

Table. Inflammatory and hemostatic biomarkers correlated with NLRP-3 inflammasome levels in patients with sepsis and suspected disseminated intravascular coagulation (DIC)

NLRP-3 inflammasome correlation	P (Mann-Whitney)	Spearman r
CD40L	.5716	-0.08028
PAI-1	.0041	0.3915
MP-TF	.1491	0.2528
Fibrinogen	.7685	0.04314
Fibronectin	.8291	-0.03067
Cortisol	.0758	0.2484
D-Dimer	.3272	0.1495

MP-TF, Microparticle-associated tissue factor; PAI-1, plasminogen activator inhibitor 1.

associated with increased levels of PAI-1 ($P < .0004$). No other inflammatory or hemostatic markers were significantly correlated with NLRP-3 inflammasomes. This is depicted in the Table.

Conclusions: The study shows a significant relationship between inflammasomes and PAI-1 levels in patients with sepsis-associated coagulopathy. The positive correlation between NLRP-3 inflammasomes and PAI-1 shows that the activation of inflammasomes may have a role in the upregulation of PAI-1 and the observed hemostatic dysregulation. The strong association between NLRP-3 inflammasome and PAI-1 in baseline samples of patients with sepsis and DIC also suggests that NLRP-3 inflammasome may contribute to the fibrinolytic dysregulation in sepsis and DIC.

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Venous Reflux Changes After Physical Exercise



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Objective: It is known that the presence of venous reflux affects the arterial inflow to the lower limb. However, the effect of changes in arterial inflow on the parameters of venous reflux has not been studied. The purpose of this investigation was to assess the influence of changes in arterial inflow during exercise on quantitative parameters of reflux.

Methods: There were 61 lower limbs of patients with primary incompetence of the great saphenous vein (GSV) included in the study. The diameter, cross-sectional area, average velocity, and reflux time (RT) were

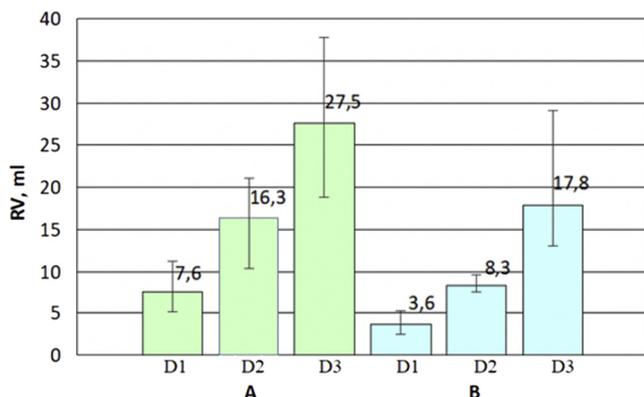


Fig 1. Reflux volume (RV) depending on diameter of the great saphenous vein (GSV). **A,** Before physical exercise. **B,** After physical exercise. All groups have statistically significant difference.

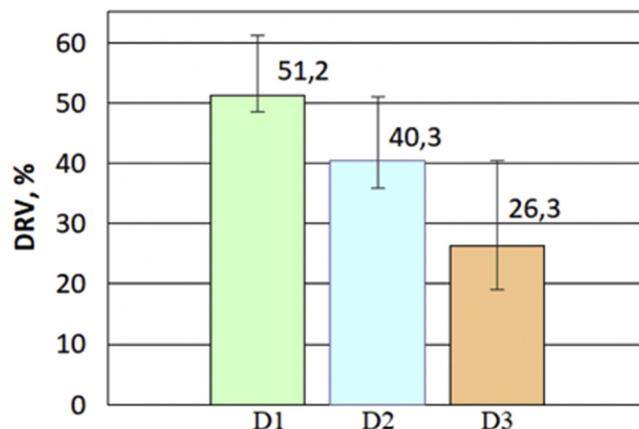


Fig 2. Decrease in reflux volume (DRV) changes depending on diameter of the great saphenous vein (GSV). D1 and D3, $P = .0002$. D1 and D2, $P = .099$. D2 and D3, $P = .0581$.

measured by duplex ultrasound. Reflux volume (RV) flow (Q) and absolute RV (ARV) were calculated. The measurements were performed standing at rest before physical exercise and 60 seconds after physical exercise (30 lifts to tiptoes at a frequency of 1 time per second). A decrease in the absolute volume of reflux (DRV) after exercise was calculated ($DRV = ARV [after] - ARV [before] / ARV [before] * 100\%$). Automatic distal compression-decompression (120 mm Hg) was used as a provoking maneuver. Median and interquartile range were used for describing quantity parameters.

Results: Before exercise, reflux parameters were as follows: RT = 4.85 (3.71-6.00) seconds; Q = 3.89 (2.03-5.81) mL/s; RV = 17.05 (10.32-25.34) mL. After physical exercise, they changed to RT = 2.86 (2.14-3.33) seconds, Q = 3.61 (2.06-6.37) mL/s, and RV = 10.07 (6.08-16.48) mL. The changes in RT and RV were statistically significant ($P < .0001$ and $P = .0007$, respectively; Fig 1).

DRV was statistically significantly different only between groups D1 and D3 ($P = .0002$; Fig 2).

DRV was reversely related to the GSV diameter ($r = -0.56$; $P < .05$) and to the disease severity measured by Venous Clinical Severity Score ($r = -0.41$; $P < .0001$).

Conclusions: The increase in arterial inflow during physical activity leads to the decrease in the volume of reflux, mainly due to decrease in RT. The decrease in the volume of reflux after exercise is inversely proportional to the diameter of the GSV.

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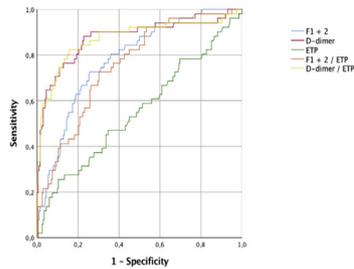
In Vivo and Ex Vivo Thrombin Generation in Noncomorbid Patients with Suspected Deep Venous Thrombosis



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Objective: Thrombin generation in vivo can be assessed by measuring prothrombin fragment 1+2 (F1+2) and D-dimer. The F1+2 fragment is generated during prothrombin conversion to thrombin and thus reflects thrombin generation. Degradation of cross-linked fibrin produces D-dimer, which reflects both ongoing coagulation and blood clot dissolution. Ex vivo, thrombin generation can be assessed by the thrombin generation assay, in which the endogenous thrombin potential (ETP) reflects the total enzymatic activity of thrombin. The aim was to compare thrombin generation in vivo and ex vivo in patients with suspected deep venous thrombosis (DVT).

Methods: Patients with clinically suspected DVT and without known comorbidities or taking anticoagulants were included. Blood samples were collected before examination with compression ultrasound of the lower extremities. In vivo parameters were analyzed with commercially



Area under the curve	
F1 + 2	0.78 (95% CI 0.72-0.85)
D-dimer	0.87 (95% CI 0.81-0.94)
ETP	0.55 (95% CI 0.46-0.65)
F1 + 2 / ETP	0.76 (95% CI 0.69-0.83)
D-dimer / ETP	0.87 (95% CI 0.81-0.94)

F1 + 2, prothrombin fragment 1 + 2; ETP, endogenous thrombin potential; CI, confidence interval.

Fig. Levels of the measured parameters in the deep venous thrombosis (DVT) negative and positive groups.

available enzyme-linked immunosorbent assay. The ETP was measured by the calibrated automated thrombogram assay. Differences between DVT-negative and DVT-positive patients were assessed with the Mann-Whitney *U* test. The area under the receiver operating characteristic curve was used to determine the overall performance of the measured parameters.

Results: The median age of the 253 patients (111 male) was 54 (range, 18-93) years. The DVT was confirmed by imaging in 51 (20%) patients. There was no significant age difference between the DVT-negative and DVT-positive groups ($P = .810$). The DVT-positive group had more men ($P < .001$). Levels of the measured parameters in the DVT-negative and DVT-positive groups are shown in the Fig.

Conclusions: A cohort without comorbidities or taking anticoagulants was selected in an attempt to show the isolated impact of lower extremity thrombosis on thrombin generation measured both in vivo and ex vivo. Levels of in vivo thrombin generation were increased in patients diagnosed with DVT vs those without. However, ex vivo ETP levels did not differ. Increased ETP levels are associated with increased risk of venous thromboembolism. Our observed discrepancy between in vivo and ex vivo parameters might be explained by a consumption of potential to generate thrombin ex vivo after an event that generates thrombin in vivo. Patients with high levels of in vivo thrombin generation parameters should thus have lower levels of ETP. A ratio of the in vivo biomarkers and ETP was therefore expected to have higher overall performance to diagnose DVT than F1+2 and D-dimer alone, which was not observed. The DVT increased the levels of F1+2 and D-dimer, but levels of ex vivo thrombin generation measured by ETP were not different from those without DVT.

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Overuse of Lower Extremity Venous Duplex by the Emergency Department for Detection of DVT: Pilot Study to Evaluate Use of D-Dimers as a Screening Tool in Low-Risk Patients



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Objective: As the cost of health care remains a major concern for patients, providers, and payers, it has become increasingly important to evaluate resource utilization behaviors. The purpose of this study was to evaluate the utilization patterns of the emergency department in the ordering of lower extremity venous duplex ultrasound examinations for detection of acute deep venous thrombosis (DVT) and the use of D-dimer as a screening test in low-risk (by Wells criteria) patients. Estimated cost

at our institution is \$15 for the D-dimer test and \$300 for the venous duplex ultrasound scan.

Methods: All venous duplex ultrasound examinations that were ordered by the emergency department during the course of 10 days were evaluated. After-hours duplex ultrasound examinations were those ordered between the hours of 9 PM and 7 AM on weekdays and between the hours of 4 PM and 7 AM on weekends. Studies were evaluated for the patient's presenting complaint, indication for duplex ultrasound as documented in the provider's notes, results of the duplex ultrasound examination (positive vs negative for DVT), D-dimer studies, and Wells criteria scores.

Results: During this 10-day period, 68 lower extremity venous duplex ultrasound examinations were performed for emergency department patients, 28% of which were performed after hours ($n = 19$). Only 13% ($n = 9$) of these patients received concomitant D-dimer serum tests, of which 56% (5/9) of results were positive; 26 studies were bilateral, and only 5 studies were positive for acute DVT in one ($n = 4$) or both ($n = 1$) legs. Of 42 unilateral studies, only 9% ($n = 4$) were positive for acute DVT.

Among patients with Wells criteria score <2 , only 5 of 63 (8%) had a D-dimer sample sent. Among these, one had a positive duplex ultrasound scan. Five (8%) other positive duplex ultrasound scans occurring in the low-risk population did not have concomitant D-dimer samples sent. No patients with negative D-dimer results had acute DVT on duplex ultrasound examination.

Conclusions: Based on the preliminary results of our pilot study, it appears there is significant overutilization of venous duplex ultrasound imaging by the emergency department for DVT screening with underutilization of D-dimer in low-risk patients. Use of D-dimer tests instead of duplex ultrasound scan in low-risk (Wells criteria score <2) patients would have potentially saved \$16,359 during a 10-day period, which would be approximately \$597,104 per annum. Larger studies are recommended to examine the overuse of duplex ultrasound in the emergency department setting.

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Reference Data from the Vascular Laboratory and Application to Chronic Venous Disease Treatment



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Objective: Several population studies have described the incidence and prevalence of chronic venous disease (CVD). This prospective study was designed to determine in detail the distribution of reflux and obstruction in all lower limb veins to provide reference data for the management of CVD patients.

Methods: Consecutive patients presenting to a university vascular clinic and undergoing a duplex ultrasound examination were included in the study. Patients with C2 CVD class or higher regardless of symptoms or cosmetic concerns were evaluated. Every patient received a detailed history and physical examination by a vascular surgeon including all demographic information. All patients then had a bilateral lower extremity venous ultrasound examination for reflux and obstruction. The examination was performed in the standing position with the exception of iliac veins and inferior vena cava, which were assessed in the supine position. Location and extent of reflux, vein diameters, and presence of obstruction were recorded. Obstruction was characterized as partial or complete for each venous segment. History of objectively documented venous thrombosis and findings on ultrasound examination indicating previous thrombosis were noted.

Results: There were 491 patients who presented for evaluation. Excluded were 241 patients, of whom 49 had undergone previous treatment and 192 had only C0 or C1 disease bilaterally. The remaining 250 patients were 32.8% male and 67.2% female. The mean body mass index was 28.3 kg/m² (range, 19.2-44 kg/m²); 55.2% identified as white, 11.2% as black/African American, 23.6% as Hispanic/Latino/Spanish origin, and 0.8% as American Indian/Alaska Native. Asymptomatic patients accounted for 17% of the cohort and symptomatic patients for 83%. Clinical, Etiology, Anatomy, and Pathophysiology (CEAP) class was distributed as 43% C2, 28.8% C3, 15.2% C4, 7.6% C5, and 4.8% C6.

In the superficial veins, 70.4% of patients had only unilateral disease; 29.6% had bilateral disease. Axial reflux was found in one vein 53.2% of