Performance Comparison of CA125 and the Combination of the Other Serum Biomarkers for the Early Detection of the Ovarian Cancer

Hye-Jeong Song¹,³, Jong-Gi Lim¹, Chan-Young Park¹,³, Yu-Seop Kim¹,³ and Jong-Dae Kim¹,³

¹ Dept. of Ubiquitous Computing, Hallym University, 1 Hallymdaehak-gil, Chuncheon, Gangwon-do, 200-702 Korea
² Dept. of Computer Engineering, Hallym University, 1 Hallymdaehak-gil, Chuncheon, Gangwon-do, 200-702 Korea
³ Bio-IT Research Center, Hallym University, 1 Hallymdaehak-gil, Chuncheon, Gangwon-do, 200-702 Korea

{hjsong, dlawhdr1, cypark, yskim01, kimjd}@hallym.ac.kr

Abstract. In this study, we compared the diagnostic performance of the cancer antigen 125 (CA125), a biomarker that is frequently used in the clinic, both alone and in combination with other biomarkers, for the early detection of ovarian cancer. The serum samples were from Korean women, including 202 patients with benign pelvic masses and 52 ovarian cancer patients. The other markers used in combination with CA125 were M1, M2, M3, and M4, which have previously shown high diagnostic performance. We determined the biomarker levels by using Luminex assay. Logistic regression was used to assess the multivariate model performance by using the area under the curve (AUC) of the receiver operating characteristic (ROC) curve. The AUC of CA125 in early ovarian cancer was 69.96% and that of the CA125 + M2 combination was 76.61%. From this study, we showed better diagnostic performance by using other markers in combination with CA125 than by using CA125 alone.

Keywords: Biomarker, Multianalyte, Ovarian Cancer, Logistic Regression

1 Introduction

The symptoms of ovarian cancer in an early stage are not noticeable, and it is hard to distinguish the benign tumor from cancer using nonradioactive diagnosis such as ultrasonography. If ovarian cancer is detected early, a 50–95% five-year survival rate can be assured. However, if detected at later stages, the survival rate is less than 25%. This is important, because almost no subjective symptoms are present for early ovarian cancer, and most cases are detected after stage III. Therefore, a diagnostic method to detect ovarian cancer early is critically required [1-2].

CA125 is a common tumor biomarker that is used to screen for ovarian cancer from
blood samples. However, since the sensitivity of this biomarker is low for detecting the early cancer stages, combining it with other methods, such as ultrasound or other markers, is necessary [1-2].

Currently, many studies have shown that using CA125 in combination with other biomarkers result in an increase in the diagnostic performance [2-4]. In particular, Moore et al. combined CA125 and the human epididymis protein 4 (HE4), analyzed the markers by using Risk of Ovarian Malignancy Algorithm, and showed improved performance [3].

In this study, we aimed to assess the diagnostic performance of the multivariate model by combining CA125 with other biomarkers (M1-M4) as shown in previous studies to obtain high diagnostic performance. Logistic regression was used to assess the multivariate model performance by using the area under curve (AUC) of the receiver operating characteristic (ROC) curve.

2 Method

The serum samples from 254 Korean women were collected from 2 hospitals. Sera from 21 patients with early stage(I/II) and 33 with late stage(III/IV) epithelial ovarian cancer, 124 patients with benign pelvic masses, were analyzed 5 proteins using Luminex xMap technology. The multivariate model for a combination of the 2 markers was calculated using logistic regression, to evaluate diagnostic performance by using the AUC of the ROC curve. The performance was evaluated for the ovarian cancer patients, including early- and late-stage cases, and benign pelvic mass patients by comparing the ROC curves and AUC. The performance between early-stage ovarian cancer and benign pelvic mass were compared.

3 Results

Table 1 and Figure 1 show the AUC and ROC curves for the total (all stages) ovarian cancer group vs. benign pelvic mass group. The AUC for CA125 alone was 80.01%; CA125 + M1, 80.71%; CA125 + M2, 74.39%; CA125 + M3, 80.27%; and CA125 + M4, 79.44%.

<table>
<thead>
<tr>
<th>Marker</th>
<th>AUC</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA125</td>
<td>80.01</td>
<td>70.88–88.67</td>
</tr>
<tr>
<td>CA125,M1</td>
<td>80.71</td>
<td>71.94–87.75</td>
</tr>
<tr>
<td>CA125,M2</td>
<td>74.39</td>
<td>63.15–83.26</td>
</tr>
<tr>
<td>CA125,M3</td>
<td>80.27</td>
<td>71.65–87.19</td>
</tr>
<tr>
<td>CA125,M4</td>
<td>79.44</td>
<td>70.35–86.08</td>
</tr>
</tbody>
</table>
Table 2 and Figure 2 indicate the AUC and ROC curve for early stages (I/II) ovarian cancer group vs. benign pelvic mass group. The AUC for CA125 alone was 70.66%; CA125 + M1, 62.10%; CA125 + M2, 74.23%; CA125 + M3, 70.03%; and CA125 + M4, 71.43%.

In both the experiments, the AUC for CA125 in combination with the other markers was higher than that for CA125 alone, and additionally, the ROC curves showed high sensitivity at high specificity.

Table 2. AUC: stages I/II vs. benign

<table>
<thead>
<tr>
<th>Marker</th>
<th>AUC</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA125</td>
<td>70.66</td>
<td>55.55–81.62</td>
</tr>
<tr>
<td>CA125,M1</td>
<td>62.10</td>
<td>44.87–76.75</td>
</tr>
<tr>
<td>CA125,M2</td>
<td>74.23</td>
<td>57.85–86.21</td>
</tr>
<tr>
<td>CA125,M3</td>
<td>70.03</td>
<td>56.59–82.29</td>
</tr>
<tr>
<td>CA125,M4</td>
<td>71.43</td>
<td>57.54–82.54</td>
</tr>
</tbody>
</table>

4 Conclusion

In this study, we assessed the diagnostic performance of CA125 alone and in combination with other biomarkers for early-stage detection of ovarian cancer.

The results show that AUC of CA125 in combination with other biomarkers, most of the marker combinations indicated diagnostic performances superior to that of CA125 alone, but some marker combinations only performed similarly. The ROC curves also showed high sensitivity at high specificity. These results show that by
using a multivariate model the diagnostic efficiency can be improved compared to using CA125 alone. Further, the degree improvement is particularly high for the detection of early-stage ovarian cancer.

![ROC curve](image)

**Fig.2.** ROC : stage I/II vs. benign

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**References**