

Contact Activation and Coagulation in Residual Venous Obstruction

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Background: Residual venous obstruction (RVO) in patients with deep vein thrombosis (DVT) has been associated with recurrent venous thromboembolism (R-VTE) and post-thrombotic syndrome (PTS). Its pathogenic relation to these adverse outcomes remains unclear. While the onset of DVT is assumed to be tissue factor (TF) driven, other pathways including the contact system may be engaged in thrombus resolution through thrombo-inflammatory pathways.

Aims: We aimed to assess the role of contact activation in relation to coagulation in patients with RVO.

Methods: Patients were recruited from an observational cohort and followed up to 5 years at Maastricht University Medical Center (MUMC). Presence of RVO was routinely assessed (at 5.4 [3.2-6.2] months), and anticoagulant treatment was prolonged if RVO was present. One month after discontinuation of anticoagulant treatment, enzyme-inhibitor complexes and TF-activated thrombin generation (TG) using the CAT-method were assessed. This study was approved by the medical ethical committee of MUMC, and all patients gave written informed consent.

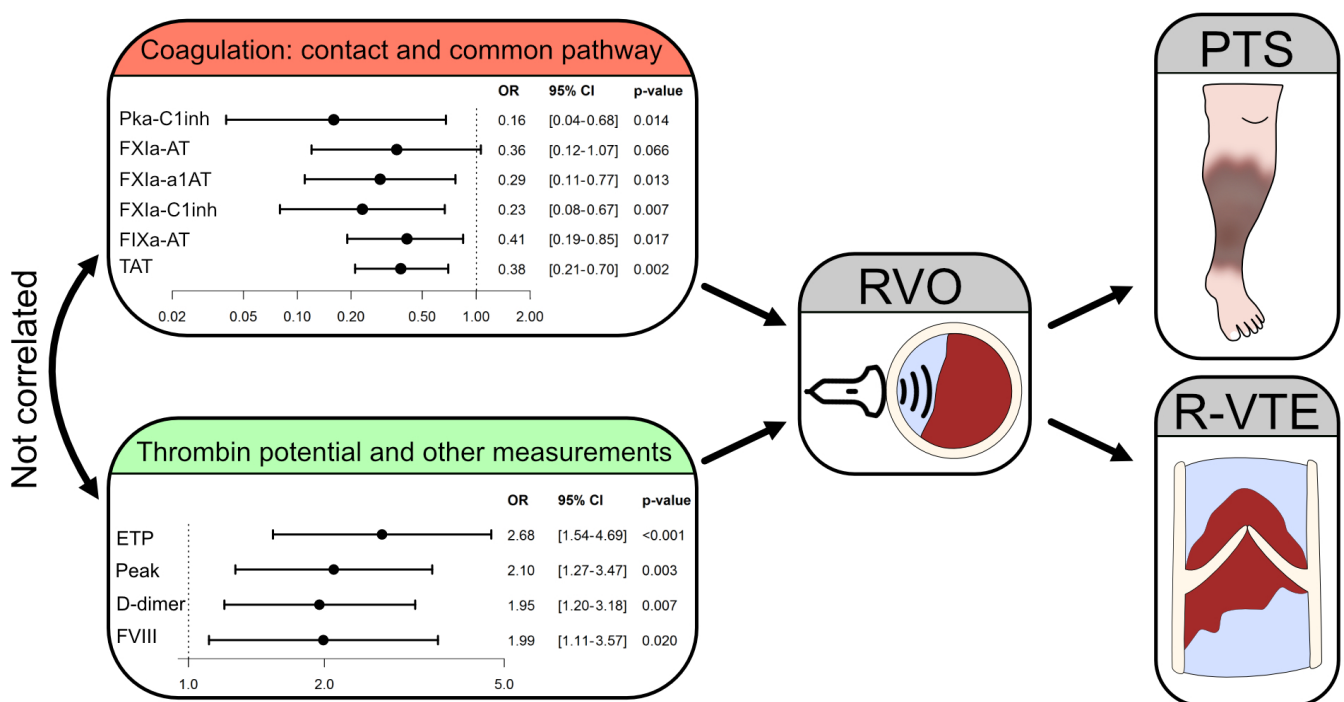
Results:

	Patients (N=306)	Missing values
Age in years (\pm SD)	55.4 (\pm 15.0)	0
Male sex (%)	157 (51.3)	0
BMI in kg/m ² (\pm SD)	27.9 (\pm 4.8)	24
Previous VTE (%)	29 (9.5)	0
Family history of VTE (%)	104 (34.2)	2
Cardiovascular risk factors (%)	100 (32.7)	0
Antiplatelet	14 (4.6)	0

drug use (%)		
Venous insufficiency (%)	16 (5.2)	0
D-dimer at diagnosis (IQR)	4000 (2200-7203)	65

Baseline characteristics of included patients.

A total of 306 patients participated in this study (Table 1). RVO was present in 102 patients (33.7%) and was associated with PTS (odds ratio [OR] 2.13, $p=0.019$). Enzyme-inhibitor complexes of both contact-activation and common pathway were lower in patients with RVO (Figure 1). However, TG was significantly enhanced (endogenous thrombin potential 1681 vs. 1579 nM.min, $p=0.005$; peak height 273 vs. 246 nM, $p=0.005$). Also, patients with RVO had more D-dimer levels $\geq 500\mu\text{g/L}$ (OR 1.95, $p=0.007$), higher levels of factor VIII activity (178 vs. 169%, $p=0.009$) and CRP (3.0 vs. 2.1, $p=0.039$). Complexes correlated well with one another, but not with other measurements, including TG.



Associations of measurements with RVO.

3.0

Conclusions: Although patients with RVO show an increased thrombin potential, in conjunction with elevated D-dimer levels, all complexes from the contact and common pathway were decreased as compared to patients without RVO. Further mechanistic studies are needed to explain this apparent paradoxical finding.

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