



Risk Factors for Impaired Cerebral Circulation in the Background of Comorbid Changes in Lower Limb Venous Insufficiency

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Abstract: *Varicose veins (varicose veins of the lower extremities), and as a result, venous thromboembolic complications, thrombophlebitis - a disease from ancient times, described by Hippocrates, Avicenna, Galen; the disease is confirmed by excavations of Egyptian burials from 1500 BC. (4, 6, 9).*

Keywords: *gender distribution, hereditary predisposition, congenital anomalies.*

According to various authors, the prevalence by gender distribution is in the range of women/ men 3 :1 (2, 4, 8). Frequent reports of the last decades are data on the detection of pathology among the younger generation (adolescence) (1, 3, 7). The causes of varicose veins remain insufficiently studied, many sources of scientific publications attribute hereditary predisposition, congenital anomalies (formed during pathological pregnancy, TORCH virus infection) (5, 7, 9). The pathomechanism of the disease is not unambiguous, it involves the fibers of the venous wall and the muscle cell, the level of collagen, the nature of the coagulation system of the body, the mechanical load of the venous valves, the static-dynamic imbalance of blood perfusion in the tissues, etc., but the main trigger of the disease is venous valve dysfunction and blood reflux (7, 8, 9). The most dangerous is the formation of blood clots, overlapping of the lumen of blood vessels and separation from the vessel wall, with entry into important parts of the body: lungs, brain. Acute stroke is a formidable complication of venous thrombosis, primarily thrombosis of the veins of the lower extremities, according to statistics, it is more than 70 %, of which more than 30% of patients die (1, 5, 7), which ranks third in terms of mortality after coronary artery disease (2, 6, 8). According to the versions of Virchow, which many scientists adhere to, it is blood clots in the veins of the lower extremities that come off the femoral segment and from the distal parts of the vessel that are dangerous (3, 7, 9). Such patients need a deep analysis of the blood composition, an assessment of the level of the cardiovascular system, the pulmonary system, neurosonography and angiopulmonography of the vessels of the extremities. All therapeutic measures should be accompanied by the supervision of a vascular surgeon, phlebologist. Currently, in the available literature, there is not enough information about the level of damage to the central nervous system against the background of venous thrombosis, varicose veins. The available literature is devoted to a greater extent to pathomorphological studies, as a post-factor of acute strokes, the etiology of which is associated with pulmonary embolism. Whether there is a chronic insufficiency of brain structures, the risk factor of which is a violation of venous insufficiency of the lower extremities, the percentage of complications, gender and age characteristics, the specifics of clinical and neurological disorders, optimization of diagnosis, treatment and prevention of patients remains a topical issue and dictates the need for study.



Target. To establish the role of venous thrombosis of the lower extremities in the development of clinical and neurological disorders of the central nervous system.

Material and research methods. The object of the study was patients with stroke, who were in the intensive care unit, neurology department of the Medical Academy of the Samara State Medical University for the period 2020-2022, 42 patients. The comparison group (CG) consisted of patients who were treated in the therapy department in the amount of 20 people of identical age and gender development (IHD diagnoses); the control group (GC) consisted of patients treated in the department of vascular surgery of the regional multidisciplinary hospital in Samarkand , 15 patients (diagnosis of varicose veins , thrombophlebitis of the lower extremities). All examined patients underwent clinical and neurological examination (daily in dynamics). Patients with stroke were assessed for the severity of the condition. Assessment of the state of the veins of the lower extremities (CEAP), laboratory blood test, according to the main parameters of hemostasis (mainly related to blood clotting factors). All patients underwent ultrasound examination of the vessels of the lower extremities, neuroimaging of the brain and lungs. Statistical processing of the results of the study was carried out on an individual computer using the standard Money Whitney test, where a significant indicator is $p < 0.05$.

Research results. Of the 42 patients, 19 patients were in the acute period (in the intensive care unit) at the time of the initial examination and the start of the study. The rest of the patients were examined in the Department of Neurology, in the stage of the acute period. A deep history taking (from the words of relatives) indicated the need for a targeted study of the lower extremities. The average age of the patients was within 50.1 ± 10.2 years. A stroke of the hemorrhagic type developed in the examined patients with a slight excess of $\approx 55\%$. The degree of severity in the examined patients with stroke was revealed as moderate and severe; in 34% of cases, ventilator assistance was used. Thrombosis of the veins of the lower extremities was noted in 21 % of cases, while thromboembolism of the pulmonary arteries in 12% of cases. These studies showed a difference with the literature indicators, in the cases of our patients, the indicators are higher, presumably this is due to the fact that the examination took place during the COVID -19 pandemic , where the potential cause of the problem was initially associated with damage to the inner wall of blood vessels, increased blood clotting and the expected reaction of the body for a virus attack. In such a situation, an analysis of the main group is brewing in comparison according to clinical, neurological, diagnostic criteria, where the OG is divided into A subgroup with thrombosis and B subgroup without thrombosis . Of the 42 patients, 25 patients had thrombosis , 17 patients without thrombosis . The guideline for dividing into subgroups was the indicators for determining the risk factor indicated in Table. one.

Table 1. Clinical and neurological risk factors for stroke in the examined patients (n =42) (%)

Indicators	OG A (n=25)	OG B (n= 17)
NIHSS scale from 2 to 3 points	83	50
Acute infection (COVID -19), pneumonia (COVID complication)	65	17
Cardiovascular insufficiency	5	1
Diabetes	7	3
Chronic varicose veins	70	26
Thromboembolism pulmonary	7	3
Hemostasis		
IX coagulation factor %	150.9 ± 10.1	80 ± 10.9
Homocystin $\mu\text{mol} / \text{l}$	11.1 ± 1.2	7.9 ± 1.0
Willibrand factor %	240 ± 10.0	152 ± 10.6



Thrombospondin - 1 ng / ml	130±15.1	60±10.3
D- demir ng /ml	> 370	> 300

Thus, it can be seen that subgroup A has a much higher level of severity in terms of motor parameters and the level of the NIHSS scale (within 3 points), the incidence of lung damage as a result of an infectious and inflammatory process, cardiovascular insufficiency; and most importantly, the presence of varicose disorders of the lower extremities, where, taking into account these indicators of patients, it is necessary to note and allocate to a group of increased risk of thromboembolic stroke. Evaluation of the results of laboratory indicators of blood hemostasis revealed changes that differ from the norm in both groups, where the level of clotting factors (VIII , IX in particular) increased, while in the OH A subgroup, the level of coagulation factor IX was significantly increased compared to OG B. Blood parameters did not have fundamental differences depending on the nature and level of brain damage, only the level of von Willibrand factor was higher in patients with ischemic stroke , compared with hemorrhagic, where patients had thrombosis , that is, in the subgroup of OH A. After the collapse of a blood clot, the index of fibrin destruction D - demir is determined in the blood , and since many of our patients had a history of COVID -19, which activates coagulation, it was necessary to study the level of the marker. D - demir has an advantage, its change is associated only if there is a simultaneous pathology of fibrinolysis and coagulation, an important component of the analysis is the change in concentration from the therapy used (anticoagulants). The level of D - demir in both groups was increased, exceeded the normal range (250 ng / ml), however, in the OG A subgroup, the indicator was 10% higher than in the OG B. Taking into account the tasks set, the next stage of the examination was a neurosonographic study of the vessels of the lower extremities, to rule out venous thrombosis . The most common level of damage was the femoral -popliteal segment (especially in overweight patients) in 35% of cases, the second place was occupied by the border of the popliteal vein and the lower leg, the third place was the level of the inner side of the thigh (in one patient, with a consequence of cholecystectomy , through 2 weeks later, a thrombus formed with pain in the inguinal region), in half of the cases the precursor of thrombus formation was infiltrative edema of the soft tissues of the lower leg, in 3 patients a Baker's cyst (hernia in the popliteal region) was noted . Neuroimaging of the brain confirmed the data of clinical and neurological disorders of acute stroke, the difference was in the level of localization, nature and type of stroke. Where in 60 % of cases the focus of infarction was recorded in the parietal lobe, at the same time, low-density foci were recorded in the temporal lobe in 21.5%. The width of the lateral ventricles in EG A was 5.05±0.09 mm, where the index of the lateral ventricles was 30.9±1.2%. Hemorrhagic transformation occurred in patients with atherothrombotic stroke, which obviously influenced the outcome of the catastrophe .

To obtain evidence-based results, risk factors for the development of stroke against the background of existing chronic venous insufficiency of the lower extremities, patients who received inpatient treatment in the department of vascular surgery served as an additional object of study. Patients were offered a questionnaire, composed of questions (arbitrarily, during the study). The reason for hospitalization turned out to be the following symptoms: pain syndrome and heaviness in the legs (long time > 3 (4) years) ; swelling and a feeling of "squeezing" in the legs in the evening; krample, not the possibility of long standing (intermittent walking). Objectively, during examination of the legs, venous patterns (spiders), or round (serpentine) reticular veins were noted. The result of the analysis of the study of the characteristics of the parameters of the state of the vessels of the lower extremities, revealed the number of refluxes, statistically without a difference in the sides, even the performed Valsalva load did not change the indicators. Thanks to colleagues who deal directly with blood vessels (vascular surgeons), a detailed study of structural and functional parameters revealed uneven vein dilatation in 22 %, reflux in 75% of cases, post-



thrombotic lesions in 6%, thrombotic mass in 7% of cases, that is, based on condition that should be in the nome. A change in vascular tone during exercise was recorded, the area of the lumen at rest is 71 Me , and under load increases 100 times (up to 175 ± 10.5 Me), the fact of an increase in the number of refluxes, under load, if before the test is 10%, but after the test increases to 23%, mainly in superficial veins , which confirms the pathological process in the venous system. Blood analysis by the level of hemostasis, increased fibrinogen levels 4.8 ± 0.40 g/l, Willibrand factor $160.9 \pm 16.7\%$, coagulation factor VIII up to $206 \pm 25\%$, Lee-White clotting time slightly increased up to 11 min (± 1.6), elevated homocystin level , all these indicators clearly confirm the possibility of thrombosis , that is, this group of patients needs preventive correction of acute cerebrovascular accident. And if during the initial examination of the determination of the level of D - demir , the level showed above 300 ng / ml, then the anticoagulant therapy leveled the indicators closer to normal (below 300 ng / ml), although the level of D - demir (according to the literature) cannot serve as a prognosis thromboembolic venous complications, but practical experience during the COVID -19 pandemic has allowed me to change my mind, respectively, D - demir can be used as a marker of thrombosis in patients with venous insufficiency in the lower extremities, to prevent severe cerebral catastrophes.

As a continuation of the study, in order to determine the leading factors in the development of venous thrombotic complications according to the type of acute cerebrovascular accident, an analysis was made of the evaluation of the results of examination of patients undergoing inpatient treatment in the therapy department. The inclusion criterion was patients with II - III degree arterial hypertension . Numerous literary sources more than once indicate the relationship of changes in venous circulation (the nature of the change in tone, volume of venous blood flow) with indicators of arterial hypertension. In addition, the inclusion criterion was patients with signs of venous insufficiency in the lower extremities (external) . Attention was drawn (during the selection of patients) and subjective indicators: swelling in the legs, intensifying in the evening, heaviness when walking, pain and convulsions (like krumpne), “fading” of the legs during prolonged standing, the presence of venous patterns ; 1 patient had a trophic ulcer. All external signs correlated with the level of arterial hypertension (AH). So, II degree in 66% corresponded more to the level of subjective changes, III the degree where the level of venous insufficiency prevailed towards focal changes. There were 23% of patients in the group who smoked, which is an important criterion for thrombosis . Laboratory standard indicators determined in patients of the therapeutic department, blood glucose, above 6 (7) mmol / l in 13%, total cholesterol exceeded the norm, above 5 mmol / l in 49% of cases; and an important fact, the duration of AH, directly adjusted with the experience of venous insufficiency in the legs. The parameters of vascular neurosonography (USDG) on the sides slightly differed from each other (Table 2).

Table 2. Ultrasound examination of the vessels of the lower extremities of patients in the control group

Indicators	Left leg	Right leg
Reflux > 0.5 sec	12%	10%
Tortuosity and difference in varicose veins	8%	4%
Wall thickness mm	0.5	0.6
Blood flow velocity cm/sec	8.9	11.3
Clearance mm ²	8	10.6
Diameter mm	2.3	3.1

The result of the analysis according to the main indicators had a slight difference in the sides of the lower extremities, but in terms of the level of the veins themselves, more often violations were noted in the saphenous veins than in the deep ones. Hemostasis indicators: elevated levels of von



Willibrand factor up to 243%, coagulation factor VIII up to 207.5%, homocystin up to 9.9 ± 2.5 $\mu\text{mol/l}$, increased blood clotting (Lee-White time) for 4 min. from the norm. That is, there is a process of thrombosis. As in the case of the comparative group, the control group of those on therapeutic treatment for elevated blood pressure, that is, indirect analysis (examination, laboratory and instrumental indicator) indicates a comorbid background of patients, venous circulatory insufficiency of the lower extremities, which needs correction and preventive treatment of acute cerebrovascular accidents.

Based on the study, it can be concluded that venous circulatory insufficiency of the lower extremities is complicated by the development of acute cerebral infarcts, and during the chronic course directly affects the formation of chronic cerebrovascular accidents, risk factors for the development of thromboembolic complications are laboratory indicators of blood coagulation more often than VIII, IX factor, the level of homocystin, von Willibrand factor, the level of D-dimer (as an indicator of the inflammatory process during the period of infectious complications), can serve as markers of thrombosis and its consequences. The study of ultrasound Doppler analysis of the vessels of the lower extremities is a timely and mandatory study of patients with even minor subjective changes in vascular lesions in the form of edema, pain, heaviness and a feeling of fullness in the legs. Preventive measures in such patients will be directed not only to reduce the symptoms associated with venous insufficiency in the legs, but also as for the prevention of acute strokes, given the high risk of thromboembolic complications.

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