# IS SCREENING FOR EXTRACRANIAL CAROTID STENOSIS EFFECTIVE IN PREVENTING ISCHEMIC STROKE? LITERATURE REVIEW

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# Abstract

This literature review shows the essence of the problem of extracranial carotid artery stenosis, since this disease is a treatable cause of ischemic stroke and can be reliably detected and assessed by using vascular ultrasound. In Kazakhstan, due to acute disorders of cerebral circulation, 11.1 thousand patients die every year. The reliability of the information in the article was obtained by using the literature data of the last 10 years. The reflection of the criteria for diagnosing stenosis of the extracranial carotid artery, the use of which, in conjunction with standard tests and other sensitive methods, makes it possible to determine the lesion of the extracranial carotid artery at an early stage, as well as a detailed description of diagnostic methods of this complication and evaluation of their effectiveness. Screening for carotid stenosis is important, and whether routine carotid ultrasound is recommended in general population for the prevention of ischemic stroke remains controversial. Screening for carotid stenosis by ultrasound is crucial not only for the daily clinical setting, but also for the management of patients with acute ischemic stroke.

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### Keywords:

Stenosis of the carotid artery, extracranial carotid artery, ischemic stroke, acute disorders of cerebral circulation, diagnosis of stenosis of the extracranial carotid artery.

Үйқы артериясының экстракраниальды стенозы бар науқастарға скрининг жүргізу ишемиялық инсультты алдын алуда тиімді ме? Әдебиет шолуы

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# Тұжырым

Бұл әдебиеттік шолу ұйқы артериясының экстракраниальды стенозы мәселесінің мәнін көрсетеді, өйткені бұл ауру ишемиялық инсульттің емделетін себебі болып табылады және қан тамырларының ультрадыбыстық көмегімен сенімді түрде анықталуы және бағалануы мүмкін. Қазақстанда ми қан айналымының жедел бұзылуынан жылына 11,1 мың науқас қайтыс болады. Бұл мақаладағы ақпараттың сенімділігі соңғы 10 жылдағы әдебиет деректерін пайдаланумен, экстракраниальды ұйқы артериясының стенозын диагностикалау критерийлерін көрсетумен түсіндіріледі, оны стандартты сынақтармен және басқада сезімтал зерттеу әдістерімен қолдану, экстракраниальды ұйқы артериясының зақымдануын ерте кезеңде анықтауға мүмкіндік береді,

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Мүдделер қақтығысы: Авторлар мүдделер қақтығысының жоқтығын мәлімдейді

### Түйінді сөздер:

ұйқы артериясының стенозы, экстракраниалды ұйқы артериясы, ишемиялық инсульт, ми қан айналымының жедел бұзылысы, ұйқы артериясының стенозының диагностикасы.

сондай-ақ осы асқынудың диагностикалық әдістерінің егжей-тегжейлі сипаттамасы және олардың тиімділігін көрсетеді. Ишемиялық инсульттің алдын алу үшін ұйқы артериясының стенозының скринингі жалпы популяцияда ультрадыбыстық зерттеу арқылы жүргізу даулы мәселе болып табылады. Алайда, жүрек қан тамыр ауруларының дамуына қауіп факторлары бар науқастарда бұл диагностикалық шаранын маңыздылығы бұл мақалада дәлелденді.

Эффективно ли проведение скрининга экстракраниальных стенозов сонных артерии для профилактики ишемического инсульта? Обзор литературы

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Конфликт интересов: Авторы заявляют об отсутствии конфликта интересов Садуакас А.Е.<sup>1,2</sup>, Шамшиев А.С.<sup>1</sup>, Куракбаев.Қ.Қ.<sup>2</sup>, Маткеримов А.Ж.<sup>1</sup>, Тергеусизов А.С.<sup>1</sup>, Демеуов Т.Н.<sup>1</sup>, Ханчи М.<sup>1</sup>, Жакубаев М.А.<sup>1</sup>, Баубеков А.А.<sup>3</sup>, Таджибаев Т.К.<sup>3</sup>, Маккамов Р.О.<sup>1</sup>, Еркинбаев Н.Н.<sup>1</sup>

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## Аннотация

Ключевые слова: стеноз сонной артерии, экстракраниальный стеноз, диагностика стеноза сонной артерии, ишемический инсульт, ОНМК. Обзор литературы отражает суть проблемы экстракраниального стеноза сонной артерии (ЭССА), так как данная патология является причиной ишемического инсульта, в свою очередь ЭССА может надежно обнаружен и оценен с помощью УЗДГ брахиоцефальных артерий. В Казахстане по причине острых нарушении мозгового кровообращения (ОНМК), в год умирает 11,1 тыс. пациентов. Достоверность полученных сведений обусловлено использованием в статье литературных данных последних 10 лет, отражением критериев диагностики ЭССА, применение которых в совокупности со стандартными тестами и другими чувствительными методами дают возможность определять поражения на раннем этапе, а так же подробным описанием диагностических методик данного осложнения и оценки их эффективности.

# Introduction

Stroke is a serious disease of global significance with a high degree of disability and high morbidity. The main cause of ischemic stroke is thromboembolism of the internal carotid artery, due to asymptomatic carotid stenosis >50%. When the plaque reaches 50% of the carotid artery lumen, it causes hemodynamically significant carotid stenosis, the treatment and diagnosis of which is currently at a turning point [2]. However, about 15% of strokes are still secondary to carotid stenosis, which can potentially be detected with effective imaging techniques.

According to the World Health Organization (WHO), 15 million people worldwide suffer from a stroke every year. Among those, 5 million die, and another 5 million remain disabled. [3]. At the beginning of the 21st century, the incidence of stroke in Europe ranged from 95 to 290 per 100,000 per year, and onemonth mortality rate ranged from 13 to 35%. [5]. Each year, approximately 795,000 people in the United States suffer from new (610,000 people) or recurrent (185,000 people) stroke. Epidemiological studies

show that 82-92% of strokes in the United States are ischemic [6].

In Kazakhstan, among the diseases of the cardiovascular system, ischemic heart disease is the leader, from which 11.3 thousand people die per year (71.7 per 100 thousand of the population); as well as due to acute disorders of cerebral circulation, 11.1 thousand patients die per year. It is significant that two thirds of deaths from stroke occur in developing countries [7]. According to the medical statistics of the Republic of Kazakhstan, more than 40 thousand Kazakhstanis suffer from stroke every year, of which about 60% become disabled. 5 thousand people die during the first 10 days of the disease. About 70% of stroke patients need outside help. Only about 10% of surviving patients can return to normal life. Diseases of the circulatory system are dangerous with a high level of disability. The incidence of stroke in the most socially active and working age is more than 60%.

According to The Global Burden of Disease Study 2019 (GBD 2019), there were 12.2 million (95% UI 11.0–13.6) cases of stroke, 143 million (133–153) DALYs

due to stroke, and 6 .55 million (6.00–7.02) deaths. Globally, stroke remained the second leading cause of death (11.6% [10.8–12.2] of total deaths) and the third leading cause of death and disability combined (5.7% [5.1–12],2]). 6 2] of the total number of DALYs) in 2019. From 1990 to 2019, the absolute number of strokes increased by 70.0% (67.0–73.0), common strokes increased by 85.0% (83.0–88.0), stroke deaths increased by 43 .0% (31.0–55.0), and DALYs due to stroke increased by 32.0% (22.0–42.0).[8]

It is predicted that the death rate from stroke will reach 7.8 million by 2030 if unified global measures to combat will not be taken [9].

Extracranial carotid stenosis is a treatable cause of ischemic stroke and can be reliably detected and evaluated using vascular ultrasonography. Up to 88% of strokes are ischemic in nature [10]. Extracranial carotid atherosclerosis is the third leading cause of ischemic stroke in the general population and the second most common non-traumatic cause in adults under 45 years of age [11].

According to the Framingham Heart Study and the Cardiovascular Health Study, the prevalence of >50% carotid stenosis is approximately 9% in men and 6-7% in women [12]. More than 5% of people over 65 years of age have extracranial stenosis of the carotid arteries with an increase of 50% or more [13].

Only in the United States of America (USA) the stroke is the third most common cause of death, with atherosclerotic extracranial carotid stenosis accounting for 20–25% of all strokes [14].

Identification of patients with carotid stenosis has the potential to allow early intervention to reduce the risk of stroke in this population. Stroke prevention strategies can be divided into medical and surgical intervention.

In 2014, the NASCET (North American Prevention Task Force) recommended that carotid artery screening should not be routinely performed. There are concerns about the risks of screening, such as investigating false positives and stroke risks associated with angiography, which can be done as a second-line study. [15]

However, the (ECST) European guidelines support targeted screening for individuals at increased risk for carotid stenosis, such as those with carotid murmurs or multiple risk factors for atherosclerosis [16]. If it were possible to identify a group with a higher prevalence of carotid stenosis and therefore a higher risk of stroke, this could lead to greater potential benefits of screening and treatment. Identifying those who should start aggressive drug therapy to prevent the occurrence of other cardiovascular diseases, as well as stroke, will be of the greatest benefit, given that the cost of treatment is estimated to be 8 times higher. [17]

There are no randomized controlled trials investigating the benefits of screening versus no screening in the general population and the impact on rates of stroke and cardiovascular diseases.

On the other hand, the desire to detect mild

carotid stenosis or atherosclerosis increases the target population and allows for earlier intervention, most likely with aggressive medical treatment, to not only prevent stroke but also reduce the risk of cardiovascular disease. In addition, it has been suggested that patients may be motivated to change their lifestyle [18].

Currently, there is no routine screening of the population for carotid stenosis. This is a complex area and needs further prospective studies. However, it has been proven that more attention should be paid to stroke prevention. Focused screening with duplex ultrasound may be appropriate in patients at high risk for atherosclerotic disease. There is also growing evidence that carotid screening can be used in conjunction with traditional risk measures to more accurately predict CVD risk.

Preventive measures for ischemic stroke

Prevention and treatment of cerebral ischemia due to extracranial carotid stenosis is the cornerstone of stroke prevention and is the subject of extensive clinical research, including numerous randomized controlled trials. Thus, timely diagnosis for choosing a method for the treatment of extracranial carotid stenosis is a preventive intervention that prevents the risk of developing primary and recurrent strokes, deaths and disability associated with a stroke.

Duplex ultrasound (DUS) is the main non-invasive screening method for assessing extracranial carotid artery stenosis and is widely used in the clinical practice to select patients for angiography and assess stroke risk stratification [19]. Duplex ultrasound (DUS) is very important in assessing the severity of carotid stenosis. DUS should be assessed using the recommended angulation (sound angle less than or equal to 60 degrees) [20]. This study uses color and spectral Doppler flow assessment, combined with grayscale plaque imaging, to determine the presence and severity of extracranial carotid artery stenosis. Since the University of Washington criteria for carotid duplex were published and widely adopted in the 1980s, there has been an ongoing effort to refine the diagnostic criteria for carotid arteries that continues to the present [21,22,23]. This method was first proposed and then developed in the 1970s at the University of Washington by Dr. D. E. Strandness, Jr., a vascular surgeon who widely introduced vascular ultrasound. His laboratory has established criteria for the interpretation of all duplex scans, including carotid disease, based on Doppler information and B-mode vessel imaging. The parameters used to classify the severity of carotid disease included peak systolic velocity (PSV), degree of spectrum expansion, end diastolic velocity, and overall waveform. These features made it possible to create a classification of carotid bifurcation stenosis, the so-called "Thread Criteria" [24]. These criteria were developed to predict carotid bulb diameter reduction using six categories of stenosis severity (none, 1-15, 16-49, 50-79, 80-99% reduction, and complete occlusion), with high sensitivity and specificity compared to with angiography. The North American Symptomatic Carotid Endarterectomy Study (NASCET), the European Carotid Surgery Study (ECST), and the Asymptomatic Carotid Artery Study (ACAS) were the main studies of symptomatic and asymptomatic carotid endarterectomy patients, respectively [25]. According to the NASCET method, the stenotic lumen is compared with the lumen of the distal internal carotid artery (ICA), so the degree of stenosis is determined in relation to the distal lumen, and according to ECST, the degree of stenosis is determined in relation to the original lumen.

This is a summary of the main steps in NASCET classification:

- 0-40% NASCET low grade stenosis:assessment in B-mode imaging, in the longitudinal and transverse planes, adding information on the percentage of diameter reduction, plaque thickness and length, and residual lumen;
- 50-60% moderate stenosis NASCET: localized velocity increase (PSV <230 cm/s) without collateral flows (this item creates further differentiation from 2003 and 2010 in PSV threshold);

Degree of stenosis consistent with NASCET ≥70%: combined assessment of hemodynamic criteria (PSV >230 cm/s, presence of collateral flows, increased end-diastolic velocity). At the same time, the assessment of the degree of reduction of the post-stenotic course allows us to differentiate 70-, 80-and 90% stenosis. [26,27] If there is any doubt about classification, contrast-enhanced magnetic resonance angiography (MRA) and computed tomography angiography (CTA) can be done. The use of intracranial MRI to predict possible extracranial carotid stenosis is rarely discussed [28].

Carotid intima-media thickness (CIM), as assessed by carotid ultrasonography, is also a widely used surrogate marker for the severity of atherosclerosis. Intima-media thickness complex (IMT) is the distance between the inner surface of the intima and the outer surface of the media. The IMT thickness of the common carotid artery is one of the independent risk factors for the development of transient ischemic attacks and stroke [29].

Ultrasound of the carotid arteries is assigned in the following cases: patients with diseases that are more often associated with stenosis or obstructive lesions of the carotid arteries (cerebrovascular diseases, impaired perfusion in the vertebral and basilar arteries, Takayasu's disease, etc.) or patients with clinical signs indicating such diseases (hemiplegia, arterial murmurs, pulse weakness, etc.) or patients who need to assess the risk of invasive treatment of atherosclerotic lesions of other organs (ischemic heart disease, arteriosclerosis obliterans, aortic aneurysm, etc.) [30]. In addition, this examination can also be appointed for patients with atherosclerosis risk factors (diabetes mellitus, dyslipidemia, arterial hypertension, smoking, obesity, etc.) and in whom the possibility of atherosclerosis progression cannot be ruled out [31].

Screening of patients with asymptomatic and symptomatic carotid stenoses is often diagnosed

by ultrasound [32,33], but there is oversight due to relatively low clinical awareness prior to the onset of ischemic symptoms [34]. However, in the presence of vascular risk factors, screening may be useful in cases where the diagnosis of extracranial carotid stenosis may have therapeutic implications. Patients with known carotid stenosis should be followed up at intervals of 6 to 12 months.

According to LeFevre ML et al., screening for coronary artery stenosis in the general population, even among patients with evidence of atherosclerosis in other vascular beds (i.e., with coronary or peripheral arterial disease), is not indicated and is not considered cost-effective [35]. The rationale against widespread screening for CS is based on the high false negative/positive rate in the general population and the potential harm of unnecessary invasive procedures. But many authors suggest that screening for CS among high-risk individuals will allow timely drug therapy to prevent stroke and cardiovascular events [36].

Non-invasive tests used to diagnose coronary artery stenosis include high-resolution duplex ultrasound, time-of-flight and contrast magnetic resonance angiography (MRI), and computed tomographic angiography (CT). All of them demonstrated sufficient sensitivity and specificity compared to the gold standard catheter digital subtraction angiography (CDSA). In real practice, doppler sonography is often preferred as a screening method due to the fact that it is inexpensive, reliable and readily available [37].

Several professional societies and accreditation institutes, including the Intersociety Accreditation Commission (IAC), the American Institute of Ultrasound (AIUM), the Society for Vascular Ultrasound (SVU), and the American College of Radiology (ACR), have been tasked with standardizing protocols and methods for describing coronary stenosis [38, 39].

Carotid ultrasonography should be used as a tool not only for risk stratification of vascular events, but also for a comprehensive interpretation of atherosclerosis or stroke etiology. [40].

# Conclusions

Screening for carotid stenosis is important, and whether routine carotid ultrasound is recommended in the general population remains controversial. Screening for carotid stenosis by ultrasound is important not only for the daily clinical setting, but also for the management of patients with acute ischemic stroke. In atherothrombotic stroke patients with severe internal carotid stenosis, surgery should be considered, and duplex ultrasound is important in assessing the severity of carotid stenosis. Physicians should be aware of the usefulness of carotid ultrasound in stratifying the risk of cerebral and cardiovascular disease based on various aspects. In addition, visual assessment or dynamic changes with carotid ultrasound can provide different and valuable insights in outpatient settings.

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