

Streszczenie w języku angielskim

OBJECTIVE: The aim of the study was to evaluate the prognostic value of selected hemostatic factors, including TF and TFPI and fibrinolysis: t-PA, u-PA and PAI-1 and the effect of adjuvant therapy on these coagulation and fibrinolysis components in invasive breast cancer. Additionally, a comparative analysis of selected hemostatic factors was performed in relation to demographic, anthropometric and clinicopathological parameters.

MATERIAL AND METHODS: In **publication number 1**, the observational and prospective study included 41 women aged 45-69 years diagnosed with primary, unilateral, invasive breast cancer without distant metastases. Patients in the study population were followed from breast cancer diagnosis to the date of breast cancer relapse or death. The study assessed the activity and concentration of the basic elements of the fibrinolytic system: t-PA, u-PA, PAI-1, PAI-1/t-PA and PAI-1/u-PA using the enzyme immunoassay technique. In **publication number 2**, the study included 60 patients with primary, invasive breast cancer with a median age of 56 years. The study assessed the activity and concentration of tissue factor (TF), tissue factor pathway inhibitor (TFPI), tissue plasminogen activator (t-PA) and plasminogen activator inhibitor 1 (PAI-1). Blood samples from the patients were collected twice - 24 hours before the planned surgery and 8 months after the tumor removal surgery. During this period, the patients underwent complementary anticancer therapy.

RESULTS: Based on the statistical analysis performed, **in the first publication** using the ROC curve, t-PA was considered to be the strongest predictor of disease recurrence among the tested fibrinolytic elements, with a concentration of 1.37 ng/ml with a specificity of 65.6% and a sensitivity of 88.9%. as the best cut-off value to distinguish patients with disease recurrence from patients without cancer recurrence. Using the analysis of Kaplan-Meier curves and the long-rank test, it was observed that patients with PAI-1 activity below 3.04 U/ml had a significantly longer disease-free survival compared to patients with PAI-1 activity above 3.04 U/ml. In turn, in the context of the t-PA biomarker, the probability of survival without cancer recurrence was significantly lower in patients with t-PA concentration below 1.37 ng/ml or 1.41 ng/ml (depending on the cut-off point used - median or Youden index). According to these Cox regression results, patients with a t-PA concentration higher than 1.41 ng/ml are 90% less likely to experience breast cancer recurrence compared to patients with a lower t-PA concentration. **In the second publication**, an extensive statistical analysis showed

that combined adjuvant therapy significantly increased plasma TF and PAI-1 concentrations, as well as TF and TFPI activity, but significantly decreased t-PA concentrations. Additionally, using the ROC curve, it was identified that pre-operative TF activity with a cut-off value of 13.32 U/ml and pre-operative PAI-1 concentration with a cut-off value of 36.46 ng/ml were the strongest predictors of cancer recurrence. In terms of comparison of individual post-treatment biomarkers, t-PA turned out to be the best prognostic factor for cancer recurrence after adjuvant treatment. The t-PA level of 3.13 ng/ml with a specificity of 59.2% and a sensitivity of 90.9% could reliably predict the effects treatment of breast cancer patients. Kaplan-Meier curves showed that high pre-treatment TF and PAI-1 concentrations and high pre-treatment TF activity corresponded to significantly shorter disease-free and overall survival. In turn, patients with higher t-PA antigen concentration after treatment had a worse prognosis in terms of disease-free survival and overall survival.

CONCLUSIONS: The conducted research obtained results confirming a significant relationship between hemostatic factors and breast cancer progression. These studies have proven that low plasma t-PA concentration is a strong prognostic factor predicting the risk of cancer recurrence. Additionally, higher pre-operative TF activity and PAI-1 levels and higher post-treatment t-PA levels have been shown to significantly increase the probability of breast cancer recurrence and death from systemic metastatic disease. As a highlight, it was observed that the use of combined adjuvant therapy in patients with primary unilateral breast cancer increased the plasma concentrations of TF and PAI-1 and the activity of TF and TFPI, and at the same time decreased the concentration of t-PA. Taking into account the role of hemostatic biomarkers and the increased impact of anticancer treatment on hypercoagulability and hypofibrinolysis, it can be suggested that breast cancer patients treated with adjuvant therapy are at a higher risk of developing venous and arterial thromboembolic complication.