Increased Thrombin Activatable Fibrinolysis Inhibitor (TAFI) and Plasminogen Activator Inhibitor-1 (PAI-1) levels in patients with a venous thromboembolism

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Background Ample research is done towards the relation between impaired fibrinolytic activity and venous thromboembolisms (VTE). Whether the association is causal or coincidental is undecided since most of the results are conflicting. The lack of standardization, the broad range of used methodology, the different study designs and the presence of confounding cardiovascular risk factors are possible reasons for these inconsistent results.

Goal Analyze the role of fibrinolysis in patients with a VTE by comparing thrombin activatable fibrinolysis inhibitor (TAFI) and plasminogen activator inhibitor-1 (PAI-1) levels of VTE patients with healthy controls (HC) thereby adjusting for different confounding factors.

Methods Plasma of 102 VTE patients (57% men and 43% women) was collected after the VTE event in a time range of 10 to 2868 days with a median of 163 days and compared with plasma of 113 HC (39% men and 61% women). Patients had either a deep vein thrombosis (DVT), a pulmonary embolism (PE) or both (DVT+PE). Intact TAFI, activation peptide of TAFI (AP), activated TAFI (TAFIa), total PAI-1 and active PAI-1 were measured with in house developed Elisa's. Additionally, we studied the association between TAFI/PAI-1 levels and clinical cardiovascular parameters such as cholesterol levels, CRP levels, D-dimer levels, age, BMI and cardiovascular risk factors such as smoking behavior, recurrent VTE, immobilization, contraceptive use.

Results Compared to HC, TAFI and PAI-1 concentrations were significantly higher in VTE patients. Intact TAFI increased 1.4-fold (14.6 μg/ml (HC) to 20 μg/ml (VTE), p<0.01), AP 15-fold (195 ng/ml (HC) to 2850 ng/ml (VTE), p<0.01), TAFIa 1.5-fold (1328 pM (HC) to 1972 pM (VTE), p<0.01), total PAI-1 22-fold (19 ng/ml (HC) to 425 ng/ml (VTE), p<0.01) and active PAI-1 4-fold (6.2 ng/ml (HC) to 24 ng/ml (VTE), p<0.01). No correlations were detected between TAFI/PAI-1 levels and the time between diagnose and analysis, neither between TAFI/PAI-1 levels and the investigated cardiovascular parameters/risk factors. No significant differences in TAFI and PAI-1 concentrations were detected between DVT patients and PE patients.

Conclusion In this study we showed that VTE patients have elevated total PAI-1, active PAI-1, intact TAFI, AP and TAFIa levels and this independently of other cardiovascular risk factors. Furthermore no association between TAFI / PAI-1 levels and the time between diagnose and analysis could be found. An increased TAFI activation as well as an increased PAI-1 concentration could be indicative for patients at risk for VTE.