Abstract:

Human kallikrein 5 (hK5; encoded by the KLK5 gene) is a secreted serine protease expressed in hormonally regulated tissues, including the breast and ovary. We have previously reported regulation of the KLK5 gene by estrogens and progestins and its clinical value as a marker of poor prognosis in breast and ovarian cancers. We thus hypothesized that hK5 may represent a potential biomarker for ovarian carcinomas, at the protein level. Using a newly developed ELISA, hK5 levels were quantified (nanograms per milligram of total protein) in 22 low malignant potential (LMP) and 132 epithelial ovarian tumors and correlated with various clinicopathological variables and outcome [progression-free survival (PFS), overall survival (OS)].

hK5 concentration in LMP tumors ranged from 0 to 2.3 ng/mg (mean = 0.24) and from 0 to 220 ng/mg (mean = 3.35) in ovarian tumor cytosols (p = 0.002). Using a cutoff value of 0.15 ng/mg, 60% of ovarian tumors were categorized as hK5 positive. We found a strong correlation between patients with hK5-positive tumors and disease stages III/IV and grade 3 tumors (all p < 0.05). Univariate survival analysis revealed that hK5-positive patients had a significantly shorter PFS and OS (p < 0.05). Kaplan-Meier survival curves further confirmed an increased risk of relapse and death in women with hK5-positive tumors (p = 0.015 and p
Multivariate analysis indicated that the prognostic value of hK5 was not independent from other parameters in the entire group of patients. When stratified by tumor grade (G1/2 vs. G3) and debulking success (optimal vs. suboptimal), univariate and multivariate analyses demonstrated that hK5 was an independent indicator of poor prognosis for patients with grade 3 tumors and with optimal debulking (p < 0.05). In patients with disease stage I/II versus III/IV, hK5 positivity was independently associated with a shorter PFS (p = 0.046) and marginally decreased OS (p = 0.08), in multivariate analysis. Lastly, we observed a fairly weak, positive, but statistically significant correlation between the expression levels of tissue hK5 and tissue CA125 (rs = 0.297; p < 0.001). Our findings provide evidence for an association between hK5 and more aggressive forms of epithelial ovarian cancer.

Stichworte: Serine proteases; Kallikreins; Cancer biomarkers; Prognostic markers; Ovarian cancer; Human kallikrein 5

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