

Associations of Residual Venous Obstruction, d-Dimers, fFactor VIII and CRP with Long-term Outcomes of Deep Vein Thrombosis

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Abstract Number: OC 64.3

Meeting: ISTH 2021 Congress

Theme: Venous Thromboembolism » VTE Epidemiology

Background: Treatment of patients with deep vein thrombosis (DVT) needs to be tailored to their risk on long-term adverse outcomes. These outcomes include recurrent venous thromboembolism (R-VTE), post-thrombotic syndrome (PTS), arterial thrombotic events (ATE) and cancer.

Aims: We aimed to assess the associations of these adverse outcomes with several measurements commonly used in clinical practice.

Methods: All patients with acute DVT treated according to an established two-year clinical care pathway (CCP) at Maastricht University Medical Center (MUMC) were followed for up to 5 years between 2003 and 2020. Only patients with cancer at baseline were excluded from the cohort. Ultrasound presence of residual venous obstruction (RVO) was routinely assessed in all patients, and if present the duration of anticoagulant treatment was prolonged once. Levels of d-dimers, factor VIII and CRP were measured one month after discontinuation of anticoagulant treatment. The study was approved by the medical ethics committee of MUMC.

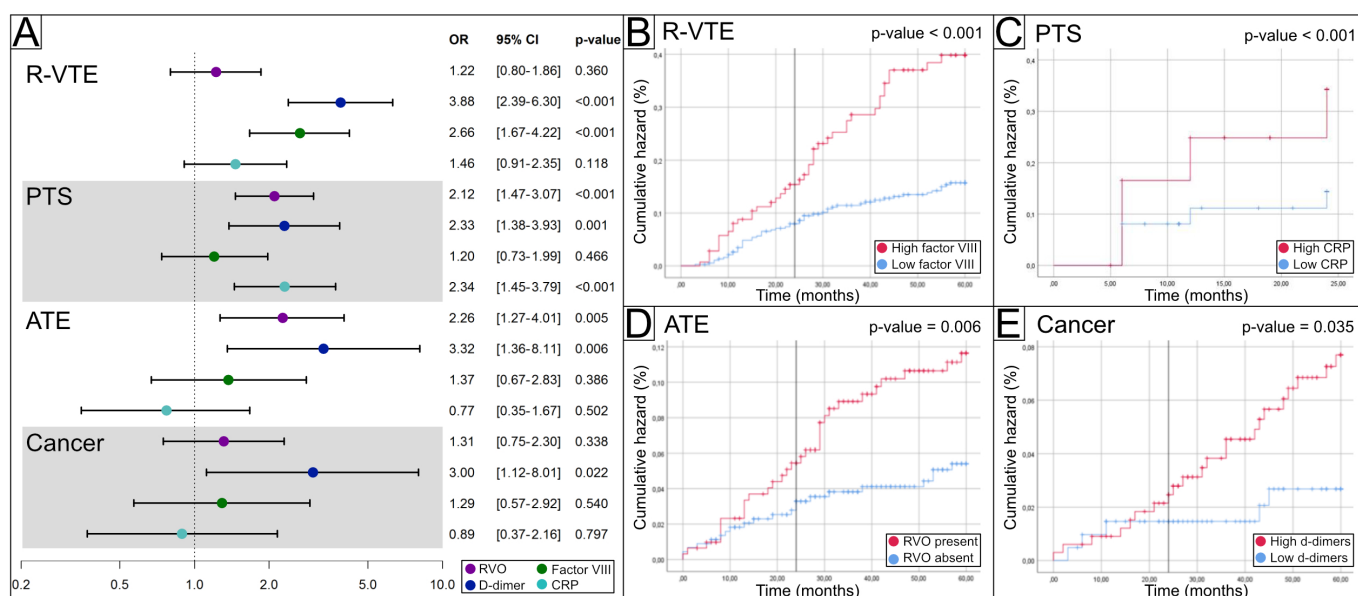
Results:

	Total cohort (N=801)	Provoked (N=343)	Unprovoked (N=458)	p-value	Discontinued cohort (N=622)	Provoked (N=296)	Unprovoked (N=326)	p-value
Age in years (±SD)	59 (±16)	53 (±16)	63 (±15)	<0.001*	57 (±16)	51 (±16)	62 (±14)	<0.001*
Male sex (%)	408 (50.9)	109 (31.8)	299 (65.3)	<0.001*	306 (49.2)	88 (29.7)	218 (66.9)	<0.001*
BMI in kg/m² (±SD)	27.9 (±5.5)	28.0 (±5.5)	27.9 (±5.5)	0.399	28.0 (±5.5)	28.0 (±5.2)	28.0 (±5.7)	0.334
Previous VTE (%)	148 (18.5)	43 (12.5)	105 (22.9)	<0.001*	51 (8.2)	15 (5.1)	36 (11.0)	0.007*
Family history VTE (%)	234 (30.0)	103 (30.8)	131 (29.4)	0.673	173 (28.5)	84 (29.1)	89 (27.9)	0.750
Cardiovascular risk factors (%)	323 (40.3)	112 (32.7)	211 (46.1)	<0.001*	225 (36.2)	80 (27.0)	145 (44.5)	<0.001*
Antiplatelet drug use (%)	80 (10.0)	38 (9.3)	48 (10.5)	0.591	54 (8.7)	21 (7.1)	33 (10.1)	0.180
Venous	81	27 (7.9)	54 (11.8)	0.069	45 (7.2)	19 (6.4)	26 (8.0)	0.454

insufficiently (%)	(10.1)							
D-dimer at diagnosis (%)	4693 (2600-8392)	4402 (2232-7841)	4900 (2844-9029)	0.069	4487 (2428-8000)	4232 (2100-7587)	4700 (2776-8633)	0.069

Baseline characteristics for the total and discontinued cohort.

Of a total of 801 patients, 780 (97.4%) completed the CCP and 49 (6.1%) were lost in the extended follow-up (median follow-up 5.0 [4.0-5.0]). In a majority of 622 patients (77.7%), anticoagulant treatment was discontinued. Patients with unprovoked DVT were significantly older and more often male, with a history of VTE and cardiovascular risk factors (Table 1). The overall incidence of R-VTE, PTS, ATE and cancer was 3.8, 11.1, 1.8 and 1.7 per 100 patient-years, respectively. Significant associations were found for RVO with ATE and PTS, high d-dimers with all outcomes, high factor VIII with R-VTE, and high CRP with PTS (Figure 1).



Associations between clinical measurements and outcomes.

Conclusions: Common clinical measurements, and in particular d-dimer levels, can be used to identify patients with increased risk of adverse outcomes. Prolonged anticoagulant treatment might negate the association of R-VTE with RVO, but the increased risk of ATE and PTS remains, suggesting an independent pathogenic relation.

To cite this abstract in AMA style:

Iding AF, Kremers B, Pallares Robles A, Pavlicic M, ten Cate H, ten Cate-Hoek AJ. Associations of Residual Venous Obstruction, d-Dimers, fFactor VIII and CRP with Long-term Outcomes of Deep Vein Thrombosis [abstract]. *Res Pract Thromb Haemost.* 2021; 5 (Suppl 1). <https://abstracts.isth.org/abstract/associations-of-residual-venous-obstruction-d-dimers-ffactor-viii-and-crp-with-long-term-outcomes-of-deep-vein-thrombosis/>. Accessed July 6, 2021.