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High preoperative plasma concentration of soluble urokinase plasminogen activators receptor (suPAR) predicts shorter overall survival in patients with ovarian cancer

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Introduction

Ovarian cancer is the leading cause of death in gynecological cancer and the fourth leading cause of death in cancer in general among women 45-64 years of age among Swedish women. The five-year survival is less than 40%, despite extensive surgery combined with chemotherapy. On the other hand, five-year survival rate for stage I is 95%. To diagnose ovarian cancer in early stage should lower the fatality rate, but there are no accurate screening tests available. The most useful tumor marker, CA125, is not reliable as a single marker because of its low sensitivity in early stage ovarian cancer. Also, combinations of ultrasound, CA125, and other markers have been found insufficient, in particular with respect to stage I tumors. A battery of tumor markers in peripheral blood would be of great help in screening for ovarian cancer.

Aim

The purpose of this study was to evaluate the plasma level of different forms of soluble urokinase plasminogen activator (suPAR) as discriminators between malignant and benign ovarian tumors, and as prognostic markers in patients with ovarian cancer.

Material and Methods

The different suPAR forms were measured in preoperative plasma samples obtained from 335 patients with adnexal lesions using three different time-resolved fluorescence assays (TR-FIAs) TR-FIA 1 measuring full length suPAR, suPAR(I-III), TR-FIA 2 measuring suPAR(I-III) and the cleaved suPAR(II-III), and finally TR-FIA 3 measuring the liberated uPAR(I). Tumors were classified as benign (n=211), borderline malignant (n=30), well (G1, n=19), moderately (G2, n=15), and poorly differentiated malignant (G3, n=60).

Results

The best area under curve (AUC) to discriminate between malignant (borderline and invasive tumors, n=102) and benign ovarian tumors (n=176) was found using the product of the suPAR(I-III)+(II-III) and CA125, AUC 0.90 (CI 95% 0.86-0.94). High levels of both suPAR(I) (HR 2.7 95%CI 1.32-5.55 p=0.006) and suPAR(I-III) (HR 2.6 95%CI 1.24-5.29 p=0.011) were independent pre-operatively predictors of poor prognosis in multivariate Cox regression analyses with CA125 and age. Analyzing suPAR(I), suPAR(I-III), CA125, age, stage, grade and residual tumor in conditional forward multivariate analyses including at the level of 0.05, high levels of suPAR(I) and residual tumor > 1cm were independent risk factors.

Conclusions

High concentration of plasma suPAR(I) and suPAR(I-III) were independent pre-operative marker for poor prognosis in patients with ovarian cancer. To differentiate between malignant and benign ovarian lesions the product of suPAR(I-III)+(II-III) and CA125 is one of the best plasma indicators published so far.