Serum CA125, HE4 and ROMA index in elderly patients with ovarian cancer

Yan-Jun Wang, Xiu-Juan Du
Department of Gynaecology, Baoji City Center Hospital, Baoji, Shaanxi 721008, China

Objective: To study the value of serum tumor markers, carbohydrate antigen 125 (CA125), human epididymis secretory protein 4 (HE4) and ovarian cancer risk factor (ROMA) index in elderly patients with ovarian cancer, so as to provide a choice for clinical diagnosis. Methods: A total of 110 cases of ovarian cancer treated in our hospital in December 2017-December 2015 were selected as malignant group. In addition, 120 cases of benign ovarian tumors in the same period were selected as the benign group, and 92 healthy women who came to the hospital for health examination were selected as the control group. Serum HE4, CA125 levels and positive rates were detected by microparticle enzyme immunochemiluminescence assay, and ROMA index values were combined to assess the risk of ovarian cancer. Results: Malignant group serum CA125, HE4 level and ROMA index were significantly higher than those in the benign group and the control group, the level of CA125 in positive group was higher than control group, but the difference in level of HE4 and ROMA index between benign group and control group was not statistically significant. The positive rates of serum CA125, HE4 and ROMA index in malignant group were 76.4%, 92.7%, 96.4%, which were significantly higher than those of HE4. The negative predictive value, positive predictive value, specificity and sensitivity of the combined ROMA index were higher than those of single diagnosis. Conclusions: Serum CA125, HE4 and ROMA index in elderly patients with ovarian cancer are significantly higher than those in elderly patients with benign ovarian tumors and healthy women. The combined diagnosis is the highest, with Gao Min’s high sensitivity and specificity, which can be popularized in clinical practice.

1. Introduction

As one of the most common three malignant tumors in clinical women, the early diagnosis of ovarian cancer lacks the specificity[1]. Studies have shown that the 5 year survival rate of ovarian cancer patients is only 25%-30%, especially for elderly patients with ovarian cancer. Because of decreased body resistance, the incidence of ovarian cancer is significantly increased, and the survival rate is significantly reduced[2]. At present, clinical ovarian cancer serum tumor markers including common carbohydrate antigen 125 (CA125), carbohydrate antigen 199 (CA199) and carcinoembryonic antigen (CEA), which has been confirmed specific and sensitivity is the highest CA125[3]. Studies have shown that CA125 can effectively evaluate the diagnosis, prognosis and recurrence of epithelial ovarian cancer, but the sensitivity of CA125 single application is low. About 20% of patients show low expression, especially 50% of patients with early ovarian cancer can have low expression[4]. As a protein found in the distal epithelia of the epididymis, whey acidic 4- two sulphide Center (WFDC) protein, human epididymal secretory protein 4 (HE4) can effectively diagnose ovarian cancer[5]. However, there are few reports on the combined diagnosis of the two, and the domestic research of the combined risk model is still less[6]. Therefore, we specially study the value of the changes of serum tumor markers CA125, HE4 and ROMA index in elderly ovarian cancer patients, and provide a choice for clinical diagnosis.
2. Materials and methods

2.1. Clinical data

A total of 110 cases of ovarian cancer treated in our hospital in December 2017-December 2015 were selected as malignant group. In addition, 120 cases of benign ovarian tumors in the same period were selected as the benign group, and 92 healthy women who came to the hospital for health examination were selected as the control group. The diagnosis of ovarian benign and malignant tumors accorded with the following criteria: (1) all of them were verified by histopathology after laparoscopic or surgical resection; all of them met the diagnostic criteria for clinical symptoms and signs of ovarian tumors; All patients or their families voluntarily participated in the study, and signed informed consent. The research program has been approved by the medical ethics committee of the hospital. The two groups were compared in age, education and other general data, the difference was not statistically significant ($P > 0.05$), and it was comparable.

2.2. Research methods

The levels of HE4 and CA125 in serum were detected by microparticle enzyme immunochemiluminescence (PL) in the three groups, and the risk of ovarian cancer was evaluated by ROMA finger value. A total of 5 mL venous blood were collected in the early morning, centrifugated at 3 000 r/min for 10 min, stored at -80°C for use. The CA125 was detected by Abbott ARCHITECTi 2000SR automatic chemiluminescence analyzer. The HE4 was detected by the ELISA-HE4 kit provided by Fujirebio Diagnostics in Sweden, and Statx Fax-2100 (AWARENESS Company) was used in the enzyme labelling instrument. On the premise of specificity of HE4 and CA125 higher than 75%, ROMA formula was used. For women with epithelial ovarian cancer risk assessment: premenopausal women aged 13.1% showed high risk, low risk <13.1%; postmenopausal women aged 27.7% showed high risk, low risk <27.7%.

2.3. Statistical analysis

Data analysis was performed by SPSS 19 software, the paired t test for group measurement data, the sample t test for measurement data between groups, $\chi^2$ test for count data rate (%), with $P < 0.05$ as the significant difference.

3. Results

3.1. Serum CA125, HE4 and ROMA indexes

Serum CA125, HE4 level and ROMA indexes in three malignant groups were significantly higher than those in the benign group and the control group ($P < 0.05$), the level of CA125 positive group was higher than control group ($P < 0.05$), but the differences in HE4 and ROMA index between benign group and control group was not statistically significant ($P > 0.05$) (Table 1).

3.2. Positive rates of serum CA125, HE4 and ROMA index in two groups of subjects

The positive rates of serum CA125, HE4 and ROMA index in malignant group were 76.4%, 92.7%, 96.4%, which were significantly higher than those in benign group (28.3%, 18.3%, 15%), ($P < 0.05$) (Table 2).

3.3. Comparison of diagnostic efficacy of serum CA125, HE4 and ROMA index in serum

The negative predictive value, positive predictive value, specificity and sensitivity of CA125 were all lower than those of HE4. The negative predictive value, positive predictive value, specificity and sensitivity of the combined ROMA index were higher than those of single diagnosis. It is shown in Table 3.

---

**Table 1.** Serum CA125, HE4 and ROMA indexes.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>CA125 (U/mL)</th>
<th>HE4 (pmol/L)</th>
<th>ROMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant group</td>
<td>110</td>
<td>437.6±102.8</td>
<td>305.6±79.9</td>
<td>83.4±24.7</td>
</tr>
<tr>
<td>Benign group</td>
<td>120</td>
<td>44.3±16.9</td>
<td>36.2±10.3</td>
<td>7.2±3.0</td>
</tr>
<tr>
<td>Control group</td>
<td>92</td>
<td>13.3±5.7</td>
<td>35.9±9.8</td>
<td>4.1±2.6</td>
</tr>
</tbody>
</table>

**Table 2.** Serum CA125, HE4 and ROMA index positive rates.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>CA125 (U/mL)</th>
<th>HE4 (pmol/L)</th>
<th>ROMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant group</td>
<td>110</td>
<td>84(76.4)</td>
<td>102(92.7)</td>
<td>106(96.4)</td>
</tr>
<tr>
<td>Benign group</td>
<td>120</td>
<td>34(28.3)</td>
<td>22(18.3)</td>
<td>18(15.0)</td>
</tr>
</tbody>
</table>

$\chi^2$ test: $P < 0.05$
4. Discussion

At present, the mortality rate of ovarian cancer ranks the leading number in gynecology. Data show that there are about 22,340 new cases of ovarian cancer in the United States every year, and about 15,280 of them die from ovarian cancer[7]. Studies have also suggested that although the ovarian cancer patients 5 years survival rate is less than 30%, but if the patients with ovarian cancer early diagnosis and effective treatment, the five-year survival rate can be as high as 85%, and advanced ovarian cancer five years survival rate is only 20%[8,9]. Therefore, the early detection and early diagnosis of elderly ovarian cancer appear to be very traditional Chinese medicine, but it is worth noting that, because of the deep anatomical position of the ovary and the early clinical symptoms, 80% of the ovarian cancer patients have been diagnosed with advanced[10].

Serum CA125, HE4 level and ROMA indexes in three malignant groups were significantly higher than those in the benign group and the control group (P<0.05), the level of CA125 positive group was higher than control group (P<0.05), but the differences in HE4 and ROMA index between benign group and control group was not statistically significant (P>0.05). Some studies have suggested that as a ovarian epithelial carcinoid associated antigen, CA125 in serum is generally less released or not released. Once ovarian malignant lesions occur, CA125 will be released by embryonic like epithelial cells, so it has a good sensitivity[11]. It is also reported that the serum CA125 of some patients with benign gynecologic lesions can also be increased, so the early diagnosis of the patients is less sensitive[12].

As the whey acidic four - two sulfide core (WFDC) protein family, HE4 is also less released in normal ovarian epithelial tissue, but early ovarian malignant tissue can be released. Once in the middle and late stage, it can also be released to serum[8,11] in high level. The difference between the two groups is also considered. There is no significant difference in serum HE4 between healthy ovarian disease patients and healthy people, and the specificity and sensitivity of HE4 are slightly higher than those of CA125[13]. In this study, the positive rate of serum CA125, HE4 and ROMA index in malignant group were 76.4%, 92.7%, 96.4%, which were higher than those in benign group (28.3%, 18.3%, 15%, respectively). The difference was statistically significant (P<0.05). The results of the study were similar to the results of this article. It was found that the positive rate of ROMA index was correlated with the state and age of menopause, and the positive rate of HE4 was also associated with age[14]. It is also reported that ROMA index does not need any other operation. It is quicker, more convenient and more accurate and objective to detect HE4 and CA125 after collecting blood from patients. Therefore, it is recommended[15]. But it is worth noting that the sample size and scale of research are relatively small. If we get more accurate conclusions, we need to have a comprehensive, extensive and multi center validation. In the study, the negative predictive value, positive predictive value, specificity and sensitivity of CA125 were lower than those of HE4. The negative predictive value, positive predictive value, specificity and sensitivity of combined ROMA index were higher than that of single diagnosis. Studies have shown that although CA125 is the first choice of tumor markers for diagnosing ovarian cancer, its specificity is lower[7] because it is susceptible to gynecological benign diseases and menstrual cycle. Therefore, the prediction model of ovarian cancer risk combined with HE4 and CA125 can be used as an important indicator for the diagnosis and differential diagnosis of ovarian benign and malignant tumors[11]. Of course, there are studies that although the sensitivity and specificity of ROMA index is the highest, the other HE4 has no obvious advantage compared with other[14], which may be related to less cases.

To sum up, serum CA125, HE4 levels and ROMA index in elderly patients with ovarian cancer are significantly higher than those in elderly patients with benign ovarian tumors and healthy women. The combined diagnosis is the highest, with Gao Min's high sensitivity and specificity, which can be popularized in clinical practice.

References


