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The relationship between CA125 status and P53, WT1 and clinical features in epithelial ovarian cancer

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Abstract: To investigate the relationship between ER status, P53, WT1, CA125 and clinical characteristics of epithelial ovarian cancer, and the differential diagnosis value of low grade and high grade serous ovarian cancer. 34 patients with epithelial ovarian cancer admitted to our hospital were selected as the research object, and divided into low grade group and high grade group according to the histological grade of ovarian cancer. The immunohistochemical expressions of ER, P53 and WT1 in the two groups were compared and analyzed, and their correlation and clinicopathological parameters were analyzed. The total positive rates of P53 and WT1 in ovarian cancer were 55.88% and 41.18%. The proportion of P53 positive expression in high-grade group was significantly higher than that in low-grade group, while the WT1 positive rate was lower than that in low-grade group, the difference was statistically significant ($P < 0.05$). The WT1 (+) &P53 (+) group had a higher level of CA125 than the non-expression group, and the difference was statistically significant ($P < 0.05$). WT1 protein was significantly correlated with pathological stage, degree of differentiation, pathological type and lymph node metastasis of epithelial ovarian cancer ($P < 0.05$), which could be used as an important prognostic factor for patients. The expression level of P53 is higher in high-grade serous ovarian cancer, while the expression level of WT1 is lower. The use of P53 and WT1 can diagnose high-grade serous ovarian cancer, and WT1 has higher diagnostic value for low-grade serous ovarian cancer. The CA125 status was significantly correlated with the expression of P53 and WT1.

Keywords: Ovarian cancer; Serous; Low level; High level

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1. Introduction

Ovarian cancer is second only to cervical cancer and endometrial cancer in the incidence of female reproductive tract malignancy, the highest mortality rate of gynecological malignancy. Ovarian cancer tissue types are highly heterogeneous, with unique clinicopathological, molecular characteristics and prognosis. Epithelial ovarian cancer is the most common ovarian cancer, accounting for about 90%. With the rapid development of medicine and related disciplines, the 5-year survival rate of cervical cancer and endometrial cancer has been significantly improved. However, the 5-year survival rate and progression-free survival time of ovarian cancer have not been significantly improved. Studies have shown that the incidence of ovarian cancer is associated with early menarche, late menopause, childbirth, breastfeeding, oral contraceptives, diabetes, obesity, talcum powder, etc. However, the results of major studies are inconsistent, and the etiology is widely recognized and accepted as genetic factors [1]. At present, serum CA125 alone or in combination has been widely used in the prevention and screening of ovarian cancer, as well as the evaluation of efficacy after treatment and the monitoring of disease during follow-up, which has certain clinical application value. However, CA125 increases in other cancers, normal menstruation, endometriosis, etc., with high sensitivity and low specificity, and serum CA125 is normal in 50% of early ovarian cancer and 10% of advanced ovarian cancer [2]. Therefore, monitoring only serum CA125 levels may be challenging for patients with advanced ovarian cancer and those with normal CA125. In recent years, there have been many clinical studies on high and low grade serous carcinoma, but there is still a lack of immunohistochemical method to compare the protein expression of high and low grade serous carcinoma [3]. Based

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on this, this study aims to further explore the immunohistochemical expression levels of WT1 and P53 in low and high grade serous ovarian cancer, in order to provide theoretical basis for clinical diagnosis and treatment, as reported below.

2. Data and methods

2.1 Clinical Data

A retrospective analysis was performed on 34 patients who were admitted to the First Affiliated Hospital of Guangdong Pharmaceutical University for ovarian cancer, who underwent comprehensive staging surgery and were pathologically confirmed as ovarian epithelial malignant tumor. The patients were 36 to 65 years old, with an average age of (52.31±5.32) years old, and had 1-4 pregnancies. Mean pregnancy times (1.98±0.21); The average yield was (2.01±0.41). This study was approved by our ethics Committee.

2.2 Inclusion and exclusion criteria

Inclusion criteria: All patients were required to meet the 2014 WHO Classification of ovarian tumor [3]; Good communication skills; Patients undergoing surgical pathological examination. Exclusion criteria: Serious heart, liver, kidney and other important organs.Functional insufficiency; Serious mental disorder, or do not cooperate with the examination; Hypertension, diabetes, hyperlipidemia and other related basic diseases; allergic constitution; with severe infectious diseases; people with coagulation disorder.

2.3 Methods

The tissue sections were dewaxed, antigen repaired and sealed according to the instructions of the immunohistochemistry kit. The PBS instead of Primary antibody was used as negative control. Results: the slides were divided into +, ++ and ++ according to the dyeing depth, and the scores were defined as 0,1,2 and 3 points respectively. The staining area was scored as 0 to 0%~25%, 1 to 26%~50%, 2 to 51%~75%, and 3 to 76%~100%. The product of staining depth and staining area ≤ 3 points was defined as negative, and >3 as positive.

2.4 Statistical methods

SPSS 25.0 statistical software was used for analysis. X2 test or Fisher's exact probability analysis was used to compare the difference in protein expression of P53 and WT1 and clinical data of CA125 status. $P < 0.05$ was considered as statistically significant.

Table 1 Expression of P53 and WT1 in ovarian cancer of the two groups

Group	cases	P53		WT1	
		negative	positive	negative	positive
low-grade group	18	12（66.67）	6（33.33）	8（44.44）	10（55.56）
high-grade group	16	3（18.75）	13（81.25）	9（56.25）	7（43.75）
X2 值		6.254		7.154	
P		0.001		0.001	

3. Results

3.1 Expression of P53 and WT1 in the two groups of ovarian cancer

In ovarian cancer, the total positive rates of P53 and WT1 were 55.88% and 41.18%, the positive rate of P53 in the high-grade group was significantly higher than that in the low-grade group, while the positive rate of WT1 was lower than that in the low-grade group, the difference was statistically significant ($P < 0.05$). See Table 1 and Figure 1.

3.2 Relationship between CA125 status, P53 and WT1 in epithelial ovarian cancer

The WT1 (+) &P53 (+) group had a higher expression of CA125 than the non-expression

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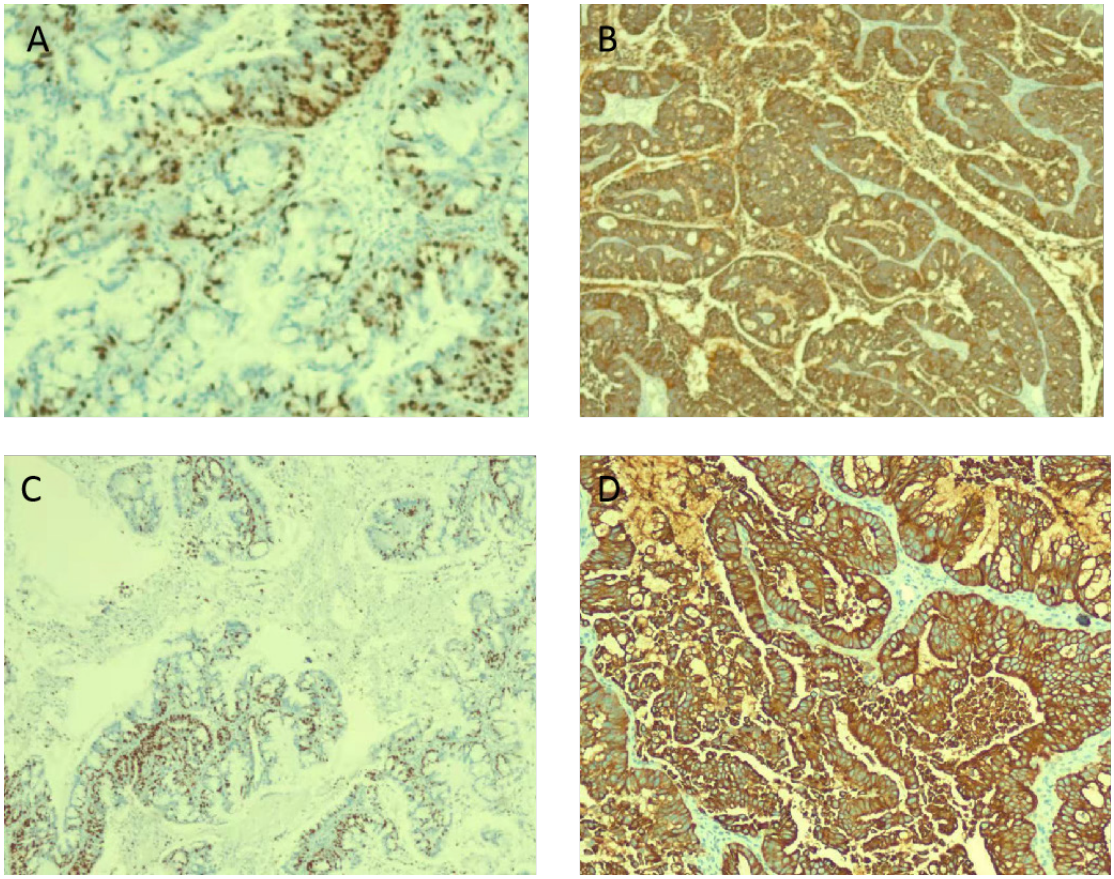

Figure 1 Expression of P53 and WT1 in the two groups of ovarian cancer (A, C: P53 was expressed in low grade and high grade ovarian cancer, B, D: WT-1 was expressed in low grade and high grade ovarian cancer)

Table 2 Relationship between CA125 status, P53 and WT1 in epithelial ovarian cancer

Group	cases	CA125		X2	P
		High level group	Low level group		
P53					
positive	19	14	5	15.214	0.001
negative	15	9	6		
WT1					
positive	17	15	2	8.471	0.001
negative	17	8	9		

group, with statistically significant difference ($P < 0.05$), as shown in Table 2. Figure 2.

3.3 Relationship between P53, WT1 and clinical features

WT1 protein was significantly correlated with pathological stage, degree of differentiation, pathological type and lymph node metastasis of epithelial ovarian cancer ($P < 0.05$), which could be used as an important prognostic factor for patients. P53 was not correlated ($P > 0.05$), as shown in Table 3.

4. Discussion

Ovarian cancer in the female reproductive tract malignancies in the incidence of the third, the fatality rate in the first, a serious threat to the

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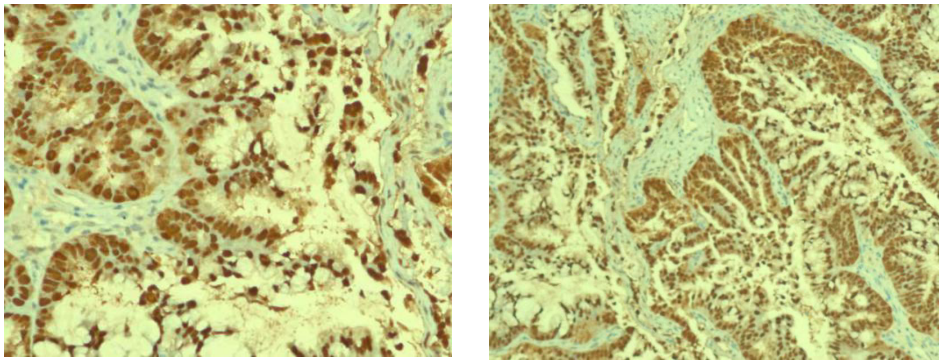

Figure 2 Positive expression of P53 and WT1 in epithelial ovarian cancer with high CA125 level group (left: P53, right: WT-1)

life of women. Its standard treatment for initial ovarian tumor cells to destroy the loss (PDS) and supplemented by postoperative platinum-based chemotherapy, for the first satisfaction evaluation cannot reduce tumor patients during operation, can be between again after neoadjuvant chemotherapy (NACT) ovarian tumor cells (IDS) to cut loss, although most patients can get better chemotherapy in the initial phase of chemotherapy response rates, However, about 70% of patients will relapse within 3 years, followed by two, three or multiple relapses. The treatment of secondary tumor cell reduction and second-line and multi-line chemotherapy are all faced with platinum-resistant and refractory, and finally there is no drug to treat, often with poor prognosis, posing great challenges to the treatment of ovarian cancer [4]. In addition, the diagnosis and treatment of EOC is still a major problem in the medical field at present, and it is also the direction we need to make efforts. A number of studies have shown that the status of

Table 3 Relationship between P53, WT1 and clinical features

Clinical parameters	Positive of P53（n=19）	Positive of WT1（n=17）
Age		
⩾ 55	8	10
＜ 55	11	7
Gender		
male	9	9
female	10	8
Differentiation		
Poorly differentiated	6	10
Moderately differentiated	5	5
High differentiation	8	2
Clinical staging		
I-II	11	5
III-IV	8	12
Lymph node metastasis		
NO	12	4
Yes	7	13

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HRD and other genes is related to the efficacy of chemotherapy and targeted therapy, and genetic testing can be used to guide clinical treatment. Therefore, the auxiliary role of genetic testing in the diagnosis and treatment of ovarian cancer should be fully played [5]. Many studies have demonstrated that targeted drugs for maintenance therapy of epithelial ovarian cancer can benefit patients in PFS or 0S, and EOC is expected to become a chronic disease in the future [6].

IHC has been widely used in the diagnosis and differential diagnosis of various diseases. Both IHC and gene testing are important auxiliary means for the diagnosis and treatment of diseases. They complement each other in the diagnosis and treatment of tumors, and also play a non-negligible role in the diagnosis and treatment of ovarian cancer. As an important tumor suppressor gene, p53 participates in and maintains the normal cell cycle, and has been proved to be closely related to the poor prognosis of colon cancer, breast cancer, head and neck tumor, leukemia and other malignant tumors [7]. According to relevant literature, P53 can inhibit excessive growth of cells, but the mutant P53 can promote tumor growth due to its lack of ability to control cell proliferation and induce apoptosis [8]. Many domestic and foreign scholars [10-11] have studied the expression and significance of P16 and P53 in ovarian serous tumors. This study showed that the positive expression rate of P16 and P53 in the high-grade group was significantly higher than that in the low-grade group, which can provide reference for clinical diagnosis and prognosis evaluation of ovarian serous tumors. P53 expression is significantly enhanced in ovarian cancer patients and is associated with lymph node metastasis [12]. In this study, no statistical differences were found in family history, lymph node metastasis and differentiation degree between p53 and EOC patients, which may be due to selection bias in sample selection. In addition, the negative or positive expression of p53 was only analyzed this time, and the difference in expression level between p53 positive patients was not specifically compared. WT1 may inhibit e-cadherin expression by activating ERK signaling pathway, and loss of WT1 significantly inhibits cell migration and invasion, reversing epithelial-mesenchymal transformation, and preventing OC cell metastasis [13]. WT1 expression is associated with tumor stage, FIGO stage and poor survival rate, and plays an important role in tumor invasion and metastasis, affecting treatment effect and prognosis, and is a biomarker of poor prognosis [14]. Statistical results of this experiment showed that WTI expression was significantly correlated with pathological type, FIGO stage and differentiation degree, and lymph node metastasis, which was consistent with the research results of YunHan et al. [15]. These results suggest that WT1 expression is significantly correlated with prognosis of patients with EOC, and may be a potential therapeutic target for ovarian cancer. In addition, the proportion of positive expression of WT1 in the high-grade group was significantly lower than that in the low-grade group, because WT1 is a tumor suppressor gene that can encode zinc finger like polypeptide isolated from Wilms tumor cells. Studies have found that almost all primitive cells can continuously express WT1, and WT1 nuclear protein can usually be detected in most primitive cells, so its expression level is higher in tumor cells with low level of tissue differentiation [16].

5. Conclusion

The expression level of P53 is higher in high-grade serous ovarian cancer, while the expression level of WT1 is lower. Therefore, P53 and WT1 can be used to diagnose high-grade serous ovarian cancer, and WT1 has higher diagnostic value for low-grade serous ovarian cancer. The CA125 status was significantly correlated with the expression of P53 and WT1.

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