Multiparametric Analysis of Six Tissue kallikreins and CA125 for Ovarian Cancer Diagnosis

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ABSTRACT:

Introduction: Early ovarian cancer diagnosis is very difficult due to absence of clinical symptoms and lack of sensitive biomarkers or imaging techniques for visualizing small tumors. Early ovarian cancer is highly curable, while late diagnosis is associated with poor patient prognosis.

Purpose: To evaluate the diagnostic value of six newly discovered ovarian cancer biomarkers (human kallikreins 5, 6, 7, 8, 10 and 11) in combination with the traditional ovarian cancer biomarker, CA125.

Methods and Material: Serum samples were collected pre-surgically from four groups: 100 women with stage I-II cancer (early cancer), 100 women with stage III-IV cancer (late cancer), 200 healthy women and 100 women with benign gynecological conditions. Samples were analyzed by conventional ELISA methodology for kallikreins and CA125.

Results: We found that CA125 correlated strongly with all measured kallikreins in the samples of ovarian cancer patients, the highest correlation being with hK8 (r=0.93). Among the kallikreins, the most significant correlation was observed between hK6 and hK8 (r=0.80) and hK6 and hK11 (r=0.81). CA125 and kallikrein values do not correlate in healthy women or in ovarian cancer patients with CA125 levels below 30 U/ml. We then constructed receiver operating characteristic (ROC) curves for each of the candidate biomarkers and the areas under the curve (AUC) were as follows: CA125 = 0.87; hK5 = 0.71; hK6 = 0.78; hK7 = 0.81; hK8 = 0.91; hK10 = 0.63 and hK11 = 0.80.

Discussion: hK8 was the most powerful, single ovarian cancer biomarker for discriminating between ovarian cancer versus patients with benign gynecological diseases and normal controls (AUC=0.91). Among all other combinations, the highest area under the curve was obtained when hK8 and hK11 were combined (AUC = 0.93). ROC analysis for all markers in Ovarian cancer versus Benign + normal with CA125 < 30U/ml

CONCLUSION: All above-mentioned kallikreins have diagnostic value for ovarian cancer.

This is augmented by combination with CA125

ROC analysis for all markers in Early cancer versus Benign + normal

CA125 correlated strongly with all measured kallikreins in ovarian cancer patients

The highest correlation being with hK8 (r=0.93)

Amongst the kallikreins, the most significant correlation was between hK6 and hK8 (r=0.80) and hK6 and hK11 (r=0.81)

No correlation was demonstrated between CA125 and kallikreins in healthy women or in ovarian cancer patients with CA125 <30U/ml

AUC on ROC curves were as follows: CA125 = 0.87; hK5 = 0.71; hK6 = 0.78; hK7 = 0.81; hK8 = 0.91; hK10 = 0.63 and hK11 = 0.80

hK8 was the most powerful, single ovarian cancer biomarker to discriminate ovarian cancer from benign gynecological diseases and normal controls (AUC=0.91)

hK8 was the single, most powerful biomarker for the detection of early stage ovarian cancer (AUC=0.86, in comparison to 0.81 for CA125)

In patients with CA125 < 30 U/ml, again the most informative, single biomarker was hK8 (AUC=0.81).

The multivariate analysis of hK6 and hK8 increased the AUC to 0.85 in this group of patients.

Among all other combinations, the highest area under the curve was obtained when hK8 and hK10 were combined (AUC = 0.93).

All above-mentioned kallikreins have diagnostic value for ovarian cancer

This is augmented by combination with CA125

hK8 was the best performing biomarker, followed by hK7, hK11, hK5, hK6 and hK10

Multivariate analysis of kallikreins with CA125 may improve sensitivity and specificity for diagnosis of early ovarian cancer

REFERENCES: