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The use of thromboelastography and the functional tests with double local hypoxia of the upper limb to assess the risk of thromboembolism in patients undergoing surgery

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Abstract

Introduction: Prothrombotic is considered a condition that leads to the development of venous or arterial thrombosis and its consequences. There are many factors that cause a violation of the hemostatic potential in patients undergoing surgery with existing risk factors for thromboembolism, a more detailed study of the blood coagulation system, including the study of the compensatory capabilities of the hemocoagulation system, should be conducted. One of these methods is a functional test with double local hypoxia of the upper limb (DLHUL) under the control of thromboelastography (TEG).

Goals: The purpose of the study - to identify the degree of thrombotic risk in patients preparing for planned surgical intervention, who belong to the risk group of thrombotic complications, to compare and evaluate the state of the hemostasis system in healthy volunteers and in this cohort of patients using a functional test with double local hypoxia of the upper limb by the method of thromboelastography.

Materials and methods: A randomized prospective study was conducted. Patients were divided into two groups depending on the presence of risk factors for thrombosis. Group 1 consisted of healthy volunteers (n = 40) who are not at risk of thrombosis. Group 2 includes patients with existing factors of thrombotic risk (n = 120) who are preparing for scheduled surgical interventions. These patients underwent a functional test of "double local hypoxia of the upper limb" (DLHUL) using thromboelastographic (TEG) methods of studying the hemocoagulation system. The main task of this functional test is to create a trigger component to determine the limits of hemostasis, the origin and duration of adaptive and compensatory reactions of the hemostasis system. Indicators of the hemostasis system are recorded using a thromboelastograph before and after the test. The links of hemostasis are reflected by the following indicators: aggregate state of blood (A0), contact coagulation intensity (CCI), coagulation drive intensity (ICD), maximum clot density - maximum activity (MA), fibrinolytic activity - clot retraction and lysis index (IRCL).

The results. Analyzing the data of thromboelastography after performing DLHUL, among the patients of Group 1, two types of reaction of the hemostasis system were found in patients without predictors of thrombotic risk: compensated (n= 20) (characterized by a decrease in the indicators of the vascular-platelet component; subcompensated (n = 20) (characterized by an increase in the indicators of the vascular -platelet component). In subjects of Group 1, TEG indicators indicate an increase in the external mechanism of prothrombinase formation, and the reaction of the procoagulant link of the blood coagulation system in response to the influence of a trigger indicates a change in the directionality of the hemostatic potential towards hypercoagulation. In subjects of group 1 with a compensated type, there is an increase in the components of fibrinolysis and a deviation of the hemostatic potential towards hypocoagulation is observed. The state of the hemostasis system in patients of Group 2 is characterized by pronounced changes in the hemostatic potential in all links. In the vascular-platelet link, a violation of platelet aggregation was noted, with an increase in indicators in response to a stimulus. When conducting the DLHUL test in the subjects of group 2, a decompensated (n = 98) and exhausted (n = 22) type of reaction to the test with local hypoxia of the upper limb was determined. That is, with increased platelet aggregation, hypercoagulation, inhibition of the anticoagulant system and fibrinolysis before the action of the trigger factor, after performing the DLHUL test, these disorders in the hemostasis system progress towards hypercoagulation, which is indicated by the increase in platelet aggregation, the strengthening of the coagulation link of the hemostatic system, the depression of fibrinolysis increases . However, the intensity of these changes is not as high as in patients of group 1 after the DLHUL test.

Conclusions: The test with double local hypoxia of the upper limb is effective as a trigger factor to determine the compensatory capabilities of the HS. Depending on the type of reaction of the platelet-vascular, coagulation components of hemostasis and fibrinolysis to the influence of the trigger, two types of reaction of the blood aggregate state regulation system are possible in people who do not have an anamnesis of factors provoking a hypercoagulable state: compensated and subcompensated. Therefore, when planning surgical intervention in this cohort of patients, the risk of thrombotic complications is low. Depending on the type of reaction of the platelet-vascular, coagulation components of hemostasis and fibrinolysis to the influence of the trigger, two types of reaction of the blood aggregate state regulation system are possible in people with an anamnesis of factors provoking a hypercoagulable state: decompensated (more often) and depleted (less often). Patients with a history of factors provoking a hypercoagulable state have a high risk of perioperative thrombotic complications and a possible risk of thrombo-hemorrhagic complications, including the syndrome of disseminated intravascular coagulation. Changes in all links of the hemostasis system in response to the DLHUL test indicate the need to use anticoagulant therapy in patients with an anamnesis of factors provoking a hypercoagulable state as one of the components of preoperative preparation.

Key words: **hemostasis; thrombosis; deep vein thrombosis; pulmonary embolism; risk of thrombosis; perioperative management; thrombotic complications; thromboelastography**

The prothrombotic stage can lead to the development of venous and arterial thrombosis and both consequences. The biological regularity of the blood aggregation regulation system (RAS) under thromboembolism, in a broad sense, is due to the inadequacy of the RAS subsystem, which makes it impossible to ensure the discreteness of the hemostatic potential in different sections of the blood flow to adequately form the minds in them. Arterial thrombosis primarily occurs after erosion or rupture of an atherosclerotic plaque and through platelet-mediated thrombi can cause ischemic damage, especially in tissues from the terminal vascular bed. Acute coronary syndrome and ischemic stroke are the most severe, but quite frequent, consequences of atherothrombosis. The basis of these consequences is tissue ischemia, which can occur slowly due to the progression of atherosclerotic disease or acutely in the case of vascular or intracardiac embolization by a thrombus.

Venous thromboembolism is the most common vascular disease after acute myocardial infarction and stroke. According to some authors, the frequency of objectively confirmed in-hospital deep vein thrombosis (DVT) reaches approximately 10 to 40% among patients undergoing general surgery and 40 to 60% after major orthopedic operations. In 25-30% of patients, the thrombosis affects the deep veins, causing DVT and can lead to pulmonary embolism (PE). In surgical and orthopedic patients, PE occurs in 10% of patients and is the main cause of hospital deaths.

VTE manifests clinically as deep vein thrombosis (DVT) or pulmonary embolism (PE). These two conditions are often interrelated when PE results from a DVT. The formation and reproduction of a thrombus depend on the presence of violations of the integrity of the vascular wall, blood flow, activation of blood coagulation components - aggregation and adhesion. The connection of these factors is known as Virchow's triad. Violations of blood flow or venous stasis often occur after prolonged immobility or bed rest, as well as the length of stay and sometimes the forced position of the patient on the operating table. The following perioperative risk factors for VTE in patients undergoing surgery are distinguished: type of operation (high risk in laparotomy compared to laparoscopic, orthopedic operations on the lower extremities, as well as large-scale operations on pelvic or abdominal organs); postoperative failure of anastomosis, history of smoking, history of venous thromboembolism; prolonged immobility and failure to activate in time, prolonged bed rest or paralysis of the lower limbs; trauma — for example, hip fracture and acute spinal cord injury; morbid obesity (body mass index more than 35 kg/m2); concomitant pathology of the cardiovascular system and respiratory system, including acute myocardial infarction, atrial fibrillation, ischemic stroke, congestive heart failure, acute and chronic respiratory failure, chronic obstructive pulmonary disease; use of estrogens in pharmacological doses — for example, oral contraceptives, hormone replacement therapy; oncological diseases - cancer, especially metastatic adenocarcinomas; age >40 years; acquired hypercoagulable conditions — lupus anticoagulant and antiphospholipid antibodies, hyperhomocysteinemia, dysfibrinogenemia, myeloproliferative disorders, such as red polycythemia; hereditary states of hypercoagulation — resistance to activated protein C (factor V Leiden mutation), protein C deficiency, protein S deficiency, antithrombin deficiency, prothrombin gene mutation.

Despite many studies of the blood coagulation system, cases of thromboembolic complications in patients at risk of thrombotic complications are becoming more frequent, especially during surgical interventions and in the postoperative period, given that the intervention is a trigger factor in the development of thromboembolism.

But thrombosis is one of the complications that can be prevented with the help of timely diagnosis, determination of the degree of risk and adequate preventive measures, both pharmacological and mechanical. And if necessary, in patients subject to planned surgical intervention, preliminary angiosurgical intervention should be performed according to the indications. When it comes to the diagnosis of prothrombotic and thrombotic conditions in patients preparing for surgery, it is usually understood the Doppler of the vessels of the lower extremities, ultrasonography of the heart, routine laboratory diagnostics, if possible, thromboelastography, which relatively recently began to gain popularity, especially in cardiac surgery and angiosurgery, and makes it possible to evaluate all links of the hemostasis system in detail in dynamics.

Despite the proven informativeness of the existing methods for assessing the state of the hemostasis system, they have a significant drawback - routine methods only provide information at a specific moment, namely at the time of blood sampling, and cannot provide an assessment of the reserve capabilities of the platelet-vascular, coagulation components of hemostasis and fibrinolysis. But, when working with patients at risk of thrombo-hemorrhagic disorders, it is important not only to have information about the level of indicators of the RAS system, but also about their functional interaction in ensuring the reference hemostatic potential in the vascular bed. This will allow us to characterize the functional activity of the RAS system and its response to a change in the hemostatic potential to one or another trigger factor, and therefore allows us to assess the compensatory capabilities of the blood coagulation and fibrinolysis system.

With the advent of thromboelastography, functional tests began to appear to detect the degree of risk of thrombo-hemorrhagic disorders. This means that a trigger component must be created to activate the hemostasis system, and further, with the help of thromboelastography, the change in the dynamics of blood coagulation and the comparative characteristics of the compensatory functions of the RAS system are monitored. One of these trigger factors is hypoxia, which increases blood coagulation and activates its fibrinolytic activity and stimulates the prostacyclin-generating activity of the vascular endothelium.

Double local hypoxia of the upper limb is a stress test that makes it possible to assess the reserve of compensatory capabilities of all links of the hemostasis system due to occlusion of the arterial and venous vessels of the upper extremity for about 5–6 min with an interval of 20–25 min.

Goals: The purpose of the study is to identify the degree of thrombotic risk in patients preparing for planned surgical intervention, who belong to the risk group of thrombotic complications, to compare and evaluate the state of the hemostasis system in healthy volunteers and in this cohort of patients using a functional test with double local hypoxia of the upper limb by the method of thromboelastography.

Materials and methods: A randomized prospective study was conducted. Patients were divided into two groups depending on the presence of risk factors for thrombosis. Group 1 consisted of healthy volunteers (n = 40) who are not at risk of thrombosis. Group 2 includes patients with existing factors of thrombotic risk (n = 120) who are preparing for scheduled surgical interventions. The criteria for inclusion in Group 2 were: anamnesis of smoking, history of venous thromboembolism, paralysis of the lower limbs, trauma (fracture of the bones of the lower limbs, etc.); morbid obesity (body mass index more than 35 kg/m^2); concomitant pathology of the cardiovascular system and respiratory system, including acute myocardial infarction, atrial fibrillation, congestive heart failure, ischemic stroke in anamnesis, obliterating atherosclerosis, chronic respiratory failure, chronic obstructive pulmonary disease, use of estrogens in pharmacological doses - for example, oral contraceptives, hormone replacement therapy, oncology, age >40 years, acquired hypercoagulation conditions, including autoimmune diseases. Exclusion factors were: taking antiplatelet and/or anticoagulant therapy.

These patients underwent a functional test of "double local hypoxia of the upper limb" (DLHUL) using thromboelastographic (TEG) methods of studying the hemocoagulation system. The basis of the method is the creation of Virchow's triad in one area of the vascular bed: damage to the vascular wall, stoppage of blood flow, change in blood rheology. The main task of this functional test is to create a trigger component to determine the limits of hemostasis, the origin and duration of adaptive and compensatory reactions of the hemostasis system. Double local hypoxia of the upper limb is achieved by occlusion of the arterial and venous vessels of the upper limb for about 5–6 min with an interval of 20–25 min using a tourniquet. Indicators of the hemostasis system are recorded using a thromboelastograph before and after the test. The links of hemostasis are reflected by the following indicators: aggregate state of blood (A0), contact coagulation intensity (CCI), coagulation drive intensity

(ICD), maximum clot density - maximum activity (MA), fibrinolytic activity - clot retraction and lysis index (IRCL).

Table 1 - Results of TEG during DLHUL

Indicator	GROUP 1				GROUP 2			
	To the test		After the test		To the test		After the test	
	M	±σ	Compensated Type	Undercompensated Type	M	±σ	M	±σ
Aggregate state of blood (A0)	225,22	13,32	211,31 ± 20,64*	269,56 ± 17,15*	435,02	22,44	462,13	30,01
Intensity of contact coagulation (CCI)	86,32	1,01	75,54 ± 1,12*	91,01 ± 1,01*	142,17	2,44	180,12	3,46*
Intensity of coagulation drive (ICD)	21,15	0,62	20,65 ± 0,46*	21,37 ± 0,41*	41,07	1,12	44,89	1,66*
Maximum clot density (MA)	513,51	31,44	490,11 ± 31,01*	600, 03 ± 33,42*	878,01	60,99	956,13	42,44
Intensity of clot retraction and lysis (IRLZ)	15,55	0,42	21,04 ± 0,42*	15,66 ± 0,44*	7,47	0,77	6,04	0,45*

Notes: * — $p < 0.05$ — statistically significant difference between the background and sample in the group; * — $p < 0.05$ — a statistically significant difference between studies after conducting a test with double local hypoxia

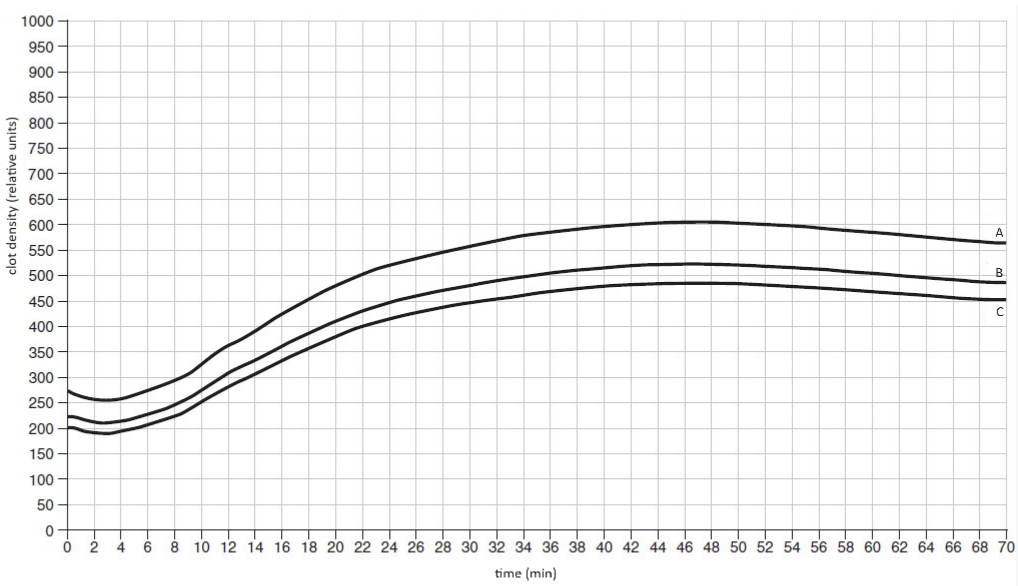

Figure 1. Changes in the state of the hemocoagulation system in Group 1 before and after a functional test with double local hypoxia of the upper limb: A — subcompensated type; B — compensated type; C — before carrying out a functional test with double local hypoxia of the upper limb.

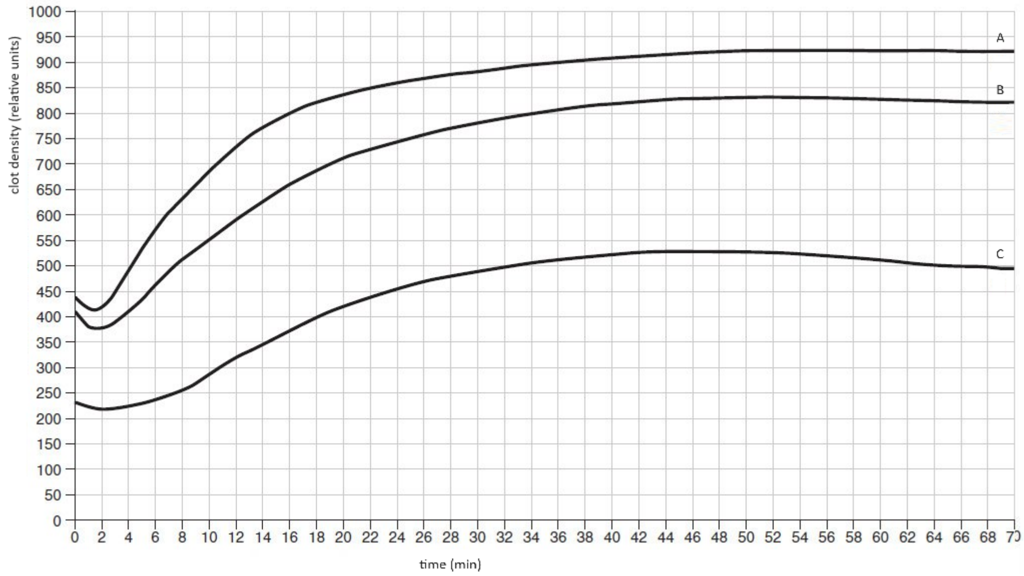

Figure 2. Thromboelastogram of changes in hemostatic potential in patients with risk factors for thrombosis (Group 2) before and after performing a functional test with double local hypoxia of the upper limb: C — averaged thromboelastogram of group 1; averaged thromboelastogram of Group 2 before B and after A performing the DLHUL test.

The results. Analyzing the data of thromboelastography after performing DLHUL, two types of reaction of the hemostasis system were found among patients of Group 1 in patients without predictors of thrombotic risk: the first type is compensated (characterized by a decrease in the indicators of the vascular-platelet component; the second type is subcompensated (characterized by an increase in the indicators of the vascular-platelet component) These two types have different TEG indicators corresponding to the compensated and subcompensated type and statistically occur with the same frequency (n1 = 20); (n2 = 20) (Table 1).

In the subjects of Group 1, who had a subcompensated type of reaction, an increase in CCI and a decrease in blood clotting time were found after the stress test. This indicates an increase in the external mechanism of prothrombinase formation. Evaluating all the TEG indicators obtained during the study, it was found that the reaction of the procoagulant link of the blood coagulation system in group 1 in response to the influence of the trigger (DLHUL test) indicates a change in the directionality of the hemostatic potential in the direction of hypercoagulation (Figure 1). In the subjects of group 1 with the compensated type, there is an increase in the components of fibrinolysis. There was a decrease in ICC compared to the subcompensated type, after the DLHUL test and an increase in blood clotting time, indicating a decrease in the external mechanism of prothrombinase synthesis. Considering the data in Table 1 and comparing the graphs in Figure 1, a hemostatic potential towards hypocoagulation is observed.

When conducting a DLHUL test in subjects of Group 2, the reaction of the hemostasis system to the trigger stimulus was determined (table 1). The state of the hemostasis system in Group 2 patients is characterized by marked changes in the hemostatic potential in all links of the hemostasis system. In the vascular-platelet link, a violation of platelet aggregation was noted, with an increase in indicators in response to a stimulus. According to TEG data (Table 1), a statistically probable deviation from the norm of A0 and CCI indicators, which characterize the aggregation properties of platelets, was found. The CCI after performing the functional test exceeds the indicator before performing the functional test by 21.07%. The initial indicator of the aggregate state of blood (A0) increased by 5.87%. An increase in the index of coagulation drive (ICD) by 8.51%, an increase in the maximum density of the MA clot by 8.17%, indicate the activation of the coagulation layer. Fibrinolytic activity, which reflects the indicator of IRCL, after performing the DLHUL test significantly decreased (by 23.67%), which indicates the inhibition of fibrinolytic activity in patients of group 2 after the functional test (Figure 2). When conducting the DLHUL test in the subjects of group 2, a decompensated (n1 = 98) and exhausted (n2 = 22) type of reaction to the test with local hypoxia of the upper limb was determined, for the most part. That is, with increased platelet aggregation, hypercoagulation, inhibition of the anticoagulant system and fibrinolysis before the action of the trigger factor, after performing the DLHUL test, these disorders in the hemostasis system progress towards hypercoagulation, which is indicated by the increase in platelet aggregation, the strengthening of the coagulation link of the hemostatic system, the depression of fibrinolysis increases. However, the intensity of these changes is not as high as in patients of group 1 after the DLHUL test.

Conclusions

1. The test with double local hypoxia of the upper limb is effective as a trigger factor for determining the compensatory capabilities of the coagulation system.

2. Depending on the type of reaction of the platelet-vascular, coagulation components of hemostasis and fibrinolysis to the influence of the trigger, two types of reaction of the blood aggregate state regulation system are possible in people who do not have an anamnesis

of factors provoking a hypercoagulable state: compensated and subcompensated. Therefore, when planning surgical intervention in this cohort of patients, the risk of thrombotic complications is low.

3. Depending on the type of reaction of the platelet-vascular, coagulation components of hemostasis and fibrinolysis to the influence of the trigger, two types of reaction of the blood aggregate regulation system are possible in people with an anamnesis of factors provoking a hypercoagulable state: decompensated (more often) and depleted (less often).

4. Patients with an anamnrsis of factors provoking a hypercoagulable state have a high risk of perioperative thrombotic complications and a possible risk of thrombo-hemorrhagic complications, including the syndrome of disseminated intravascular coagulation.

5. Changes in all links of the hemostasis system in response to the DLHUL test indicate the need to use anticoagulant therapy in patients with a history of factors provoking a hypercoagulable state as one of the components of preoperative preparation.

Conflict of interest. The author declares that there is no conflict of interest and no financial interest in the preparation of this article.

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