Abstract:

PURPOSE: Proteolytic factors of the human tissue kallikrein (hK) family and the plasminogen activation system play a key role in tumor progression in various malignancies. We determined antigen levels of urokinase-type plasminogen activator (uPA), its inhibitor PAI-1, and hK5-8, hK10, hK11, and hK13 by ELISA in primary tumor tissue extracts of 142 International Federation of Gynecology and Obstetrics (FIGO) I to IV ovarian cancer patients (median follow-up 41 months). RESULTS: After radical surgery, absence of macroscopically visible residual tumor (RT) was achieved in 72 patients; all patients received postoperative platinum-containing chemotherapy. Significant univariate predictors of poor progression-free survival (PFS) were RT (>0), FIGO stages (III/IV versus I/II/III), ascites volume>500 mL, nodal status, and the difference between PAI-1 and uPA (fractionally ranked). In multivariate analysis, significant independent factors for poor PFS were RT (HR, 4.53) and low hK11 fractional rank (HR, 0.30). Univariate predictors of poor overall survival were RT, FIGO stages, nodal status, ascites volume, nuclear grade, and low hK10 and hK13. In multivariate analysis, significant independent factors for poor overall survival were RT (HR, 7.49), ascites (HR, 1.97), and low hK10 (HR, 0.196). We constructed a multivariate scoring model estimating RT probability, based on ascites [odds
ratio (OR, 13.1], nuclear grade (OR, 2.92), hK6 (OR, 8.54), and hK13 (OR, 0.14), with good in-sample predictive performance (area under receiver operating characteristic, 0.833). CONCLUSIONS: In view of risks and benefits of radical surgery, such a score could support preoperative risk stratification and identify candidates for alternative therapeutic strategies. These results highlight the distinct roles of the hKs for different disease end points in ovarian cancer and their potential to support individualized therapy decisions.

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