LONG-TERM RESULTS OF PATHOGENETICALLY-GROUNDED METHODS OF TREATMENT OF PATIENTS WITH POSTTHROMBOTIC SYNDROME OF THE LOWER EXTREMITIES ACCORDING TO THREE-YEAR FOLLOW-UP

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The aim of this study was to evaluate the effectiveness of surgical treatment using a modified method of correction of venous hemodynamic disorders of the lower extremities by the state of function of the leg muscle pump during long-term follow-up in the postoperative period of patients with postthrombotic syndrome of the lower extremities. 148 patients with lower limb postthrombotic syndrome (C5, 6, S, Es, As, d, p, Pr, LI by CEAP classification) were divided in two groups. The first group included 71 patients, which were treated by traditional methods of surgical intervention (crossectomy and venecseresis). The second group consisted of 77 patients who underwent closed separation of the perforating veins and paratibial fasciotomy in the complex of surgical treatment. The function of the leg muscle pump was studied using three methods: a 6-minute marching test measuring the circumference of the limbs, the amplitude indices of movements in the ankle joint with a protractor, and electromyography using a multichannel electromyography with skin electrode application. The quality of life was studied using the CIVIQ questionnaire, the severity of venous pathology by the VCSS scale and disability rates by the VDS disability scale. The examination was performed before the surgery, after 1 year and after 3 years of observation. In both groups of patients, there was a decrease in the basal levels of a 6-minute marching test, the movement amplitude in the ankle joint, the electromyography indicators, the presence of a strong correlation between these parameters, indicating venous dysfunction in the lower extremities. In the postsurgical period (in 1 and 3 years), there was a reduced circumference of the legs during the marching test, an increased amplitude of movements in the ankle joint with a protractor, and electromyography indicators – the mean and maximum amplitude of oscillations. In patients of group II, the results were better than in patients of group I. In the pre-surgical period, a significant deterioration of the life quality was observed in terms of the CIVIQ questionnaire, the severity of venous pathology – by the VCSS scale and a decrease in working capacity – by the VDS disability scale in both groups. In the long-term postsurgical period, there was an improvement of these indicators, more pronounced in patients of group II. Clinical study of long-term results of the closed separation of perforating veins and paratibial fasciotomy operation confirmed the high efficiency of this method and allowed us to consider it as a pathogenetically-grounded method of surgical treatment of patients with postthrombotic syndrome of the lower extremities.

Key words: postthrombotic syndrome, paratibial fasciotomy, chronic venous diseases

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Reферат. Віддалені результати патогенетично обґрунтованих методів лікування хворих на посттромботичний синдром нижніх кінцівок за даними трирічного спостереження. Оринчак В.А., Гудз О.І. Метою дослідження було оцінити ефективність оперативного лікування із застосуванням модифікованого методу корекції порушень венозної гемодинаміки нижніх кінцівок за станом функції м'язової помпи гомілки при довготривалиму спостереженні в післяоперативному періоді хворих на посттромботичний синдром нижніх кінцівок. Під спостереженням перебувало 148 хворих на посттромботичний синдром нижніх кінцівок (C5, 6, S, Es, As, d, p, Pr, LI згідно з міжнародною класифікацією CEAP), які були розподілені на дві групи. До першої групи залучено 71 хворий, яким були проведені традиційні методи оперативного втручання (кросcktомія та венексерез). Другу групу склали 77 хворих, яким у комплексі оперативного лікування було застосовано закрите
As of today, according to the international statistics, up to 83.6% of the world's population suffers from chronic venous diseases (CVD) [10]. Patients with postthrombotic syndrome (PTS) of lower extremities occupy a large share in the structure of CVD. By various authors, this disease affects from 1.5% to 5% of population. Among such patients, people of working age from 20 to 50 years old predominate [4, 11]. In case of no adequate treatment, 2-5 years later, half of patients with PTS develop severe forms of CVD, including venous ulcers. And if in European countries CVD are complicated by trophic ulcers in 2% of cases, in Ukraine this figure is much higher. Thus, according to the all-Ukrainian epidemiological study "DETECT 1000", 7.4% of patients were found to develop trophic venous ulcers – healed C5 (4.2%) and active C6 (3.2%) [3]. It is caused by social and medical problems, as well as surgeons’ usual passive attitude to these patients. The presence of PTS of lower extremities reduces patients’ life quality (LQ) and ends in their severe disability complicated with trophic disorders and venous ulcers [5].

Given that the tibial fasciocompression syndrome plays an important role in pathogenesis of trophic ulcers in patients with PTS of lower extremities, the performance of closed separation of perforating veins and paratibial fasciotomy will improve the prognosis of CVD course [1]. However, the literature contains no data on the results of long-term observation over such patients. At the same time, there exist no clearly developed and unified criteria for assessing the quality of treatment of such patients [12]. Often, in the postoperative period, despite the lack of clear clinical signs of PTS of lower extremities, patients are dissatisfied with their LQ. Therefore, when assessing the quality of treatment, it is necessary to take into account both objective indices and subjective feelings of patients, which finally determined the purpose of our research work.

The purpose of research work was to evaluate the effectiveness of surgical treatment using a modified method of correction of venous hemodynamic disorders of the lower extremities by the state of function of the leg muscle pump during long-term follow-up in the postoperative period of patients with postthrombotic syndrome of the lower extremities.

**MATERIALS AND METHODS OF RESEARCH**

Within the period from 2015 to 2020, 148 patients with PTS of lower extremities were observed (C5, 6, S, Es, As, d, p, Pr, L1 according to international classification CEAP [7]); they were hospitalized to the Vascular Surgery Department of the Ivano-Frankivsk Regional Clinical Hospital.

The research was approved by the Biomedical Ethics Commission of Ivano-Frankivsk national medical university and was conducted in accordance with the principles of bioethics set out in the WMA Declaration of Helsinki – “Ethical principles for medical research involving human subjects” and “Universal Declaration on Bioethics and Human Rights” (UNESCO).

The patients were divided into two groups. The first group included 71 patients, mean age – 56.5±0.8 years (24 – men, 47 – women), who underwent traditional methods of surgery (crossectomy and veneseresis). The second group consisted of 77 patients, mean age – 57.1±1.1 years (28 – men, 49 – women), who underwent closed separation of perforating veins and paratibial fasciotomy in the complex of surgical treatment (Patent of Ukraine No. 115035 "Method of treatment of postthrombotic syndrome of lower extremities"), using the self-developed tools (Patents...
of Ukraine No. 29760 "Device for separation of fascia" and No. 46002 "Device for separation of perforating veins"). Along with the main disease, some patients were diagnosed with various comorbidities: coronary heart disease, atherosclerotic cardiiosclerosis detected in 23 (32.4%) patients of group I and 24 (31.2%) patients of group II; hypertension I-II stages – in 20 (28.2%) patients of group I and 23 (29.9%) patients of group II; obesity I-II stages – in 11 (15.5%) patients of group I and 13 (16.9%) patients of group II; vegetative-vascular dystonia by hypertensive type – in 4 (5.6%) patients of group I and 5 (6.5%) patients of group II. Consequently, both groups of patients were statistically comparable in terms of gender, age, concomitant pathology and the nature of venous blood flow disorders (p>0.05). The control group consisted of 40 healthy individuals showing no signs of CVD, mean age – 55.7±0.9 years (15 – men, 25 – women).

The rationale for closed separation of perforating veins and paratibial fasciotomy was both the literature data [12] and our own results, indicating the development of chronic compartment syndrome with dysfunction of the muscle pump in the late stages of PTS. For this, in the upper third of the lower leg, 4 cm from the medial edge and 2 cm from the lateral edge of the tibia, vertical skin incisions 3-4 cm long were made. After blunt separation of the subcutaneous tissue, the fascia of the lower leg was cut longitudinally along the entire length of the wound. At the next stage, the spatula was alternately introduced into the wounds subfascially to separate the perforating veins and destroyed them towards the ankle joint over the entire width of the lower leg. After compression of the lower leg for 5 minutes to stop bleeding from the severed perforating veins, the fascia was dissected along both surfaces of the lower leg using a fasciotome. The operation was completed by draining both subfascial areas according to Redon, suturing the skin and elastic bandaging. After surgery, patients were prescribed strict bed rest for 5 days with the appropriate appointment of low-molecular-weight heparins for the prevention of venous thromboembolism. The drains were removed the next day after the operation. It should be noted that in both groups there were no patients who underwent autodermoplasty of the ulcer. Postoperative management of patients in both groups included constant adequate compression therapy, as well as standard medical treatment. The choice of treatment was guided by the recommendations of the world phlebological societies regarding the long-term pathogenetically justified use of the micronized purified fraction of flavonoids in patients with CVD symptoms and the presence of trophic skin disorders in particular [1].

Apart from the general clinical examination, all patients underwent Doppler and Duplex examination – in order to diagnose and define the severity of venous reflux in deep veins of the affected limb (Logiq C-5, producer General Electric). The function of muscle pump of tibia was studied using three methods: a 6-minute march test along with measuring the circumference of extremities; the amplitude indices of movements in the ankle joint (AMAJ) using a goniometer; electromyography using a multichannel electromyograph with cutaneous application of electrodes (M-TEST 4, producer DX-Systems).

The protocol of a 6-minute march test was as follows: the patient was placed in horizontal position for 10 minutes with his lower limbs raised at the angle of 45 degrees, and after that the circumference of his right tibia was measured. Then the patient stood up on his left leg and was standing in this position for 10 minutes without touching the floor with the right foot, while the circumference of his right leg was re-measured. Afterwards, the patient was suggested to walk at a normal pace for 6 minutes and the circumference of his right tibia was measured. Similarly, the circumference of left tibia was measured [14].

During the research of AMAJ, the patient was placed in horizontal position. The measurements were made with the relaxed Achilles tendon, the knee joint was bent for that. The measurements were performed using a goniometer, the foot was set in the position of extreme extension (dorsiflexion) and flexion (plantar flexion) [6].

Electromyography was performed by standard methods: electrodes were put on the skin in the area of calf muscle under study, whereas the indices of bioelectrical activity of muscles were recorded. Then the patient stood up on his toes, thus causing the contraction of muscles involved in functioning of the muscle pump, and the muscular activity was recorded during physical exercises [9].

The parameters of LQ were studied using the CIVIQ questionnaire [13]. This questionnaire included 20 questions. On the basis of the points collected, the patients’ LQ was assessed for the previous four weeks. But since the total score per each factor depends on the number of questions, the scores collected are difficult to be compared. Therefore, the absolute scores are translated into a relative scale with values from 0 to 100% by the formula:

$$X = \frac{a - b}{c - b} \times 100\%,$$

where X – the rate of LQ, a – the actual score, b – theoretically minimal score, c - theoretically maximal score.
Given that the worst LQ corresponds to a higher score on this scale, the term "disease-related LQ limitations" is used to describe the impact of this index.

Referring to the recommendations for assessing the condition of patients with CVD of lower extremities, the American Forum of Phlebologists has worked out the clinical scale of venous pathology – VCSS (Venous Clinical Severity Score) and the scale of working ability reduction – VDS (Venous Disability Score) [8]. These scales are reliable and clinically convenient, so that they allow to quantify the results of surgical treatment of PTS of lower extremities.

All the studies were performed after admission to hospital and before surgery, also 1 and 3 years after surgery during follow-up examinations.

The statistical processing of the results obtained was performed using the statistical analysis program STATISTICA 6.1 (StatSoft Inc., serial number AGAR909E415822FA). Student’s t-criterion was used to compare the quantitative indices. Correlation analysis was used to establish the dependencies. The statistically significant level of reliability was considered p<0.05 [2].

RESULTS AND DISCUSSION

All patients had a history of deep vein thrombosis, and during duplex examination, pathological blood reflux was found in the femoral (3.5±0.4 sec.), popliteal (3.1±0.3 sec.) and perforating veins of the leg (more than 0.5 sec.), which indicates a violation of the venous hemodynamics of the lower extremities [5].

One of the reasons causing the disorder of venous hemodynamics in PTS of lower extremities is the dysfunction of tibial muscle pump. As revealed by the examination, before surgery after passive standing in patients of both groups, the tibial circumference increased by +2.5±0.3 cm. After a 6-minute march test, the tibial circumference decreased to +1.4±0.2 cm. In patients of the control group, the tibial circumference slightly increased due to passive standing (less than by +1 cm), and during the 6-minute test it almost returned to the baseline, regarded by us as normal functioning of the muscle pump [14]. One year after surgery, in patients of group I after a 6-minute march test, the tibial circumference decreased from +2.1±0.2 cm to +1.1±0.1 cm (p<0.05), in patients of group II – from +1.9±0.3 cm to +1.0±0.2 cm (p<0.05); after 3 years follow-up, the circumference of the legs in group I decreased from +1.8±0.2 cm to +0.8±0.1 cm (p<0.05), and in group II – from +1.5±0.1 cm to +0.5±0.1 cm (p<0.05). A significant increase in the tibial circumference during passive standing and preservation of venous stasis after walking indicates some malfunction of the muscle pump [14]. Thus, in the postoperative period (1 and 3 years later) there was a tendency to the reduction of tibial circumference during a march test, while in patients of group II the results were better than in those of group I.

When measuring the AMAJ of the affected lower extremity before surgery in patients with PTS of lower extremities of both groups, we established the evident reduction (p<0.05) in the total scope of foot flexion and extension as compared with patients in the control group – i.e. 1.6 times less, indicating the dysfunction of muscular pump of tibia (Table 1) [6].

### Table 1

<table>
<thead>
<tr>
<th>Clinical group</th>
<th>Follow-up period</th>
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<tbody>
<tr>
<td></td>
<td>before surgery</td>
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<tr>
<td>Group I</td>
<td>32.5±1.7°</td>
</tr>
<tr>
<td>(n=71)</td>
<td>(n=67)</td>
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<tr>
<td>Group II</td>
<td>31.6±1.6°</td>
</tr>
<tr>
<td>(n=77)</td>
<td>(n=74)</td>
</tr>
<tr>
<td>Control group</td>
<td>51.3±2.4°</td>
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<td>(n=40)</td>
<td>(n=39)</td>
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Notes: 1. ° – unit of measurement in degrees; 2. * – p<0.05 comparing with the indices in control group (Student’s t-criterion); 3. ** – p<0.05 comparing with the indices in group I (Student’s t-criterion).

1 year after surgery, the index of foot flexion and extension in patients of group II was 13% higher than in patients of group I (p<0.05); 3 years later – 17% higher (p<0.05). Thus, in the postoperative period, the patients of group II demonstrated a higher rate of foot flexion and extension than the patients of group I, which proves better functioning of the tibial muscle pump.
pump upon performing the closed separation of perforating veins and paratibial fasciotomy [11].

The bioelectrical profile of tibial muscles during electromyography was significantly impaired in patients with PTS of lower extremities (Table 2). In case of PTS of lower extremities, the reduction of average amplitude indices 1.5 times less (p<0.05) and maximum amplitude indices 1.9 times less (p<0.05), if compared with the similar indices in control group, indicated a significant decrease in muscle tone and weakening of functional ability of tibial muscles. 1 and 3 years after surgery, the indices of average and maximum amplitude have improved, moreover, the indices of average amplitude in patients of group II were 10% higher than in patients of group I (p<0.1), and the indices of maximum amplitude were 14% higher (p<0.1).

Table 2

<table>
<thead>
<tr>
<th>Clinical group</th>
<th>Index</th>
<th>Follow-up period</th>
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<tr>
<td></td>
<td></td>
<td>Before surgery</td>
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<tr>
<td>Group I</td>
<td>Ampl. average, mcV</td>
<td>337.4±13.1*  (n=71)</td>
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<td></td>
<td>Ampl. maximum, mcV</td>
<td>841.1±80.4*  (n=71)</td>
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<tr>
<td>Group II</td>
<td>Ampl. average, mcV</td>
<td>341.6±13.3*  (n=77)</td>
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<tr>
<td></td>
<td>Ampl. maximum, mcV</td>
<td>849.5±82.2*  (n=77)</td>
</tr>
<tr>
<td>Control group</td>
<td>Ampl. average, mcV</td>
<td>518.8±57.2  (n=40)</td>
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<td></td>
<td>Ampl. maximum, mcV</td>
<td>1593.4±222.9 (n=40)</td>
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Notes: * – p<0.05 comparing with the indices in control group (Student’s t-criterion); ** – p<0.1 comparing with the indices in group I (Student’s t-criterion).

The results of correlation analysis in patients with PTS of lower extremities before surgery indicate the presence of an inverse correlation between the tibial circumference during a 6-minute test with AMAJ (group I – r= -0.63, p<0.05; group II – r= -0.58, p<0.05), and also with the average amplitude during electromyography (group I – r= -0.55, p<0.05; group II – r= -0.57, p<0.05). Besides, the direct correlation was found between AMAJ and average amplitude of oscillation (group I – r= 0.65, p<0.05; group II – r= 0.69, p<0.05).

The disease-related overall rate of LQ limitation in the preoperative period significantly differed from the norm in both groups of patients. 1 year after surgery, in patients of both groups there was a significant decrease in the overall rate of LQ limitation: in group I – 1.5 times less – from 57.4±3.3% to 38.3±2.8% (p<0.05), in group II – 2.0 times less – from 58.2±3.3% to 29.1±2.2% (p<0.05), LQ in group II was 1.3 times better, than in group I (p<0.05). 3 years after surgical treatment, the overall rate of LQ restriction in group I was 34.2±2.5%, which is 1.7 times better than before surgery (p<0.05); in group II – 23.1±1.8%, which is 2.5 times better than in the preoperative period (p<0.05). The LQ in group II was 1.5 times better than in group I (p<0.05). The analysis of pain, physical, social and psychological factors in the postoperative period 1 and 3 years later revealed a clear tendency to improvement, which was regarded by us as the evidence of positive effect on LQ of the suggested method of surgical treatment [1, 13].

In the preoperative period, both groups of patients demonstrated a severe course of PTS of lower extremities with a significant deviation from the normal score by the VCSS scale [8]. One year after surgery, patients in both groups showed a significant decrease in the number of points by the VCSS scale: in group I – 2.7 times less from 16.8±3.3 to 6.2±1.9 points (p<0.05); in group II – 4.4 times less from 16.9±3.6 to 3.8±1.4 points (p<0.05); the severity of the disease in group I was 1.6 times worse than in group II group (p<0.05). 3 years after surgery, the score by the VCSS scale in group I was 5.5±1.4 points, which is 3.1 times less than the one before surgery (p<0.05); in group II – 3.0±0.9 points, which is 5.6 times less than in the preoperative period (p<0.05). The severity of the disease
in group I was 1.8 times worse than in group II (p<0.05), which indicates the advantages of closed separation of perforating veins and paratibial fasciotomy.

As a result of analysis of patients’ working ability indices by the VDS scale, it was found out that 68 (95.8%) patients of group I and 74 (96.1%) patients of group II had impaired working ability prior to surgery [8]. One year after surgery, in group I the working ability was impaired in 14 (20.9%) patients, while in group II – in 9 (12.2%) patients. Three years after surgery, in group I 11 (18.0%) patients had a disability and 7 (10.3%) patients – in group II. Thus, in the postoperative period there was a significant recovery in both groups, but in group II the number of able-bodied patients was 1.7 times higher than in group I (p<0.05).

Before surgery, the patients with PTS of lower extremities had a direct correlation of general index of LQ restriction by the VCSS scale (group I – r=0.71, p<0.05; II – r=0.73, p<0.05), as well as worsening of working ability (group I – r=0.69, p<0.05; II – r=0.65, p<0.05). A direct correlation was found between the score by the VCSS scale and worsening of working ability (group I – r=0.61, p<0.05; II – r=0.64, p<0.05).

During the ultrasound duplex scanning, 1 year after surgery 5 (7.5%) patients of group I showed insufficient perforating veins in the tibial area, while group II showed insufficient perforating veins solely in 2 (2.7%) patients, which is 2.8 times less than in group I (p<0.05). Three years after surgery, insufficient perforating veins were found in 6 (9.8%) patients of group I and 3 (4.4%) patients of group II, which is 2.2 times less than in group I (p<0.05). The duration of reflux along the femoral and popliteal veins was 1.5±0.3 sec. Three years after surgery in group I 11 (18.0%) patients had a disability and 7 (10.3%) patients – in group II. Thus, in the postoperative period there was a significant recovery in both groups, but in group II the number of able-bodied patients was 1.7 times higher than in group I (p<0.05).

Thus, the long-term 3-year follow-up over patients with PTS of lower extremities using a 6-minute march test, measurement of AMAJ, electromyography, as well as study of LQ, severity of venous pathology and working ability of patients confirms a high effectiveness of the pathogenetically-grounded method of surgical treatment that was developed by us.

CONCLUSIONS

1. In the long-term postoperative period in patients with postthrombotic syndrome of lower extremities after closed separation of perforating veins and paratibial fasciotomy, the quality of life improves (1.3 times after 1 year (p<0.05) and 1.5 times after 3 years (p<0.05)), the severity of venous pathology decreases (1.6 times after 1 year (p<0.05) and 1.8 times after 3 years (p<0.05)) and working ability increases (1.7 times after 1 and 3 years (p<0.05)), compared with traditional methods of surgical treatment.

2. In patients with postthrombotic syndrome of lower extremities, closed separation of perforating veins and paratibial fasciotomy improve the function of tibial muscle pump: the results of march test improve (leg circumference decreases after exercise (p<0.05)), the amplitude of movements in the ankle joint increases (by 13% after 1 year (p<0.05) and 17% after 3 years (p<0.05) compared with traditional operations) along with the biopotentials of tibial muscles and the severity of venous pathology and working ability of patients confirms a high effectiveness of the pathogenetically-grounded method of surgical treatment that was developed by us.

3. Evaluation of the results of ultrasound duplex scanning based on the data of a three-year follow-up (after 1 year in group II, 2.8 times less number of insufficient perforating veins of the leg (p<0.05) and a decrease in the duration of reflux along the femoral and popliteal veins by 1.3 times (p<0.05); after 3 years – 2.2 times less number of insufficient perforating veins of the leg (p<0.05) and a decrease in the duration of reflux – 1.5 times (p<0.05) compared with group I) makes it possible to consider the use of closed separation of perforating veins and paratibial fasciotomy as a justified method of surgical treatment of patients with postthrombotic syndrome of the lower extremities of late stages.

Contributors:
Orynchak V.A. – conceptualization, methodology, investigation, writing – original draft; Gudz O.I. – formal analysis, investigation, writing – review & editing.

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