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Carotid stenosis as a risk factor for ischemic stroke

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Abstract

Aim – to analyze the effect of carotid stenosis of varying severity in combination with other factors on the risks of primary and recurrent ischemic stroke, using methods of mathematical regression analysis.

Material and methods. The study included 606 patients, examined by a neurologist, contrast-enhanced CT scan of the brain, ultrasound of the vessels of the head and neck, other tests and instrumental studies. The degree of carotid stenosis was assessed using the NASCET method (stenosis 0-49%, 50-69%, 70% or more). For the purpose of mathematical analysis, patients were divided into 3 comparison groups: those without a history of stroke, patients with a single stroke, and a group of patients with two or more ischemic strokes. In patients with a history of stroke, the size of the ischemic lesion was assessed according to CT data, the severity of neurological deficit according to the NIHSS scale and the recovery degree, and the functional outcome of ischemic stroke (Rankin scale, Rivermead index). The study used logistic regression analysis to assess the relationship between the dependent variable (presence of primary or recurrent stroke) and a set of predictors, which were a number of clinical and instrumental indicators.

Results. The presence of carotid stenosis of 50-69%, when combined with pathology of the cardiovascular system, acts as a factor that significantly increases the risk of developing primary ischemic stroke. Stenosis exceeding 70% has a high level of significance in the risk of recurrent ischemic stroke, this fact should be taken into account for secondary prevention of stroke.

Conclusion. A preliminary assessment and analysis of carotid stenosis degree and other comorbid factors co-influencing the risks of primary and recurrent ischemic stroke has an undoubted potential. This approach can reduce the risk of recurrent vascular accidents and help organizing a personalized approach to surgical treatment of patients.

Keywords: carotid stenosis, ischemic stroke, risk factors, regression analysis.
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Каротидный стеноз как фактор риска развития ишемического инсульта

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Аннотация

Цель – проанализировать влияние каротидного стеноза различной степени выраженности в сочетании с другими факторами на риски возникновения первичного и повторного ишемического инсульта, с применением методов математического регрессионного анализа.

Материал и методы. Обследованы 606 пациентов (осмотр невролога, КТ головного мозга с контрастным усилением, УЗИ сосудов головы и шеи, иные анализы и инструментальные исследования). Степень каротидного стеноза оценивалась по методике NASCET (стенотическое поражение 0–49%, 50–69%, 70% и более). В целях математического анализа пациенты были разделены на 3 группы сравнения: не имеющие инсульт в анамнезе; пациенты с единственным инсультом; с двумя и более ишемическими инсультами. При наличии инсульта в анамнезе оценивались размер очага ишемии по данным КТ, выраженность неврологического дефицита по шкале NIHSS и степень его восстановления, функциональный исход ишемического инсульта (шкала Рэнкина, индекс Ривермид). В исследовании применен логистический регрессионный анализ для оценки взаимосвязи между зависимой переменной (наличие первичного или повторного инсульта) и набором предикторов, в качестве которых выступал комплекс клинических и инструментальных данных.

Результаты. Наличие каротидного стеноза 50–69% при сочетании с патологией со стороны сердечно-сосудистой системы выступает в качестве

фактора, существенно повышающего риски развития первичного ишемического инсульта. Превышение величины стенотического поражения более 70% имеет высокий уровень значимости в вероятности возникновения повторного ишемического инсульта, что необходимо учитывать в качестве вторичной профилактики инсульта.

Выводы. Предварительная оценка и анализ степени каротидного стеноза и других коморбидных факторов, в совокупности влияющих на риски развития первичного и повторного ишемического инсульта, имеют несомненный потенциал для снижения вероятности возникновения повторных сосудистых катастроф и организации персонализированного подхода к хирургическому лечению пациентов.

Ключевые слова: каротидный стеноз, ишемический инсульт, факторы риска, регрессионный анализ.

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Список сокращений
ИИ – ишемический инсульт; ОНМК – острое нарушение мозгового кровообращения; КТ – компьютерная томография; УЗИ – ультразвуковое исследование.

INTRODUCTION

Cerebrovascular diseases are leading in the statistics of reasons for mortality and disablement of adult employable population [1] and bringing a marked economic loss [2]. Among cerebrovascular diseases, cerebrovascular accidents (CVA) are to be seen as the major medico-social problem of international scale [3]. The modern status of the problem justifies the high importance of studying the risk factors of stroke development, development of new and improvement of existing methods of diagnostics [4], treatment and prevention of this condition [5]. According to the WHO data, diseases of the circulation organs due to atherosclerosis become the reason of death of more than 16 million people every year; and the prevalence of ischemic stroke associated with atherosclerosis among patients aged 50–55 increases by 1.8–2.0 times in every successive decade of life. Within 12 months from the old CVA, 40-45% patients die [6], every fifth patient develops a second stroke in the successive years [7]. Among survivors, up to 90% of patients become disabled [1], and 20% of them would require nursing care [8]. Less than 10% of patients would be able to return to labor and regular life after a stroke [9]. Modern clinical practice of management of stroke patients sees its primary and secondary prevention as priorities. A complex study of factors relevant to the risk of stroke development will enable a more efficient approach to prevention of this disease [10].

The pathogenic mechanism of ischemic stroke (IS) is the hypoxia of the brain that can be aggravated with various comorbidities [11], including carotid stenosis [12]. Underlying diseases may acts as isolated or complex risk factors for the development of stroke, and their therapy is the basis for the primary and secondary prevention of the stroke [13]. One of the most significant reasons for the development of chronic hypoperfusion of the brain is the lesion of the great vessels [14], including constrictive lesions of the major arteries of the head and neck [15].

The carotid arteries play a major role in the formation of the total volume of cerebral circulation [16], providing for approx. 75% of cerebral blood flow [17]. Since the stenosis of the carotid artery due to atherosclerosis disrupts the normal cerebral blood flow, it surely increases the risk of CVA. In 80% of the cases, the atherosclerotic process affects the area of bifurcation of the arteria carotis communis, and multiple atherosclerotic lesions are seen much more often that isolated ones. Therefore, the stricture formation of the extracranial sections of the carotid arteries by an atherosclerotic plaque is the most frequent reason of defects of perfusion of the brain tissue, which might be accompanies with chronic [18] and acute cerebrovascular circulation deficiencies [19].

Atherosclerotic carotid plaques are often found in elderly patients and individuals with a high risk of other cardiovascular diseases. The stenosis of the carotid artery, as a rule, us the consequence of systemic atherosclerosis, and its prevalence demonstrates an age-associated dynamic and is seen in approx. 7.5% men and 5% women aged over 80 [20]. There are many risk factors contributing to atherosclerosis, namely, smoking, hyperlipidemia, male sex, age that may increase the risks of stenosis of the carotid artery. A plaque occupying over 50% of the carotid arterial lumen is considered to cause substantial constriction of the vessel known as hemodynamically significant stenosis of the carotid artery [21], which may be accompanied with clinically relevant decrease of brain tissue perfusion with blood [22]. Patients with severe stenosis of the carotid artery demonstrate higher degrees of cardiac accidents and mortality; with asymptomatic carotid stenosis of over 75% of the lumen, the risk of the stroke is 5.5% per year; with asymptomatic stenosis of 60% of the vessel lumen, 11% over 5 years. The lesions of carotid arteries are related to a third of all strokes. This data shows the importance of early diagnosis and treatment of carotid stenosis to prevent complications such as CVA [23].

Despite the numerous studies of various aspects of epidemiology, pathogenic mechanisms, diagnostics and prevention of IS, there are some problems the solution of which would allow a more efficient prognosis of the outcome

[24] and improve prevention of CVA in these patients [25]. One of the aspects that is still needs more research are the specifics of risks of development of first and second ischemic stroke associated with carotid stenosis of different degrees or associated with other risk factors.

MATERIAL AND METHODS

An open retrospective study was conducted to assess risk factors for primary and recurrent stroke in patients with carotid stenosis of varying severity. The subjects of the study were 606 patients who were treated in neurological departments, as well as patients who sought outpatient care. The study included 292 women (48.2%) and 314 men (51.8%) aged from 39 to 89, the median age of patients being 67.4 (84.25; 50.56) years. The study was conducted in accordance with the standards of good clinical practice and the principles of the Declaration of Helsinki. The study protocol was approved by the ethics committee of the Federal State Budgetary Educational Institution of Higher Education SSMU of the Ministry of Health of Russia, written informed consent was obtained from all patients before participating in the study.

Depending on the degree of stenosis of the major vessels of the head and the neck (based on the stenosis degree evaluation method NASCET – North American Symptomatic Carotid Endarterectomy Trial), the patients were divided into three groups (**Table 1**). In 446 patients (73.6% of the total number of patients within the study), stenosis was identified without hemodynamically significant damage to the major vessels of the head and the neck (stenosis of 0–49%), in 85 patients (14.0%) stenosis was between 50–69%, and the group of patients with stenosis damage of 70% and above included 75 people (12.4%).

The pathogenic subtype of the ischemic stroke was identified using the TOAST criteria, Trial of ORG 10172 in Acute Stroke Treatment (1993): atherothrombotic, cardioembolic, lacunar, or of other identified ethiology.

At the same time, the patients were divided into three comparative groups: no history of stroke; one stroke; two cases of IS and more (**Table 2**).

The comparison of study groups was performed against the fact of history of first or second IS. In post-stroke patients, the size of the ischemic site was assessed using computed tomography (CT) scans of the brain, manifestation of the neurologic impairment using the NIHSS scale (National Institutes of Health Stroke Scale) and the degree of its restoration, functional outcome of IS (Rankin scale, Rivermead index). The study did not include patients with hemorrhagic stroke and patients with adverse outcome of disease.

All patients were examined by a neurologist and underwent computed tomography (CT) of the brain with contrast enhancement or CT angiography as indicated. Other examinations included ultrasonic dopplerography of the brachiocephalic arteries (BCA USDG), duplex ultrasonic scanning (DUSS) of the vessels of the head and the neck combined with color flow mapping (CFM). If necessary, other studies, analyzes and consultations with relevant specialists were carried out. Patients with stroke received therapy in accordance with the standards of medical care for this disease, and a set of rehabilitation measures was also carried out as part of the first stage of rehabilitation.

The statistical analysis was performed using the SPSS Statistics software suite, Ver. 27. Both parametric and nonparametric statistical methods were used to analyze the data in the study. The parametric methods included a t-тест and regression analysis. Nonparametric methods were used to analyze data that did not meet the requirements of normality of distribution or homogeneity of variances and included the Mann-Whitney test and Wilcoxon's test. The assessment of the distribution type was performed using the Shapiro-Wilt test and Kolmogorov-Smirnov test.

The study used logistic regression analysis to assess the relationship between the dependent variable (presence of primary or recurrent stroke) and a set of predictors, which were a set of clinical and instrumental data. Logistic regression was used to estimate the probability of the occurrence of primary or recurrent IS when changing the values of the predictors. The critical level of significance when testing statistical hypotheses was taken equal to 0.05.

RESULTS

Analysis of individual risk factors is not a sufficiently objective method for analyzing the risk of CVA in a patient, since a combination of them is observed, as a rule. From a practical point of view, the most promising thing is to study a set of clinical and instrumental indicators that correspond to the risk of developing a primary or recurrent stroke, which is a reflection of the effectiveness of primary / secondary prevention and requires special attention. The use of models considering a complex of clinical and instrumental parameters allows for a personalized approach towards assessment of their dynamics in the course of primary and secondary prevention.

Regression analysis of a complex of clinical and instrumental parameters of a group of patients without a history of stroke

Age	0–49%		50–69%		≥ 70%		Total	
	Abs.	%	Abs.	%	Abs.	%	Abs.	%
below 50	37	8,3	1	1,2	1	1,3	39	6,4
50–59 y.o.	86	19,3	17	20,0	15	20,0	118	19,5
60–69 y.o.	142	31,8	19	22,4	35	46,7	196	32,4
70–79 y.o.	123	27,6	28	32,9	14	18,7	165	27,2
80 and above	58	13,0	20	23,5	10	13,3	88	14,5
TOTAL	446	100,0	85	100,0	75	100,0	606	100,0

Table 1. *Distribution of patients depending on the carotid stenosis severity*

Таблица 1. *Распределение пациентов в зависимости от степени выраженности каротидного стеноза*

Patient group	Carotid stenosis of 0– 49% (n, %)	Carotid stenosis of 50–69% (n, %)	Carotid stenosis of ≥ 70% (n, %)
No stroke history	223 (36,8%)	10 (1,6%)	3 (0,5%)
First stroke	134 (22,1%)	47 (7,8%)	20 (3,3%)
Second stroke	89 (14,7%)	28 (4,6%)	52 (8,6%)
TOTAL	446 (73,6%)	85 (14,0%)	75 (12,4%)

Note: n – total number; % – relative number from the total number of patients within the study.

Table 2. *Distribution of patients into study groups*

Таблица 2. *Распределение пациентов по группам сравнения*

Variable	Coefficient (β)	Standard error	p-value	Odds ratio
Constant term	-0,537	0,079	-	-
Third-degree CHF	21,740	0,301	0,049	1,876
Stenosis on opposite side 50–69%	0,624	0,306	0,041	1,867

Table 3. *Predictor values in the equation of clinical and instrumental indicators of groups of patients without a history of ischemic stroke and having a history of ischemic stroke in the carotid territory*

Таблица 3. *Показатели предикторов уравнения клинических и инструментальных показателей групп пациентов без ишемического инсульта в анамнезе и с перенесенным ишемическим инсультом в каротидном бассейне*

and with a history of stroke demonstrated the participation of a small number of regressors in the formation of the regression model (**Table 3**).

The equation describing the probability of classification of clinical and instrumental indicators as matching the risk of development of the first stroke is as follows:

$$y = -0{,}537 + 21{,}740*(\text{3-degree CHF}) + 0{,}624*(\text{Stenosis on opposite side 50-69\%})$$

The presence of significant concomitant diseases is a separate risk factor for the development of IS, but their presence aggravates the risks of stroke in patients with stenosis of 50–69%. Thus, the presence of hemodynamically significant carotid stenosis in the presence of a pronounced comorbid condition in the form of grade 3 CHF can be considered as an indication for its surgical treatment, since the risks of developing IS increase by 1.8 times. It is known that asymptomatic stenosis of 60% is accompanied by a probability of stroke within 5 years in only 11% of cases [23].

The quality of the proposed model can be characterized by the following indicators: -2Log-likelihood, Cox and Snell R Square and Nigelkerk R Square, the values of which were 966.893; 0.016 and 0.022, respectively.

Studied group	Without history of IS	With history of IS	Correct indications
Without history of ischemic stroke	433	22	95,2
With history of ischemic stroke	253	28	10,0

Table 4. *Classification of clinical and instrumental parameters of patients without a history of ischemic stroke and having a history of ischemic stroke in the carotid territory*

Таблица 4. *Таблица классификации показателей клинических и инструментальных показателей пациентов из групп без ишемического инсульта в анамнезе и с перенесенным ишемическим инсультом в каротидном бассейне*

Area	Standard error	Asymptotic significance	Asymptotic 95% confidence interval	
			Lower threshold	Upper threshold
0,526	0,022	0,236	0,483	0,569

Table 5. *The ROC curve area values when comparing clinical and instrumental indicators of patients without a history of ischemic stroke and having a history of ischemic stroke in the carotid territory*

Таблица 5. *Показатели площади под ROC-кривой при сравнении клинических и инструментальных показателей пациентов без ишемического инсульта в анамнезе и с перенесенным ишемическим инсультом в каротидном бассейне*

Despite the completeness of the model, one cannot assert its high quality with respect to its specificity (**Table 4**). According to the general summary, the percentage of correctly identified states is only 62.6%.

Table 5 shows the parameters of the ROC-curve of the formed model (**Fig. 1**). It is to be noted that the model is not sufficiently reliable for use in clinical practice. Not all risk factors of stroke development are considered when building the module. This is indeed supported by the volume of data that was involved in the analysis. Thus, clinical and instrumental data were limited to the results of vascular ultrasound, CT scan of the brain, and the presence of concomitant diseases of the cardiovascular system.

The next stage of the analysis was the study of factors influencing the occurrence of recurrent stroke, which can be interpreted as insufficient effectiveness of secondary prevention of ischemic stroke.

The major predictors involved in the increase of the risk of development of second stroke are shown in **Table 6**.

The equation describing the probability of development of second stroke based on the analyzed complex of clinical and instrumental data is as follows:

$$y = -20{,}0 - 0{,}366*(\text{Rankin2}) - 3{,}564*(\text{Ht higher than 181 mmHg}) - 6{,}306(\text{Stenosis on the focal side over 70\%}) - 5{,}700*(\text{Stenosis on the opposite side over 70\%})$$

The quality of the proposed model may be characterized with the following indicators: -2Log-likelihood, Cox and Snell R Square and Nigelkerk R Square, the values of which were 28.037; 0.595 and 0.975, respectively.

The performance indicators of the model are shown in **Table 7**. The model is characterized with a rather good sensitivity and specificity of classification of a complex

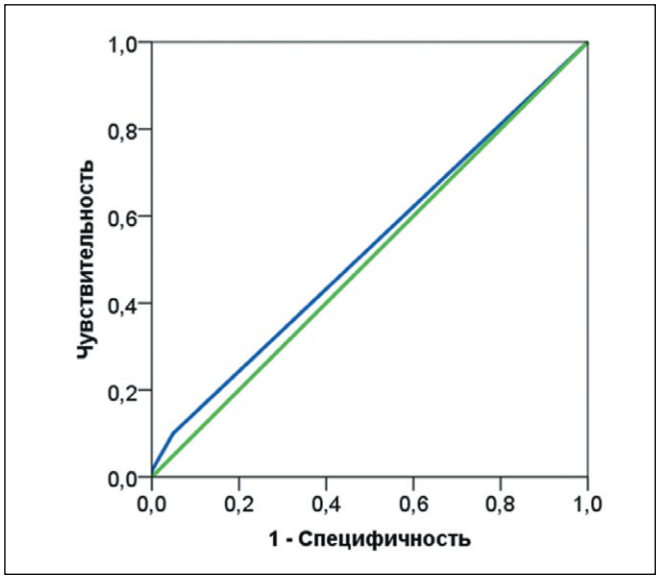

Figure 1. *The ROC curve for the differences between the group of patients without a history of ischemic stroke and having a history of ischemic stroke in the carotid territory.*

Рисунок 1. *ROC-кривая, отражающая различия между группой пациентов без ишемического инсульта в анамнезе и с перенесенным ишемическим инсультом в каротидном бассейне.*

Variable	Coefficient (β)	Standard error	p-value	Odds ratio
Constant term	-20,000	1478,916	-	-
Rankin2	-0,366	0,196	0,042	0,693
HT above 181 mmHg	-3,564	1,685	0,034	0,028
Stenosis on the side of the site over 70%	-6,306	1,514	0,000	0,002
Stenosis on the opposite side over 70%	-5,700	1,661	0,001	0,003

Table 6. *Predictors values in the equation of clinical and instrumental parameters of patients with primary and recurrent ischemic stroke in the carotid territory*

Таблица 6. *Показатели предикторов уравнения клинических и инструментальных показателей пациентов с первичным и повторным ишемическим инсультом в каротидном бассейне*

of parameters. The total percentage of correctly classified conditions was 99.3%.

Table 8 shows the indicators of the ROC-curve of the formed model, and its graphical representation is shown on the graph (**Fig. 2**).

It was revealed that patients with carotid stenosis of more than 70% after stroke have a high risk of developing a recurrent stroke. Thus, correction of changes in the vessels of the carotid territory should be considered as an important aspect of secondary prevention of IS.

Taking into account the critical role of the preventive approach in the management of neurological patients and the global medical and social significance of acute vascular pathology of the brain, continuous improvement of existing diagnostic and rehabilitation approaches is necessary [26, 27], as well as complex stratification of risks [28] in the development of the stroke [29, 30]. The introduction of

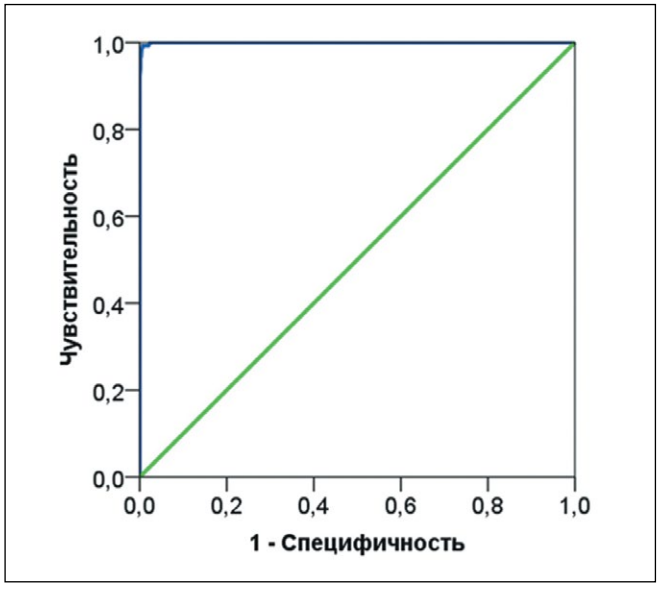

Figure 2. *The ROC curve showing the differences between the group of patients with primary and recurrent ischemic stroke in the carotid territory.*

Рисунок 2. *ROC-кривая, отражающая различия между группой пациентов с первичным и повторным ишемическим инсультом в каротидном бассейне.*

Study group	First stroke	Second stroke	Correct indications
First stroke	602	257	99,7
Second stroke	365	129	97,7

Table 7. *Classification of clinical and instrumental parameters of patients with primary and recurrent ischemic stroke in the carotid territory*

Таблица 7. *Таблица классификации показателей клинических и инструментальных показателей пациентов с первичным и повторным ишемическим инсультом в каротидном бассейне*

Area	Standard error	Asymptotic significance	Asymptotic 95% confidence interval	
			Lower threshold	Upper threshold
1,000	0,000	0,000	0,999	1,000

Table 8. *The ROC curve area values when comparing clinical and instrumental indicators of patients with primary and recurrent ischemic stroke in the carotid territory*

Таблица 8. *Показатели площади под ROC-кривой при сравнении показателей клинических и инструментальных показателей пациентов с первичным и повторным ишемическим инсультом в каротидном бассейне*

methods for modeling the pathological process, including the use of regression analysis, provides prediction of the risk of stroke, and makes it possible to develop new approaches to effective prevention of patients with a combination of comorbidities [31, 32].

DISCUSSION

Carotid artery stenosis of varying severity as a comorbid condition and a serious medical problem is characterized by positive correlations with the age of patients and high cardiovascular risk and depends on a number of other factors, including, for example, smoking status, hyperlipidemia, and male gender. Therapy of carotid artery stenosis may include conservative medical and surgical methods, the most accessible of which are carotid endarterectomy [33] and carotid artery stenting [34]. Despite the fact that any of the therapeutic approaches is aimed at reducing the risk of cerebral ischemia and is an important aspect of primary and/or secondary prevention of IS, the decision on the tactics of surgical / endovascular intervention or the optimal choice in favor of conservative medical treatment remains controversial and difficult in many cases. Moreover, the level of restoration of neurological deficiency in the early post-stroke period, and, respectively, the rehabilitation potential directly depends on the severity of atherosclerotic changes of the major vessels of the neck and the head [35]. Therefore, a personalized approach to the evaluation of exceptional features of the clinical and demographical status of the patient, determination of the main and dependent risk factors and, in particular, the degree of influence of carotid stenosis on the course and prognosis of IS [36] will definitely improve the treatment outcomes, optimize care [37] and, in the future, reduce the probability of onset of cerebrovascular accidents [38].

CONCLUSIONS

The study found that hemodynamically significant stenotic lesions of the great vessels of the head and neck, with carotid stenosis values of 50-69%, significantly increase the risk of developing ischemic stroke (IS) when combined with cardiovascular system pathology. As a secondary prevention

measure, it is crucial to focus on the degree of carotid stenosis. Mathematical models indicate that a stenotic lesion exceeding 70% significantly increases the likelihood of recurrent ischemic stroke (IS). Additionally, poor recovery from an initial stroke, as measured by the Rankin Scale, is a significant predictor of recurrent stroke.

Thus, carotid stenosis independently serves as a risk factor for the development of acute cerebrovascular accidents (CVA), a finding corroborated by several clinical studies. Studying the impact of a combination of factors on the likelihood of primary and recurrent ischemic stroke, manifesting against the backdrop of carotid stenosis, allows for a reduction in the risk of subsequent vascular events. It also facilitates a personalized approach to treatment strategy selection and helps determine the optimal timing for preparing patients for surgical interventions.

ADDITIONAL INFORMATION	ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ
Ethical expertise. Protocol No. 202 of the SamSMU Bioethics Committee meeting dated 09.10.2019.	***Этическая экспертиза.*** Протокол №202 заседания комитета по биоэтике при СамГМУ от 09.10.2019.
Study funding. The study was the authors' initiative without external funding.	***Источник финансирования.*** Работа выполнена по инициативе авторов без привлечения финансирования.
Conflict of Interest. The authors declare that there are no obvious or potential conflicts of interest associated with the content of this article.	***Конфликт интересов.*** Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с содержанием настоящей статьи.
Contribution of individual authors. I.E. Poverenova – developed the study idea. A.S. Tkachenko – developed the study idea, wrote the first draft of the manuscript. A.V. Zakharov – provided data analysis. I.V. Shirolapov, T.V. Romanova – wrote the first draft of the manuscript. S.A. Ananyeva, M.S. Sergeeva – provided detailed manuscript editing and revision. N.P. Romanchuk – wrote the first draft of the manuscript, provided data analysis. A. Khan – visualized the study results and conclusions. All authors gave their final approval of the manuscript for submission, and agreed to be accountable for all aspects of the work, implying proper study and resolution of issues related to the accuracy or integrity of any part of the work.	***Участие авторов.*** И.Е. Повереннова – идея статьи. А.С. Ткаченко – идея статьи, написание текста. А.В. Захаров – анализ данных. И.В. Широлапов, Т.В. Романова – написание текста статьи. С.А. Ананьева, М.С. Сергеева – редактирование и корректировка ошибок. Н.П. Романчук – написание текста статьи, анализ данных. А. Хан – презентация результатов и выводов. Все авторы одобрили финальную версию статьи перед публикацией, выразили согласие нести ответственность за все аспекты работы, подразумевающую надлежащее изучение и решение вопросов, связанных с точностью или добросовестностью любой части работы.

REFERENCES / ЛИТЕРАТУРА

1. Gusev EI, Skvortsova VI, Stakhovskaya LV. The problem of stroke in the Russian Federation: time for active joint actions. *S.S. Korsakov Journal of Neurology and Psychiatry.* 2007;107(8):4-10. (In Russ.). [Гусев Е.И., Скворцова В.И., Стаховская Л.В. Проблема инсульта в Российской Федерации: время активных совместных действий. *Журнал неврологии и психиатрии имени С. С. Корсакова.* 2007;107(8):4-10].
2. Adams HP Jr, del Zoppo G, Alberts MJ, et al. Guidelines for the early management of adults with ischemic stroke: a guideline from the American Heart Association/ American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists. *Circulation.* 2007;115(20):e478-534. https://doi.org/10.1161/CIRCULATIONAHA.107.181486
3. Kopczak A, Schindler A, Sepp D, et al. Complicated Carotid Artery Plaques and Risk of Recurrent Ischemic Stroke or TIA. *J Am Coll Cardiol.* 2022;79(22):2189-2199. https://doi.org/10.1016/j.jacc.2022.03.376
4. Suslina ZA, Varakin YuYa. *Clinical guidelines for early diagnosis, treatment and prevention of vascular diseases of the brain.* M., 2017. (In Russ.). [Суслина З.А., Варакин Ю.Я. *Клиническое руководство по ранней диагностике, лечению и профилактике сосудистых заболеваний головного мозга.* М., 2017].
5. Van Dam-Nolen DHK, Truijman MTB, van der Kolk AG, et al. Carotid Plaque Characteristics Predict Recurrent Ischemic Stroke and TIA: The PARISK (Plaque At RISK) Study. *JACC Cardiovasc Imaging.* 2022;15(10):1715-1726. https://doi.org/10.1016/j.jcmg.2022.04.003
6. Fassbender K, Lesmeister M, Merzou F. Prehospital stroke management and mobile stroke units. *Curr Opin Neurol.* 2023;36(2):140-146. https://doi.org/10.1097/WCO.0000000000001150
7. Kandyba DV. Stroke. *Russian Family Doctor.* 2016;20(3):5-15. (In Russ.). [Кандыба Д.В. Инсульт. *Российский семейный врач.* 2016;20(3):5-15]. https://doi.org/10.17816/RFD201635-15
8. Skvortsova VI, Shamalov NA. Modern approaches to the management of patients with stenosis of the carotid arteries. *Consilium medicum.* 2009;8:11-14. (In Russ.). [Скворцова В.И., Шамалов Н.А. Современные подходы к ведению больных со стенозами сонных артерий. *Consilium medicum.* 2009;8:11-14].
9. Suslina ZA, Piradov MA, Domashenko MA. Stroke: the review of the problem (15 years after). *S.S. Korsakov Journal of Neurology and Psychiatry.* 2014;114(11):5-13. (In Russ.). [Суслина З.А., Пирадов М.А., Домашенко М.А. Инсульт: оценка проблемы (15 лет спустя). *Журнал неврологии и психиатрии им. С.С. Корсакова.* 2014;114(11):5-13].
10. Repina LA, Romanova TV, Poverennova IE, Murtazina AKh. A prognostic model for ischemic stroke outcome. *Science and Innovations in Medicine.* 2023;8(3):181-188. (In Russ.). [Репина Л.А., Романова Т.В., Повереннова И.Е., Муртазина А.Х. Прогностическая модель исхода ишемического инсульта. *Наука и инновации в медицине.* 2023;8(3):181-188]. https://doi.org/10.35693/2500-1388-2023-8-3-181-188
11. Barber PA. Magnetic resonance imaging of ischemia viability thresholds and the neurovascular unit. *Sensors (Basel).* 2013;13(6):6981-7003. https://doi.org/10.3390/s130606981
12. Markus HS. The global burden of stroke. *Int J Stroke.* 2023;18(6):632-633. https://doi.org/10.1177/17474930231181677
13. Levin OS, Bril EV. Primary and secondary prevention and counseling. *Modern therapy in psychiatry and neurology.* 2016;1:4-7. (In Russ.). [Левин О.С., Бриль Е.В. Первичная и вторичная профилактика и консультирование. *Современная терапия в психиатрии и неврологии.* 2016;1:4-7].
14. Chang RW, Tucker LY, Rothenberg KA, et al. Incidence of Ischemic Stroke in Patients With Asymptomatic Severe Carotid Stenosis Without Surgical Intervention. *JAMA.* 2022;327(20):1974-1982. https://doi.org/10.1001/jama.2022.4835
15. Micheel A, Konietschke F, Hinterseher I, et al. Perioperative risk prediction using the POSSUM and V-POSSUM models in symptomatic carotid stenosis. *Vasa.* 2022;51(3):150-157. https://doi.org/10.1024/0301-1526/a000997
16. Lelyuk VG, Lelyuk SE. Ultrasound angiology. M., 2007:179-210. (In Russ.). [Лелюк В.Г., Лелюк С.Э. *Ультразвуковая ангиология.* М., 2007:179-210].
17. Medvedkova EY, Berdalin AB, Orlova EV, Lelyuk VG. Microembolic Signals in Arteries of the Base of the Brain after Ischemic Stroke. *Bull Exp Biol Med.* 2022;173(2):193-198. https://doi.org/10.1007/s10517-022-05517-z
18. Pokrovsky AV, Beloyartsev DF, Timina IE, et al. Clinical manifestations and diagnosis of pathological deformation of the internal carotid artery. *Angiology and vascular surgery.* 2011;17(3):7-18. (In Russ.). [Покровский А.В., Белоярцев Д.Ф., Тимина И.Е., и др. Клинические проявления и диагностика патологической

деформации внутренней сонной артерии. *Ангиология и сосудистая хирургия*. 2011;17(3):7-18].

19. Yaghi S, Albin C, Chaturvedi S, Savitz SI. Roundtable of Academia and Industry for Stroke Prevention: Prevention and Treatment of Large-Vessel Disease. *Stroke*. 2024;55(1):226-235. https://doi.org/10.1161/STROKEAHA.123.043910

20. Lineback CM, Stamm B, Sorond F, Caprio FZ. Carotid disease, cognition, and aging: time to redefine asymptomatic disease? *Geroscience*. 2023;45(2):719-725. https://doi.org/10.1007/s11357-022-00688-z

21. Messas E, Goudot G, Halliday A, et al. Management of carotid stenosis for primary and secondary prevention of stroke: state-of-the-art 2020: a critical review. *Eur Heart J Suppl*. 2020;22(Suppl M):M35-M42. https://doi.org/10.1093/eurheartj/suaa162

22. Abbott AL. Extra-Cranial Carotid Artery Stenosis: An Objective Analysis of the Available Evidence. *Front Neurol*. 2022;13:739999. https://doi.org/10.3389/fneur.2022.739999

23. Warlow C, Sudlow C, Dennis M, Wardlaw J, Sandercock P. Stroke. *Lancet*. 2003;362(9391):1211-1224. https://doi.org/10.1016/S0140-6736(03)14544-8

24. Puig N, Solé A, Aguilera-Simon A, et al. Novel Therapeutic Approaches to Prevent Atherothrombotic Ischemic Stroke in Patients with Carotid Atherosclerosis. *Int J Mol Sci*. 2023;24(18):14325. https://doi.org/10.3390/ijms241814325

25. Pospelova ML, Zaitsev DE, Lepekhina AS, et al. Asymptomatic carotid stenosis. Problem status and prospective directions for ischemic stroke prediction. *Medical News of North Caucasus*. 2021;16(3):332-338. (In Russ.). [Поспелова М.Л., Зайцев Д.Е., Лепехина А.С., и др. Асимптомные каротидные стенозы. Состояние проблемы и перспективные направления прогнозирования ишемического инсульта. *Медицинский вестник Северного Кавказа*. 2021;16(3):332-338]. https://doi.org/10.14300/mnnc.2021.16080

26. Pyatin VF, Shirolapov IV, Nikitim OL. Vibrational physical exercises as the rehabilitation in gerontology. *Advances in Gerontology*. 2009;22(2):337-342. (In Russ.). [Пятин В.Ф., Широлапов И.В., Никитин О.Л. Реабилитационные возможности вибрационной физической нагрузки в геронтологии. *Успехи геронтологии*. 2009;22(2):337-342].

27. Zakharov AV, Bulanov VA, Khivintseva EV, et al. Stroke Affected Lower Limbs Rehabilitation Combining Virtual Reality With Tactile Feedback. *Front Robot AI*. 2020;7:81. https://doi.org/10.3389/frobt.2020.00081

28. Alawieh A, Zhao J, Feng W. Factors affecting post-stroke motor recovery: Implications on neurotherapy after brain injury. *Behav Brain Res*. 2018;340:94-101. https://doi.org/10.1016/j.bbr.2016.08.029

29. Malik AN, Tariq H, Afridi A, Rathore FA. Technological advancements in stroke rehabilitation. *J Pak Med Assoc*. 2022;72(8):1672-1674. https://doi.org/10.47391/JPMA.22-90

30. Pyatin VF, Kolsanov AV, Shirolapov IV. Recent Medical Techniques for Peripheral Nerve Repair: Clinico-Physiological Advantages of Artificial Nerve Guidance Conduits. *Advances in Gerontology*. 2017;7(2):148-154. https://doi.org/10.1134/S2079057017020126

31. Arasu R, Arasu A, Muller J. Carotid artery stenosis: An approach to its diagnosis and management. *Aust J Gen Pract*. 2021;50(11):821-825. https://doi.org/10.31128/AJGP-10-20-5664

32. Volkers EJ, Algra A, Kappelle LJ, et al. Prediction Models for Clinical Outcome After a Carotid Revascularization Procedure. *Stroke*. 2018;49(8):1880-1885. https://doi.org/10.1161/STROKEAHA.117.020486

33. Mohd AB, Alabdallat Y, Mohd OB, et al. Medical and Surgical Management of Symptomatic and Asymptomatic Carotid Artery Stenosis: A Comprehensive Literature Review. *Cureus*. 2023;15(8):e43263. https://doi.org/10.7759/cureus.43263

34. Rosário M, Fonseca AC. Update on Biomarkers Associated with Large-Artery Atherosclerosis Stroke. *Biomolecules*. 2023;13(8):1251. https://doi.org/10.3390/biom13081251

35. Piegza M, Więckiewicz G, Wierzba D, Piegza J. Cognitive Functions in Patients after Carotid Artery Revascularization-A Narrative Review. *Brain Sci*. 2021;11(10):1307. https://doi.org/10.3390/brainsci11101307

36. Howard DPJ, Gaziano L, Rothwell PM. Risk of stroke in relation to degree of asymptomatic carotid stenosis: a population-based cohort study, systematic review, and meta-analysis. *Lancet Neurol*. 2021;20(3):193-202. https://doi.org/10.1016/S1474-4422(20)30484-1

37. Nies KPH, Smits LJM, Kassem M, et al. Emerging Role of Carotid MRI for Personalized Ischemic Stroke Risk Prediction in Patients With Carotid Artery Stenosis. *Front Neurol*. 2021;12:718438. https://doi.org/10.3389/fneur.2021.718438

38. Bir SC, Kelley RE. Carotid atherosclerotic disease: A systematic review of pathogenesis and management. *Brain Circ*. 2022;8(3):127-136. https://doi.org/10.4103/bc.bc_36_22