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# THE FUNCTIONAL STATE OF THE HEMOSTASIS SYSTEM IN PATIENTS WITH CAROTID ARTERY STENOSIS WHICH SUBJECT TO CAROTID ENDARTERECTOMY AGAINST THE BACKGROUND OF ANTICOAGULANT THERAPY

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**THE FUNCTIONAL STATE OF THE HEMOSTASIS SYSTEM IN PATIENTS WITH CAROTID ARTERY STENOSIS WHICH SUBJECT TO CAROTID ENDARTERECTOMY AGAINST THE BACKGROUND OF ANTICOAGULANT THERAPY**

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The study is dedicated to assessing the functional state of the hemostasis system in patients with carotid artery stenosis (CAS) who underwent carotid endarterectomy against the background of anticoagulant therapy with rivaroxaban and enoxaparin. The aim of the research was to determine the state of the hemostasis system using low-frequency piezoelectric thromboelastography (LPTEG) and to find optimal methods for preventing thromboembolic complications in the perioperative period.

The study involved 40 patients with CAS who received treatment between 2022 and 2024, as well as a control group of 20 healthy individuals. The patients were randomized into two groups: the first group received enoxaparin, while the second group was treated with rivaroxaban post-surgery. Hemostasis dynamics were evaluated before surgery and on the 1st, 3rd, 5th, and 7th postoperative days.

**The results** showed that patients with CAS exhibited hypercoagulation and suppressed fibrinolysis against the background of increased vascular-platelet activation. After surgery, patients receiving rivaroxaban demonstrated faster normalization of hemostasis parameters compared to those receiving enoxaparin.

**Conclusion.** The use of rivaroxaban ensures a faster normalization of hemostasis system parameters in patients with CAS after carotid endarterectomy, leading to a more effective reduction in the risk of thromboembolic complications.

**Key words:** carotid artery stenosis, atherosclerosis, carotid endarterectomy, hemostasis system, rivaroxaban, enoxaparin, low-frequency piezoelectric thromboelastography.

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# ФУНКЦІОНАЛЬНИЙ СТАН СИСТЕМИ ГЕМОСТАЗУ У ПАЦІЄНТІВ ЗІ СТЕНОЗОМ СОННИХ АРТЕРІЙ, ЯКІ ПІДЛЯГАЛИ КАРОТИДНІЙ ЕНДАРТЕРЕКТОМІЇ НА ТЛІ АНТИКОАГУЛЯНТНОЇ ТЕРАПІЇ

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Дослідження присвячене оцінці функціонального стану системи гемостазу у пацієнтів зі стенозом сонних артерій (ССА), які піддавалися каротидній ендартеректомії на тлі антикоагулянтної терапії ривароксабаном і еноксапарином. Метою дослідження було визначення стану системи гемостазу за допомогою низькочастотної п'єзоелектричної тромбоеластографії (LPTEG) та пошук оптимальних методів профілактики тромбоемболічних ускладнень у періопераційному періоді.

У дослідженні взяли участь 40 пацієнтів із ССА, які отримували лікування у період з 2022 по 2024 рік, та контрольна група із 20 здорових осіб. Пацієнти були рандомізовані на дві групи: перша отримувала еноксапарин, а друга – ривароксабан після операції. Динаміка стану гемостазу оцінювалась до операції, на 1-й, 3-й, 5-й і 7-й післяопераційні дні.

**Результати** показали, що у пацієнтів із ССА на тлі підвищеної судинно-тромбоцитарної активації спостерігалася гіперкоагуляція та пригнічення фібринолізу. Після операції пацієнти, які отримували ривароксабан, демонстрували швидшу нормалізацію показників гемостазу порівняно з пацієнтами, які отримували еноксапарин.

**Висновок.** Використання ривароксабану забезпечує більш швидку нормалізацію параметрів системи гемостазу у пацієнтів із ССА після каротидної ендартеректомії, що дозволяє ефективніше зменшити ризик тромбоемболічних ускладнень.

**Ключові слова:** стеноз сонних артерій, атеросклероз, каротидна ендартеректомія, система гемостазу, ривароксабан, еноксапарин, низькочастотна п'єзоелектрична тромбоеластографія.

**Introduction.** This article explores the hemostasis system on anticoagulant management by rivaroxaban vs enoxaparin and considerations of patients undergoing CEA.

Stenosis of the brachiocephalic vessels is one of the most common causes of ischemic strokes, which are the leading causes of death and disability in our world. According to the World Health Organization (WHO), in 2020, more than 13 million people in the world suffered a stroke, of which about 5 million people became disabled, and almost 6 million died from this disease. Among the factors that contribute to the development of strokes, an important role is played by atherosclerosis of brachiocephalic vessels, which is the main cause of their stenosis [1; 2]. Atherosclerotic plaques that form in these vessels can lead to reduced blood flow to the brain, causing severe neurological impairment and increasing the risk of strokes [2; 4].

According to the results of epidemiological studies, stenosis of brachiocephalic vessels accounts for about 20–30% of all cases of ischemic stroke [1; 4; 5]. The problem is especially relevant in older people, in whom the frequency of this disease increases significantly due to changes in the windows in the vessels and the development of concomitant pathologies, such as arterial hypertension and diabetes [6; 7]. Thus, recognition and treatment of brachiocephalic vessel stenosis is a critical task to reduce disability and mortality from stroke [8].

Changes in the hemostasis system, which are observed in the supply with brachiocephalic vessel stenosis, are one of the aspects affecting the risk of thrombosis and strokes [9]. Atherosclerosis increases the coagulation activity in the blood, which increases the probability of thrombus formation in the places of atherosclerotic plaques. This can lead to the formation of blood clots that restrict or completely block blood flow in important vessels such as the carotid arteries that feed the brain [4; 9]. Thus, changes in the hemostasis system are an important part of the pathogenesis of the disease, and monitoring and correction of these disorders in patients with brachiocephalic vessel stenosis can significantly reduce the risk of thromboembolic complications [10; 11].

The relevance of monitoring the hemostasis system during reconstructive operations on brachiocephalic vessels is also of great importance. Reconstructive interventions such as carotid endarterectomies and stenting of brachiocephalic vessels are effective methods of treating stenosis of these vessels, but they are accompanied by certain risks, including thrombus formation, thromboembolic complications, and the development of stroke [2; 3]. According to studies conducted in various clinical centers, if necessary, those who have undergone reconstructive surgery on brachiocephalic vessels have an increased risk of developing coagulation disorders, which requires significant monitoring and stasis correction systems during surgery and in the postoperative period [3].

In connection with the above, it is important to develop optimal approaches to managing the reserve with brachiocephalic vessel stenosis, taking into account not only anatomical changes in the vessels, but also changes in the hemostasis system. If the effectiveness of treatment and the reduction of the risk of complications depend on the correct monitoring and management of hemostasis, it is necessary to improve the methods of diagnosis and treatment of damage to hemostasis in the case of stenosis of brachiocephalic vessels, in particular during reconstructive operations. In this context, this study aims to reveal the mechanisms of changes in the hemostasis system in patients with stenosis of brachiocephalic vessels, as well as to evaluate the role of monitoring and correction of hemostasis during surgical interventions [12; 13].

**The purpose is** to determine the functional state of the hemostasis system in patients with carotid artery stenosis using a low-frequency vibrating piezoelectric thromboelastograph (LPTEG), search and improvement of the optimal method of prevention of thromboembolic complications in the perioperative period.

**Materials and methods.** The reaction of the hemostasis system was studied in 40 patients who have undergone treatment for carotid artery stenosis (CAS) in the period from 2022 to 2024. Blood sampling for the study was performed under the same conditions according to the standard method from cubital vein of the subjects. To study the system of hemostasis and rheological properties of blood, hardware and software complex ARP-01M "Mednord" was used for continuous registration of the basic parameters of the process of blood clot formation and its lysis.

All patients underwent surgical intervention in volume carotid endarterectomy. Adding a patient with CAS to a particular group occurred randomly. Patients of both groups were examined in the same way, received the same intensive care therapy, indications for surgical intervention were set on the basis of the same criteria. Patients in the comparative (1st) group (20 patients) received analgesia during surgery and in the postoperative period based on regional anesthesia of bupivacaine, their treatment

regimen included enoxaparin 0.4 ml (40 00 anti-XA ME) 2 times a day subcutaneously into the anterolateral surface of the abdominal wall from the first postoperative day for 7 days.

Patients of the studied (2nd) group (20 patients) received analgesia during surgery and in the postoperative period on the basis of regional administration of bupivacaine, they also took rivaroxaban 15 mg 2 times a day orally on the first postoperative day in their treatment regimen for seven days. The control group included 20 practically healthy volunteers. The dynamics of the state of the hemostatic system in both groups of patients with CAS was evaluated using LPTEG before surgery, on the first day and on the 3rd, 5th and 7th postoperative days. CAS treatment included gastroprotective, rheological, antioxidant, metabolic and infusion therapy.

**Results.** In patients with CAS on the background of increased vascular-platelet hemostasis, there is a significant structural and chronometric hypercoagulation and inhibition of fibrinolysis. After surgery according to LPTEG in the first group, changes in indicators toward hypercoagulation were established: in patients with CAS, numerous of ICC and ICD reduction in patients with CAS were noted. Hypercoagulation with increased thrombin activity ICC and activation of fibrinolysis IRCL. The recorded amplitude of the indicator of the intensity of the contact phase coagulation (ICC) 145.38 ± 3,17 r.u. (in the 1st group), at the rate of 84.4 ± 10.76 r.u., which indicates an increase in spontaneous platelet aggregation. An increase in the amplitude and shortening of the time constants of hemocoagulation were also noted. Following data were obtained with the healthy group: in the first group an increase in the intensity of coagulation drive (ICD) by 97.1% and an increase in the rate of retraction and clot lysis (IRCL) by 47.27%. In the second group, similar changes were observed before the start of treatment compared to the group of healthy volunteers. In the second group, the activation of the fibrinolysis system was observed, an increase in IRCL by 39.32% compared to the norm. The **third day** after surgery showed in both groups showed a change in ICC of 65,78% in group 1 and 18.22% in group 2 in compared to healthy volunteers. A statistically significant deviation from the norm of LTPEG indices was revealed: the registered amplitude of the indicator of the intensity of the contact phase of coagulation (ICC) 139.75 ± 3.06 r.u. in group 1 and 119.25 ± 1.76 r.u. in group 2, at a rate of 84.2 ± 10.9 r.u., which indicates a significant increase spontaneous platelet aggregation. An increase in the amplitude and shortening of the time constants of hemocoagulation were also noted.

Comparing the results with the healthy group were obtained: the intensity of coagulation drive (ICD) accelerated by 77.74% in Group 1 and 54.05% in Group 2. The nature of the changes indicates the presence of hypercoagulation due to increased activity and vascular-platelet and procoagulant hemostasis, as well as deviation from the norm, which characterizes fibrinolytic activity (IRCL) decrease by 39.32% in the 1st group and by 33.10% in 2'd group compared to healthy volunteers. On the third day after surgery changes in the hemostasis system indicated a decrease in hypercoagulation, hyperaggregation with the orientation of both groups toward normocoagulation, which are more significant in the second group, which we believe is associated with the use of rivaroxaban as a component of treatment in patients of the second group. **On day 5**, according to the LPTEG, the first group revealed statistically unreliable deviations from the indicators of healthy volunteers: ICC, which characterises the aggregation capacity of platelets, and the indicator that characterize hemocoagulation potential – ICD, as well

as the indicator responsible for changes in the fibrinolytic blood system (IRCL). In the second group, these indicators are almost indistinguishable from those of the norm, indicating a more substantial change towards normalization in patients of the second group. The registered value of the intensity of the contact phase of coagulation (ICC) 127.82 ± 1.95 r.u. (in the 1st group), at the rate of 84.2 ± 10.9 r.u., this indicates the preservation of hyperagregation against the background of the trend towards normalization in patients the first group. When comparing the results with the healthy group, the following data were obtained: the intensity of coagulation drive ICD by 53.36% in the first group, intensity of retraction and clot lysis (IRCL) by 25.72% in the first. In the second group statistically significant changes towards normalization of indicators with preservation of moderate hypercoagulation were revealed: indicators characterizing hemocoagulation potential of blood ICD. The recorded amplitude of the indicator of the intensity of the contact phase of coagulation (ICC) 99.65 ± 2.03 r.u. (in the 2nd group), at the rate of 84.33 ± 10.93 r.u., this indicates a significant ($p<0.05$) increase in spontaneous platelet aggregation. Also observed is the increase in the amplitude and the reduction of the time constants of hemocoagulation. When comparing the results with the healthy group, the following data were obtained: an increase in ICD by 5.97%. Those changes indicate that patients in the second group show a marked tendency toward normalization of all parameters of the hemostasis system, while maintaining a slight hypo-coagulation, hyperaggregation and activation of fibrinolysis. Changes on 5th day after surgery indicated that patients in rivaroxaban group show a marked tendency toward normalization of all parameters of the hemostasis system, while maintaining a slight hypo-coagulation, hyperaggregation and activation of fibrinolysis. **On day 7**, according to the LTPEG, in the first group, statistically significant deviation from the norm of indicators towards moderate hypercoagulation was revealed: ICC, which characterises the aggregation capacity of platelets and the indicator that characterises hemocoagulation, ICD, as well as the indicator responsible for changes in the fibrinolytic blood system. In patients of the second group normalization of all indicators of the hemostasis system is noted.

The recorded amplitude of the coagulation contact phase (ICC) intensity index is 114.76 ± 1.77 r.u. (in the 1st group), at the rate of 84.4 ± 10.76 r.u., which indicates the preservation of activation of spontaneous platelet aggregation. Consideration was also given to increasing the amplitude and reducing the time constants of hemocoagulation in patients of the first group compared with the group of healthy volunteers. When comparing the results with the healthy group, the following data were obtained: an increase in the intensity of coagulation drive ICD by 3.28% in the first group, activation of the intensity of the retraction and clot lysis (IRCL) by 20.19% in the first. In the second group, statistically significant ($P <0.05$) normalization of all indicators which characterize hemocoagulation potential of blood ICD, and ICC which characterize platelet aggregation capacity is detected, as well as normalization of an indicator, responsible for changes in the fibrinolytic blood system. The recorded amplitude of the indicator of the intensity of the contact phase coagulation (ICC) 84,42 ± 1,62 r.u. (in the 2nd group), at the rate of 84.4 ± 10.76 r.u., indicates a reliable normalization of the parameters. Normalization of the amplitude and time constants of hemocoagulation is also noted. The nature of the thromboelastogram indicates the normalization of all hemostatic system on the background of treatment on the 7th day after surgery.

**Conclusion.** Comparing the dynamics of indicators in both groups, we can note faster and more positive dynamics towards normalization in patients of the second group. All of the above indicates: ICC, ICD, IRCL more significant changes toward normalization in patients in the second study group who received rivaroxaban and as therapy, compared with those of the first comparator who received enosaparin as therapy.

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