ULTRASOUND DIAGNOSIS OF VENOUSTHROMBOSIS IN THE COURSE OF PROPHYLACTIC DRUG THERAPY IN THE ACUTE PHASE OF TRAUMA

L.O. Mezhebitskaya, E.Y. Trofimova, P.A. Ivanov, E.V. Kungurtsev

N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Healthcare Department, Moscow, Russian Federation

INTRODUCTION High risk of venous thrombosis in patients with multisystem trauma is associated with a number of precipitating factors, such as direct damage to vessels, prolonged immobilization, major changes in the hemostatic system, as well as possible surgical intervention.

PURPOSE OF THE STUDY Analysis of the incidence, echosemiotics, and evolution of venous thrombosis in the course of various prophylactic drug therapies in patients with polytrauma.

METHODS The results of leg veins ultrasonography in 610 patients with various prophylactic drug therapies have been analyzed over time. Antiplatelet agentswere received by 314 patients of the first group, low molecular weight heparins - 186 patients of the second group, oral anticoagulants - 110 patients of the third group.

RESULTS Evolved thromboses varied in frequency (52.5% in the first group, 15.6% in the 2nd group and 10% in the 3rd group), prevalence, nature of the proximal border, with an increase in the proportion of non-occlusive lesions in the 2nd and 3rd groups, as well as in start time and degree of recanalization.

CONCLUSION Low molecular weight heparins and oral anticoagulants reduce the risk of venous thrombosis by 3.3 and 5 times respectively, compared to the group of patients who did not receive anticoagulants in the early posttraumatic period; recanalization begins 1-2 weeks earlier with more effective restoration of the lumen. As the number of thromboses in the course of modern anticoagulants decreases, the proportion of non-occlusive thromboses including the floating ones grows, requiring ultrasound observation.

Keywords: ultrasonic study, deep vein thrombosis, anticoagulants, polytrauma.

AAs – antiplatelet agents

CFV – common femoral vein

DVTLE – deep vein thrombosis of the lower extremities

LMWHs – low molecular weight heparins

OAs – oral anticoagulants

PE – pulmonary embolism

VTEC – venous thromboembolic complications

INTRODUCTION

High risk of venous thrombosis in patients with multisystem injury is associated with a number of predisposing factors, such as direct damage to vessels, prolonged immobilization, major changes in the hemostatic system, as well as possible surgery [1-4].

The incidence of venous thromboembolic complications (VTEC) in these patients ranges from 5.8 to 58%, depending on the nature of the injury, preventive measures and diagnostic method [5-7].

In the acute phase there is a risk of pulmonary embolism (PE), often leading to death [8, 9]. In the long-term period chronic venous insufficiency may occur, which significantly reduces the quality of life.

Proximal spread of deep leg veins thrombosis on day 5-7 is noted in 25% of cases even in the course of treatment, while the effectiveness of anticoagulation is the more effective the earlier it had been initiated [10-12]. However, in some cases, the risk of hemorrhagic complications in patients with trauma is the cause of the delay in adequate prevention of VTEC [13, 14].

Since 80% of cases of deep veins thrombosis of the lower extremities (DVTLE) are asymptomatic, their active detection and monitoring is especially important [15]. The most informative and accessible method of diagnosis is the ultrasound duplex compression scan [16-18].

The purpose of the study is to estimate the frequency, echosemioics and evolution of venous thrombosis, developed in the course of various drug prevention in patients with polytrauma.

MATERIAL AND METHODS

We analyzed the results of ultrasonography of veins of the lower extremities over time in 610 patients with multisystem trauma, 420 men and 190 women, aged 17 to 76 years (mean age 39.8 years) who were treated at the Sklifosovsky Research Institute for Emergency Medicine from 2001 to 2012.

Non-pharmacological prevention of VTEC included gymnastics, methods of elastic pneumocompression and early mobilization.

According to the nature of drug prevention patients were divided into three groups. The first (control) group consisted of 314 patients who had been treated with antiplatelet agents (AAs) – Trental 400 mg / day, Xantinol nicotinate 0.3-0.6 g / day, Rheopolyglukin since the first day of hospital stay. Of these, 200 patients were treated in the hospital from 2001 to 2003, before the adoption of standard prevention of pulmonary embolism with low molecular weight heparins (LMWHs) [19], and 114 patients had contraindications to anticoagulants associated with a high risk of bleeding or hypocoagulation (multiple rib fractures with alung injury – 31, intrahepatic hematoma – 16, subcapsular splenic rupture – 13, intracranial hematoma – 20, gastric ulcer and duodenal ulcer – 23, severe diabetes – 4, chronic renal failure – 5, thrombocytopenia - 2).

The second group consisted of 186 patients who received LMWHs as a preventive measure. Fraxiparine was administered in a dosage according to the weight of the victim – 0.1 ml / 10 kg of the body weight 2 times daily (starting no later than 3 days since the date of admission to the hospital as soon as possible sources of bleeding were excluded), and canceled after the activation of the patient in the absence of DVTLE (by ultrasound data).

In 110 patients of the group 3, oral anticoagulants (OAs) have been included into the set of preventive measures since 2010. Among them, 60 patients were treated with the direct thrombin inhibitor dabigatran etexilate (Pradaxa) at a dosage of 220 mg / daily and 50 people received the factor *Xa* inhibitor rivaroxaban (Xarelto) – 10 mg once daily.

Treatment of revealed thrombosis in patients of all groups was performed using direct and indirect anticoagulants according to the conventional scheme.

Ultrasound of lower extremities veins was performed on *Siemens Sonoline Omnia* and *Logiq* – P-6 of *General Electric*, equipped with multifrequency linear transducers with a frequency range of 5.0-7.5 MHz to locate veins of lower leg and femoral-popliteal segment by a convex transducer with a working frequency of 3.5-5.0 MHz for the study of the lower hollow and iliac vein.

Ultrasound study was performed at least once a week, starting with day 3-5 from the time of injury. Patients requiring surgery, underwent the study starting on day 1-2 before the upcoming surgery, followed by weekly monitoring, beginning with the day 2-3 in the postoperative period. When identifying the floating thrombus, intervals between ultrasound studies were reduced (3-5 days) to eliminate the threat of embolism. Standard evaluation criteria in gray-scale and color-coded modes were used for the diagnosis of thrombosis, special tests were performed. Since the thrombosis often develops in the veins of the contralateral limb, we always adhered to bilateral scanning.

In assessing the prevalence of the process and fixing of the thrombus on the proximal level of thrombosis, V.S. Savelyev classification was used [20]. Considering the special importance of the common femoral vein (CFV) in the formation of embologenic blood clots due to its large diameter and the presence of large inflows in our research, we have identified three levels of the proximal border: 1) distal, not reaching the lumen of CFV; 2) intermediate, which involves CFV; 3) proximal, involving the lower hollow and iliac vein.

Statistical processing was performed using the computer program *Statistica.* When comparing the numerical parameters in groups we used the Student's *t-test,* χ^2. Statistically significant level was $p \leq 0.05$.

RESULTS AND DISCUSSION

In group 1, affected at different times after injury, DVTLE was diagnosed in 165 patients (52.5%) out of 314 people, including bilateral thrombosis in 22 cases (13.3%). Thus, venous thrombosis developed in veins of 187 limbs.

Data on the location and nature of the proximal border of thrombosis are presented in Table 1.

Table 1

The location and nature of thrombosis in the course of its prevention using antiplatelet agents

Location of thrombosis	Character of thrombosis						Total	
	occluding		parietal		floating			
	abs.	%	abs.	%	abs.	%	abs.	%
Distal	52	44.8	57	49.2	7	6.0	116	100
Intermediate	10	19.2	18	34.6	24	46.2	52	100
Proximal	4	21.1	11	57.8	4	21.1	19	100
Total	66	35.3	86	46.0	35	18.7	187	100

As can be seen from the table, in the largest number of observations, distal thrombosis with occlusive and parietal character of fixation occurred. It should be noted that the proximal level of DVTLE often reached the ostium of the femoral vein. In the lower leg veins, associated thrombotic occlusion involving the paired trunks occurred that strongly impaired the venous outflow.

Among patients of the group 2, thrombosis was detected in 29 cases (15.6%).

In 2 of them (6.2%), we diagnosed bilateral DVTLE (31 limbs in total).

Distal thrombosis developed in the veins of 10 limbs (32.3%). In the veins of 19 limbs (61.2%) the process extended to the lumen of the CFV, and in 3 cases (10.3%) deep femoral vein became its source, but maintained normal outflow through the greater distal vessel (Fig. 1).

In 2 patients (6.5%), tops of floating thrombi extended to the iliac segment, reaching the ostium of the common iliac vein in one of them (Fig. 2).

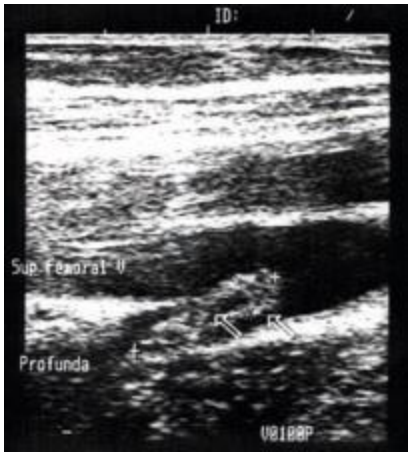

Fig 1. Floating thrombus in the distal common femoral vein, coming from deep femoral vein

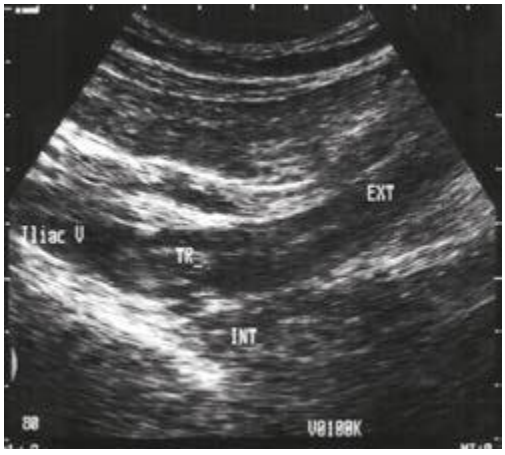

Fig 2. Floating thrombus in the external and common iliac vein

Character of thrombotic masses fixation on different levels is shown in Table 2.

Table 2

The location and nature of thrombosis in the course of its prevention using low molecular weight heparins

Location of thrombosis	Character of thrombosis						Total	
	occlusive		parietal		floating			
	abs.	%	abs.	%	abs.	%	abs.	%
Distal	2	20	4	40	4	40	10	100
Intermediate	1	5.3	3	15.8	15	78.9	19	100
Proximal	-	-	-	-	2	100	2	100
Total	3	9.7	7	22.6	21	67.7	31	100

As the table shows, patients of the group 2 had mostly non-occlusive thrombosis, extending into the lumen of the CFV, where 15 of the 21 identified floating tops of length from 3 to 8 cm were located.

In patients of the group 3, DVTLE was detected in 11 cases (10%) in the veins of one limb (bilateral lesions were not observed). Distal thrombosis occurred in 6 patients (54.5%), intermediate – in 4 patients (36.4%) and proximal – in one patient (9.1%).

There were 5 cases of thrombosis with parietal fixation and 6 cases of thrombosis with a floating proximal part of the thrombus. Occlusive thrombosis in the studied group of patients was not found. Changes were characterized by small extension, involving no more than two venous segments. In 3 cases, the process was limited to isolated lesions of the lower leg veins, and

in 3 other cases the lesion spread to the popliteal and femoral vein. In 4 patients, floating thrombi were found in the lumen of the CFV, and 3 of them had the base at the ostium of the deep femoral vein, and one was fixed on the venous valve cusp (Fig. 3).

Segmental floating thrombus in the lumen of the external iliac vein with a base in the paravalvulvar area of CFV was found in one case.

Thus, the victims of the 1st group (AAs) often had femoral-popliteal thrombosis, extending from the veins of the lower leg to the ostium of the femoral vein (Fig. 4). Ascending thrombosis, reaching the lumen of the CFV was more frequent in patients treated with LMWHs – 61.2% vs. 27.8% in patients treated with AAs. As already noted, in the group of patients treated with the OAs, thromboses were of small extention, segmental character and were also revealed with the same frequency both in the distal part of the vessel and in CFV. Statistically significant difference in the incidence of DVTLE with proximal localization was not found: 10.2% – in group 1, 6.5% – in group 2 and 9.1% – in group 3, $p > 0.05$.

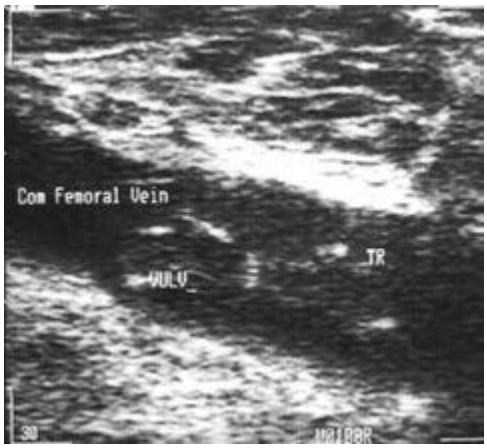

Fig. 3. The floating thrombus with a base on the valve cusp

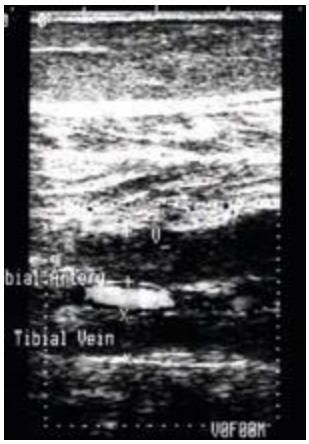

Fig. 4. Occlusive tibial veins thrombosis

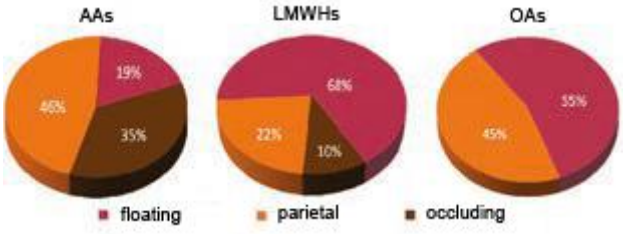

Fig. 5. The nature of the proximal border of thromboses in different types of drug prevention

Notes: AAs - antiplatelet agents; LMWHs - low molecular weight heparins; OAs - oral anticoagulants

The share of occlusive thrombosis in strong violation of the venous outflow using AAs was significantly higher than in the group, which used LMWH for the prevention – 35.3% compared to 9,7% ($p < 0.01$). In the third group where patients received OAs, there were no occlusive lesions. Accordingly, the relative amount of floating changes in the structure of thrombosis in patients treated with AAs was lower – 18.7% versus 67.7% in the group 2 and versus 54.5% in the group 3 ($p < 0.01$) that is demonstrated in Fig. 5.

In repeated ultrasound spread of thrombosis in the proximal direction was observed in 35 patients. In 32 cases (19.4%) patients were of the 1st group. In 24 of them, the growth of DVTLE was completed by the end of the 1st week, and in 8 cases, the growth of the lesion continued even on the 2nd week after the detection of thrombosis. Among the victims of the 2nd group, the growth of thrombosis in the proximal direction was revealed in 3 (10.3%) patients. In other cases, the growth thrombosis was not observed.

In patients treated with OAs, repeated studies did not reveal the growth of thrombosis (Fig. 6). In patients with thrombosis, which developed in the course of the use of AAs and, therefore, with the later order of anticoagulants for therapeutic purposes, the first signs of recanalization were found only on the third week in 6%, and the restoration of a functioning lumen by 30% in diameter – in 19 of patients in the 4th week of observation.

In group 2, the signs of recanalization were found in 7.4% of patients on the 2nd week. On week 3-4 of observation, restoration of functioning lumen by more than 30% in diameter was observed in 35.7% of cases (Fig. 7).

In patients treated with OAs, segmental parietal changes before the discharge from the hospital were observed in 3 cases. In 8 cases (72.7%), lysis of blood clots, recanalization with full restoration of the lumen and the maintenance of the function of the valve apparatus were observed on week 3.

The rate of recanalization in groups of patients are shown on Fig. 8.

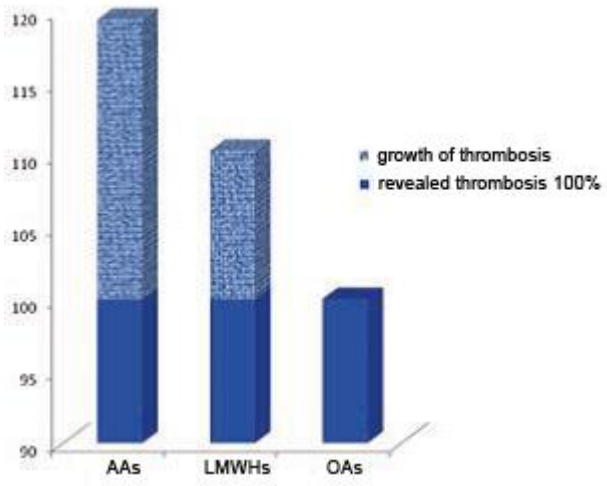

Fig. 6. Growth of thrombosis in groups with different prevention on repeated ultrasound examinations.

Notes: AAs - antiplatelet agents; LMWHs - low molecular weight heparins; OAs - oral anticoagulants

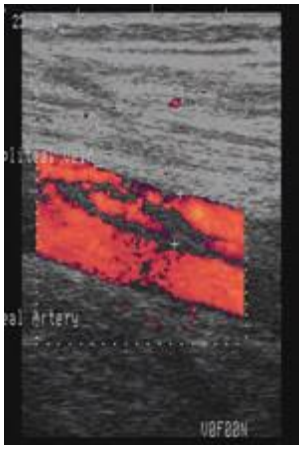

Fig. 7. Multi recanalization of the popliteal vein

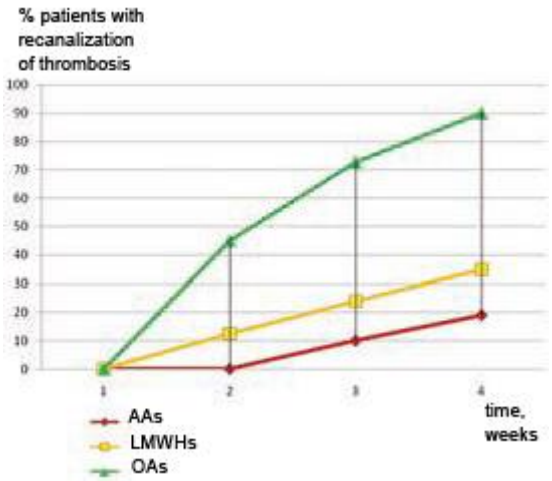

Fig. 8. The rate of recanalization of thrombosis in the course of various drug prevention.

Notes: AAs - antiplatelet agents; LMWHs - low molecular weight heparins; OAs - oral anticoagulants

CONCLUSIONS

1. Ultrasound of the lower extremities veins over time showed that the use of different methods of drug prevention affected the incidence, sonographic characteristics and processes of thrombosis evolution.
2. In the course of low molecular weight heparins and oral anticoagulants, venous thromboembolic complications occur 3.3 and 5.2 times less often, respectively, than in the patients treated in the early posttraumatic period only with antiplatelet agents.
3. In patients receiving anticoagulants from the first days after the injury, recanalization begins 1-2 weeks earlier and with more efficient restoration of the lumen, which reduces the risk of chronic venous insufficiency.
4. When using modern preventive medications, against a significant decrease in the frequency of venous thrombosis, the rate of non-occlusive ones grows, including embologenic floating cases, which necessitates ultrasound monitoring for timely correction of management.

Article received on August 2, 2014

For correspondence:

Mezhebitskaya Lyudmila O.,

Cand. Sc. Med., Researcher of the Ultrasound and Minimally Invasive Ultrasound-guided Treatment Department

N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Healthcare Department, Moscow, Russian Federation

e-mail: amezhebitskiy@yandex.ru

.

REFERENCES

1. Van Hensbroek P.B., Haverlag R., Ponsen K.J., et al. Prevention of thrombosis in traumatology. *Ned Tijdschr Geneeskd*. 2007; 151 (4): 234–239.
2. Lippi G., Franchini M. Pathogenesis of venous thromboembolism: when the cup runneth over. *Semin Thromb Hemost.* 2008; 34 (8): 747–761.
4. AndersonF.A., Spencer F.A. Risk factors for venous thromboembolism. Circulation. 2003; 107 (23) Suppl. 1: 9–16.
5. Giannadakis K., Leppek R., Gotzen L.,Stiletto R. Thromboembolism complication in multiple trauma patients: an underestimated problem? Results of a clinical observational study of 50 patients. *Chirurg*. 2001; 72 (6): 710–716.
6. Knudson M.M., Lewis F.R., Clinton A., et al. Prevention of venous thromboembolism in trauma patients. *J Trauma*. 1994; 37 (3): 480–487.
7. Rogers F.B. Venous thromboembolism in trauma patients: a review. Surgery. 2001; 130 (1): 1–12.
8. Lazarenko V.A., Mishustin V.N. Tromboemboliya legochnoy arterii u bol'nykh s travmoy [Pulmonary embolism in patients with trauma]. Angiologiya i sosudistaya khirurgiya. 2005; 4: 101–104. (In Russian).
9. Savelyev V.S. *Venoznyje trombozy i tromboemboliya legochnoy arterii* (venoznyje tromboembolicheskiye oslozhneniya): metod. Rekomendatsii [Venous thrombosis and pulmonary embolism (venous thromboembolism): method. recommendations]. Moscow, 2007. 20 p. (In Russian).
10. Geerts W.H., Jay R.M., Code K.I., et al. A comparison of low-dose heparin with low-molecular-weight heparin as prophylaxis against venous thromboembolism after major trauma. *N Engl J Med*. 1996; 335 (10): 701–707.
11. Kearon C. Natural history of venous thromboembolism. *Circulation*. 2003; 107 (23) Suppl. 1: 22–30.
12. Robinson D.M., Wellington K. Fondaparinux sodium: a review of its use in the treatment of acute venous thromboembolism. *Am J Cardiovasc* Drugs. 2005; 5 (5): 335–346.
13. Shchelokov A.L., Zubritsky V.F., Nikolayev K.N., et al. Kombinirovannaya profilaktika venoznykh tromboembolicheskikh oslozhneniy u postradavshikh s perelomami proksimal'nogo otdela bedrennoy kosti [Combination prevention of venous thromboembolic events in patients with fractures of the proximal femur]. *Vestnik travmatologii i ortopedii*. 2007; 1: 16–21. (In Russian).
14. Geerts W.H., Pineo G.F., Heit J.A.Prevention of venous thromboembo- lism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest*. 2004; 126 Suppl. 3: 338S–400S.
15. Asamov R.E., Tulyakov R.P., Muminov Sh.M., et al. Bessimptomnyje flebotrombozy i nasledstvennaya trombofiliya u bol'nykh so skeletnoy travmoy [Asymptomatic phlebothrombosis and inherited thrombophilia in patients with skeletal trauma]. *Angiologiya i sosudistaya khirurgiya*. 2008; 3: 73–76. (In Russian).
16. Krüger K., Wildberger J., Haage P., Landwehr P. Diagnostic imaging of venous disease: Part I: methods in the diagnosis of veins and thrombosis. *Radiologe*. 2008; 48 (10): 977–992.
17. Tomkowski W.Z., Davidson B.L., Wisniewska J., et al. Accuracy of compression ultrasound in screening for deep venous thrombosis in acutely ill medical patients. *Thromb Haemost*. 2007; 97 (2): 191–194.
18. Balakhonova T.V. Sovremennyje instrumental'nyje metody diagnostiki tromboza: ul'trazvukovoye dupleksnoye skanirovaniye [Modern instrumental methods of diagnosing thrombosis: ultrasound duplex scanning]. *Profilaktika tromboembolicheskikh oslozhneniy v travmatologii* i ortopedii: materialy gor. simp. [Prevention of thromboembolism in traumatology and orthopedics: proceedings of the city symposium]. Moscow, December 10, 2002. 12–17.
19. Ob utverzhdenii otraslevogo standarta vedeniya bol'nykh. Profilaktika tromboembolii legochnoy arterii pri khirurgicheskikh i inykh invazivnykh vmeshatel'stvakh: prikaz MZ RF № 233 ot 09.06.2003 [Approval of industry standard management of patients. Prevention of pulmonary embolism in surgical and other invasive procedures: the Ministry of health of the Russian Federation No. 233 dated 09.06.2003]. Available at: http://www.zakonprost.ru/content/base/63044/.(Accessed February 26, 2015) (In Russian).
20. Savel'ev V.S. Flebologiya [Phlebology]. Moscow: Meditsina Publ., 2001. 664 p.