, and CA125+CEA for the diagnosis of breast cancer were 50.00%, 48.00%, and 26.00% respectively; the sensitivity of the three joint tests is the highest, reaching 53.00%, while the specificity of the joint tests was lower than the individual tests. *Conclusion:* Detection of peripheral blood CTC, CA125, CA153, and CEA levels has specific reference significance for the treatment and prognosis of DCIS patients.

Keywords: Ductal carcinoma in situ; CTC; CA125; CA153

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1. Introduction

Ductal carcinoma in situ (DCIS) is the most common tumor in breast ducts, accounting for 10% to 15% of breast cancers. Among surgical specimens, approximately 70% of cases have a pathological diagnosis of carcinoma in situ. DCIS is clinically divided into papillary DCIS, intraductal carcinoma in situ, and intraductal invasive. The diagnosis of intraductal carcinoma in situ is mainly based on the tumor's histological type and histological grade. The judgment of grade mainly depends on the clinician's understanding of the disease and pathological examination. With the continuous development of molecular technology and

immunohistochemistry technology in recent years, tumor-related molecular markers are playing an increasingly important role in the diagnosis of malignant tumors, prognosis assessment, drug selection, and prognosis prediction. Recent studies have shown that molecular markers such as the detection of circulating tumor cells (CTCs), cancer antigen 125 (CA125), CA153, and carcinoembryonic antigen (CEA) are of great significance for the diagnosis, efficacy evaluation, and prognosis prediction of tumors [1-6]. However, there are no CTC or relevant reports of CA153 in the diagnosis and prognosis evaluation of breast cancer. This study intends to explore the changes in peripheral blood CTC, CA125, CA153, and CEA levels in patients with breast cancer and their clinical significance.

2. Materials and methods

2.1. General information

Two hundred ten patients who underwent breast cancer surgical treatment in our hospital from January 2019 to December 2022 were selected as the research subjects. According to the postoperative pathology, 100 cases were divided into a breast cancer group and 110 benign breast tumor group, and 110 healthy physical examination patients were selected as the control group during the same period.

Inclusion criteria included: (1) Patient age > 40 years old; (2) Clinical diagnosis of breast ductal carcinoma in situ; (3) No other systemic severe diseases such as heart, brain, or kidney; (4) No history of other malignant tumors, or are undergoing chemotherapy, radiotherapy, and other treatments. Exclusion criteria included: (1) Recently suffered from acute infectious diseases, such as viral hepatitis or tuberculosis; and (2) Recently suffered from severe heart, brain, kidney, and other systemic diseases.

2.2. Detection method

The enzyme-linked immunosorbent assay (ELISA) method was used to detect the serum CTC, CA125, CA153, and CEA levels. Nanjing Jiancheng Bioengineering Institute provided the reagents which were subjected to strict quality control before use.

2.3. Statistical processing

SPSS 24.0 statistical software was used for data analysis. Measurement data were expressed as mean ± standard deviation (SD), and a *t*-test was performed. Count data were expressed as percentages, and the χ^2 test was performed. $P < 0.05$ was considered as a statistically significant difference.

3. Results

3.1. Comparison of CA153, CA125, and CEA levels among three groups

The levels of CA153, CA125, and CEA in the breast cancer group were significantly higher than those in the benign breast tumor group ($P < 0.05$); the levels of CA153, CA125, and CEA in the breast cancer group were significantly higher than those in the control group ($P < 0.05$); the levels of CA153, CA125, and CEA in the benign breast tumor group were all higher than those in the control group. However, the differences were not statistically significant. See **Table 1**.

Table 1. Comparison of CA153, CA125, and CEA levels among three groups (mean ± SD)

Group	CA153 (U/mL)	CA125 (U/mL)	CEA (ng/mL)
Breast cancer group (n = 100)	35.19 ± 17.02	21.64 ± 12.47	6.90 ± 4.73
Breast benign tumor group (n = 110)	8.72 ± 4.02	15.30 ± 8.07	1.64 ± 0.85
Control group (n = 110)	8.33 ± 3.87	14.86 ± 6.91	1.58 ± 0.67

Note: Comparisons between the breast cancer group and the benign breast tumor group as well as the breast cancer group and the control group were all $P < 0.05$; the comparison between the benign breast tumor group and the control group was $P > 0.05$.

3.2. Evaluation of single and combined detection in breast cancer diagnosis

Among the three tumor markers, CA153 has the highest sensitivity at 39.00%, CA125 has the second highest sensitivity at 18.00%, and CEA has the lowest sensitivity at 17.00%; the combinations of two tumor markers, CA153+CA125, CA153+CEA, and CA125+CEA showed a sensitivity of 50.00%, 48.00%, and 26.00%, respectively; the sensitivity of the three combined tests is the highest, reaching 53.00%, while the specificity of the combined tests is lower than that of the individual tests. See **Table 2**.

Table 2. Evaluation of single and combined detection in breast cancer diagnosis

Test items	True-positive	False-negative	True-negative	False-positive	Sensitivity (%)	Specificity (%)
CA153	39	61	109	1	39.00	99.10
CA125	18	82	110	0	18.00	100
CEA	17	83	110	0	17.00	100
CA153+CA125	50	50	104	6	50.00	94.55
CA153+CEA	48	52	105	5	48.00	95.45
CA125+CEA	26	74	105	5	26.00	95.45
CA153+CA125+CEA	53	47	102	8	53.00	92.73

Note: Sensitivity = number of true positive cases / (number of true positive cases + number of false negative cases) × 100%; specificity = number of true negative cases / (number of true negative cases + number of false positive cases) × 100%.

4. Discussion

Breast cancer is a highly heterogeneous malignant tumor with complex and diverse pathogenesis [7]. Breast cancer is a type of tumor with multi-stage evolution characteristics. Its pathogenesis is closely related to the mutations and changes in expression levels of multiple genes, which brings significant challenges to its personalized treatment [8]. In recent years, there has been a notable rise in the incidence of breast cancer. To enhance the survival rates, improve the quality of life of patients, and prolong the life of patients, it is imperative to attain the objectives of early detection and diagnosis. This can be accomplished by integrating comprehensive treatment methods with tailored cancer treatment plans, resulting in improved diagnostic and therapeutic outcomes for patients. Currently, standard clinical breast ultrasound, MRI, needle biopsy, mammography, and other technologies are subject to a certain degree and are expensive or non-invasive. Therefore, there is an urgent clinical need for a fast and simple technology that enables repeated testing to improve breast cancer diagnosis. Tumor markers refer to antigens produced by tumor cells that cause malignant lesions due to the expression of oncogenes. They can be detected in the blood of patients with malignant tumors, and the results are often much higher than usual [9]. However, it is rarely found in the serum of patients

with either non-cancerous or benign tumors. In the early stages of most malignant tumors, before corresponding clinical symptoms and imaging changes appear, positive expression can be detected through tumor markers in the blood [10]. Because serum tumor markers have the clinical advantages of being simple, rapid, non-invasive, and easy to continuously monitor, they are considered an early diagnostic method for malignant tumors accepted by clinicians. Therefore, the joint determination of multiple cancer molecular markers has significant application value in early breast cancer diagnosis.

Peripheral blood CTCs are tumor cells present in the peripheral blood. These cells have been released from the primary tumor and spread to other parts through the blood circulation [11-13]. The number of CTCs is often related to tumor size, stage, grade, and other factors. Studies have shown that the number of CTCs in peripheral blood may be related to the development and prognosis of DCIS. In some cases, peripheral blood CTC numbers may increase, indicating an increased risk that DCIS has developed into invasive breast cancer. Therefore, monitoring the number of CTCs in peripheral blood can be used to assess the risk of DCIS progression. It should be noted that the number of CTCs in peripheral blood is not only related to DCIS but also to other factors such as age, gender, obesity, genetics, and other health conditions. Therefore, these factors need to be considered when interpreting CTC numbers.

CA125 is a glycoprotein commonly used to detect ovarian cancer. It can also be elevated in certain other types of cancer (such as lung and gastrointestinal cancer). In breast cancer, CA125 levels may be elevated in some cases, significantly when the breast cancer has progressed to more advanced stages. However, CA125 levels may not be significantly elevated in most DCIS patients. For people with elevated peripheral blood CA125 levels, it may indicate that some tumor has occurred [14,15]. However, the specific cause of elevated CA125 requires further evaluation and investigation. When evaluating elevated CA125, a comprehensive judgment needs to be made in conjunction with the patient's other examination results and clinical manifestations. It should be noted that the detection of tumor-associated antigens such as CA125 is not a specific detection method for breast cancer, and they may also be elevated in other types of cancer and other diseases. Therefore, other factors need to be considered when interpreting the results of these biomarkers, and a comprehensive evaluation should be carried out in the context of the patient's specific situation.

CA153 is a glycoprotein not present in normal breast tissue but is highly expressed in breast cancer cells. Therefore, CA153 levels are often elevated in breast cancer patients and are related to the malignancy and stage of the tumor. In patients with DCIS, elevated CA153 levels may indicate the development of invasive breast cancer because, during the progression of DCIS to invasive breast cancer, tumor cells will release CA153 into the blood circulation [16]. For people with elevated peripheral blood CA153 levels, it may indicate that some tumor has appeared. However, the specific cause of CA153 elevation requires further evaluation and investigation. When evaluating CA153 elevation, a comprehensive judgment needs to be made in conjunction with the patient's other examination results and clinical manifestations.

CEA is a broad-spectrum tumor marker that can be found in various tumors, such as colon, rectal, and gastric cancer. CEA levels may also be elevated in breast cancer, but the elevation in CEA levels in patients with DCIS may not be particularly pronounced. Likewise, CEA expression levels in DCIS patients did not correlate with levels in peripheral blood.

The results of this study showed that the levels of CA153, CA125, and CEA in the breast cancer group were significantly higher than those in the benign breast tumor group and the control group ($P < 0.05$). However, the specificity of the joint detection of the three tumor markers decreased, and the sensitivity was significantly higher. For any single item or pairwise combined detection, the sensitivity can reach 53.00%, so it has excellent value in the clinical diagnosis of breast cancer. In this data, there are some breast cancers whose

three test results are within the reference range of expected values and do not show positivity, which may have a particular relationship with the pathological staging of breast cancer patients. The positive rate of the three tests for patients in the middle and advanced stages is relatively high.

In contrast, the test results of early-stage patients may produce false negatives, significantly reducing the positive rate. Preliminary work has proven that the combination of CA153, CA125, and CEA can improve the sensitivity of breast cancer and reduce its missed diagnosis rate, which is of great significance to the early diagnosis and postoperative follow-up monitoring of breast cancer. With the continuous development of immune marker technology, research believes that more tumor markers will be detected in plasma, which will play a critical role in the early diagnosis of cancer, evaluation of treatment effects, and judgment of prognosis, providing clinicians with more options for treatment options.

In summary, the detection of peripheral blood CTC, CA125, CA153, and CEA levels has certain reference significance for the treatment and prognosis of DCIS patients.

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Disclosure statement

The authors declare no conflict of interest.

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