

RISK ASSESSMENT OF DEEP VEIN THROMBOSIS WITH D-DIMER LEVEL IN PATIENTS ELIGIBLE FOR VASCULAR SURGERY

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ABSTRACT

Objectives: Venous thrombosis represents a major clinical problem, both because of its high incidence and the fact that is often complicated with fatal pulmonary embolism. D-dimer level is the diagnostic parameter used to exclude venous thrombosis and to confirm thrombosis revealed by diagnostic imaging studies. The aim of this study was to assess D-dimer levels in a group of patients scheduled for femoropopliteal bypass and to compare results of this laboratory test to those obtained in a group of volunteers without lower limb ischaemia.

Material and methods: The study group consisted of 102 patients presenting with lower limb ischaemia (50 with stage IIb according to Fontaine's classification and 52 with stage III) and 49 individuals in the control group.

Results: Levels of D-dimer differed significantly between the groups. In patients presenting with Fontaine's stage IIb, Fontaine's stage III, and in control group they were, respectively: $0.87 \pm 0.31 \mu\text{g/ml}$, $0.90 \pm 0.95 \mu\text{g/ml}$, and $0.44 \pm 0.21 \mu\text{g/ml}$.

Conclusions: In comparison with healthy controls, D-dimer levels were significantly higher in patients presenting with lower limb ischaemia.

Key words: D-dimer, lower limb ischemia, risk of venous thromboembolic events.

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INTRODUCTION

D-dimer (DD) is the end product of fibrin degradation by plasmin [1], and an increased level of DD indicates activation of the coagulation system and fibrinolysis. The main diagnostic value of DD is its ability to indirectly assess the intensity of thrombin generation and the conversion of fibrinogen to fibrin catalysed by thrombin in both arteries and veins. The upper limit of DD is usually set at 500 ng/ml fibrinogen equivalent units (FEU) [2].

It is estimated that about 40% of patients with elevated DD levels are at risk of developing venous thromboembolism, which includes deep vein thrombosis (DVT) and pulmonary embolism (PE). However, many other clinical states are associated with elevated DD, including disseminated intravascular coagulation, myocardial infarction, ischaemic stroke, neoplasm, patients after surgical procedures and trauma, inflammatory pathologies such as inflammatory bowel disease, infections (particularly bacterial ones), and severe post-thrombotic syndrome with large varicose veins or ulcerations [3-6]. Thromboembolic complications represent a major problem in general surgery patients. Vascular surgery patients are at even higher risk. Up to 15-25% of patients not receiving

thromboprophylaxis can postoperatively develop DVT [7]. This concerns particularly patients after major general surgical interventions and patients presenting with risk factors for thromboembolism. The risk of thrombotic complications seems to be even higher in patients with initially high levels of DD [8].

Atherosclerotic peripheral arterial occlusive disease, which in some patients requires surgical reconstruction, is a relatively common disease. Prevalence of peripheral arterial occlusive disease is estimated to be at the level of 3-10% of adults and it increases with age. As many as 15-20% individuals older than 70 years present with clinical signs of peripheral arterial occlusive disease [5]. In Poland 40,000 new cases are noted each year [9]. Immobility, which is due to severe occlusive atherosclerosis, is often associated with increased risk of venous thromboembolism. In spite of the fact that patients scheduled for vascular reconstructions present with risk of thromboembolism, current guidelines do not recommend routine thromboprophylaxis [7, 10].

The aim of this study was to assess D-dimer levels in a group of patients scheduled for femoropopliteal bypass and to compare results of this laboratory test to those obtained in a group of volunteers without lower limb ischaemia.

MATERIAL AND METHODS

We included two research groups and one control group in our study. Group I ($n = 50$) suffered from stage IIb lower-limb ischaemia according to Fontaine’s classification, and group II ($n = 52$) from stage III lower-limb ischaemia. The control group ($n = 49$) consisted of persons without ischaemia of lower extremities but with comorbidities typical for their age group, who spend their free time in one of Wrocław’s senior clubs.

Inclusion criteria for groups I and II: stage IIb or III lower limb ischaemia according to Fontaine’s classification.

Relative criteria for groups I, II, and control groups (at least one of the listed below):

- type 2 diabetes mellitus,
- qualification for femoropopliteal bypass surgery,
- history of myocardial infarction,
- history of ischaemic stroke without subsequent motor disability,
- hypertension controlled with pharmacotherapy.

Exclusion criteria:

- trophic changes in the lower limbs,
- sensory disturbances resulting from ischaemia (sensory neuropathy) without intermittent claudication,
- comorbidities that permanently impair motor function,
- diagnosed mental illness,
- lack of an informed and voluntary consent to participate in the study,
- neoplastic disease.

The numbers of participants in each arm of the study are presented in Figure 1.

Samples of venous blood were collected to determine levels of DD. Levels of DD were measured using quantitative agglutination and immunoassay tests. These laboratory investigations were performed in the laboratory of University Teaching Hospital in Borowska Street, Wrocław. Demographic and clinical characteristics of patients and controls are presented in Table 1.

Statistical methods

In a case of nonrepudiation of the hypothesis on normal distribution, the distributions were compared using the one-way analysis of variance (ANOVA). The F-test that was used in the analysis when comparing two means consisted of Student’s t -test squared. The correlations of categorised variables (of discrete distribution) were evaluated using the chi-squared test (χ^2). The statistical significance was determined with the significance level set at $\alpha = 0.05$. The calculations were performed using Statistica 8.0 and GNU Octave 4.0.0 software.

RESULTS

DD levels did not significantly differ between patients presenting with stage IIb and stage III of lower limb ischaemia. However, values of DD differed significantly between patients and controls (Table 2). There was no monotonic relationship between DD levels and patient’s age. A rising trend was noted in group I, while simultaneously, a significant decrease was observed in the group of patients from 56 to 65 years of age ($0.7 \mu\text{g/ml}$). On the other hand, in the age group over 66 years, the mean DD value increased to $1.1 \mu\text{g/ml}$. The situation is slightly different in the second group, with DD value decreasing from 1.3 to $0.8 \mu\text{g/ml}$ with the age of the patients, but still remaining high in the last subgroup. In the control group, a strong growing tendency can be observed when comparing the medians of the DD level between the age groups; the DD_r level doubles between the age groups from 58 to 60 years and 65 to 69 years (from 0.2 to 0.4) (Table 3, Fig. 2).

DISCUSSION

Atherosclerotic peripheral arterial occlusive disease chronically impairs patient’s mobility. In addition, comorbidities such as diabetes and hypertension contribute to the unfavourable clinical prognosis. In this paper we analysed one of the risk factors for thromboembolism. We tried to assess whether chronic ischaemia of the lower limbs influences DD levels.

Our study demonstrated that DD levels were elevated in comparison with the control group. Our research also indicated that while D-dimer levels decreased with

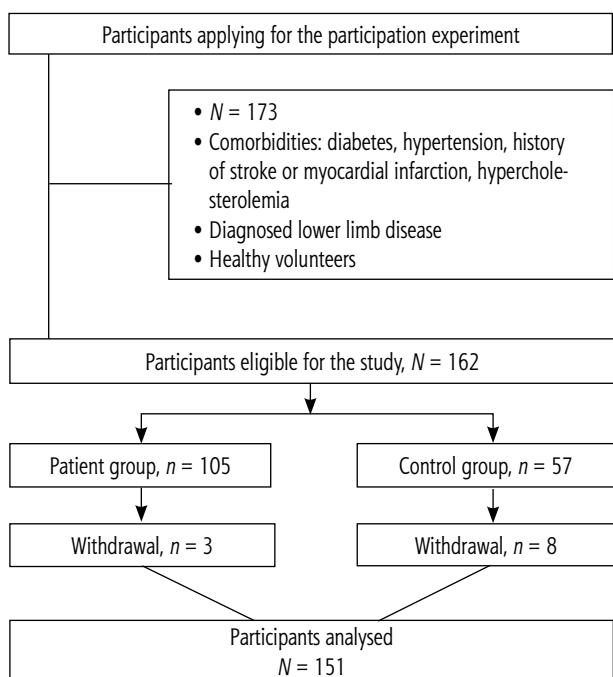


Fig. 1. Consort diagram

Table 1. Characteristics of patients and controls

Variable		Group I	Group II	Control group
Gender	female	12 (24%)	19 (37%)	31 (63%)
	male	38 (76%)	33 (63%)	18 (37%)
Mean age	female	62.7 ±6.9	65.2 ±3.7	65.8 ±5.6
	male	64.4 ±6.0	65.2 ±5.8	68.2 ±5.6
BMI kg/m ²		27.1 ±3.8	27.1 ±4.1	27.2 ±3.7
Previous occupation	blue collar	35 (70%)	35 (67%)	19 (39%)
	white collar	15 (30%)	17 (33%)	30 (61%)
Comorbidities	diabetes type 2	32%	50%	8%
	hypertension	46%	65.3%	12%
	history of stroke	8%	17.3%	17%
	history of myocardial infarction	12%	11.5%	65%
	hypercholesterolaemia	1.5%	7.7%	50%

Table 2. Mean DD levels in patients and controls

D-dimers µg/ml		
Group I	mean	0.87 ±0.31
Group II	mean	0.90 ±0.95
Control group	mean	0.44 ±0.21
ANOVA test	<i>F</i>	9.58
	<i>p</i>	0.0001

Table 3. Age of the participants in relation to DD levels

D-dimers (µg/ml)			
Age (years)	Group I	Group II	Control group
46-55	0.9 ±0.4	1.3 ±0.1	0.2 ±0.0
56-65	0.7 ±0.7	0.9 ±0.3	0.4 ±0.2
> 66	1.1 ±1.2	0.8 ±0.3	0.5 ±0.2
ANOVA test			
<i>F</i>	0.702	6.311	2.981
<i>p</i>	0.501	0.004	0.061

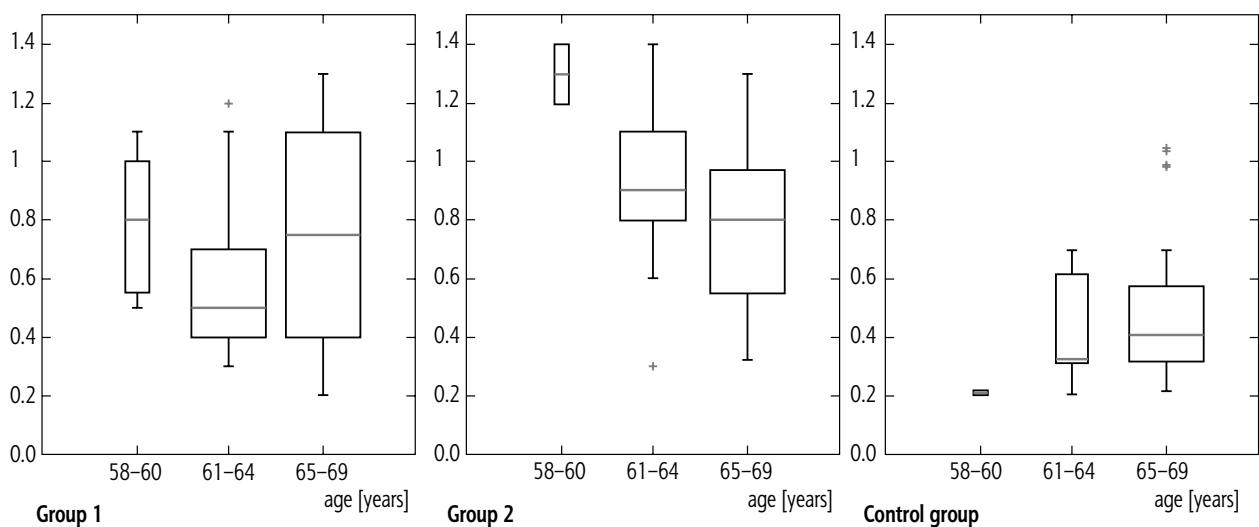


Fig. 2. DD levels in different age groups

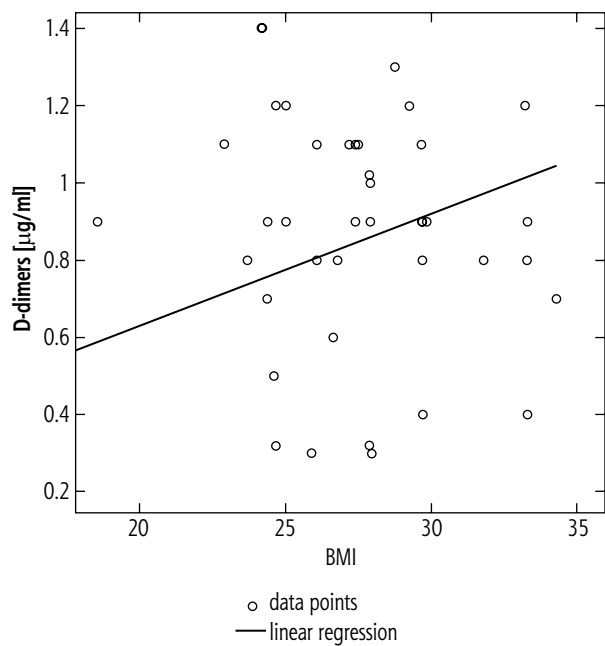


Fig. 3. D-dimer levels in the function of BMI in the research group

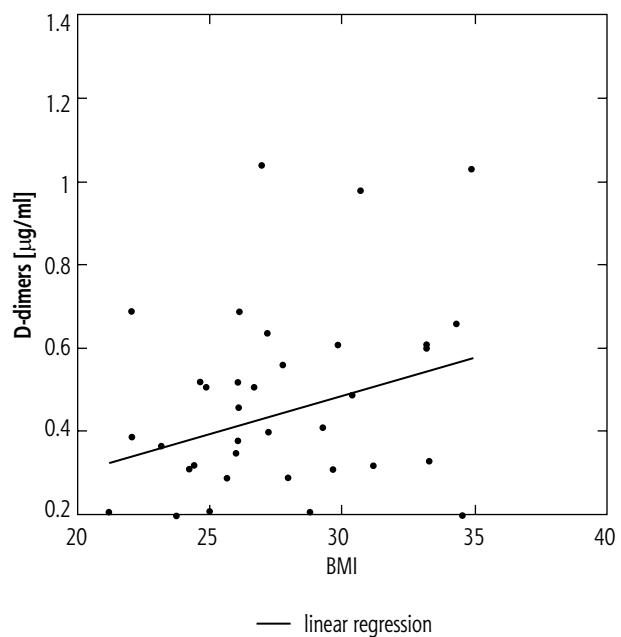


Fig. 4. D-dimer levels in the function of BMI in the control group

age from 1.3 µg/ml to 0.8 µg/ml while still being elevated in one of the groups (group II), they had a tendency to increase in the other group (group I) from 0.9 µg/ml to 1.1 µg/ml. Ntourakis *et al.* [11] observed high D-dimer levels in patients over 70 years of age, and the difference between the age groups was statistically significant. Natkaniec *et al.* [12], however, did not observe a correlation between the age of the patient and coagulation parameters, including D-dimer levels [13]. Känel *et al.* [14] in their study on 116 persons also noted a statistically significant correlation between the age and D-dimer levels, which probably increases the risk of myocardial infarction, unstable angina pectoris, or vascular disorders [9].

Garg *et al.* [15] assessed the risk factors of thromboembolic events depending on age, gender, and BMI. Although the BMI differences between the groups were small and not statistically significant, there was a positive correlation between the BMI and D-dimer levels; a D-dimer level increase was noted with the increase of BMI (Figs. 3 and 4). A similar study by Grygiel-Górniak [16] assessed patients with diabetes and high BMI, particularly with abdominal fat distribution. The patients had high D-dimer levels and elevated thromboembolic risk. Nwose *et al.* [17], who sought to correlate the D-dimer levels with diabetes progression in overweight patients, managed to observe a correlation between these variables. Moreover, prolonged duration of the disease also proved to increase the prothrombotic markers [18].

Ambiguity of the results encourages closer examination of patients with lower-limb ischaemia in the context of D-dimer levels.

CONCLUSIONS

DD levels are higher in patients presenting with chronic lower-limb ischaemia, but the clinical stage of ischaemia does not correlate with the levels of DD.

No strong correlation between the age of patients or controls and DD levels was revealed.

The authors declare no conflict of interest.

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