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## COMPARATIVE EFFICACY OF ANTICOAGULANT AND THROMBOLYTIC THERAPY IN PATIENTS WITH ACUTE THROMBOSIS OF THE INFERIOR VENA CAVA

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138 patients with thrombosis in the system of the inferior vena cava was examined and treated. Thrombolytic therapy (TLT) as a basic method of treatment was used in 52 (37,7 %) patients. Of these, 20 (14,5 %) was performed catheter-controlled thrombolysis and 32 (23,2 %) patients had systemic thrombolytic therapy. The 86 (62,3 %) patients in the basic treatment had anticoagulant therapy (ACT). In the long-term results of thrombolytic therapy significantly exceed the results of ACT. The 70 % of this patients had signs of post-thrombotic disease with mild chronic venous insufficiency, and 100% of patients with ACT had more forms of postthrombotic disease.

**KEY WORDS:** acute thrombosis in the inferior vena cava, anticoagulant therapy, thrombolytic therapy

## СРАВНИТЕЛЬНАЯ ОЦЕНКА ЭФФЕКТИВНОСТИ АНТИКОАГУЛЯНТНОЙ И ТРОМБОЛИТИЧЕСКОЙ ТЕРАПИИ У БОЛЬНЫХ С ОСТРЫМ ТРОМБОЗОМ В СИСТЕМЕ НИЖНЕЙ ПОЛОЙ ВЕНЫ

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Проведено обстеження і лікування 138 пацієнтів з тромбозами в системі нижньої порожнистої вени. Тромболітична терапія (ТЛТ) в якості базового методу лікування була застосована у 52 (37,7 %) пацієнтів. З них у 20 (14,5 %) був здійснений катетер-керований тромболізіс та у 32 (23,2 %) пацієнтів була застосована системна тромболітична терапія. У 86 (62,3 %) пацієнтів базовим методом лікування була антикоагулянтна терапія (АКТ). У віддаленому періоді результати ТЛТ значно перевершують результати АКТ. У 70 % пацієнтів, пролікованих ТЛТ, спостерігали у віддаленому періоді ознаки посттромбофлебітичної хвороби (ПТФХ) з легким ступенем хронічною венозною недостатністю (ХВН), а у 100 % пацієнтів, котрі отримали курс АКТ, відзначені більш важкі форми ПТФХ.

**КЛЮЧЕВЫЕ СЛОВА:** острый тромбоз в системе нижней полой вены, антикоагулянтная терапия, тромболитическая терапия

## ПОРІВНЯЛЬНА ОЦІНКА ЕФЕКТИВНОСТІ АНТИКОАГУЛЯНТНОЇ ТА ТРОМБОЛІТИЧНОЇ ТЕРАПІЇ У ХВОРИХ НА ГОСТРИЙ ТРОМБОЗ У СИСТЕМІ НИЖНЬОЇ ПОРОЖНИСТОЇ ВЕНИ

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**КЛЮЧОВІ СЛОВА:** гострий тромбоз в системі нижньої порожнистої вени, антикоагулянтна терапія, тромболітична терапія

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Acute deep vein thrombosis (DVT) in the inferior vena cava is more than 95% of venous thrombosis and is often complicated by pulmonary embolism (PE) [1, 2]. In Ukraine, each year about 260 cases of DVT and its complications per 100 thousand people with mortality from pulmonary embolism at the level of 20–25 % [3, 4]. In addition to a life-threatening pulmonary embolism, deep venous thrombosis is a serious consequence of the post-thrombotic disease (PTD) with severe manifestations of chronic venous insufficiency (CVI) of the lower extremities [4, 5]. Subsequent progression PTD accompanied by the formation of venous ulcers, which constitute 19,7 % of the etiology of venous ulcers [1, 6].

Despite the use of different methods of treatment of deep venous thrombosis in the inferior vena cava, the immediate and long-term results of their application can not fully meet the professionals [7–10]. This fact was the basis for a comparative analysis of the effectiveness of various methods of treatment of acute deep venous thrombosis in the inferior vena cava.

In our study, we conducted a comparative evaluation of the efficacy of thrombolytic therapy compared with anticoagulation in patients with deep venous thrombosis of the pelvis and lower extremities, and to determine the severity of chronic venous insufficiency caused PTD.

**The purpose** of the study is to evaluate the efficacy of thrombolytic and anticoagulant therapy in patients with deep venous thrombosis of the pelvis and lower extremities, and to determine the severity of CVI due PTD, in the long term.

Work performed as part of the scientific program of the SI «Institute of General And Emergency Surgery» NAMS of Ukraine and a fragment of a comprehensive the research work: «To develop a differentiated therapeutic, diagnostic and preventive tactics in patients with acute thrombosis of the inferior vena cava» (№ state registration 011V002288).

## **MATERIALS AND METHODS**

The examination and treatment of 138 patients with DVT of the pelvis and lower extremities, in 20 cases complicated by pulmonary embolism. Said patients have been applied to different types of treatment in 52 (37,7 %) — thrombolytic and in 86 (62,3 %) — anticoagulant therapy.

The examinees were 79 (57,2 %) men and 59 (42,8 %) of women aged 20 to 78 years. Pa-

tients came for treatment in terms of 3 to 20 days after onset of clinical signs of disease. Anamnestic prescription thrombosis in 83 (60,1 %) of the patients was 7 or more days. Under the complex clinical and instrumental and laboratory examination, including ultrasound scanning of and on the testimony of a radiopaque angiography revealed widespread acute thrombosis involving the iliac-femoral and/or femoral-popliteal venous segments. All patients were identified occlusive thrombi specified location. 20 patients hospitalized for DVT, PE is complicated, while 18 (90 %) of them had sub massive and 2 (10 %) — massive form of the disease. Patients admitted to hospital with DVT combined with PE, were in a state of moderate severity.

Thrombolytic therapy as a basic method of treatment was used in 52 (37,7 %) patients. Of these, 20 (14,5 %) performed catheter-controlled thrombolysis (CCT) [11] using the Streptase at 100 000 units/hour with an average duration of treatment up to 3 days. The drug was administered through a catheter inserted in the posterior tibial vein thrombosis affected lower limb.

For systemic thrombolytic therapy (STLT) [6, 7] in 32 (23,2 %) patients used Streptokinase (100,000 units/hour), Urokinase (4400 U/kg/h) and Actilyse (100 mg for 2 hours).

In 86 (62,3 %) patients had baseline treatment anticoagulant therapy (ACT) using low molecular weight heparin (LMWH), 57 (41,3 %) and unfractionated heparin (UFH) 29 (21 %) patients. Low molecular weight (fractionated) heparin (mainly — Enoxaparin) administered at a dose of 1mg/kg body weight of the patient two times per day subcutaneously to a patient on Warfarin transfer when the target INR. Also used UFH, which was administered once intravenously at a dose of 5000 ED.i then continued treatment by continuous intravenous infusion at a daily dose of UFH 20000–35000 units, ensuring the maintenance of APTT values are 1,5–2 times larger than the original and controlling her every 6 hours. The duration of infusion of UFH was a minimum of 5 days or more, depending on the performance INR. Patients treated with ACT, parallel to the prescribed anticoagulants of indirect action (AIA). The dose of these drugs were selected individually under the control of prothrombin ratio (50–60 %) or INR (2,0–3,0), and recommended taking AIA for at least 4–6 months in an outpa-

tient setting. In addition to this therapy during the hospital stay, patients received Movalis, Detralex, Flebodia, Cyclo 3 Fort in standard doses, use elastic bandages or compression stockings individualized.

In accordance with the protocol of the study, all patients were assessed hemostasis prior to and throughout the hospital treatment period.

Assessment of the immediate results of the treatment of patients with acute deep vein thrombosis of the lower limbs and pelvis was performed with the following parameters:

- the dynamics of the regression of clinical symptoms;
- the degree of patency of the venous bed;
- the effectiveness of the prevention of pulmonary embolism;
- the type and number of complications associated with treatment.

Assessment of long-term results of treatment was carried out in the absence or presence of clinical signs and PTD indicators such as:

- functional class CVI according to the International Classification of CEAP;
- the degree of patency of the venous bed (partial or complete recanalization) according to duplex scanning.

Statistical analysis was performed using a standard office suite «Microsoft Office XP» with the application package «Microsoft Excel» and statistical software for biomedical research «Biostatistics» (Statistical Graphics Corp., USA), Version 4.03 for Windows.

## RESULTS AND DISCUSSION

In general, the immediate clinical outcomes were positive in 83 (74,1 %) patients.

In patients who received CCT, there was a rapid regression of the main clinical signs of acute iliofemoral venous thrombosis. By the end of the first day in these patients significantly reduced bursting pain in the lower extremities. On the third day of the CCT remained only mild pain in the limbs, the volume of which was significantly smaller than the original. On the 12th day of the clinical manifestations of the disease were absent. An ultrasound and angiography in 14 of 20 patients receiving CCT, marked by full and 6 — partial lysis of blood clots. Under STLT after the first day of treatment start regression of clinical symptoms was observed in 6 (22,2 %), and on the third day — in 14 (51,9 %) patients. At 12 days of the clinical manifestations of DVT in 22 (83,3 %) patients were minimal. According to the ultrasound group STLT complete patency affected segments there thrombosis in 5 (18,5 %) and partial — 17 (63 %) patients. In this group, 24 patients (88,9 %) had normalization of hemodynamics in the pulmonary circulation, and only 3 patients (11,1 %) were observed moderately pronounced signs of pulmonary hypertension. System-administration of a thrombolytic agent was unsuccessful in 5 (18,5 %) patients. Importantly, treatment of thrombolytic agents are not accompanied by a clinically significant bleeding complications were observed only subcutaneous hematoma. The results of anticoagulant and thrombolytic therapy in patients with acute venous thrombosis in the inferior vena cava in the table.

Table

**Comparative evaluation of the effectiveness of anticoagulant and thrombolytic therapy in patients with acute venous thrombosis**

The result of treatment (number of patients n)	TLT		ACT		Total
	STLT	CCT	LMWH	UFH	
The treatment	32 (23,2 %)	20 (14,5 %)	57 (41,3 %)	29 (21,0 %)	138 (100 %)
Examined the results of Treatment	27 (84,4 %)	20 (100 %)	48 (84,2 %)	17 (58,6 %)	112 (81,2 %)
Positive direct results	22 (81,5 %)	20 (100 %)	32 (66,7 %)	9 (52,9 %)	83 (74,1 %)
The development of severe chronic venous insufficiency (C5-C6)	3 (11,1 %)	0	11 (22,9 %)	5 (29,4 %)	19 (17,6 %)

Of the 65 patients who received a course of ACTs in 41 (63,1 %), there was progression of the thrombotic process. In 12 (18,5 %) patients had an ultrasound examination revealed signs of recanalization of the thrombosed veins, and earlier recanalization was observed in patients treated with LMWH. In 24 (36,9 %) cases, the

course of the ACP has not led to a positive effect of the treatment due to progression of the thrombotic process. However, in any case for DVT is not complicated by pulmonary embolism. Conducted a comprehensive treatment of deep vein thrombosis of the pelvis and lower extremities prevented the development of pul-

monary embolism. Recurrence of DVT, no deaths reported in all groups of patients.

In the long-term in terms from 3 months to 10 years were examined 108 (80,5 %) patients, of whom 43 (39,8 %) patients received TLT and 65 (60,2 %) — a course of ACT.

In 20 patients, the treatment of which was the base of TCS, in the late period showed no signs of chronic venous insufficiency associated with PTD. In the group of 32 patients, the primary treatment which was to STLTL, and 4 marked C1-C2, and 4 — C3-C4 and 3 — C5-C6 CVI (CEAP). In patients who received TLT, there was varying degrees (from full to partial) recanalization of the deep veins by ultrasound. In the group of 57 patients who were treated with LMWH, 12 registered C2-C3 and 10 — and 11 C4-C5-C6 CVI (CEAR). Among the 29 patients treated with UFH, in 3 marked C2 in 6 — C3-C4, and 5 — C5-C6 CVI (CEAP).

Application TLT patients with DVT pelvis and lower limbs and pulmonary embolism caused rapid regression or complete elimination of the major clinical signs of venous thrombosis and pulmonary embolism, while in anticoagulant treatment in 16 (52,3 %) patients remained significant clinical manifestations of CVI.

In 14 (70 %) of 20 patients who received CCT, there was a complete and in 6 (30 %) — a partial lysis of blood clots. Under full restore patency STLTL deep vein was observed in 18,5 % and partial — 63 % of patients. The resumption of blood flow in the major tributaries of the iliac and femoral veins contributed to the rapid improvement of venous hemodynamics and eliminate clinical symptoms of DVT. In the course of the TLT clinically significant bleeding complications were not recorded, and subcutaneous hematoma occurred gradually disappeared without treatment. According to the results of the late period TLT methods significantly outperform the conservative therapy with anticoagulants. 70 % of patients treated with TLT had a long-term PTD with mild to moderate chronic venous insufficiency. In contrast, all patients who received a course of ACP marked PTD, with more severe manifestations of chronic venous insufficiency observed in those who was treated with UFH and LMWH are not.

Thus, the use of anticoagulant and thrombolytic therapies makes it possible to reduce the likelihood of PTD and reduce the severity

of chronic venous insufficiency of the lower extremities in the long term.

## **CONCLUSIONS**

1. Application of thrombolytic therapy in patients with DVT pelvis and lower limb leading to rapid regression or complete elimination of the major clinical signs of venous thrombosis. According to the results of the late period TLT methods significantly outperform the conservative therapy with anticoagulants. Thus, only three (6,3 %) patients treated TLT had a pronounced long-term signs PTD while treatment with anticoagulants in 16 (52,3 %) patients remained severe clinical manifestations of CVI.

2. According to our observations, the regional administration of thrombolytics more fully and quickly in comparison with systemic thrombolytic therapy allows you to resume the blood flow in the deep veins of the pelvis and lower extremities. Thus, in 14 (70 %) who received CCT, there was a complete and in 6 (30 %) — a partial lysis of blood clots. In the group of patients treated with STLTL full recovery of deep vein patency was observed in 5 (18,5 %) of 27 patients and partial — in 17 (63 %) patients.

3. The use of ACT has prevented the progression of the thrombotic process in 41 (63,1 %) patients, of whom 32 (66,7 %) of patients receiving LMWH and in 9 (52,9 %) — NFG. In addition, an ultrasound examination, the earlier recanalization of the thrombosed veins was observed in patients treated with LMWH course. In 24 (36,9 %) cases, the course of the ACP has not led to a positive effect of the treatment due to progression of the thrombotic process. However, in any case for DVT is not complicated by pulmonary embolism.

4. ACT does not remove the blood clots deep veins of the pelvis and lower extremities, accompanied by a sustained regression of clinical signs of DVT and in the long term often leads to the development of moderate to severe PTD. However, the ACP may be effective in preventing pulmonary embolism. When ACT drugs of choice are the LMWH. These drugs should be used after the CUT or STLTL in prevention of recurrence of DVT.

Prospects for future research is to study and compare the effectiveness of methods of regional and systemic thrombolysis in patients with acute thrombosis in the inferior vena cava.

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