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Ultrasonography screening of carotid arteries in asymptomatic patients

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Abstract:
Objective: to identify the most important predictors of carotid artery stenosis in ambulatory patients of Saratov and Saratov Oblast, using multivariate analysis, and to specify an ideal patient for ultrasonographic screening.
Materials and methods. In 2014-2018, field consultations and ultrasonographic examinations were performed for asymptomatic patients with suspected carotid artery disease at outpatient clinics of Saratov and Saratov Oblast. Such patients were referred for screening by neurologists and general practitioners. The study encompassed 470 medical charts. The multivariate regression analysis was performed to identify independent predictors of carotid artery stenosis of 50 per cent or more.
Results. Carotid artery stenosis of ≥30% was detected in 24.5% (i.e., 115 of 470) of study participants; of ≥50% in 10.2% (48 of 470) patients, and of ≥70% stenosis in 2.9% (14/470) of participants. The multivariate analysis revealed that the odds of finding stenosis of ≥50% in patients, selected by neurologists and general practitioners for ultrasonographic screening, were significantly higher in the presence of the following factors: age exceeding 72, male gender, acute cerebrovascular event in anamnesis > 6 months ago, atherosclerosis of leg arteries, and episodes of speech impairment. We developed the point scale for risk assessment. A point scale for risk assessment has been created. In the absence of prognostic factors, the absolute risk of detecting stenosis ≥50% was just 3%, with 1 point it was 16%, and with 4 points it amounted to >50%.
Conclusion. Our analysis enabled us to specify the most significant predictors of carotid artery stenosis in patients observed at outpatient clinics of Saratov and Saratov Oblast, and to obtain a patient model helping to optimize optimize selection for ultrasonographic examination.

Keywords: carotid artery stenosis, asymptomatic carotid stenosis, ultrasonography, screening.

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Introduction

Stroke is among foremost causes of death and disability in the Russian Federation. In Saratov Oblast, the incidence of stroke in 2016 was 90.2 cases per 100 thousand inhabitants [1]. Atherosclerosis of the aortic arch vessels is the main cause of ischemic strokes, accounting for one-fifth of all strokes, while up to 80% of these events occur without previous symptoms. This fact justifies the need to examine patients who belong to risk groups. The rate of carotid stenosis progression cannot be accurately predicted. The likelihood of its rapid development is approximately the same as the probability of its stable course.

Carotid stenosis is most often diagnosed after a stroke or if the patient has symptoms of transient ischemic attacks (TIA), such as temporary speech impairment; dizziness and confusion; sudden loss or deterioration of vision; facial numbness on one side; weakness in one arm, or leg, or one side of the body. Patients with atherosclerotic lesions of carotid arteries are considered symptomatic if they have had TIA or ischemic stroke in the region of carotid artery stenosis within the last six months [2]. However, in most cases, patients are unaware of the presence of significant stenosis, since this pathology may not manifest itself in any way. The prevalence of significant asymptomatic stenosis of carotid arteries in the general population, according to different studies, ranges from 0 to 3.1% [3, 4]. Even if stenosis of carotid arteries is asymptomatic, the patient is at increased risk, hence the prognosis of stroke development within a year increases by 3% annually, despite up-to-date medical treatment [5].

Every year, stenosis of carotid arteries, as well as atherosclerosis in general, are diagnosed at a younger age than before. Early detection of lesions in the carotid arteries would allow to correct risk factors and prescribe modern medicamentous therapy to prevent the progression of stenosis, and in case of significant damage, to propose timely surgical treatment in order to prevent stroke.

Carotid artery duplex scan is used as a screening method to assess the risk of atherosclerotic lesions of the carotid arteries [2]. Although cervical auscultation is a standard part of physical examination, murmur detection is more closely correlated with systemic atherosclerosis than with significant carotid stenosis. The sensitivity and positive predictive value for hemodynamically significant stenosis is low. The NASCET (North American Symptomatic Carotid Endarterectomy Trial) study established that sensitivity of carotid arteries

auscultation is only 63%, and the specificity is 61% [6]. Several studies have stated that the sensitivity of auscultation of the carotid arteries for detecting stenosis of over 70% varies from 46 to 77%, and the specificity ranges from 61 to 98% [6, 7]. In a broad study, the prevalence of asymptomatic carotid stenosis of over 35% in patients without murmur symptoms was 6.6%, and the prevalence of stenosis of over 75% was 1.2% [8].

Ultrasonography of the carotid arteries is widely available and associated with a low risk and discomfort. However, medical and economic studies have not shown the feasibility of mass ultrasound screening of the adult population [2, 9-11]. Besides, low specificity of carotid artery duplex scan in routine mass screening may lead to abundant false positive results [12], thereby increasing the frequency of unnecessary aggressive medicamentous and surgical treatment.

In the present-day realities of the Russian Federation, ultrasonographic screening is limited due to large financial costs, as well as due to low provisioning of regional polyclinics, especially in smaller towns and urban-type settlements, with equipment and ultrasound examination specialists. Thus, despite the fact that ultrasonography is a simple and effective method for diagnosing lesions of the carotid arteries, screening of the entire population with an asymptomatic course of the disease is impractical. It is necessary to identify risk groups of carotid artery disease and purposefully conduct examination of these patients in order to increase the effectiveness of ultrasound screening. Several population studies have shown that conventional risk factors, including smoking, high low-density lipoprotein cholesterol content, low high-density lipoprotein cholesterol content, hypertension and diabetes mellitus, increase the risk of carotid atherosclerosis in men and women regardless of their age [4]. We analyzed already published studies to detect risk factors for carotid artery disease, as well as carried out a study, based on polyclinics in Saratov Oblast, during which we attempted to identify the most significant predictors, using multivariate analysis, and clarify the optimal patient model for ultrasonography screening in our region.

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Patient information	Risk factors
Name	Stroke in anamnesis
Date of birth M A	Myocardial infarction in anamnesis
Weight kg Height Cm	Arterial hypertension
Address	Diabetes mellitus
Tel.	Smoking
Date of screening	Cardiac arrhythmia
Complaints	**Ultrasonography results**
Headaches Tinnitus	Norm
Dizziness Syncope	Atherosclerosis
Speech impairment Memory Impairment	Tortuosity
Weakness/numbness in an arm and/or a leg	Side of lesions right left
Temporary loss of vision in one eye	<30%
Other:_____	30-50%
	50-70%
	>70%
	occlusion

Figure 1. Protocol for ultrasonographic screening of carotid arteries

Materials and methods

In the clinics of Saratov and Saratov Oblast (the cities of Balashov, Rtishchevo, Krasnoarmeysk, Pugachev, Balakovo, Engels), over 2014 – 2018, field consultations and examination of patients with suspected carotid arteries lesions, referred by neurologists and therapists, were conducted. The survey encompassed the collection of complaints and anamneses; for each patient, a questionnaire was filled out, where, in addition to passport and anthropometric data, risk factors and ultrasonography results were noted (*Figure 1*).

Over 600 patients were examined, and 470 correctly completed patient medical records were finally included into the study. The study did not include symptomatic patients – i.e., those with a stroke or TIA over the last 6 months; transient or persistent focal neurological symptoms; previously identified carotid artery stenosis; as well as with incomplete or incorrectly completed questionnaires. The study was carried out in accordance with Good Clinical Practice and the principles of the Declaration of Helsinki. Informed consent was obtained from all participants prior to their enrollment. Ultrasonography was conducted on the Medison SonoAce R3 portable device. A broadband linear sensor with a scanning frequency of 5-15 MHz and a broadband convex sensor with a frequency of 2.0-5.0 MHz were used. In the process of examination, we used B-mode imaging, color and power Doppler mapping, and Doppler ultrasonography. The presence of stenosing plaques in the bifurcation of the carotid artery was considered with subsequent gradation of stenosis degree *sensu* the ECST criteria [13]: <30, 30-50%, 50-70%, and >70 (%).

Based on examination results, patients with a degree of stenosis of >50% were allocated to a separate group, since they needed continuing attendance and appointment of optimal medicamentous therapy or surgical intervention. Statistical data processing was carried out, using Microsoft Office Excel 13 with the application package and IBM SPSS Statistics 21.0. The distribution normality was checked using the Kolmogorov-Smirnov and Shapiro-Wilk tests. When distribution of parameter values was not normal, the group median and interquartile range were used to describe quantitative features. Qualitative traits were presented in absolute values and percentages.

When comparing groups by quantitative characteristics, the methods of nonparametric statistics were used, such as Mann-Whitney U test (two-sided test). Comparison of groups by qualitative characteristics was carried out by evaluating contingency tables and calculating the Pearson's χ^2 criterion (two-sided test; Fisher's exact test at the number of observations in the table cells less than 5). The revealed differences ($p < 0.2$) were further included in the multivariate analysis. To determine the optimal cut-off values of continuous variables, sensitivity and specificity analysis was used to construct ROC curves and calculate the Youden's index (Youden's J statistic: J = sensitivity + specificity – 1).

Multivariate analysis was performed, using binary logistic regression via forced inclusion with an inclusion probability of 0.05 and an exclusion probability of 0.10 or above. The odds ratios (OR) were determined with a 95% confidence interval (significance level $p < 0.05$). The predictors identified in the multivariate analysis were used to create a scoring scale for the risk of detecting carotid artery stenosis ≥50%. Discriminant analysis was used to estimate the normalized coefficients of the canonical discriminant function of

independent predictors. We then used the hierarchy of these coefficients to create the predictive scale by converting them into integer components (points). The absolute risk of detecting stenosis (%) was computed for different scores.

Results

A total of 470 completed questionnaire cards were included into the study. Among patients, referred by neurologists and therapists, the vast majority were women (81.7%, 382/470). The age of patients ranged from 17 to 87 years; the median age was 67 (60; 75) years. Most were overweight: body mass index (BMI) was 28 (25; 32) kg/m2. Among the risk factors were the following: arterial hypertension (62%), cardiac arrhythmias (37%), a history of acute cerebrovascular accident (over 6 months) (17%), diabetes mellitus (17%), ischemic heart disease (16%), a history of myocardial infarction (16%), atherosclerosis of leg arteries (11%), smoking (8%). The main complaints were: dizziness (66%), headaches (61%), tinnitus (56%), memory loss (63%), visual impairment (15%), episodes of speech impairment (7%), and episodes of syncope (7%).

Among these patients, carotid artery stenosis ≥30% was detected in 24.5% (115/470). Stenosis ≥50% was found in 10.2% (48/470) of patients. Consequently, on average, one patient of ten had a lesion of carotid arteries, requiring dynamic monitoring and aggressive treatment of atherosclerosis. Stenosis ≥70% was detected in 2.9% study participants (14/470). These were the patients, for whom surgical treatment may has already been indicated (approximately every thirtieth patient). Of these, 12 patients underwent further carotid endarterectomy or stenting at the Department of Nerosurgery of the Research Institute of Traumatology, Orthopedics and Neurosurgery, SSMU.

Table 1 shows main characteristics of all patients and a comparison of two groups, depending on the presence of carotid artery stenosis ≥50%. The revealed significant differences between the groups (p <0.2) were further included in multivariate analysis (binary logistic regression). To convert quantitative characteristics (age and height) into qualitative traits, threshold values were determined, using sensitivity and specificity analysis, while constructing ROC curves, and the Youden's index was calculated.

Multivariate analysis showed that the risk of detecting stenosis ≥50% in the group of patients, selected by neurologists and therapists for screening, was significantly higher in the presence of the following factors: age over 72 years old, male gender, acute cerebrovascular accident in the history of over six months, atherosclerosis of leg arteries, and episodes of speech impairment (*Figure 2*).

In the course of discriminant analysis, a scoring scale for detecting carotid artery stenosis of ≥50% among patients, selected for screening, was obtained (*Table 2*).

In the absence of these prognostic factors, the absolute risk of detecting stenosis ≥50% was only 3%; 16% with a score of 1 point; and over 50% with a score of 4 points (*Table 3*).

Discussion

At the moment, there is no direct evidence of the need for screening to detect asymptomatic carotid stenosis. There are several opinions on the need for mass screening. Due to potentially adverse effects of false positive and false negative results in the general population, lack of cost effectiveness, and low absolute benefit of various types of invasive interventions, the American Heart Association guidelines for the primary prevention of ischemic stroke do not support the idea of mass population screening for asymptomatic carotid stenosis. From the point of view of the US Preventive Services Task Force, as well as American Heart Association/American Stroke Association, American College of Cardiology, and others, it is not recommended to screen for carotid stenosis in patients without neurologic symptoms and a history of stroke or TIA – i.e., existing screening methods have insufficient sensitivity, which could lead to unnecessary surgery and serious complications (death, stroke, or myocardial infarction) [14-16]. Russian national recommendations are as follows, 'Ultrasonographic carotid artery duplex scan is not recommended for routine screening of neurologically asymptomatic patients who do not have clinical manifestations or risk factors for atherosclerosis' (Evidence C) [2].

Table 1. Descriptive statistics of all patients and comparison of two groups based on the presence of carotid artery stenosis of ≥50%

Parameters*	All patients (n=470)	Stenosis of <50% or none (n=422)	Stenosis of ≥50% (n=48)	*p***
Age, years	67 (60-75)	**66.5 (60-74)**	**72 (64-80)**	**0.001**
Male gender, n (%)	88 (18.7)	**66 (15.6)**	**22 (45.8)**	**<0.001**
Weight, kg	73 (65-85)	73 (65-85)	76 (70-83)	0.271
Height, cm	162 (156-167)	**162 (156-166)**	**165 (159-170)**	**0.003**
BMI, kg/m²	28 (25-32)	28 (25-31)	28 (26-30)	0.529
Risk factors:				
ACA in anamnesis over 6 months, n (%)	79 (16.8)	**62 (14.7)**	**17 (35.4)**	**0.001**
MI in anamnesis, n (%)	42 (8.9)	35 (8.3)	7 (14.6)	0.176
ASHD, n (%)	73 (15.5)	61 (14.5)	12 (25.0)	0.089
DM, n (%)	79 (16.8)	70 (16.6)	9 (18.8)	0.686
AH, n (%)	293 (62.3)	263 (62.3)	30 (62.5)	0.557
CA, n (%)	172 (36.6)	154 936.5)	18 (37.5)	0.876
Atherosclerosis of leg arteries, n (%)	50 (10.6)	**40 (9.5)**	**10 (20.8)**	**0.024**
Smoking, n (%)	36 (7.7)	30 (7.1)	6 (12.5)	0.244
Complaints:				
Headaches, n (%)	287 (61.1)	255 (60.4)	32 (66.7)	0.438
Dizziness, n (%)	312 (66.4)	283 (67.1)	29 (60.4)	0.420
Speech impairment, n (%)	32 (6.8)	**23 (5.5)**	**9 (18.8)****	**0.003**
Weakness and numbness of legs, n (%)	265 (56.4)	236 (55.9)	29 (60.4)	0.646
Temporary loss of vision, n (%)	68 (14.5)	60 (14.2)	8 (16.7)	0.665
Tinnitus, n (%)	261 (55.5)	233 (55.2)	28 (58.3)	0.760
Syncope, n (%)	35 (7.4)	30 (7.1)	5 (10.4)	0.385
Memory impairment, n (%)	296 (63)	264 (62.6)	32 (66.7)	0.638

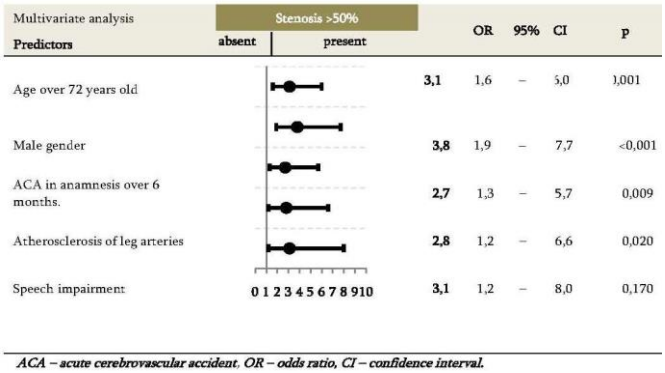

Figure 2. Predictors of detecting carotid artery stenosis over 50% among patients selected for screening (multivariate analysis)

Table 2. Risk score for detecting carotid artery stenosis ≥50% among patients selected by physicians and neurologists for screening

Predictive factor	Discriminant function coefficient	Predictive model score *
Age over 72 years old	0.396	1
Male gender	0.591	2
ACA in anamnesis over 6 months	0.364	1
Atherosclerosis of leg arteries	0.332	1
Speech impairment	0.354	1

Description of the model: Wilks' lambda is 0.887, χ^2 is 55.12, p <0.001; * – rounded up to an integer, multiple of the minimum coefficient of the discriminant function; ACA – acute cerebrovascular accident.

Table 3. Prevalence of carotid artery stenosis ≥50% vs. presence of risk factors

Score (number of points)	Number of patients with stenosis (total number of patients)	Absolute risk of detecting stenosis ≥50%
0	6 (208)	3%
1	11 (132)	16%
2	12 (69)	24%
3	10 (44)	31%
4	6 (12)	53%
5	3 (5)	60%

Despite available recommendations and research, the issue of the need to diagnose stenosis in asymptomatic people remains open. Is it worth identifying and subsequently subjecting asymptomatic patients to further examinations and treatment? The term asymptomatic carotid artery stenosis was proposed in the ACAS study (Asymptomatic Carotid Artery Stenosis Study) in 1995 [17]. It means the absence of transient or persistent focal neurological symptoms, while the patient may have certain nonspecific signs of dyscirculatory encephalopathy.

Some researchers, primarily cardiovascular surgeons, insist on the need to actively identify and treat patients with asymptomatic carotid stenosis. They argue that the first clinical manifestation of carotid artery stenosis is often represented by the stroke. Based on the results of randomized clinical trials (RCTs), conducted in the 1990s, carotid artery occlusion is detected, when restoration of full cerebral blood flow is no longer possible, in a large percentage of ischemic stroke cases. However, in three studies, evaluating carotid endarterectomy (CEA) benefits in asymptomatic patients – ACAS [17], VACS (Veterans Affairs Cooperative Study) [18], ACST (Asymptomatic Carotid Surgery Trial) [19] – the absolute risk reduction of ipsilateral stroke with stenosis >60% after the surgery was significant, even though quite small: 5.9% (ACAS); and 5.4% (ACST), with women having either no risk reduction, or smaller reduction than in men (*Table 4*).

Opponents of active detection and surgical treatment of asymptomatic stenosis, who are mainly neurologists, also point out significant limitations of the RCTs. For example, the studies did not include patients selected for outpatient screening. In addition, many of registered patients were not completely asymptomatic, 20 to 24% had a history of carotid endarterectomy, and 25-32% had a history of TIA or stroke over 6 months prior to the surgery. The ACAS study included patients with symptoms related to the contralateral artery (over 45 days before surgery). Medicamentous therapy has not been well standardized. Although all patients received aspirin, only 7-11% received statins in 1993, although 80-82% did in 2007 studies. Currently, best medical therapy is a combination of antiplatelet therapy (usually dual therapy), intensive medicamentous treatment of arterial hypertension, dyslipidemia, diabetes mellitus, as well as lifestyle changes aimed at quitting smoking, preventing obesity and increasing the frequency of physical activity. Surgeons have been carefully selected to participate in clinical trials based on observed low morbidity and mortality rates.

Table 4. Randomized clinical trials comparing surgical vs. medicamentous treatment for asymptomatic carotid artery stenosis

Clinical study	Stenosis degree	Sample size	Observation time, years	Primary effects	CEA, %	OMT, %	*p*
VACS (1983-1987)	≥50%	444	4	TIA, transient blindness, or stroke	8.0	20.6	0.001
ACAS (1987-1993)	≥60%	1662	2.7	Stroke or death	5.1	11.0	0.004
ACST-1 (1993-2003)	≥60%	3120	5	Stroke or death	6.9	10.9	0.0001
			10		13.4	17.9	0.009

TIA – transient ischemic attack; CEA – carotid endarterectomy; OMT – optimal medical therapy; VACS – Veterans Affairs Cooperative Study [18]; ACAS – Asymptomatic Carotid Artery Stenosis Study [17]; ACST-1 –Asymptomatic Carotid Atherosclerosis Study [19].

Table 5. Randomized clinical trials currently underway to compare different treatment techniques for asymptomatic carotid stenosis

	Comparison	Started	Inclusion criteria	Recruited (total/goal)	Outcomes	Duration	Results
SPACE-2	CEA+OMT vs. OMT CAS+OMT vs. OMT	2008	Stenosis ≥70% (based on USG)	513/1998 (2013)	30-day stroke/death, ipsilateral stroke 5 years	5 years	30-day stroke / death: 1.97% – 0% (CEA – OMT), 2.54% – 0% (CAS – OMT) *
ECST-2	CEA/CAS vs. OMT	2012	Stenosis ≥50% (based on USG)	364/2000 (October 2018)	Stroke, ICH, death 2 years; stroke and non-stroke death 5-10 years	10 years	After 2022
CREST-2	CEA vs. OMT	2014	Stenosis ≥70% based on AG or USG (obvious)	1100/2480 (February 2019)	Periprocedural stroke/death, ipsilateral stroke 4 years	6 years	After 2020

SPACE – Stent Protected Angioplasty versus Carotid Endarterectomy; ECST – European Carotid Surgery Trial; CREST – Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Trial; AG –angiography; USG – ultrasonographic examination; CEA – carotid endarterectomy; CAS – carotid artery stenting; OMT – optimal medical therapy; ICH – intracerebral hemorrhage; * – slow recruitment of patients, did not recruit the required number, continued monitoring of already recruited patients.

Thus, the presence of asymptomatic stenosis is not yet 100% indication for surgery. More research is needed to compare current optimal medicamentous therapy and surgical management for asymptomatic stenosis. A number of such studies are currently underway with results expected after 2020-2022. (*Table 5*).

The planned study CREST-2 (Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Trial) may be one of the most informative for future recommendations. CREST-2 plans to enroll 2,400 patients with stenosis greater than 70% that will be randomly assigned to groups. Different management tactics will be compared. The carotid artery stenting group with optimal medicamentous therapy will be compared with the optimal medicamentous therapy group. The carotid endarterectomy group with optimal medicamentous therapy will be compared with the optimal medicamentous therapy group [20]. The randomized clinical trial SPACE-2 (Stent Protected Angioplasty versus Carotid Endarterectomy), which was conducted in Germany, Austria and Switzerland, had methods similar to CREST-2, but, unfortunately, due to problems with patient selection, instead of planned 1998 patients, only 513 patients were recruited. The study per se was completed, but the follow-up study of already recruited patients continues for inclusion in further meta-analyzes [21].

Given the fact that there is not only a significant improvement in pharmaceutical drug treatment, but also a decrease in complications after surgical treatment, the future outcome of the research is not clear [22]. Currently, in surgical treatment, the risk of stroke / death is 1.2%, the risk of death is 0.4%, which is associated with a higher technical level of the operation, increased use of statins and dual antiplatelet therapy; more effective postoperative blood pressure control; more careful patient selection; centralized surgery of carotid arteries; patch use for suturing arteriotomy or performance of eversion carotid endarterectomy; and abandonment of open surgery in favor of stenting in high-risk patients. However, simple mathematical calculations show that, in the ACAS and ACST studies, 1000 patients with asymptomatic stenosis had to be operated to prevent 50-60 strokes, and 940-950 patients underwent unnecessary surgery. Even a significant improvement in surgical outcomes at this time would not significantly change these statistics. In simple terms, the reduction in the incidence of perioperative death / stroke is nothing less than good news for the individual patient, but in fact, it has little effect on reducing the number of patients who would ultimately undergo unnecessary intervention [23].

Life expectancy is also a very important criterion for assessing the effectiveness of the discussed treatments. Comparing the ratios of postoperative deaths / strokes after surgery and deaths from natural causes / stroke without surgery, we can conclude that they are approximately equal. Thus, the question arises: is it advisable to operate on asymptomatic screened-only patients over 75 years of age? Indeed, these patients usually have several competing diseases that are potentially life-threatening.

Recent recommendations from various medical communities agree that surgery is indicated for a specific group of asymptomatic patients with risk factors. In addition to the need to identify patients who already need surgical treatment, screening makes it possible to promptly start aggressive medicamentous therapy, identify a group of patients for follow-up (Russian national guidelines indicate

the need to repeat ultrasonography every year to assess the progression of the disease in patients with stenosis over 50%), and prevent the development of a stroke. It has been shown that, even in the presence of obvious indications for statin therapy (for example, after suffering a cerebrovascular accident or myocardial infarction), many doctors persistently refuse to prescribe these pharmaceutical drugs, referring to the danger of side effects [24], or prescribing them in insufficient doses [25]. Despite the fact that frequency and effectiveness of antihypertensive treatment has increased, the achievement of target blood pressure values in Russia is significantly lower than in most developed countries [26]. Hence, the need to identify risk groups and standardize medicamentous therapy for atherosclerotic lesions of carotid arteries in Russia is an important factor in favor of screening.

From the economic point of view, conducting total screening using ultrasonography is unprofitable and requires unreasonable labor costs [27]. Screening can only be cost-effective when it is conducted in a population with a higher prevalence of the disease [28]. According to Yin D, et al. (1998), screening is cost-effective if the prevalence of carotid stenosis is 4.5% or above, the specificity of the screening test (carotid artery duplex scan) is 91% or more, the stroke rate in patients with optimal medicamentous therapy is 3.3% or more, the relative risk reduction for stroke is not less than 37%, and the cost of ultrasound examination is US $300 or less [29].

One of the limitations of ultrasound screening is the large number of false positive and false negative results. Sensitivity and specificity for detecting carotid artery stenosis greater than 70% is 90% (95% CI 84-94%) and 94% (95% CI 88-97%), respectively [4]. For example, for a population where the adult population is 100,000 and the prevalence of significant carotid artery stenosis is 1%, ultrasonography will yield 940 true positive results and 7920 false positives (with a specificity of 92%). If additional examinations are not carried out, then many unnecessary surgical interventions may follow [4].

Thus, total screening for carotid artery pathology has neither economic nor clinical justification. However, there is evidence of the feasibility of screening and subsequent preventive surgical treatment within risk groups [30]. The American neuroimaging community has recommended screening among people over 65 years of age who have three or more risk factors for cardiovascular disease as opposed to full screening of all population. The community recommends screening among asymptomatic patients with carotid murmur who are potential candidates for carotid revascularization, and screening for those undergoing coronary artery bypass graft.

Following foreign and Russian national recommendations, we could single out the factors of high stroke risk: silent cerebral infarct sensu computed tomography (CT) or magnetic resonance imaging (MRI); progression of stenosis degree; unstable plaque sensu ultrasonography, CT or MRI (large area of the plaque, large area of the soft core of the plaque, hypoechoic plaque, hemorrhages in the plaque according to MRI, spontaneous embolization sensu transcranial Doppler); decreased cerebrovascular reserve; history of TIA or acute cerebrovascular accident in the contralateral arterial network, diabetes mellitus, male gender, age over 60 years old. The patients with above-listed factors, even if they are with asymptomatic course of the disease, are most likely indicated for surgical treatment and, accordingly, for ultrasound screening.

Russian national guidelines recommend to pay attention to the following markers and risk factors when conducting ultrasonography: previous acute cerebrovascular accident or TIA, damage to other vascular networks (arteriosclerotic heart disease, atherosclerosis of leg arteries, aortic aneurysm, etc.), hereditary hyperlipidemia, diabetes mellitus, bad habits (smoking, alcohol abuse), arterial hypertension, thrombophilia, and overweight [2]. Carotid artery duplex scan is recommended to neurologically asymptomatic patients with auscultatory murmur over the carotid arteries, over 50 years old, who have two or more of the following risk factors: arterial hypertension, hyperlipidemia, smoking, family history among close relatives with cases of atherosclerosis when under 60 years of age, or family history of ischemic stroke (level of evidence C).

However, despite the significance of the listed risk factors for stroke, it is problematic to use these data in actual practice, since almost every patient over 60 years old, who seeks a help of neurologist or therapist, has one or more of the listed risk factors. In Russia, due to high morbidity and mortality from stroke, the low availability of ultrasonography in many regions, the issue of screening is more acute.

In studies on various populations, the following risk factors for revealing significant stenosis of the carotid arteries were identified: age over 65 years old, smoking, hypercholesterolemia, cardiovascular diseases, and arterial hypertension [31, 32]. As a result of our study, we identified the most significant risk factors and developed a point scale, the use of which could help in deciding whether it is necessary to conduct an ultrasonography: age over 72 years old, male gender, a history of acute cerebrovascular accident over 6 months, atherosclerosis of leg arteries, and episodes of speech impairment. The presence of at least one factor increases the likelihood of detecting carotid artery stenosis by 13%, while the presence of four factors augments the probability by 50%.

It is worth noting that the most frequent complaints, with which neurologists and therapists sent patients for ultrasound screening (headaches, dizziness, tinnitus, weakness and numbness in the extremities), had no connection with the detection of the carotid arteries stenosis. This fact suggests that, first of all, it is necessary to pay attention to risk factors rather than to non-specific patient complaints.

During the analysis, we noticed that there were just 16-17% of the patients, selected for ultrasonography, with such risk factors, as diabetes mellitus and coronary heart disease. Perhaps, this is due to the fact that such patients are more often observed by endocrinologists and cardiologists. Probably, with an increase in the proportion of such patients, these risk factors would become significant in our study. From this finding, we can conclude that such specialist physicians should be involved in the selection of patients for the screening.

An episode of acute cerebrovascular accident in the anamnesis over 6 months ago has become a significant risk factor. This evidence once again confirms the fact that, first of all, it is necessary to conduct ultrasonography in patients after acute cerebrovascular accident and TIA (episodes of speech impairment, episodes of temporary loss of vision in one eye, and episodes of weakness in half of the body), regardless of the limitation period.

Male gender was the most significant predictor of carotid atherosclerosis. This is in line with the global statistics on the high prevalence of atherosclerosis in men. It should be noted that, among the patients selected for ultrasound screening, the absolute risk of detecting carotid artery stenosis in men with atherosclerosis of leg arteries increased by almost 30%. Perhaps, it is necessary to provide greater involvement of general surgeons into selecting patients for screening, because they observe patients with atherosclerotic lesions of the arteries of lower extremities in most polyclinics.

Our research had a number of limitations:

– Only 470 patients were included in the analysis. When assessing the required sample size using the calculation formula sensu M. Bland method, the power of our study does not exceed 80%, which corresponds to a study of average accuracy;

– The sample was biased, since the patients were selected for screening by therapists and neurologists, and we did not conduct weighting to obtain greater uniformity of the sample;

– Major, but not all, risk factors were included in the questionnaire – i.e., family history, hypercholesterolemia, thrombophilia and some other factors were not taken into account;

– Conducting a comprehensive ultrasonography has disadvantages in the form of false positive and false negative results. For example, evaluating the accuracy and reliability of ultrasound examination to detect carotid stenosis in three meta-analyses and three large studies, Jonas DE, et al. (2014) reported a sensitivity of 98% (95% CI, 97-100%) and specificity of 88% (95% CI 76-100%) for detecting carotid artery stenosis ≥50% [4]. There is no doubt that ultrasound screening in our study had lower values of sensitivity and specificity.

Conclusion

Our analysis enabled us to clarify the most significant predictors of carotid artery stenosis in patients observed in outpatient clinics of Saratov and Saratov Oblast, and to develop a patient model that would help optimize selection for ultrasound screening. The resulting patient model for ultrasonographic examination can be recommended to neurologists, therapists, cardiologists and related specialists. This model may help to refer patients to ultrasonography – those, who actually need it most, which could make all the difference at regional polyclinics and hospitals, where ultrasonography of blood vessels is in high demand due to shortage of equipment and specialists.

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Conflict of interest

The authors declare no conflict of interest.

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