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ABSTRACT

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FEATURES OF SUPERFICIAL VEIN THROMBOSIS IN PATIENTS WITH A LARGE DIAMETER OF GREAT SAPHENOUS VEIN

Introduction. Superficial vein thrombosis is characterized by the formation of thrombi in the superficial veins with subocclusion or occlusion of the venous lumen and its inflammatory reaction, which occurs more often in the lower extremities. Chronic venous disease in 75–88% of cases is the most important clinically identified factor in the development of superficial vein thrombosis. The great saphenous vein is affected in 60–80% of cases. A population-based study found that the chronic venous disease is a risk factor for venous thromboembolism and correlates with an increased risk of mortality in patients. Venous thromboembolism is a major burden of the disease worldwide, with approximately 10 000 000 cases per year.

Objective: to assess the prevalence of superficial vein thrombosis in patients with chronic venous disease and to identify the relationship between the diameter of the great saphenous vein and superficial vein thrombosis.

Materials and methods. Total of 925 chronic venous disease cases were analyzed from January 2019 to December 2021 at the Clinical Department of Surgery, Traumatology, Orthopedics, and Phthisiology of Sumy State University (Sumy Laser Clinic, LLC) for the prevalence of superficial vein thrombosis in patients with chronic venous disease who were undergoing treatment. The patients with superficial vein thrombosis were examined for the diameters of great saphenous vein and venous reflux using ultrasound 10 mm below the sapheno-femoral junction, in the upper and lower thirds of the thigh.

Results: Of 925 chronic venous disease cases, superficial vein thrombosis was observed in 53 cases, which accounted for 5.73 % of the total. Women accounted for 67.9 % (36), men – for 32.1 % (17). The study included patients aged 25 to 69 years (mean age 52.62 ± 10.48 years). In 69.8 % (37) of superficial vein thrombosis cases, the diameter of great saphenous vein was ≥ 10 mm at a level 10 mm below the sapheno-femoral junction; in 49 % (26) of cases – in the upper third of the thigh; in 30.2 % (16) of cases – in the lower third of the thigh. That is, the extension of the sapheno-femoral junction trunk to the lower third of the thigh was preserved in 43.24% of cases.

Conclusion. The results of the study revealed a high prevalence (5.73%) of superficial vein thrombosis. 69.8% of all cases of superficial vein thrombosis was registered in patients with a large diameter (≥ 10 mm) of great saphenous vein.

Keywords: superficial vein thrombosis, great saphenous vein, large diameter, chronic venous disease.

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РЕЗЮМЕ

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ОСОБЛИВОСТІ ТРОМБОФЛЕБІТУ ПРИ ВЕЛИКОМУ ДІАМЕТРІ ВЕЛИКОЇ ПІДШКІРНОЇ ВЕНИ

Вступ. Тромбофлебіт поверхневих вен характеризується утворенням тромбів у поверхневих венах з субокклюзією або оклюзією просвіту вени та запальною її реакцією, що частіше трапляється в нижніх кінцівках. Хронічні захворювання вен у 75–88 % випадків є найважливішим клінічно ідентифікованим фактором розвитку тромбофлебіту поверхневих вен. Велика підшкірна вена вражається у 60–80 % випадків. Популяційне дослідження показало, що наявність хронічних захворювань вен є фактором ризику венозної тромбоемболії та корелює з підвищеним ризиком смертності у пацієнтів. Венозна тромбоемболія є основним тягарем захворювання у всьому світі, приблизно 10 000 000 випадків на рік

Мета – оцінити поширеність тромбофлебіту поверхневих вен у хворих на хронічні захворювання вен; виявити залежність між діаметром великої підшкірної вени і тромбофлебітом поверхневих вен.

Матеріали та методи. Було проаналізовано 925 випадків хронічних захворювань вен з січня 2019 року по грудень 2021 року на клінічній базі кафедри хірургії, травматології, ортопедії та фтизіатрії СумДУ (ТОВ «Сумська клініка лазерної медицини») щодо поширеності тромбозу поверхневих вен у пацієнтів з хронічними захворюваннями вен, які перебували тут на лікуванні. У хворих з тромбофлебітом поверхневих вен оцінювали діаметри великої підшкірної вени та венозний рефлюкс на ультразвуковому дослідженні на 10 мм нижче сафено-феморального з'єднання, у верхній та нижній третинах стегна.

Результати. Із 925 випадків лікування хронічних захворювань вен тромбофлебіт поверхневих вен спостерігався у 53 випадках, що склало 5,73 % від загальної кількості. Особи жіночої статі склали 67,9 % (36), чоловіки – 32,1 % (17). До дослідження було включено осіб у віці від 25 до 69 років (середній вік склав 52,62 ± 10,48 років). Діаметр великої підшкірної вени у нашому дослідженні був ≥ 10 мм на рівні на 10 мм нижче сафено-феморального з'єднання у 69,8 % (37) випадків тромбофлебіту поверхневих вен; у верхній третині стегна – у 49 % (26) випадків тромбофлебіту поверхневих вен; у нижній третині стегна – у 30,2 % (16) випадків тромбофлебіту поверхневих вен. Тобто розширення стовбура великої підшкірної вени аж до нижньої третини стегна зберігалося у 43,24 % випадків.

Висновки. Результати дослідження виявили високу поширеність (5,73 %) тромбофлебіту поверхневих вен. 69,8 % всіх випадків тромбофлебіту спостерігалися у хворих з великим діаметром (≥ 10 мм) великої підшкірної вени.

Ключові слова: тромбофлебіт поверхневих вен, велика підшкірна вена, великий діаметр, хронічні захворювання вен.

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INTRODUCTION / ВСТУП

Abbreviations
CVD – chronic venous disease;
DVT – deep vein thrombosis;
GSV – great saphenous vein;
NSAIDs – nonsteroidal anti-inflammatory drugs;
PE – pulmonary embolism;
SFJ – sapheno-femoral junction;
SPJ – safeno-popliteal junction;
SSV – small saphenous vein;
SVT – superficial vein thrombosis;
VTE – venous thromboembolism

Superficial thrombophlebitis, or superficial vein thrombosis (SVT), is characterized by the formation of thrombi in the superficial veins, with subocclusion or occlusion of the venous lumen and an inflammatory reaction during it, which is more common in the lower extremities. The frequency of SVT is 0.3 to 0.6 per 1 000 in young patients and 0.7 to 1.5 per 1 000 in elderly patients. SVT can affect any vascular area. Most often it is localized in the superficial veins of the lower extremities, less often in the veins of the chest, abdomen, neck, and upper extremities. [1, 2]. The great saphenous vein (GSV) is affected in 60–80% of cases, the small saphenous vein (SSV) – in 10–20% of cases, bilateral damage – in 5–10% [3]. The prevalence in the general population is estimated at 3–11%. The prevalence of deep vein thrombosis (DVT) and pulmonary embolism (PE) combined is about twice as low. In a retrospective cohort study conducted in the Netherlands, the incidence of coded SVT events was 1.3 per 1 000 patients per year [4].

It was previously thought that SVT was easily diagnosed and treated only symptomatically. However, it has become clear that SVT, DVT, and PE are related diseases that can occur simultaneously or sequentially [5, 6]. In a meta-analysis by Minno et al., including 4358 patients in 22 studies, the prevalence of DVT was 18.1 % and 6.9 % of PE together with SVT [7, 8]. Recent studies have provided evidence that SVT should be considered a form of venous thromboembolism (VTE) along with DVT and PE [9]. During the COVID-19 pandemic, mortality rates from venous thrombosis tended to increase [10, 11]. Cui et al. (2020) reported that the prevalence of VTE in patients with COVID-19 is 25 % [12].

The etiology of SVT is multifactorial, generally related to the Virchow triad. The main causes are inflammatory, chemical, biological, and infectious processes, mechanical injuries, varicose veins [13].

There can be many reasons for the risk of developing SVT, but the following are a decrease venous blood flow (sedentary lifestyles, prolonged immobilization, chronic venous disease (CVD), pregnancy), damage to the inner lining of the veins (superficial injuries, injecting drugs), increased susceptibility to thrombosis or hypercoagulable state (surgical interventions, malignant tumors, hormone therapy, coagulation disorders), infections and viral diseases, hereditary factor or a combination thereof. It can develop against the background of vasculitis and other immunological syndromes (Trussus or Mondor syndromes) [13]. SVT can be a symptom of some inherited thrombophilias. Previous cases of SVT increase the risk of the following. This disease can also develop without any obvious favorable factor, often against the background of CVD. CVD in 75–88% of patients is the most important clinically identified factor in the development of SVT [7, 14, 15]. Venous stasis within dilated and incompetent main subcutaneous trunks leads to the formation of a

thrombus, which can spread to neighboring veins, including the deep venous system.

SVT begins with microscopic thrombosis. Microscopic thrombi in vascular wall damage, venous stasis or abnormal coagulation can spread and form macroscopic thrombi. Damage to the vascular endothelium significantly leads to thrombosis, causing an inflammatory reaction that leads to immediate adhesion of platelets. Thrombin and thromboxane A2 mediate platelet aggregation [16].

The clinical picture of SVT depends on the location of thrombosis, the prevalence of the thrombotic process, the degree of involvement in the inflammatory process of the surrounding tissues, and the presence of complications. In most cases, acute thrombophlebitis develops suddenly, for no apparent reason. Sometimes it is preceded by the trauma of a varicose vein, an infectious disease, a long bed rest. Complaints of pain in the area of thrombosed veins, the appearance of signs of inflammation, general weakness, fever, limb dysfunction. Examination reveals hyperemia of the skin, edema of the tissues along the thrombosed vein, slight edema and pastosity in the ankle and foot. Palpation along the thrombosed vein determines painful strands of varying density, local fever, hyperesthesia of the skin and paravasally painful dense infiltrates of various sizes, the presence of foci of fluctuation indicates purulent-septic melting of blood clots. Inflammation and other symptoms usually last for 3–4 weeks, but sometimes the process can take longer. The patient may experience a thrombosed vein for several months. Clinical manifestations are often benign and self-limiting [1, 13, 15]. However, it is important to consider the high risk of other VTEs [7, 8].

The diagnosis of SVT is made on the basis of clinical examination. However, for the final diagnosis, an instrumental examination is required, which will help to establish accurately: the presence of a blood clot; its position in the vessel and nature (floating or non-floating, occlusive or non-occlusive); the level of spread in the vascular system – whether the blood clot has passed into the deep veins. To do this, it is recommended to conduct a duplex ultrasound. Ultrasound examination is indicated in cases where the clinical picture is not clear (differential diagnosis); there are concomitant clinical signs indicating DVT; SVT is above the mid-thigh, especially if close to the sapheno-femoral junction (SFJ) (risk of thrombosis passing through the SFJ to the femoral vein; or if thrombophlebitis is located in the upper leg near the perforating veins of the knee, which also pass into the popliteal vein), Duplex ultrasound should show superficial and deep veins to characterize superficial venous insufficiency, which can be treated accordingly after the acute phase of the disease. [19] Van Langevelde K et al. or perforating veins in the popliteal region, the greater the likelihood of DVT and pulmonary embolism [20]. Leizorovicz A. et al. [21] and Galanaud et al. [22] believe that SVT in the GSV or SSV at a distance of 3 cm from the SFJ or safeno-popliteal junction (SPJ) is associated with a risk of PE similar to DVT, and in these cases, patients should be prescribed anticoagulant drugs [13]. In addition, the patient may be assigned laboratory tests such as clinical blood tests, coagulogram and blood D-dimer test. However, the determination of the level of D-dimer is not informative for the differential diagnosis of SVT and DVT [17, 18]. In patients with SVT without a provoking factor, it is necessary to conduct a detailed diagnosis to exclude cancer or thrombophilia [1].

The development of the disease can lead to life-threatening consequences. The treatment of thrombophlebitis cannot be postponed. The aim of SVT treatment is to alleviate local symptoms, as well as to prevent the spread of the process to the deep vein system and the development of PE.

In order to control the symptoms and reduce the spread of thrombosis and the risk of developing PE, a distinction is made between low-risk and high-risk SVT treatment [14]. Low-risk SVT is characterized by the absence of other thromboembolic diseases and a predisposition to them. It includes areas of thrombophlebitis with an extension of ≤ 5 cm, which are not near the SPJ or SFJ. High-risk SVT is characterized by a site of thrombophlebitis in the lower extremity ≥ 5 cm long; SVT is proximal to the knee, especially within 30 mm of the SFJ, regardless of its length; the presence of severe symptoms; the presence of a history of active malignancy or recent surgery, as well as previous SVT or VTE [16].

Symptoms of low-risk SVT can be alleviated with nonsteroidal anti-inflammatory drugs, elevated lower extremities, and compression stockings [19, 23]. It is recommended that the patient begin motor activity as soon as possible (immobilization increases the risk of DVT). Nonsteroidal anti-inflammatory drugs are often used to relieve pain, but do not affect the risk of thromboembolism [19].

According to the Cochrane review, high-risk SVT treatment is either an average therapeutic dose of low molecular weight heparins (e.g. enoxaparin 60 mg once daily) or a prophylactic dose of fondaparinux subcutaneously (2.5 mg once daily) for 45 days [24].

In 2017, the SURPRISE study [25] was published to determine the effectiveness of oral inhibitors of factor X – Rivaroxaban. Treatment was compared between rivaroxaban (10 mg once daily per os) and fondaparinux (2.5 mg once daily subcutaneously) for 45 days. Rivaroxaban has been shown as effective as fondaparinux. Thus, oral rivaroxaban may be a less burdensome and expensive alternative to subcutaneous fondoparinux injection. Additional studies are needed, but treatment with rivaroxaban may already be considered for high-risk patients with SVT. The practicality of rivaroxaban is its effectiveness [25]. There is no evidence of the effectiveness of other new oral anticoagulants. The Cochrane Review recommended further studies on its use and other direct oral inhibitors of factor X or thrombin [24, 26]. In addition, he recommended further research on the use of nonsteroidal anti-inflammatory drugs and low molecular-weight heparins [24].

Pregnancy is usually a criterion for exclusion from SVT treatment studies. However, it is a risk factor for the development of CVD, SVT, and VTE. Unfractionated heparin and low molecular weight heparins do not cross the placenta and are the drugs of choice. During pregnancy, unfractionated heparin is prescribed, which the woman takes throughout pregnancy and 6 weeks after delivery. If the criteria for anticoagulant therapy described above are not met, the patient may take oral NSAIDs that relieve symptoms but do not affect thrombosis. However, long-term oral NSAIDs are not recommended during pregnancy after 26–28 weeks of gestation [27, 28]. Topical NSAIDs may also be prescribed in addition to anticoagulant therapy [28]. Women with low-risk DVT and those who do not require symptom control should be monitored only. Clinical follow-up of these women should take place within 7–10 days with repeated duplex ultrasound every week [27, 28].

The use of graduated elastic compression stockings as the only treatment did not give advantages in comparison with the control group. However, their use in combination with other treatments (NSAIDs, anticoagulants) provides a more pronounced clinical improvement compared to that observed in groups that do not use elastic knitwear [29].

Topical application of an anticoagulant cream may alleviate the local symptoms of venous thrombosis, but there is no evidence that it can prevent the spread of thrombosis to deep veins [13].

Antibiotic therapy is not required and should be prescribed only in case of a concomitant infectious process [14].

SVT associated with the use of intravenous catheters is usually not treated with systemic anticoagulants. First-line treatment involves catheter removal and topical treatment and/or, if necessary, the administration of nonsteroidal anti-inflammatory drugs [6]. In this case, SVT in the Cochrane Review does not provide consensus recommendations on safety, required dose, or duration of therapy for topical treatments, nonsteroidal anti-inflammatory drugs, or systemic anticoagulants [30].

The Cochrane Review also evaluated local and surgical treatments, but noted that data on these treatments and their effects on VTE are too limited, so further research is currently recommended [16, 24]. Surgery on superficial veins is aimed at reducing the risk of recurrent SVT and other secondary VTE. It eliminates the source of venous stasis and varicose veins, can avoid recurrence and reduce both symptoms and progression of SVT. High subcutaneous vein ligation has often been used to treat solid waste that is close to the deep venous system [13]. Although surgery or ablation performed in the early stages after a SVT event may eliminate the possibility of the thrombotic process passing through the junction into the deep venous system, this approach is not without risk. There is a possibility of post-procedural VTE due to the inability to remove large segments of GSV and/or SSV and in combination with a potentially generalized prothrombotic state. Prolonged thromboprophylaxis may be a solution to this problem. Surgical treatments may be recommended after the acute phase, i.e. three months after the last episode of SVT. Planned surgical treatment of superficial veins should be considered for patients in whom repeated venous thrombosis affects the same areas on the background of CVD. Although this approach is rational and widely practiced, this approach is not based on evidence [19].

The main principle of SVT prevention is timely detection and adequate treatment of chronic venous diseases. This involves surgical treatment of early (uncomplicated) stages of CVD [16, 19].

The aim of the study was to assess the prevalence of SVT in patients with CVD; identify the relationship between the diameter of the great saphenous vein and SVT.

Materials and Methods

We analyzed 925 cases of CVD from January 2019 to December 2021 at the Clinical Department of Surgery, Traumatology, Orthopedics and Phthisiology of Sumy State University (LLC «Sumy Laser Clinic») for the prevalence of SVT in patients who were undergoing treatment. All patients included in the study signed the informed consent to participate in accordance with the World Medical Association's Declaration of Helsinki (WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects). The study was approved by the Bioethics Commission of the Academic and Research Medical Institute of Sumy State University (Protocol № 3/12 of 14 December 2020).

Exclusion criteria were pregnancy or lactation, deep vein thrombosis, connective tissue disease, cancer, severe comorbidities, recent surgery or trauma, prolonged immobilization, hormone therapy.

The diameters of GSV and venous reflux were assessed on ultrasound 10 mm below the SFJ, in the upper and lower thirds of the thigh. It was determined using ultrasound the SonoScape S6 apparatus with an L741 linear probe (frequency range of 7–13 MHz) in the gray-scale B-mode (Figure 1). Pathological reflux was determined by duration ≥ 0.5 seconds. In addition, ultrasound results were used to assess the degree of thrombosis, exclude the presence of DVT, and determine superficial and/or deep venous insufficiency.

To optimize the work created an electronic database using Microsoft Excel 2016. For the obtained indicators, the arithmetic mean (M) and standard error of the mean (m) were calculated. To rate the degree of significance of differences between the groups, a simple Student's t test (t) was used.

Results and Discussion

925 cases of CVD treatment at LLC «Sumy Laser Clinic», Ukraine, from January 2019 to December 2021 were analyzed. Of these, SVT was observed in 53 cases, which accounted for 5.73 % of the total. According to gender, women accounted for 67.9 % (36), men – for 32.1 % (17). The study included patients aged 25 to 69 years (mean age 52.62 ± 10.48 years).

Figure 1 – Ultrasound examination of the lower extremities

A population-based study found that CVD is a risk factor for VTE and correlates with an increased risk of mortality in patients [31]. A recent retrospective cohort study during a median follow-up of 7.5 years found a 4-fold increase in the risk of DVT in patients with CVD [32]. VTE is a major disease burden worldwide, with approximately 10 000 000 cases per year [33].

When evaluating patients with CVD, a common parameter that is often measured and recorded is the diameter of the main subcutaneous vein. Labropoulos et al. [34], Conway et al. [35] and Yang et al. [36] reported a significantly larger subcutaneous vein diameter in patients with C4–C6 CEAP clinical, etiological, anatomical, and pathophysiology classification compared to patients with C2–C3 class; those classified as C4 and C5 had statistically significant larger diameters of the perforated calf veins than those with class C2.

The diameter of GSV in our study was ≥ 10 mm at a level 10 mm below the SFJ in 69.8 % (37) of SVT cases; in the upper third of the thigh – in 49 % (26) of cases of SVT; in the lower third of the thigh – in 30.2 % (16) of cases of SVT (P > 0.05). That is, the extension of the SFJ trunk to the lower third of the thigh was preserved in 43.24 % of cases.

CONCLUSIONS / ВИСНОВКИ

The results of the study showed a significant prevalence (5.73%) of SVT in patients with CVD. SVT is registered in 69.8% with a diameter of the great saphenous vein ≥ 10 mm.

PROSPECTS FOR FUTURE RESEARCH / ПЕРСПЕКТИВИ ПОДАЛЬШИХ ДОСЛІДЖЕНЬ

Given the relationship between thrombosis and the diameter of the GSV, the prospects for further research are the availability of a non-invasive outpatient surgery approach to the treatment of CVD. This will allow the use of prevention and treatment regimens to prevent the progression of CVD complications. There is an urgent need to develop new approaches to reduce the risk of VTE.

CONFLICT OF INTEREST / КОНФЛІКТ ІНТЕРЕСІВ

The authors declare no conflict of interest.

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None.

AUTHOR CONTRIBUTIONS / ВКЛАД АВТОРІВ

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A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

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