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Lacunar Stroke in Young Men

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Abstract: ischemic strokes (IS) at a young age are one of the pressing problems of modern reality, since they develop in people of working age. These vascular accidents are of great economic importance. Lacunar stroke (LI) due to small vessel occlusion is one of the main subtypes of IS with a variety of modifiable risk factors for its development.
Key words: ischemic strokes, Lacunar stroke

Introduction: to evaluate the main risk factors, features of the course of stroke and the state of endothelial function in young men (18–50 years old) with LI.
Material and methods: the study included 46 men aged 18–50 years with LI. To objectify the severity of existing clinical symptoms and assess severity and IS, the NIHSS neurological deficit assessment scale, the modified Rankin scale and the Rivermead mobility index were used . Patients underwent computed and/or magnetic resonance imaging of the brain, ultrasound and duplex scanning of the vessels of the neck and head, ECG, echocardioscopy and laboratory examination. To assess the vasomotor function of the endothelium, an ultrasound cuff test (UCT) was used.
Study results: in the examined patients, the main risk factors were arterial hypertension (HTN) (97.8%), smoking (67.4%), dyslipidemia (41.3%) and obesity (8.7%). At the same time, a combination of hypertension and smoking was observed in 67.4% of cases, a combination of hypertension, smoking and regular alcohol consumption - in 17.4% of cases, atherosclerotic lesions of the main arteries of the head - in 56.5% of cases. In 22.2% of cases, isolated stenosis of the common carotid artery (CCA) was observed, the degree of which varied from 20 to 35%, in 50% - stenosis of the internal carotid artery (ICA) (from 20 to 40%) and in 33.3% - combined stenoses in the CCA and ICA territories (from 25 to 60%). Ultrasound MP revealed a disorder in the form of decreased vasomotor reactivity in 20 (58.8%) of 34 examined.
Conclusion: In men aged 18–50 years with LI, multiple modifiable risk factors are identified. Ultrasound signs of endothelial dysfunction were detected in more than half of the patients.

Key words: lacunar stroke, young age, modifiable risk factors, endothelial dysfunction, ultrasound cuff test.

Introduction

Worldwide, more than 2 million young people suffer from ischemic strokes (IS) every year [1, 2]. Stroke in young (18 to 50 years old) people accounts for approximately 10–14% of all strokes in high-income countries [3, 4]. Strokes in young adults are associated with high early mortality [5] and disability [6] and are of particular economic importance for working-age adults [7].

According to the TOAST classification (Trial of Org 10172 in Acute Stroke Treatment) [8] distinguish several pathogenetic subtypes of IS. Lacunar stroke (LI), due to occlusion of small vessels, accounts for a quarter of all IS [9]. The development of LI is associated with an occlusive lesion of one of the perforating arteries. These occlusions develop as a result of destruction of microvessels (lipohyalinosis or arteriolosclerosis) or against the background of a local atherosclerotic process [10]. G. Lammie et al . [11] presented data from a pathomorphological study of 70 brain specimens with verified microangiopathy of perforating arteries, in which the morphological changes were the same in the form of concentric hyaline thickening of the walls of small vessels with simultaneous narrowing of their lumen (lipohyalinosis). Currently, according to the TOAST classification (criteria), LI includes IS having the following characteristics: one of the classic lacunar syndromes and the absence of symptoms of damage to the cerebral cortex; a history of diabetes mellitus (DM) or arterial hypertension (AH) supports the diagnosis; lesions in the trunk or subcortex with a diameter of <1.5 cm or no changes on computed tomography (CT)/magnetic resonance imaging (MRI); absence of criteria for stroke due to damage to large vessels or cardioembolism [8].

In European countries, according to various studies, the frequency of LI in young people varies from 3–5 to 16–22% [12–17]. According to our data, among 145 men and women aged 18–45 years, LI occurred in 24% [18].

Purpose of the study: to evaluate the main risk factors, features of the course of stroke and the state of endothelial function in young men (18–50 years old) with LI.

Material and methods

A clinical and instrumental study of 46 young men with LI was conducted. To assess the severity of clinical symptoms and severity and AI, generally accepted scales were used: National Institute of Health Stroke Scale (NIHSS), modified Rankin Scale and Rivermead Mobility Index [19–21].

Inclusion criteria for the study: men aged 18–50 years admitted to the regional vascular center with a diagnosis of acute ischemic cerebrovascular accident, lacunar subtype; availability of voluntary informed consent to participate in the study.

Among the risk factors, we analyzed the presence of hypertension, coronary heart disease, a history of myocardial infarction, a history of acute cerebrovascular accident, smoking (duration and number of cigarettes smoked per day), diabetes, dyslipidemia , regular alcohol consumption, including on the eve of a stroke.

Dyslipidemia was defined as fasting serum triglyceride levels greater than 1.7 mmol /L and low-density lipoprotein (LDL) levels greater than 3.4 mmol /L [22].

Upon admission, all patients underwent a CT scan of the brain, if necessary, MRI, ultrasound and duplex scanning of the vessels of the neck and head, ECG, echocardioscopy , biochemical blood test, blood test for lipid spectrum, coagulogram , blood test for HIV, syphilis, rheumatic tests .

To assess the vasomotor function of the endothelium, an ultrasonic cuff test (MP) was used according to the DS Celermajer method et al . [23] with the study of flow-dependent vasodilation

of the brachial artery (BA) (endothelium-mediated reaction). Flow-dependent VA dilatation was calculated as the ratio of the change in VA diameter during reactive hyperemia (dmax) to the VA diameter in the initial state (dref), expressed as a percentage [24]. A normal VA reaction in a test with reactive hyperemia is considered to be its dilation by more than 10% of the initial diameter, and vasodilation of less than 10% or vasoconstriction are considered pathological conditions [25, 26].

The study was approved by the local ethics committee of the Federal State Budgetary Educational Institution of Higher Education YSMU of the Ministry of Health of Russia (protocol No. 26 of October 11, 2018) and was conducted in compliance with international standards and bioethical norms.

Statistical analysis of the obtained data was carried out using the Statistica 10.0 program (StatSoft Inc. , USA), methods of descriptive statistics. Group data are presented as mean (M) ± standard deviation (δ) in the sample for quantitative variables, and in the sample for qualitative variables the absolute value and frequency of occurrence (%) were indicated.

Research results

The study included 46 men aged from 22 to 50 years (mean age 41.4±6.4 years) with LI, among whom 38 (82.6%) patients had a primary stroke, 8 (17.6%) had a recurrent stroke. 4%). The average age at the primary stroke was 41.1±6.4 years, at the second stroke - 43.3±5.3 years. In the group as a whole, IS developed in the territories of the left or right middle cerebral arteries in 63% of cases, in the territory of the posterior cerebral artery in 26.1%, in the territory of the anterior cerebral artery in 6.5%, and in 4.4% in the vertebrobasilar system. At the time of admission, the average severity of neurological changes on the NIHSS scale in patients was 4.85±2.5 points; the average score on the Rankin scale , which assesses the degree of disability after a stroke, was 3.7±0.83; the average value of the Rivermead mobility index is 3.88±3.74 points.

The main risk factors in patients with LI were hypertension (n=45, 97.8%), while 7 (15.6%) patients regularly took antihypertensive drugs. Other risk factors included smoking (67.4%), dyslipidemia (41.3%), obesity (8.7%), and type 1 (2.2%, n=1) and type 2 diabetes (4.3%, n=1). n=2). Atherosclerotic lesion of the main arteries of the head (MAG) occurred in 56.5% of patients. A combination of hypertension and smoking was observed in 67.4% of cases, a combination of hypertension, smoking and regular alcohol consumption - in 17.4% of cases. Both patients with type 2 diabetes had hypertension (regularly took antihypertensive drugs) and were smokers. The patient with type 1 diabetes did not smoke, did not drink alcohol, and did not have hypertension.

Atherosclerotic lesions of the carotid arteries were localized predominantly in the area of the bifurcation of the common carotid artery (CCA) with transition to the ostia of the internal carotid artery (ICA), while the distal sections remained patent. Atherosclerotic plaques in the area of the CCA bifurcation on the right were detected in 12 (46.2%) patients, on the left - in 11 (42.3%), while in 8 patients they were bilateral. The degree of stenosis varied from 45 to 80%. In the group as a whole, stenosis of the CCA and ICA occurred in 39.1% of cases. Among patients with stenoses, isolated stenoses of the CCA were observed in 22.2% of cases (from 20 to 35%), stenoses of the ICA - in 50% (from 20 to 40%), and combined stenoses in the CCA and ICA territories - in 33.3% (from 25 to 60%) of cases.

The average value of the intima-media complex in CCA was 1.01+0.33 mm. According to echocardioscopy, aortic thickening was recorded in 25 (54.3%) patients.

When considering separately the subgroup with recurrent stroke, it turned out that the average age of these patients was 43.3 ± 5.3 years and they were older than patients with primary stroke. All of these patients had hypertension and regularly took antihypertensive drugs, smoked from 10 to

40 cigarettes per day, three (37.5%) of them regularly drank alcohol. At the time of admission, in patients with repeated stroke, the average severity of neurological changes on the NIHSS scale was higher - 6±3.7 points, reflecting a greater severity of neurological symptoms than in the case of a primary stroke (4.7 points); the average score on the Rankin scale was also higher - 4±0.87 (with primary - 3.6±0.81) and the average Rivermead mobility index was 3.1±3.3 points (with primary - 4.03±3, 4).

When performing ultrasound MP, the initial velocity (V out) along the VA in patients with LI was 64±0.4 cm/s, the initial diameter (d out) of the VA was 4.47±0.26 mm. After MP, Vmax in PA in patients with LI was 157±2.3 cm/s, dmax PA was 4.85±0.33 mm. V max values for PA increased by an average of 146.2±27.6%. The degree of maximum expansion of the VA after MP in patients with IS was 8.47±3.59%. Dilation of the VA against the background of reactive hyperemia by more than 10% of the initial diameter was considered a normal reaction; insufficient vasodilation was recorded with an increase in diameter from 3 to 10%, and vasoconstriction with an increase of less than 2.9% [23, 27]. Among patients with LI, a normal VA reaction in a test with reactive hyperemia with its dilation by more than 10% of the initial diameter was detected in 41.1% (n=14) of cases, vasodilation of less than 10% - in 47.1% (n=16)) and vasoconstriction - in 11.8% (n=4) of cases. Ultrasound MP revealed a disorder in the form of decreased vasomotor reactivity in 20 (58.8%) of 34 examined.

Discussion

Stroke is the second most common cause of death among people over 60 years of age and the fifth most common cause of death among people aged 15 to 59 years, according to the World Health Organization [28]. Over the past 2–3 decades, the incidence of AI has increased worldwide. The most commonly used age range for defining stroke in young adults is 18–49 years [29]. The incidence of stroke in young patients has increased [30]. According to the Danish National Patient Registry, the incidence of initial hospitalizations for stroke and transient ischemic attack in young people has increased significantly since the mid-1990s, while the incidence of hospitalizations for intracerebral hemorrhage and subarachnoid hemorrhage has remained stable [31]. There is a predominance of men with this pathology, although it is more common in women under 30 years of age [3, 14].

Much of the literature indicates that traditional risk factors—hypertension, diabetes, and dyslipidemia —are still the most common, with hypertension ranking first. Other risk factors among young people with IS include smoking, excessive alcohol consumption, drug use, oral contraceptive use, and migraine [32].

According to the results obtained, in our study the average age of patients with LI with a primary stroke was 41.1 ± 6.4 years, with a second stroke - 43.3 ± 5.3 years, which is consistent with the data of other studies [33, 34].

Among the examined patients, the main risk factors were hypertension (97.8%), smoking (67.4%), dyslipidemia (41.3%) and obesity (8.7%). At the same time, a combination of hypertension and smoking was observed in 67.4% of cases, a combination of hypertension, smoking and regular alcohol consumption - in 17.4% of cases. Atherosclerotic lesion of the MAG occurred in 56.5% of cases. In 22.2% of cases, isolated stenoses of the CCA were observed, the degree of which varied from 20 to 35%, in 50% - stenoses of the ICA (from 20 to 40%) and in 33.3% - combined stenoses in the CCA and ICA basins (from 25 up to 60%). These results are comparable to those of other studies [3, 30, 35, 36–38]. In a recently published study by A. Schwarzwald et al . [39] showed that among 689 patients aged 16–55 years without taking into account the subtype of IS in men (they amounted to 60.8%), the following modifiable risk factors were more common:

dyslipidemia (57.9%), smoking (45.0%), overweight (40.3%). According to R. Renna et al . [33], all young patients with LI suffered from hypertension and most of them had additional risk factors. It was also noted that the incidence of hypertension, diabetes and dyslipidemia increased with age [34]. In some series of young patients with IS, alcohol consumption was described as one of the main risk factors [13, 16, 40, 41], as in our study.

Recent work in the field of LI associated with small vessel occlusion has focused on elucidating two pathogenetic mechanisms: endothelial dysfunction and blood-brain barrier disruption [42], and endothelial dysfunction may be most important for the development of LI. The endothelium regulates vascular tone, fibrinolysis /coagulation, and is involved in inflammation and angiogenesis . Its dysfunction reflects a shift towards vasoconstrictor, procoagulative , proinflammatory and proliferative effects [43]. It is believed that hypertension is the most important factor causing endothelial dysfunction [44, 45]. The endothelium is subject to structural and functional damage. Further damage leads to disruption of autoregulation and vascular vasodilation , contributing to the deterioration of cerebral perfusion [44]. The vessel wall thickens as connective tissue replaces normal wall layers with eventual luminal narrowing, thrombosis, and occlusion [42].

During MP, restoration of blood flow through the VA after its occlusion leads to a temporary increase in shear stress, which, in turn, is normally accompanied by the release from the endothelium of a number of substances with vasodilator activity, which causes an increase in the diameter of the VA [23, 24]. In studies [46, 47] in young patients with spontaneous dissection of the MAG and in middle-aged patients with IS, disturbances in flow-mediated vasodilation . A recently published study [48] noted the presence of endothelial dysfunction in stroke patients aged 18 to 49 years.

In our sample, men aged 18–50 years had a flow-mediated disorder vasodilation was observed in 58.8% of cases (20 out of 34 examined). The degree of maximum expansion of the VA after MP in our patients with LI was 8.47±3.59%. Our data indicate the presence of ultrasound signs of endothelial dysfunction. This is comparable to data from previous studies, but in these studies the patients were older [24, 49]. The ultrasound signs of endothelial dysfunction we identified in men with LI at a younger age, the majority of whom had hypertension (97.8%), correspond to the data on the relationship between endothelial dysfunction and hypertension [24, 50, 51]. It has been shown that hypertension contributes to the development of functional disorders in the vascular endothelium and, at the same time, is itself a consequence of them [52]. Several studies in young adults without stroke have shown that male gender, family history, increasing age, weight, alcohol consumption, smoking, diabetes and lipid disorders were associated with endothelial dysfunction [53–55]. Therefore, we can say that the main strategy of medical work is mass coverage of the population with screening for the presence of these risk factors and close attention to identified patients, as well as work to reduce risk factors in this group of people [56].

Conclusion

Thus, in young men (18–50 years old) with LI, the main risk factors are hypertension, smoking, alcohol consumption and dyslipidemia , and most of them had several modifiable risk factors. More than half of the patients with LI had a flow-mediated disorder vasodilation , which indicates the presence of endothelial dysfunction. The high incidence of traditional risk factors in young patients highlights the need to optimize primary and secondary prevention plans.