

Concomitant acute deep venous thrombosis and superficial thrombophlebitis of the lower limbs

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Abstract

Introduction: Some patients may have deep venous thrombosis (DVT) and superficial thrombophlebitis (ST) of the lower limbs at the same time. **Aims:** To analyze the frequency of risk factors for thrombosis (RF), other than thrombophilias, in patients with concomitant DVT and ST. **Patients and methods:** Clinical examination, plasma D-dimers and duplex ultrasonography were performed in 88 consecutive patients (mean age 64.9±13.9 years) admitted in Medical Clinic in 2007. Patients with DVT were divided into two groups: A (with ST – 30 subjects, 34.1%) and B (without ST – 58 patients, 65.9%). **Results:** Conditions known as RF were the following (Group A versus B): varicose veins (17 vs 21 patients, p=0.11), obesity (12 vs 19, p=0.66), previous venous thromboembolism (8 vs 16, p=0.87), malignancy (4 vs 10, p=0.44), chronic obstructive lung disease (4 vs 7, p=0.56), sepsis (2 vs 3, p=0.56), stroke and chemotherapy (1 vs 2, p=0.73), bed rest more than three days (1 vs 7, p=0.17), major surgery (1 vs 1, p=0.57), family history of DVT (1 vs 0, p=0.57), immobilizing plaster cast (0 vs 1, p=0.57). **Conclusion:** One third of patients with DVT had ST. None of those conditions considered as RF for DVT correlated with DVT-ST association.

Keywords: deep venous thrombosis, superficial thrombophlebitis, risk factors, thrombosis

Rezumat

Introducere: Unii pacienți pot prezenta la nivelul membrelor inferioare, în același timp, tromboză venoasă profundă (TVP) și tromboflebită superficială (TS). **Obiectiv:** Analiza frecvenței factorilor de risc trombotic (FR), alții decât trombofilii, la pacienții cu TVP și TS. **Pacienți și metodă de lucru:** Am investigat, prin examen clinic, D-dimeri plasmatici și ultrasonografie duplex, 88 de pacienți consecutivi (vârstă medie de 64,9±13,9 ani) internați într-o clinică medicală în anul 2007. Pacienții cu TVP au fost împărțiți în două grupuri: A (cu TS – 30 bolnavi, 34,1%) și B (fără TS – 58 pacienți, 65,9%). **Rezultate:** Condițiile cunoscute ca FR au fost următoarele (grupul A versus B): varicele (17 vs 21 de pacienți, p=0,11), obezitatea (12 vs 19, p=0,66), antecedentele personale tromboembolice (8 vs 16, p=0,87), cancerul (4 vs 10, p=0,44), bronhopneumopatia cronică obstructivă (4 vs 7, p=0,56), septicemia (2 vs 3, p=0,56), accidentul vascular cerebral și chimioterapia (1 vs 2, p=0,73), repausul la pat de peste trei zile (1 vs 7, p=0,17), operațiile majore (1 vs 1, p=0,57), antecedentele trombotice familiale (1 vs 0, p=0,57), aparatul gipsat (0 vs 1, p=0,57). **Concluzie:** O treime din pacienții cu TVP au prezentat TS. Niciunul dintre FR pentru TVP nu s-a corelat cu asocierea TVP-TS.

Cuvinte cheie: tromboză venoasă profundă, tromboflebită superficială, factori de risc, tromboză

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Introduction

Deep vein thrombosis (DVT) and/or pulmonary embolism (PE) define venous thromboembolism. The incidence of DVT increases with age, reaching 10/1000 persons/year [1-3]. Risk factors (RF) associated with development of DVT may be categorized as strong, as major general surgery and fractures are. Other RF are moderate, eg cancer and thrombophilia, while others are

weak, as, for example, varicose veins and obesity [4]. In the case of obesity, the risk depends on the body-mass index (BMI). In Caprini's classification of risk level for DVT, patients with BMI between 30 and 40 receive one point. Those subjects with a BMI between 40 and 50 have two points. In patients with BMI over 50, the risk increases by another point. Similarly, patients previously diagnosed with cancer receive two points on the scale of thrombotic risk, while those with present cancer or chemotherapy get three points [5]. In recent years, some researchers have found a correlation between risk factors for atherosclerosis, such as smoking and hyperlipidemia, and the presence of DVT [6-9].

Varicose veins, trauma, stasis and abnormalities of blood clotting factors are the main RF for superficial thrombophlebitis (ST). Because of the existence of varicose veins, ST has a seasonal pattern of occurrence. Increased incidence of ST during the summer can be explained by poor patient compliance and lack of usage of elastic stockings [10]. The strongest relation was with hypercoagulable states [11-13]. In recent years, increasingly more evidence has appeared about the relationship between cancer and ST. Unprovoked ST may be considered a paraneoplastic phenomenon [14,15]. However, the strength of this association remains unknown [11,16,17].

The ST is not always benign because it may coexist with DVT [11,12]. There are two types of links between the deep and superficial venous system: the ostium of the superficial veins and the communicant veins. Because of these connections, the thrombus, located in the superficial venous system, can reach deep venous system, therefore, in some cases, occult DVT can complicate ST [18,19].

There are few prospective randomized studies on ST, so, the relation between DVT and ST remains controversial [11,18,20]. The POST (Prospective Observational Superficial Thrombophlebitis) Study found that 210 of the 844 patients with ST (24.9%) developed DVT in the next three months [21]. Dewar *et al* have followed 79 patients with ST for six months and found that three subjects developed DVT (4%, 95% CI 0.8%-11%) [22]. In their meta-analysis, Leon *et al* found that ST and DVT coexist in 6-53% of patients [11].

If researchers used venography as diagnostic method, results were as follows: 12% (Skillman *et al*, 1990), 20% (Prountijos *et al*, 1991) and 44% (Bergqvist and Jaroszewski, 1986) [23-25]. But in most studies, diagnosis of DVT and ST was based on ultrasound. In some studies, the frequency of DVT-ST association was less than 10%: 0.9-3.6% (Decoussus, 2003), 5.6% (Belcaro *et al*, 1999), 5.96% (Bounameaux *et al*, 1997), 7% (Fard *et al*, 2001), 8.6% (Blumenberg *et al*, 1998), 9.3% (Hill *et al*, 2008) [18,19,26-29].

Other authors have found that the frequency of this association was between 10% and 20%: 11% (Chengelis *et al*, 1996), 14% (Krause *et al*, 1998), 15.4% (Nopeney *et al*, 2006), 17% (Gillet *et al*, 2001), and 19% (Plate *et al*, 1985) [30-34]. According to other studies, the frequency of DVT-ST combination is greater than 20%: 21.6% (Sobreira *et al*, 2009), 23% (Jorgensen *et al*, 1993), 23.5% (Rohrbach *et al*, 2003), 24.9% (Decousus *et al*, 2010), 25.3% (Murgia *et al*, 1999), 28% (Lutter *et al*, 1991) [20,21,35-38]. In other studies, the frequency of this association is even higher than 40%: 44% (Blättler and Frick, 1993) and 53.48% (Lohr *et al*, 1992) [39,40].

The purpose of this study is to determine if some RF for venous thromboembolism (other than thrombophilias) are associated with ST in patients with concomitant DVT and thrombophlebitis of the great saphenous vein.

Patients and methods

We have investigated a total of 88 patients diagnosed with DVT, admitted into the 5th Medical Clinic of the „Juliu Hațieganu” University of Medicine and Pharmacy, Cluj-Napoca, Romania, from January to December 2007. The study protocol was approved by the local Ethics Committee.

The diagnosis of acute DVT was based on three elements: Wells pre-test probability score, plasma D-dimer test and real-time compression ultrasonography [41,42]. Wells's criteria for assessment of pre-test probability are: active cancer, paralysis, recent plaster immobilization, major surgery in the last month, bed rest of more than three days, entire leg swelling, calf circumferences of two legs differing by *more than 3 cm*, and dilated superficial veins, alternative diagnoses as likely as or more than that of DVT [41,43]. Diagnostic ultrasound criteria for DVT were: lack of compressibility (the major criterion), increased cross-sectional diameter, heterogeneous intraluminal material, absence of Doppler signal, and collateralization. Thrombosis was classified into two categories, depending on location: proximal (involving the iliac, femoral and popliteal veins) and distal (involving the below-knee deep veins) [44,45]. The ST was diagnosed based on symptoms (tenderness, erythema, and indurated cord) and ultrasonographic findings (increased cross-sectional diameter, heterogeneous intraluminal material, and lack of compressibility) [46]. Patients were examined using a Hitachi EUB-405 duplex ultrasound machine equipped with a 7.5 MHz linear transducer.

In all those 88 DVT patients were studied several parameters: demographics (age, gender), anamnesis (RF, criteria for assessment of pre-test probability), physical exam findings (cardiac and respiratory failure criteria,

paralysis, obesity, varicose veins, edema, and cardinal signs of inflammation), blood tests (plasma D-dimers, complete blood count, coagulation, metabolic disorders), and above-mentioned ultrasound findings.

Patients were divided into two groups: A (patients with acute DVT and concomitant greater saphenous vein thrombosis) and B (DVT subjects without ST).

Our study was an observational transversal one. Statistical analysis was performed using Epi Info computer package, version 3.3.2. The arbitrary statistical significance level was $p=0.05$.

Results

Of the 88 DVT patients, 47 were men (53.4%). Patients' mean age was 64.9 ± 13.9 years (range 23-86 years). Age distribution was as follows: under 40 years – 10 subjects (11.4%), 41-59 years – 22 patients (25%), 60-74 years – 34 individuals (38.6%), and over 75 years – 22 patients (25%).

Among the strong RF, major general surgery was the most commonly encountered (2 patients - 2.2%). There were no patients with DVT related to hip or knee replacement, major trauma and spinal cord injury as strong RF. Personal history of DVT, malignancy and respiratory failure were the most frequent moderate RF (24 subjects - 27.2%, 14 patients - 15.9%, and 11 individuals – 12.5% respectively). None of the patients presented moderate RF such as hormone replacement therapy, oral contraceptives and postpartum period. Varicose veins and obesity were the most common weak RF (38 patients – 43.1% and 31 subjects – 35.2%, respectively). There were no cases of pregnant women with DVT. A total of 13 patients (14.7%) had PE as a complication of DVT.

Characteristics of patients included in groups A and B are presented in the table I. There was no statistically significant correlation of RF with the presence of acute ST in patients with acute DVT.

Table I. Patient characteristics

Parameters	Group A N=30	Group B N=58	OR*	95% CI**	p
Men	19	28	1.85	0.68-5.05	0.26
Age (mean±standard deviation, median, range)	61.7±16.7 63.5 (23-86)	66.5±12.1 70 (31-83)	–	–	–
40 years	4	6	–	–	–
41-59 years	10	12	–	–	–
60-74 years	8	26	0.34	0.09-1.26	0.12
75 years	8	14	0.63	0.15-2.52	0.66
Major general surgery***	1	1	1.97	0.0-75.16	0.57
Immobilizing plaster cast	0	1	1.97	0.0-75.16	0.57
Arthroscopic knee surgery	0	1	1.97	0.0-75.16	0.57
Malignancy	4	10	0.74	0.17-2.93	0.44
Chemotherapy	1	2	0.97	0.0-14.49	0.73
Respiratory failure	4	7	1.12	0.25-4.83	0.56
Congestive heart failure	0	1	1.97	0.0-75.16	0.57
Stroke**	1	2	0.97	0.0-14.49	0.73
Previous venous thromboembolism	8	16	0.95	0.31-2.86	0.87
Bed rest > three days	1	7	0.25	0.01-2.23	0.17
Long-haul flights	1	0	1.97	0.0-75.16	0.57
Varicose veins	17	21	2.3	0.86-6.26	0.11
Obesity	12	19	1.37	0.5-3.76	0.66
Smoking	6	7	1.82	0.48-6.94	0.25
Immobilization < three days	3	9	0.6	0.12-2.75	0.36
Sepsis	2	3	1.31	0.14-10.47	0.56
Family history of DVT	1	0	1.97	0.0-75.16	0.57
Hyperlipidemia	10	18	1.11	0.39-3.14	0.98

* Odds ratio; ** 95% confidence interval; *** in the last 30 days

The 88 subjects included in this study had 183 affected deep venous segments. Left-sided DVT was diagnosed in 43 patients (48.8%). A total of 33 subjects had right-sided DVT (37.5%) - left-to-right ratio 1.30. Proximal location of DVT was found in 57 patients (64.8%). The remaining 31 subjects had both proximal and distal DVT (35.2%).

Of the 30 patients with concomitant DVT and ST only one had bilateral greater saphenous vein thrombosis (3.3%). Of the 29 subjects with unilateral ST, 15 had left-sided lesions (51.7%) - left-to-right ratio 1.07.

In the figure 1 and figure 2 is illustrated the concomitant involvement of the right common femoral vein and greater saphenous vein. Changes in the two veins located in the left leg are shown in figure 3 and 4.

Discussion

Diagnosis of acute greater saphenous vein has been established in 30 patients with DVT (34%). In our study, the frequency of this association is close to that found by several authors such as: Marcović *et al*, 1997 (28%), Gillet *et al*, 2004 (28.6%), Pulliam *et al*, 1991 (30%), and Ascer *et al*, 1995 (40%) [47-50].

There were no statistically significant differences regarding age and gender of patients in both groups. Regarding gender, our results conflict with those of Andreou *et al* (2008) and Bauersachs *et al* (2010). These authors have analyzed over 1300 DVT patients and found that the prevalence of DVT was higher in men than in women [51,52].

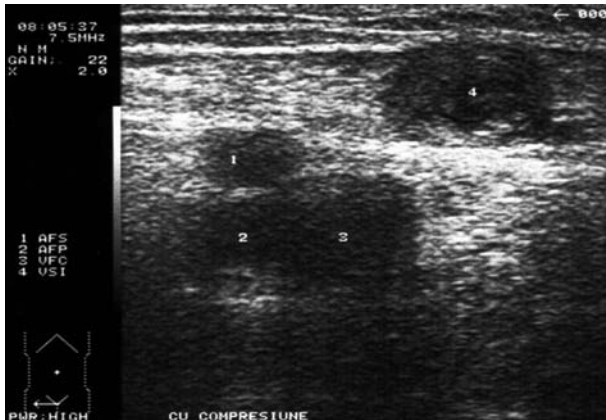


Fig 1. Cross section with compression through the vessels located in the right femoral triangle. Dilated common femoral vein and greater saphenous vein with occlusive thrombus. 1 – superficial femoral artery, 2 – deep femoral artery, 3 – common femoral vein, 4 – greater saphenous vein.



Fig 2. Transverse image of the right femoral triangle. Compression ultrasonography. Heterogenous intraluminal material dilating the common femoral vein, greater saphenous vein and its ostium. 1 – common femoral artery, 2 – common femoral vein, 3 – greater saphenous vein.

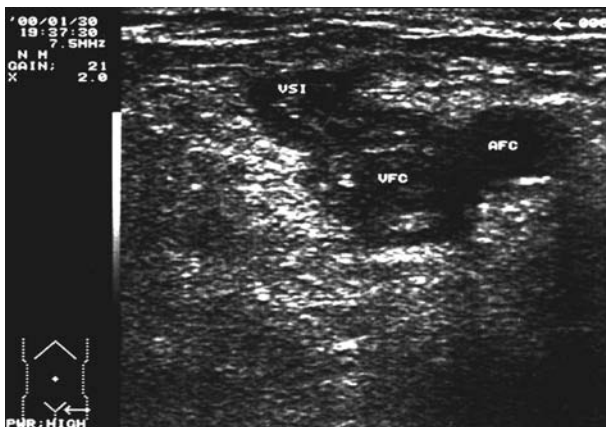


Fig 3. Transverse view of the left common femoral vessels. Increased cross-sectional diameter of the common femoral vein and of the greater saphenous vein. VSI – greater saphenous vein, UFC – common femoral vein, AFC – common femoral artery.

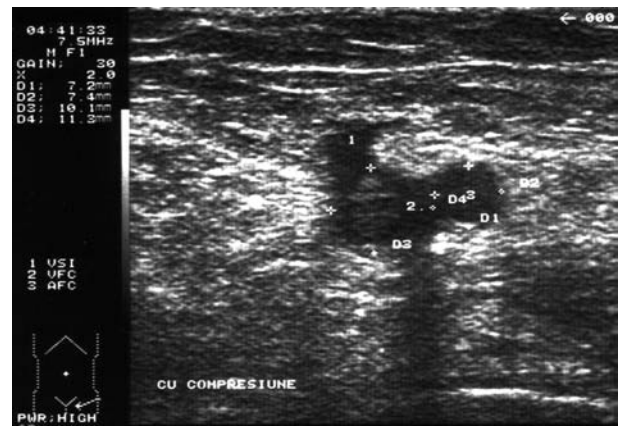


Fig 4. Cross section with compression through the left femoral triangle. Dilated common femoral vein with heterogenous occlusive thrombus. 1 – greater saphenous vein, 2 – common femoral vein. 3 – common femoral artery.

There were no statistically significant differences in the frequency of RF in patients of two groups. Some strong and moderate RF were rarely detected in patients who were included in our study: stroke, chemotherapy, congestive heart failure, immobilizing plaster cast, and arthroscopic knee surgery.

We would have expected that previous venous thromboembolism, major general surgery, stroke, and malignancy to be more common in patients in Group B than in those from Group A. In his classification of RF for DVT, Caprini gave three points to the personal history of DVT [5]. In our study, eight of the 30 patients in Group A and 16 of the 58 patients in Group B had previous venous thromboembolism (26.6% and 27.5%, respectively). It is possible that the personal history of DVT has been more common because it is known that the clinical presentation of DVT is often nonspecific and patients do not go immediately to the emergency room.

It is known that DVT and PE are among the main preventable extracerebral complications of stroke [53,54]. Also, cancer is associated with an increased prevalence of DVT, as Heit *et al* (2000) have shown. The authors have included in their population-based case-control study more than 600 people and followed them for 15 years. They proved that cancer is an independent RF for DVT (OR 4.1; 95% CI 1.9-8.5) [55].

It would also be expected that varicose veins to be more frequent in patients in Group A than in those from Group B. A total of 17 of the 30 patients included in the first group and 21 patients in the second group had varicose veins (56.6% and 36.2%, respectively). This means that approximately 43% of patients in group A had non-varicose ST.

Hyperlipidemia was diagnosed in 10 of the 30 patients in Group A and in 18 of the 58 patients in Group B (33.3% versus 31% - nonsignificant). We have not found information in the medical literature about the association between hyperlipidemia and ST.

The PE was diagnosed in 13 patients (14.7%) – three of Group A (10%) and 10 of Group B (17.2%) – OR 0.53, 95% CI 0.11-2.38, $p=0.28$. Meta-analysis of Leon *et al* (2005) showed that PE occurred in 0-33.3% of patients with DVT-ST association [11].

Limitations

Because the study was transversal, we could not determine in which of our patients ST occurred before or after DVT. Other limitations were the small number of patients included in the study, absence of some RF (such as pregnancy, oral contraceptive therapy and major trauma) and the inability to perform diagnostic tests for thrombophilia, because of lack of money.

Conclusions

Thrombosis of the greater saphenous vein was diagnosed in one third of patients with DVT. None of those conditions considered as RF for DVT correlated with DVT-ST association.

Conflict of interest: none

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