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EFFECTIVENESS OF ANTICOAGULANT-BASED COMPREHENSIVE THERAPY IN PATIENTS WITH SUPERFICIAL VEIN THROMBOSIS

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Abstract

Superficial vein thrombosis (SVT) of the lower extremities remains a clinically relevant condition due to its risk of thromboembolic complications and variability in response to anticoagulant therapy. The aim of this study was to evaluate the clinical and ultrasound effectiveness of anticoagulant therapy and to identify factors influencing thrombus regression. A prospective observational study included 104 patients with acute SVT associated with varicose vein disease who received anticoagulant therapy with dynamic clinical and duplex ultrasound monitoring over 8 weeks. Clinical improvement was observed in 87.5% of patients and was accompanied by thrombus disorganization, decreased echogenicity, and, in some cases, partial recanalization. Two patterns of response were identified: rapid regression (27.9%) and delayed regression (72.1%), associated with the severity of inflammatory changes, thrombus structure, and early presentation. The effectiveness of anticoagulant therapy was also influenced by local hemodynamic conditions. These findings highlight the importance of combined clinical and ultrasound assessment for predicting treatment outcomes.

Keywords

superficial vein thrombosis; anticoagulant therapy; varicose veins; duplex ultrasonography; thrombus morphology; thrombus regression; venous thrombosis; inflammation; periphlebitis; hemodynamics; low-molecular-weight heparin; recanalization.

Introduction

Superficial vein thrombosis of the lower extremities (SVT) is a common vascular disorder traditionally regarded as a complication of varicose vein disease. According to epidemiological studies, the incidence of SVT in the general population is comparable to, or even exceeds, that of deep vein thrombosis (DVT), reaching up to 3–11% among patients with chronic venous insufficiency[2].

Despite its relatively “benign” clinical course, superficial vein thrombosis should not be considered an isolated condition. According to current evidence, SVT is associated with concomitant deep vein thrombosis in 18–29% of cases, while the risk of pulmonary embolism (PE) reaches 4–7%, which significantly alters the clinical relevance of this condition [2,1].

The key pathogenetic mechanism underlying the development of superficial vein thrombosis is the combination of factors described by Virchow’s triad: venous stasis, endothelial injury, and hypercoagulability. In varicose vein disease, the leading role is played by chronic venous stasis and structural remodeling of the venous wall, accompanied by inflammatory infiltration and hemodynamic disturbances [3].

In contrast to deep vein thrombosis, in which the coagulation component predominates, superficial vein thrombosis is characterized by a pronounced inflammatory process (phlebitis/paraphlebitis), which determines the morphology of the thrombus. It has a denser structure, is more often adherent to the venous wall, and is associated with reactive changes in

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the surrounding tissues. This factor has a fundamental impact on the effectiveness of anticoagulant therapy, as the inflammatory component may limit drug penetration into the area of thrombosis [4]. Current guidelines are shifting the focus of SVT management toward conservative therapy. The most compelling evidence for the efficacy of anticoagulants was obtained in the randomized CALISTO trial, in which the use of fondaparinux significantly reduced the risk of thrombus progression and the development of thromboembolic complications [1].

Nevertheless, despite the existing evidence base, a number of unresolved issues remain. In particular, most studies focus on clinical outcomes (pain, inflammation, progression) but do not give sufficient attention to the morphological dynamics of the thrombus and the factors influencing its lysis. Moreover, in clinical practice there is considerable variability in the response to anticoagulant therapy, ranging from rapid thrombus lysis to its prolonged organization without significant recanalization. This underscores the need for a more detailed analysis of prognostic factors, including the ultrasound characteristics of the thrombus.

Duplex ultrasonography is currently considered the “gold standard” for the diagnosis of venous thrombosis and allows not only confirmation of thrombus presence but also assessment of its structure, echogenicity, degree of fixation, and the extent of inflammatory changes, thereby enabling dynamic monitoring and prediction of disease course [5].

Thus, despite the proven efficacy of anticoagulant therapy, the question of factors determining its effectiveness in superficial vein thrombosis remains relevant.

The aim of the study was to evaluate the clinical and ultrasound effectiveness of anticoagulant therapy in superficial vein thrombosis of the lower extremities.

Materials and Methods.

A prospective observational study was conducted at Clinic No. 1 of the Samarkand State Medical University and included 104 patients with acute superficial vein thrombosis of the lower extremities associated with varicose vein disease, who received anticoagulant therapy as part of comprehensive conservative treatment. All patients were treated in a surgical inpatient setting followed by outpatient follow-up. The time from the onset of clinical symptoms to seeking medical care ranged from 1 to 12 days, with a mean of 4.8 ± 2.1 days. Depending on disease duration, patients were conditionally divided into two subgroups: early presentation (within 3 days, n=46) and late presentation (more than 3 days, n=58).Inclusion criteria: acute superficial vein thrombosis of the lower extremities confirmed clinically and by duplex ultrasonography; presence of varicose vein disease; disease duration not exceeding 14 days; provision of informed consent to participate in the study and the possibility of dynamic follow-up.

Exclusion criteria: embolism-prone forms of thrombosis (floating proximal segment); involvement of deep veins; presence of open trophic ulcers; acute infectious and inflammatory diseases (including erysipelas); decompensated somatic diseases; forced immobilization; inability to comply with the anticoagulant therapy regimen and subsequent follow-up.

A total of 104 patients were included in the study, with a predominance of women — 72 (69.2%), while men accounted for 32 (30.8%). The age of the examined patients ranged from 29 to 79 years, with a mean age of 55.1 years (95% CI: 51.8–58.4 years).

In all patients, the thrombotic process developed in the setting of varicose vein disease, clinically manifested by dilation, tortuosity, and nodular transformation of the superficial veins. The duration of varicose vein disease ranged from 3 to 48 years, with a mean of 24.9 years (95% CI: 21.6–28.2 years), indicating the chronic nature of venous pathology and its significant role in thrombogenesis.Clinical examination was performed according to a standard algorithm

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and included a detailed assessment of patient complaints with evaluation of pain severity, the degree of hyperemia, and soft tissue infiltration along the course of the affected vein. Particular attention was paid to determining the extent of the thrombotic process, which was documented using skin marking.Additionally, the boundaries of paravasal inflammation were assessed, which made it possible to objectively quantify the dynamics of the local inflammatory process and to monitor its regression during therapy. This approach ensured comparability between clinical and ultrasound data throughout the follow-up period.

Clinical examination and duplex ultrasonography of the lower extremity veins were performed in all patients at the time of initial presentation. Subsequent monitoring was carried out dynamically: daily during the first 5–7 days of treatment, followed by assessments at 7-day intervals throughout the entire observation period, which lasted up to 8 weeks. This schedule allowed evaluation of both early and delayed changes in the thrombotic process.

During ultrasound monitoring, the main clinically relevant characteristics of the thrombus were analyzed. These included its localization and extent, the degree of propagation along the venous system, the presence of a free proximal segment and its length. In addition, echogenicity and structural features of the thrombotic masses in different segments were assessed, as well as the severity of inflammatory changes in the venous wall and surrounding tissues.

Particular attention was paid to the dynamics of these parameters during treatment, which made it possible to objectively assess the effectiveness of therapy. Positive ultrasound dynamics were defined as signs indicating regression of the thrombotic process, including a reduction in thrombus size, decreased echogenicity, the appearance of a heterogeneous (reticular) structure, as well as a reduction in the thickness of the inflamed venous wall and paravasal tissue.

A comprehensive assessment of clinical manifestations and ultrasound findings provided an objective means of monitoring disease progression and allowed correlation of subjective symptoms with morphological changes in the area of thrombosis.

At initial duplex ultrasonography, signs of embolism-prone thrombosis were identified in a subset of patients. In 18 cases (17.3%), the thrombus was localized in the proximal segments of the superficial venous system at the level of the thigh and had a free-floating segment.

These patients were classified as a high-risk group for thromboembolic complications and underwent emergency surgical intervention in the form of crossectomy. The indication for surgical treatment was the presence of an ascending thrombotic process with a floating proximal segment exceeding 4 cm in length, consistent with generally accepted criteria for embolic risk.

The remaining patients (n = 86) received conservative therapy. In the operated group, anticoagulant treatment was initiated in the early postoperative period, typically within the first 24 hours, whereas in non-operated patients it was started immediately after diagnosis.

Comprehensive therapy included the use of low-molecular-weight heparins at therapeutic doses (enoxaparin, fraxiparine), topical anti-inflammatory agents, as well as mandatory compression therapy using class II compression stockings.

All patients were advised early mobilization from the first day, including graded walking and elements of therapeutic exercise, which contributed to improved venous outflow and reduced the risk of thrombus progression.

The duration of patient follow-up was 8 weeks, allowing for the assessment of both early and long-term changes in the thrombotic process.

Data analysis was performed using specialized statistical software. Quantitative variables are presented as mean values with standard deviation, as well as 95% confidence intervals.

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Results

In all patients included in the study, disease onset was characterized by the acute development of clinical symptoms typical of superficial vein thrombosis. The leading manifestations were localized tenderness along the course of the affected vein, cutaneous hyperemia, and soft tissue infiltration of varying severity.

The intensity of inflammatory changes ranged from moderate hyperemia with mild tenderness to pronounced infiltration with a dense, painful cord along the vein, reflecting different stages of the thrombotic process at the time of presentation.

The distribution of involvement by side was relatively even: thrombosis of the left lower extremity was recorded in 54 patients (51.9%), and of the right in 50 patients (48.1%).

Initial clinical assessment demonstrated that the thrombotic process had variable localization. Isolated involvement of the thigh veins was identified in 20 patients (19.2%), confinement of the process to the lower leg in 45 (43.3%), while combined involvement of both the lower leg and thigh veins was observed in 39 patients (37.5%).

Analysis of anatomical localization demonstrated that in the majority of cases the great saphenous vein system was involved in the pathological process. Isolated involvement of the trunk of the great saphenous vein was recorded in 59 patients (56.7%), and its tributaries in 32 (30.8%). Simultaneous involvement of both the trunk and tributaries of the great saphenous vein was observed in 7 patients (6.7%).

Involvement of the small saphenous vein was significantly less frequent. Isolated thrombosis of its trunk was identified in 2 patients (1.9%), while combined involvement of the trunk and tributaries was observed in 1 patient (1.0%). Concurrent involvement of both the small and great saphenous veins was diagnosed in 3 patients (2.9%).

In the subgroup of patients receiving conservative treatment (n = 86), duplex ultrasonography revealed variability in the localization of the proximal segment of the thrombus.

In 38 patients (44.2%), the proximal portion of the thrombus was located at the level of the thigh. Among them, signs of a free, non-adherent segment were identified in 6 patients (7.0%). The length of the free segment ranged from 1.4 to 2.6 cm, with a mean of 1.9 cm (95% CI: 1.3–2.4 cm). True flotation, manifested by oscillatory movements of the thrombus synchronous with respiration, was observed only in isolated cases—namely in 1 patient (1.2%), with a free segment length exceeding 2.5 cm.

In the remaining 48 patients (55.8%), the proximal segment of the thrombus was localized at the level of the lower leg. A free segment in this group was detected in 8 patients (9.3%), with a wider range of lengths—from 1.0 to 4.2 cm, averaging 1.9 cm (95% CI: 0.9–3.3 cm). Signs of flotation in this subgroup were likewise rare and were identified in 1 patient (1.2%) at the maximum length of the free segment.

In the subgroup of patients who underwent surgical treatment (n = 18), duplex ultrasonography demonstrated that in all cases the proximal segment of the thrombus was localized at the level of the thigh, indicating an ascending pattern of the thrombotic process.

A free proximal segment of the thrombus was identified in 12 patients (66.7%). Its length ranged from 2.5 to 14.8 cm, with a mean of 7.2 cm (95% CI: 4.6–9.8 cm). In most cases, this segment was characterized by high mobility.

Thrombus flotation, manifested by pronounced oscillatory movements synchronous with respiration, was observed in 11 patients (61.1%). The length of the floating segment in these cases ranged from 4.0 to 14.8 cm, with a mean of 7.6 cm (95% CI: 5.1–10.2 cm).

Against the background of anticoagulant therapy, positive clinical dynamics were observed in the majority of patients (n = 91; 87.5%), as evidenced by a reduction in

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inflammatory changes and regression of pain syndrome. In the remaining patients (n = 13; 12.5%), clinical manifestations persisted for a longer period; however, no signs of thrombotic progression were observed.Regression of clinical symptoms followed a sequential pattern. Initially, a reduction in cutaneous hyperemia was observed, followed by a decrease in pain intensity, and finally resolution of soft tissue infiltration, reflecting gradual attenuation of the inflammatory component.

According to duplex ultrasonography, positive ultrasound dynamics were characterized by a reduction in thrombus extent, decreased echogenicity, and the formation of a heterogeneous structure with areas of low echogenicity. Concurrently, a decrease in the thickness of the inflamed venous wall and paravasal tissue was observed.

At the same time, it was established that the rate of regression of the thrombotic process varied significantly. Based on the rate of ultrasound changes, two main patterns of disease course were identified.

In 29 patients (27.9%), a relatively rapid positive dynamic was observed, with significant changes in thrombus structure detected within the first week of treatment. In this group of patients, early reduction in thrombus echogenicity and the appearance of signs of its disorganization were noted.

In the majority of patients (n = 75; 72.1%), the dynamics were more gradual. In these cases, pronounced ultrasound changes were predominantly observed within 10 to 30 days, corresponding to progressive remodeling and partial recanalization of the thrombotic masses.

The subgroup of patients with relatively rapid regression of the thrombotic process comprised 29 individuals (27.9%). This category was characterized by early presentation for medical care—within 2 days from disease onset, with a mean of 1.6 days (95% CI: 1.2–2.0 days).

Clinically, these patients predominantly exhibited moderately expressed inflammatory changes, manifested by limited hyperemia and mild soft tissue infiltration along the course of the affected vein.

According to duplex ultrasonography, signs of structural heterogeneity of the thrombus were already noted at the initial examination. The proximal segment was characterized by indistinct contours and the presence of areas of varying echogenicity with the formation of a reticular structure, indicating its relative “immaturity.”The thickness of the inflamed venous wall and paravasal tissue in the region of the proximal segment ranged from 3 to 6 mm, with a mean of 3.5 mm (95% CI: 3.0–4.1 mm). In the middle portion of the thrombus, this parameter was slightly higher, ranging from 4 to 8 mm, with a mean of 5.4 mm (95% CI: 4.9–5.9 mm).

Against the background of anticoagulant therapy, patients in this group demonstrated rapid regression of inflammatory changes. Clinical resolution of signs of paravasal inflammation was observed within 2 to 6 days, with a mean of 3.6 days (95% CI: 2.9–4.3 days). Ultrasound dynamics were pronounced and occurred early. A significant decrease in the echogenicity of thrombotic masses was already observed within the first week of treatment, indicating the onset of thrombus disorganization.

Lysis of the proximal segment of the thrombus, including its free portion when present, occurred within 3 to 7 days, with a mean of 5.2 days (95% CI: 4.4–6.0 days). Notably, the free portions of the thrombus regressed most rapidly, likely due to their lower degree of fixation and greater exposure to blood flow.

In cases where a free proximal segment was absent, positive dynamics manifested as gradual changes in the internal structure of the thrombus, including an increase in areas of reduced echogenicity and the formation of a pronounced heterogeneous, “reticular” structure.

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The group of patients with a slower regression of the thrombotic process comprised 75 individuals (72.1%). In this group, presentation for medical care occurred at later stages—between 3 and 10 days from disease onset, with a mean of 5.5 days (95% CI: 4.9–6.1 days).
Despite ongoing anticoagulant therapy, positive dynamics in these patients were delayed. A significant reduction in the echogenicity of thrombotic masses, according to duplex ultrasonography, was predominantly observed at later time points—between 10 and 30 days, with a mean of 12.1 days (95% CI: 10.8–13.4 days).
Comparative analysis demonstrated that baseline clinical manifestations in this group were more pronounced, including intense pain, marked hyperemia, and dense soft tissue infiltration along the course of the affected vein.
The ultrasound findings also indicated a greater degree of thrombus "maturity." At initial examination, both proximal and distal segments of the thrombotic masses were characterized by high echogenicity and well-defined contours, reflecting a more advanced stage of thrombus organization.The thickness of inflamed paravasal tissue in the region of the proximal segment ranged from 5 to 20 mm, with a mean of 8.1 mm (95% CI: 7.0–9.2 mm). In the distal segments, these changes were even more pronounced—ranging from 7 to 22 mm, with a mean of 10.4 mm (95% CI: 9.5–11.3 mm).
Positive ultrasound dynamics in this group manifested as a gradual increase in areas of reduced echogenicity within the thrombus and the formation or enhancement of its heterogeneous ("reticular") structure.
It should be noted that changes within the thrombotic masses occurred more slowly than the regression of inflammatory changes in the surrounding tissues. According to clinical and ultrasound data, signs of paravasal inflammation resolved within 6 to 15 days, with a mean of 7.8 days (95% CI: 7.1–8.4 days).

The dynamics of the thrombotic process were analyzed separately in patients who underwent crossectomy. It was established that in this category of patients, thrombus regression occurred at later time points compared not only with patients exhibiting rapid dynamics but also with those in the slow-course group.
A probable explanation for this phenomenon is the alteration of hemodynamics following ligation of the trunk of the great saphenous vein, accompanied by reduced blood flow in the area of the thrombosed segment. This, in turn, may slow the processes of disorganization and lysis of thrombotic masses.

The obtained observations indirectly confirm the importance of preserving and stimulating venous blood flow as one of the factors contributing to more effective thrombus regression during conservative treatment.

In addition, in a subset of patients (n = 9; 8.7%), elective surgical intervention in the form of miniphlebectomy was performed after resolution of the acute inflammatory process, aimed at eliminating varicose veins as the primary pathogenetic factor of the disease.

Discussion

The present study demonstrates that the effectiveness of anticoagulant therapy in superficial vein thrombosis is heterogeneous and largely determined by baseline characteristics of the thrombotic process, particularly the severity of inflammation, thrombus structure, and timing of presentation.

Although clinical improvement was achieved in the majority of patients (87.5%), ultrasound findings revealed substantial variability in the rate and pattern of thrombus regression. Two distinct trajectories were identified: rapid regression (27.9%) and delayed

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regression (72.1%), indicating that anticoagulant therapy does not produce uniform effects across patients.

Early presentation (within 2 days) was strongly associated with faster thrombus resolution. In this subgroup, thrombi were characterized by structural heterogeneity, indistinct contours, and lower echogenicity, suggesting a less organized ("immature") state. These features were accompanied by less pronounced inflammatory changes and thinner paravasal tissue involvement (mean 3.5 mm proximally), which likely facilitated both anticoagulant penetration and the effect of blood flow on thrombus disorganization. As a result, thrombus lysis—particularly in free segments—occurred within the first week of treatment (mean 5.2 days).

In contrast, delayed presentation was associated with slower thrombus regression. In these patients, thrombi demonstrated higher echogenicity, well-defined contours, and greater structural organization, indicating a more advanced stage of thrombus maturation. This was accompanied by more pronounced inflammatory changes, including increased thickness of paravasal tissue (up to 10.4 mm distally), which likely impaired local hemodynamics and limited the effectiveness of anticoagulant therapy. As a result, significant ultrasound changes were delayed, occurring predominantly between 10 and 30 days.

An important finding is that regression of inflammatory changes consistently preceded structural remodeling of the thrombus. Clinical and ultrasound signs of paravasal inflammation resolved earlier (mean 3.6 days in the rapid group and 7.8 days in the slow group), suggesting that reduction of the inflammatory component may serve as an early indicator of treatment response.

The distribution of thrombus regression also demonstrated segmental differences. The most pronounced and rapid changes occurred in proximal and especially free segments of the thrombus, which are more exposed to blood flow. In contrast, distal segments, particularly in the presence of marked inflammation, exhibited slower lysis, reflecting a higher degree of thrombus organization and reduced hemodynamic influence.

The role of hemodynamics was further supported by findings in patients who underwent crossectomy. Despite subsequent anticoagulant therapy, thrombus regression in this group was delayed compared to non-operated patients. This is likely explained by reduced blood flow following ligation of the great saphenous vein, which may limit mechanical and biochemical factors contributing to thrombus disorganization.

Taken together, these findings indicate that the effectiveness of anticoagulant therapy depends not only on pharmacological intervention but also on thrombus morphology, inflammatory burden, and venous blood flow. Duplex ultrasonography provides critical information for identifying these factors and allows stratification of patients according to expected treatment response.

Thus, a combined clinical and ultrasound approach is essential for optimizing management strategies and predicting outcomes in patients with superficial vein thrombosis.

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