

## Impact of Proteolytic Factors on Surgical Success and Survival in Ovarian Cancer

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**Abstract:** **Background:** Proteolytic factors of the plasminogen activation system and the human tissue kallikreins (hK4-15) have been implicated in tumor progression in ovarian cancer. **Methods:** In 142 ovarian cancer patients FIGO 1-4 operated on between 1985 and 1999 in the Dept. of OB&GYN of Munich Technical University (median follow-up 33 months), uPA, PAI-1, hK5-8,10,11,13 were measured by ELISA in primary tumor tissue extracts; 72 patients were optimally debulked. All patients received postoperative platinum-containing chemotherapy. **Results:** In univariate Cox models of progression free survival (PFS) including these measurements (fractionally ranked) plus age, pN, grading, ascites volume, and residual tumor, the strongest single predictor was presence of residual tumor (HR=4.37; 2.55-7.47). pN (HR=1.94; 1.12-3.38) and ascites volume (HR=2.37; 1.45-3.88) were also separately significant, but none of the others. In multivariate analysis of PFS, residual tumor (HR=4.76; 2.75-8.23) and hK11 (HR=0.30; 0.12-0.77) both entered the model, higher values of hK11 being associated with improved survival. Due to the strong impact of residual tumor on PFS, any factor influencing residual tumor, thus predicting surgical outcome could also be of considerable clinical interest. hK5 and 13 had significant impact on residual tumor. In univariate logistic regression, higher hK5 significantly predicted poor surgical outcome (OR=1.52; 1.25-16.6). In multivariate analysis, both hK5 and hK13 entered the model: Higher hK5 was strongly associated with residual tumor (OR=6.4; 1.63-25.0), whereas higher hK13 was associated with better surgical outcome (OR=0.16; 0.03-0.74). A ROC curve from this model classifies surgical success with AUC=0.65 (0.56-0.75). For OS, residual tumor (HR=8.7; 4.1-18.3) and hK10 (HR=0.21; 0.07-0.64) were significant in multivariate analysis. hK13 (HR=0.27; 0.08-0.85) was significant in univariate analysis only. Higher hK10 and hK13 are associated with better OS. **Conclusions:** Our results demonstrate that proteolytic factors are linked to tumor aggressiveness in ovarian cancer and have the potential to support clinical therapy decisions. Validation in independent data sets is currently being performed.