

# PREDICTORS OF STROKE DEVELOPMENT AFTER CAROTID REVASCLARIZATION. REVIEW

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## Abstract

Stroke is one of the leading causes of death and disability. According to the WHO, mortality due to stroke and other cerebrovascular diseases ranks second after cardiovascular disease. Timely revascularization of the carotid arteries has been shown to be effective in reducing the risk of cerebrovascular accident in patients with symptomatic carotid stenosis of atherosclerotic genesis. However, despite the high efficiency, there are risks of ischemic stroke in the postoperative and long-term period. This review presents statistical data on recurrent strokes and predictors of stroke development after carotid endarterectomy and carotid artery stenting.

Ұйқы артериясын ревазуларизациялаудан кейін инсульт дамуының предикторлары. Әдебиет шолуы.

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## Аңдатпа

Инсульт – өлім мен мүгедектіктің негізгі себептерінің бірі. ДДҰ мәліметтері бойынша, инсульт пен цереброваскулярлық басқа аурулардан болатын өлім-жітім жүрек-қан тамырлары ауруларынан кейін екінші орында. Каротид артерияларының уақытылы ревазуларизациясы атеросклеротикалық генездің каротидті симптоматикалық стенозы бар емделушілерде цереброваскулярлық апат қаупін төмендетуде тиімді екені дәлелденді. Алайда, жоғары тиімділікке қарамастан, операциядан кейінгі және ұзақ мерзімді кезеңде ишемиялық инсульт қаупі бар. Бұл шолу каротидтық эндартерэктомия мен ұйқы артериясын стенттеуден кейінгі қайталанатын инсульт пен инсульттің дамуының болжаушылары туралы статистикалық деректерді ұсынады.

Предикторы развития инсульта после ревазуларизации сонных артерий. Обзор литературы.

Таджибаев Т.К., Маткеримов А.Ж., Демеуов Т.Н., Тергеусизов А.С., Баубеков А.А., Жакубаев М.А., Ханчи М.

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## Аннотация

Инсульт является одной из лидирующих причин смертности и инвалидности. По данным ВОЗ, смертность по причине инсульта и других цереброваскулярных заболеваний занимает 2 место после сердечно-сосудистой патологии. Своевременная ревазуларизация сонных артерий доказала свою эффективность в снижении риска возникновения нарушения мозгового кровообращения у пациентов с симптомными стенозами сонных артерий атеросклеротического генеза. Однако, несмотря на высокую эффективность, существуют риски развития ишемического инсульта в послеоперационном и отдаленном периоде. В данном обзоре представлены статистические данные повторных инсультов и предикторов развития инсульта после каротидной эндартерэктомии и стентирования сонных артерий.

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**Conflict of interest**  
The authors declare that they have no conflicts of interest

## Keywords

Ischemic stroke, stroke predictors, carotid endarterectomy, carotid artery stenting, restenosis

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## Конфликт интересов

Авторы заявляют об отсутствии конфликта интересов

## Ключевые слова

Ишемический инсульт, предикторы инсульта, каротидная эндартерэктомия, стентирование сонных артерий, рестеноз

## Introduction

Stroke is the result of deterioration in the blood supply to the brain. This condition occurs when there is a violation of the patency or integrity of the arteries that feed the brain (internal carotid and vertebral arteries). In other words, a stroke is an acute violation of cerebral circulation, accompanied by a sudden dysfunction of the brain [1]. This is always a complication of acute or chronic diseases. Most of all, the vessels of the brain suffer from atherosclerosis, arterial hypertension, and diabetes mellitus, especially when they are combined. Therefore, it is these extremely common diseases that are most often complicated by stroke. It turns out that our brain is so sensitive to the insufficient blood supply that areas deprived of a normal blood supply die within a few minutes [1].

Atherosclerosis is an inflammatory process that affects medium and large vessels in the circulatory system [2,3]. Early atherosclerotic changes develop already in childhood and adolescence as a result of exposure to several risk factors [4,5]. These include smoking, physical inactivity, unhealthy diet, harmful use of alcohol, hypertension, diabetes, elevated blood lipids, obesity, poverty and low educational status, advanced age, male gender, genetic predisposition, and psychological factors.

Carotid stenosis is a narrowing of the lumen of the carotid artery. The most common cause of narrowing is atherosclerotic plaque. Unique hemodynamics in carotid artery bifurcation predisposes this area to atherosclerosis [6]. Most patients have light to medium plaques, while some develop full stenosis up to complete closure (occlusion) of the arterial lumen. A small percentage of plaque may rupture and embolize, occluding intracranial arteries (causing transient ischemic attack or stroke) or occluding retinal arteries (for causing amaurosis fugax or retinal stroke).

Often, carotid stenosis is detected when there are significant neurological symptoms, or a transient ischemic attack (TIA) or ischemic stroke (symptomatic stenosis) develops, creating a high risk of death.

In most cases, carotid stenosis occurs when an ischemic stroke or TIA has occurred. Moreover, such patients have a high risk of recurrent strokes. When assessing the risk of recurrent stroke during the year in these patients, it was found that the presence of atherosclerosis of the carotid arteries increases the risk of stroke by 2 times, all other things being equal (blood pressure, high grade of LDL, the presence of diabetes, etc.).

## Statistics on the development of recurrent stroke

A meta-analysis of 13 studies obtained from different stroke registries found a cumulative risk of stroke recurrence of 3.1% (OR 95% CI, 1.7-4.4%)

within 30 days, 11.1% (OR 95% CI, 9.0-13.3%) within 1 year, 26.4% (OR 95% CI, 20.1-32.8%) after 5 years and 39.2% OR (95% CI, 27, 2-51.2%) within 10 years [7].

In North Dublin, a study by Callaly et al. the cumulative rate of stroke recurrence for 2 years was 10.8%, and the mortality rate was 38.6% [8]. Also, according to the MONICA stroke registry in northern Sweden, out of 6,700 patients with ischemic or hemorrhagic stroke from 1995 to 2008, the cumulative risk of recurrence was 6% within 1 year, 16% within 5 years, and 25% within 10 years [9]. It is worth noting that approximately 62% of all recurrent strokes after hemorrhagic stroke were ischemic.

In the 2016 REGARDS study, approximately 10% of participants with prior stroke experienced a recurrent stroke during a median follow-up of 6-8 years [10].

## Social predictors of stroke

Social predictors, such as income distribution or educational level, indirectly affect the health of the cardiovascular system in particular and the health of a person in general. These determinants determine the set of socio-economic positions in the hierarchy of power, prestige, and access to resources. Several structural mechanisms are responsible for the formation of a particular person's social status, including the public administration system, the education system, labor market structures, and the presence or absence of a mechanism for redistributing income within the social security system. Social stratification forms the individual health status of an individual, as well as cerebrovascular diseases outcomes, are determined by social stratification by influencing the behavioral and metabolic risks of cardiovascular diseases, socio-psychological status, living conditions, and health care system [11,12].

According to a study by Eshak ES et al. adverse working conditions, including job loss and unemployment, were associated with the risk of stroke. The cohort included 21,902 Japanese males and 19,826 females, with a follow-up period of 19 years. Job loss (change in job status within the first 5 years after placement) was associated with a greater than 50% increase in the incidence of stroke and a 2-fold increase in stroke mortality (over the follow-up period) [13].

A meta-analysis by Kivimäki M. et al. results from 24 cohort studies from the United States, Europe, and Australia found a dose-dependent effect on the relationship between working hours (more than 40 hours per week) on increased stroke incidents [14].

The ARIC (Atherosclerosis Risk in Communities) study presented an interesting observation that

people with little social relationships (i.e., fewer family members, friends, and neighbors) had a 44% higher risk of stroke over 18.6 years. even after accounting for demographic and other relevant risk factors [15].

Findings from the MESA trial have documented associations between other psychosocial factors, including depressive symptoms, chronic stress and hostility, and incident, with participants in the highest-rated versus lowest-rated category with a 1.5-2-fold increase in the risk of stroke (median follow-up 8.5 years).

### **Predictors of stroke after carotid endarterectomy (CEA)**

ECST (European Carotid Surgery Trial) reported various features that were associated with an increased risk of perioperative stroke, including (1) female gender (10.4% versus 5.8%,  $p = 0.0001$ ); (2) peripheral arterial disease (12.0% versus 6.1%,  $p = 0.0001$ ); (3) systolic blood pressure (<120 mm Hg 3.4%; 121-159 6.5%; 160-180 7.7%; > 180 mm Hg 13.0%,  $p = 0.04$ ); and (4) the focus of the previous lesion in symptomatic stenosis (retina [3.2%], stroke in the hemisphere [6.3%], TIA in the hemisphere [9.1%],  $p = 0.006$ ) [16].

NASCET also reported clinical / visual features associated with a significant increase in stroke rate after CEA, including (1) events in the hemisphere versus retina (6.3% versus 2.7%; OR 2.3, 95% CI 1.1- 5.0); (2) FEA left or right (6.7% versus 3.0%; OR 2.3, 95% CI 1.4-3.6); (3) contralateral occlusion (9.4% vs. 4.4%; OR 2.2, 95% CI 1.1-4.5); (4) ipsilateral infarction on CT / MR (6.3% versus 3.5%; OR 1.8, 95% CI 1.2e2.8); and (5) irregular (unstable) AS plaque (5.5% versus 3.7%; OR 1.5, 95% CI 1.1e2.3) [17].

A meta-analysis of 170 studies (over 70,000 patients) revealed that contralateral occlusion in patients was associated with a high risk of procedural stroke after CEA, but this does not apply to carotid artery stenting [18].

### **Predictors of stroke after carotid artery stenting**

In the CAVATAS (Carotid and Vertebral Artery Transluminal Angioplasty Study) study, an increase in stenosis length was an independent risk factor for procedural stroke/death. A pooled analysis from EVA-3S, SPACE, and ICSS found that performing CAS in the first 7 days after symptom onset was associated with a threefold increased risk of death/stroke (compared to CEA) (9.4% vs. 2.8%; OR 3.4, OR 95% CI 1.01-11.8 [19] As a result of a special analysis of the data by the ICSS study, it was found that patients with CAS who had an age-related change in the white matter of the brain (ARWMC), assessed as 7 points or more on the preoperative

CT / MRI scans faced an increased risk of perioperative stroke compared with patients whose ARWMC score was <7 (HR 2.76, 95% CI 1.17-6.51,  $p = 0.021$ ). However, for patients receiving CEA, there were no associations between ARWMC scores and perioperative stroke (HR 1.18, 0.4e3.55,  $p = 0.76$ ) [20]. Recently CREST reported that the incidence of postoperative stroke was significantly higher after CAS in patients with lesion length > 13 mm and sequential lesions distant from the main ICA stenosis [21]. In addition to the generally accepted calculation methods for predicting ischemic stroke after cerebral revascularization, there are dissertations and publications of scientific interest in the public domain. So, in the work of Dyuba D.Sh. et al. demonstrated the role of C-reactive protein, homocysteine, and the main indicators of the blood lipid spectrum as markers of stroke severity in patients in the prognosis of management after carotid endarterectomy. The importance of correcting these indicators has been demonstrated [22]. Also, a group of authors led by Barabash L.S. a method was developed for predicting the risk of developing adverse cardiovascular events within a year after carotid endarterectomy in patients with multifocal atherosclerosis, including the identification and scoring of unfavorable risk factors for cardiovascular diseases, characterized in that as unfavorable risk factors for cardiovascular diseases are determined the level of interleukin-12 in the preoperative period, the presence of dyslipidemia in the anamnesis and hemorrhages in the atherosclerotic plaque, as well as the presence of an atherosclerotic plaque in the carotid arteries of more than 2 cm, and if they are present, the following weight coefficients are assigned: 30.3 points at the level of interleukin-12 preoperative period more than 102.15 ng / ml; 24.1 points with a history of dyslipidemia; 23.4 points if the length of the atherosclerotic plaque in the carotid arteries is more than 2 cm; 22.2 points for hemorrhage in an atherosclerotic plaque, and the probable risk (Y) is assessed based on the formula:  $Y = X1 + X2 + X3 + X4$ , where X1 is the weight coefficient of interleukin-12, X2 is the weight coefficient of dyslipidemia, X3 is the weight coefficient the length of the atherosclerotic plaque, X4 is the weight coefficient of the presence of hemorrhage in the atherosclerotic plaque, the prognosis is carried out on the basis of comparing the obtained Y value with the risk scale of the development of an unfavorable prognosis one year after carotid endarterectomy, where 0-20 points is a low risk, 21-40 points is a lower risk average, 41-60 points - average risk, 61-80 points - risk above average, 81-100 points - high risk. The method makes it possible to predict the risk of adverse cardiovascular events in patients

with multifocal atherosclerosis within a year after carotid endarterectomy [23]. Thus, given the high risk of stroke and mortality, especially the first 30 days after undergoing vascular interventions, there is a need to develop methods for predicting and preventing adverse outcomes from the cardiovascular system.

## Conclusion

At the moment, there are generally accepted prognostic criteria for the risk of ischemic stroke

after interventions on the carotid arteries. However, in Kazakhstan, algorithms, approaches and methods of rehabilitation of patients after carotid interventions have not been developed.

Thus, the development of preventive measures not only reduce the risk of restenosis and other undesirable consequences, but also contribute to an increase in economic and social efficiency due to a decrease in the cost of care, social services, an improvement in the quality of life, and a decrease in disability.

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