**STROKE:** **A COMPREHENSIVE OVERVIEW OF TRENDS, PREVENTION, AND TREATMENT (LITERATURE REVIEW)**

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**ИНСУЛЬТ: ТЕНДЕНЦИЯЛАРҒА, АЛДЫН-АЛУҒА ЖӘНЕ ЕМДЕУГЕ ЖАН-ЖАҚТЫ ШОЛУ (ӘДЕБИЕТТЕРГЕ ШОЛУ)**

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**ИНСУЛЬТ: ВСЕСТОРОННИЙ ОБЗОР ТЕНДЕНЦИЙ, ПРОФИЛАКТИКИ И ЛЕЧЕНИЯ (ОБЗОР ЛИТЕРАТУРЫ)**

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**Конфликт интересов:** Авторы заявляют об отсутствии конфликта интересов

**Abstract**

Stroke, a critical medical emergency commonly referred to as a cerebrovascular accident, arises when the brain's blood supply is disrupted, depriving brain tissue of oxygen and essential nutrients. This interruption can lead to rapid neurological impairments and, if not promptly addressed, permanent brain damage or even death. Stroke is primarily categorized into two types: ischemic, resulting from arterial blockage, and hemorrhagic, caused by a ruptured blood vessel. Conditions such as acute cerebral circulatory disorder, atherosclerosis, and carotid artery stenosis are strongly associated with an increased stroke risk. Understanding these underlying factors is crucial for effective prevention, early detection, and management of stroke.

Globally, stroke ranks as the second leading cause of disability and mortality, disproportionately affecting low- and middle-income countries. Efforts in stroke prevention emphasize the significance of early detection, management, promoting healthy lifestyles, and implementing legislative measures. The healthcare costs associated with stroke are substantial and projected to grow significantly. Socioeconomic factors and adverse working conditions also influence stroke incidence. Advancements in surgical revascularization techniques, such as carotid endarterectomy and stenting, have demonstrated efficacy in reducing stroke risk.

Continuous research and development of optimal treatment strategies and monitoring protocols are essential for improving stroke outcomes and mitigating its global burden.

**Key words:** stroke, acute cerebral circulatory disorder, carotid endarterectomy, carotid artery stenting, atherosclerosis

**Түйіндеме**

Инсульт, әдетте цереброваскулярлық апат деп аталатын шұғыл медициналық көмек, мидың қанмен қамтамасыз етілуі бұзылған кезде пайда болады, бұл ми тінін оттегі мен қажетті қоректік заттардан айырады. Бұл үзіліс тез неврологиялық бұзылуларға, егер жедел емделмесе, мидың тұрақты зақымдалуына немесе тіпті өлімге әкелуі мүмкін. Инсульт, ең алдымен, екі түрге бөлінеді: артериялық бітелу нәтижесінде пайда болатын ишемиялық және қан тамырларының жарылуынан туындаған геморрагиялық. Церебральды қан айналымының жедел бұзылуы, атеросклероз және ұйқы артериясының стенозы сияқты жағдайлар инсульт қаупінің жоғарылауымен қатты байланысты. Осы негізгі факторларды түсіну инсульттің тиімді алдын алу, ерте анықтау және емдеу үшін өте маңызды.

Дүние жүзінде инсульт мүгедектік пен өлім - жітімнің екінші себебі болып табылады, бұл табысы төмен және орташа елдерге пропорционалды емес әсер етеді. Инсульттің алдын алу бойынша күш-жігер ерте анықтаудың, басқарудың, салауатты өмір салтын насихаттаудың және заңнамалық шараларды жүзеге асырудың маңыздылығын көрсетеді. Инсультпен байланысты денсаулық сақтау шығындары айтарлықтай және айтарлықтай өседі деп болжануда. Инсульт жиілігіне әлеуметтік-экономикалық факторлар мен қолайсыз еңбек жағдайлары да әсер етеді. Каротидті эндартерэктомия және стенттеу сияқты хирургиялық реваскуляризация әдістерінің жетістіктері инсульт қаупін азайтудың тиімділігін көрсетті.

Инсульттің нәтижелерін жақсарту және оның жаһандық ауыртпалығын азайту үшін емдеудің оңтайлы стратегиялары мен бақылау хаттамаларын үздіксіз зерттеу және әзірлеу өте маңызды.

**Түйін сөздер:** инсульт, церебральды қан айналымының жедел бұзылуы, каротид эндартерэктомиясы, каротид артериясының стенттелуі, атеросклероз

**Аннотация**

Инсульт, неотложная медицинская помощь, обычно называемая нарушением мозгового кровообращения, возникает, когда нарушается кровоснабжение мозга, что лишает ткани мозга кислорода и необходимых питательных веществ. Это нарушение может привести к быстрым неврологическим нарушениям и, если своевременно не принять меры, к необратимому повреждению мозга или даже к смерти. Инсульт в основном подразделяется на два типа: ишемический, возникающий в результате закупорки артерий, и геморрагический, вызванный разрывом кровеносного сосуда. Такие состояния, как острое нарушение мозгового кровообращения, атеросклероз и стеноз сонной артерии, тесно связаны с повышенным риском инсульта. Понимание этих основополагающих факторов имеет решающее значение для эффективной профилактики, раннего выявления и лечения инсульта.

Во всем мире инсульт занимает второе место среди основных причин инвалидности и смертности, непропорционально сильно затрагивая страны с низким и средним уровнем дохода. Усилия по профилактике инсульта подчеркивают важность раннего выявления, ведения пациентов с инсультом, пропаганды здорового образа жизни и принятия законодательных мер. Расходы на здравоохранение, связанные с инсультом, значительны и, по прогнозам, значительно возрастут. Социально-экономические факторы и неблагоприятные условия труда также влияют на частоту возникновения инсульта. Достижения в области хирургических методов реваскуляризации, таких как каротидная эндартерэктомия и стентирование, продемонстрировали эффективность в снижении риска инсульта.

Постоянные исследования и разработка оптимальных стратегий лечения и протоколов мониторинга необходимы для улучшения исходов инсульта и снижения его глобального бремени.

**Ключевые слова:** инсульт, острое нарушение мозгового кровообращения, каротидная эндартерэктомия, стентирование сонной артерии, атеросклероз.

**Introduction**

Stroke, a medical emergency commonly referred to as a cerebrovascular accident, occurs when the brain's blood supply is interrupted or significantly diminished, depriving brain tissue of oxygen and essential nutrients. This disruption can precipitate the rapid onset of neurological impairments and, without timely intervention, may culminate in permanent brain damage or death.1 Stroke can be categorized into two principal types: ischemic, stemming from a blockage in an artery supplying blood to the brain, and hemorrhagic, resulting from a rupture in a cerebral blood vessel.

Several conditions are associated with stroke and increase the risk of its occurrence. Acute cerebral circulatory disorder is a sudden impairment of blood flow to the brain, often leading to transient ischemic attacks or more severe strokes. Atherosclerosis, the accumulation of fatty deposits within arterial walls, narrows and hardens the arteries, significantly elevating the risk of ischemic stroke.2,3 Carotid artery stenosis, the narrowing of the carotid arteries supplying the brain, frequently stems from atherosclerosis and poses a critical stroke risk by potentially reducing blood flow or causing embolism formation.4 Comprehending these conditions is vital for the prevention, early identification, and management of stroke.

Stroke ranks as the second most prevalent cause of disability and mortality globally, with the greatest burden of the condition concentrated in low- and middle-income nations.5 The 2016 GBD study used statistical models to report incidence, prevalence, mortality, and cause-specific mortality for 315 conditions across 195 countries. Globally, cerebrovascular disease affected 80.1 million people, with 67.6 million having ischemic stroke and 15.3 million having hemorrhagic stroke. From 1990 to 2016, ischemic stroke prevalence increased by 2.7%, while hemorrhagic stroke decreased by 6.8%. However, the more recent decline from 2006 to 2016 was only 1.7%. The highest cerebrovascular disease rates were in Eastern Europe, Russia, and East Asia, for both ischemic and hemorrhagic stroke (Figure 1, Figure 2).6

**Figure 1.** Age-standardized prevalence rates of cerebrovascular disease worldwide for both sexes per 100,000 people



Source: (Global Burden of Disease Study 2016. Global Burden of Disease Study 2016 (GBD 2016) results. Seattle, WA: Institute for Health Metrics andEvaluation (IHME), University of Washington; 2016.)

**Figure 2.** Age-standardized prevalence rates of ischemic stroke worldwide for both sexes per 100,000 people



Source: (Global Burden of Disease Study 2016. Global Burden of Disease Study 2016 (GBD 2016) results. Seattle, WA: Institute for Health Metrics andEvaluation (IHME), University of Washington; 2016.)

In 2010, there were an estimated 11.6 million ischaemic stroke incidents and 5.3 million haemorrhagic stroke incidents, of which 63% of ischaemic strokes and 80% of haemorrhagic strokes occurred in middle-income countries.7 Between 1990 and 2010, the incidence of ischaemic stroke showed a 13% decrease (RR 95% CI 6-18%) in high-income country settings. However, no significant improvements were observed in low- or middle-income nations. This may be attributed not only to the development and implementation of the latest clinical guidelines for diagnosing, treating, and preventing narrowing of the cerebral arteries, but also to the introduction of modern treatment approaches like carotid artery stenting.

In 2016, the global death rate from cerebrovascular disease was 5.5 million. The absolute number of cerebrovascular deaths worldwide increased by 28.2% from 1990 to 2016, while age-standardised mortality decreased by 36.2%. From 2006 to 2016, the absolute number of cerebrovascular deaths worldwide increased by 5.1%, but the age-standardised mortality rate decreased by 21.0% over the 10-year period. Globally, a total of 2.7 million people died from ischaemic stroke and 2.8 million from haemorrhagic stroke.6

Eastern Europe, Eastern, South-Eastern and Central Asia and sub-Saharan Africa had the highest CVD mortality rates. Mortality from haemorrhagic stroke was highest in Eastern and South-Eastern Asia, the Pacific Islands and parts of sub-Saharan Africa. Countries in Eastern Europe and Central Asia have one of the highest mortality rates associated with ischaemic stroke, reaching up to 114 per 100000 people (Figure 3).

In 2010, the median age of death from stroke in high-income countries was 80.4 years compared with 72.1 years in low- and middle-income countries.8 From 1990 to 2010, ischaemic stroke mortality decreased by 37% in high-income countries and 14% in low- and middle-income countries.7

**Figure 3.** Age-standardized mortality rates from ischemic stroke worldwide for both sexes per 100,000 people.



Source: (Global Burden of Disease Study 2016. Global Burden of Disease Study 2016 (GBD 2016) results. Seattle, WA: Institute for Health Metrics andEvaluation (IHME), University of Washington; 2016.)

Despite the observed downward trend in mortality from cerebrovascular diseases in the Russian Federation, these conditions remain among the leading causes of death. The incidence of cerebrovascular disease (CVD) in the country was 6,058.9 cases per 100,000 adults in 2010, with 734.2 new diagnoses. Cerebral infarctions accounted for 198 cases per 100,000 adults that year. Cerebral infarction comprises an average of 27% of primary morbidity and is a major contributor to disability. The number of surgical interventions on the arteries supplying blood to the brain has steadily increased, reaching nearly 18,000 in the Russian Federation by 2010. There has been a convergence of perspectives among neurologists, cardiovascular surgeons, and specialists in X-ray endovascular diagnostic and treatment methods for this patient population. Consequently, determining the optimal treatment approach for both symptomatic and asymptomatic patients is of paramount importance. The impact of novel pharmacotherapies and endovascular procedures necessitates a careful re-evaluation of existing clinical approaches to develop informed recommendations for institutions and practitioners managing extracranial arterial diseases.9

Stroke remains a paramount medical and societal issue globally, including in Kazakhstan, owing to its high rates of incidence, mortality, and disability.10]

In Kazakhstan, the incidence of stroke is high, at 370 cases per 100 000 population. Mortality and disability rates are also quite high. Mortality is 108 cases per 100 000 population, which is 26 % in the structure of total mortality. Stroke is the leading cause of disability, the frequency of which is 104.6 per 100 000 population.11 A study from Kazakhstan also indicates a rise in all cause mortality rate almost 2 times in the stroke population.12

The allocation and appropriate distribution of resources dedicated to combating ischemic stroke is of paramount importance. This encompasses not only the identification, diagnosis, and treatment of the condition, but also the promotion and facilitation of healthy lifestyles and choices, as well as the implementation of pertinent legislation and policies. Crucially, preventing and detecting these diseases at the earliest possible stage can help minimize human suffering, while ensuring the provision of comprehensive, high-quality healthcare throughout the lifespan, including empowerment, rehabilitation, and palliative care. According to 2013 data from the World Health Organization, healthcare expenditures are reported as a percentage of gross domestic product (Figure 4).

**Figure 4.** World map showing the amount of healthcare spending as a percentage of gross domestic product.



Source:World atlas of cardiovascular disease prevention and control. Edited by: Mendis S, Puska P, Norrving B. World Health Organization, Geneva, 2013.

According to estimates from the National Heart, Lung, and Blood Institute (NHLBI) and the Medical Expenditure Panel Survey (MEPS) in the United States between 2014 and 2015, the average annual cost of stroke was $45.5 billion. The estimated direct medical cost of stroke was $28.0 billion, encompassing expenses for hospital outpatient or inpatient consultations, inpatient stays, doctor visits, medication prescriptions, and home care.13 The average direct care costs per patient in the United States are estimated at $7,902.13 Moreover, the total number of direct medical expenses aimed at addressing stroke is projected to double from $36.7 billion to $94.3 billion between 2015 and 2035, with a significant portion of the increase directed towards care for elderly patients aged 80 years and above.14,15

The social determinants of health, such as income and education, play a crucial role in shaping cardiovascular health and human wellbeing. These define a hierarchy of socioeconomic positions with varying power, prestige, and resource access. Structural mechanisms, including public administration, education, labor markets, and social security, shape individual social position. This stratification fundamentally impacts health and cardiovascular disease by influencing behavioral, metabolic, socio-psychological, and healthcare factors.16,17

Job loss and unemployment were associated with increased stroke risk and mortality, according to Eshak et al.18 A meta-analysis by Kivimäki et al revealed a dose-dependent relationship between work duration and stroke incidents.19

Studies have found that fewer social relationships, depressive symptoms, chronic stress, and hostility were associated with 44-100% higher stroke risk.20

A meta-analysis of 13 studies from different stroke registries found a pooled risk of stroke recurrence of 3.1% (95% CI, 1.7-4.4%) at 30 days, 11.1% (95% CI, 9.0-13.3%) at 1 year, 26.4% (95% CI, 20.1-32.8%) after 5 years, and 39.2% (95% CI, 27.2-51.2%) at 10 years.21 In the North Dublin study by Callaly et al, the cumulative rate of stroke recurrence at 2 years was 10.8% and mortality was 38.6%.22 Also, according to the MONICA stroke register in northern Sweden, of 6700 patients with ischaemic or haemorrhagic stroke from 1995 to 2008, the cumulative risk of recurrence was 6% at 1 year, 16% at 5 years, and 25% at 10 years.23 It is worth noting that approximately 62% of all recurrent strokes after haemorrhagic stroke were ischaemic.

In the 2016 REGARDS study, among participants with prior stroke, approximately 10% had a recurrent stroke during a mean follow-up period of 6.8 years.24

Substantial work was done in the 2016 GBD study to calculate 1-year and 5-year recurrent stroke mortality rates with age, sex, and race distributions (Figure 5).

**Figure 5.** Probability of stroke mortality within 1-year and 5-year



Source: Pooled data from the Framingham Heart Study, Atherosclerosis Risk in Communities Study, Cardiovascular Health Study, Multi-Ethnic Study of Atherosclerosis, Coronary Artery Risk Development in Young Adults, and Jackson Heart Study of the National Heart, Lung, and Blood Institute 2017.25

**Materials and methods**

A comprehensive literature search was conducted using PubMed, Google Scholar, and Cochrane Library databases. Keywords included "stroke epidemiology", "cerebrovascular disease", "cardiovascular events", "carotid artery stenosis" and "carotid endarcterectomy". Articles published between 2000 and 2024 were included. Both clinical and experimental studies were reviewed to provide a holistic understanding of stroke prevention and treatment methods.

**Results and discussion**

**Etiopathogenetic aspects of the development of ischemic stroke**

One of the key factors in the development of cerebral stroke is disruption in the regulation of cerebrovascular reactivity, characterized by an imbalance between vasoconstriction and vasodilation.26 Accordingly, the assessment of cerebrovascular reactivity to carbon dioxide (CO2) can be used to predict the risk of stroke.27 This parameter, known as cerebrovascular reactivity to CO2 (CVRCO2), refers to the highly sensitive changes in cerebral blood flow velocity in response to fluctuations in arterial CO2 levels.28

Atherosclerosis is the predominant vascular disorder, characterized by the accumulation of lipid and cholesterol deposits within blood vessels, resulting in arterial occlusion and/or inadequate perfusion to organs and tissues.29 Consequently, atherosclerosis underlies the pathogenesis of various cardiovascular diseases, including myocardial infarction, coronary artery disease, stroke, and peripheral artery disease.30 Despite the availability of therapeutic interventions aimed at reducing blood lipid and cholesterol levels, atherosclerosis remains the leading cause of disability and premature mortality worldwide.31

Recent scientific studies have revealed that the pathogenesis of atherosclerosis is primarily associated with inflammatory reactions involving both innate and adaptive immune cells.32,33 Inflammation has been shown to play a pivotal role throughout the progression of atherosclerosis.34 Early in the disease process, trapped oxidized low-density lipoprotein in the vessel wall leads to endothelial dysfunction and increased expression of adhesion molecules, promoting the recruitment and migration of leukocytes into the subendothelial region. Macrophages and dendritic cells engulf lipids, transforming into foam cells, while simultaneously producing various inflammatory cytokines.35 The accumulation of macrophages and lipid droplets within the vascular intima culminates in the formation of early atherosclerotic plaques. Additionally, both macrophages and dendritic cells express toll-like receptors, mediating the activation of antigen-presenting cells and the production of inflammatory cytokines.36 CD4+ T cells also play a significant role in the development of atherosclerosis, secreting inflammatory cytokines such as IFN-γ.37 This cytokine amplifies vascular inflammation by activating antigen-presenting cells, enhancing lipid uptake by macrophages, and increasing the expression of endothelial adhesion molecules, further promoting the recruitment of leukocytes to the site of injury. The ongoing recruitment of leukocytes into atherosclerotic arteries leads to the perpetuation of inflammatory reactions, which in turn exacerbate the progression of this disease.38

**Current trends in the approach to cerebral revascularization**

Prompt surgical revascularization of the brachiocephalic arteries has been demonstrated as an effective intervention for mitigating the risk of cerebrovascular accidents in patients with lesions of the extracranial arteries.39 The primary treatment modalities for managing carotid artery pathology include open surgical procedures such as carotid endarterectomy, as well as carotid artery stenting. Timely surgical treatment of carotid artery disease has been shown to significantly decrease the incidence of acute ischemic cerebrovascular events and also reduce the severity of associated cognitive impairment.40,41

Carotid endarterectomy is a common reconstructive surgical procedure performed on the carotid artery bifurcation. The primary goal is to eliminate stenosis and restore the patency of carotid arteries affected by atherosclerosis. During the procedure, the patient's head is positioned away from the side of the affected carotid artery. The skin and underlying tissues are dissected along the inner edge of the sternocleidomastoid muscle, exposing the common, external, and internal carotid arteries. After administering heparin, the arteries are clamped individually. The anterior wall of the common carotid artery is dissected, and the dissection is extended to the internal carotid artery. Utilizing specialized instruments, the surgeon removes any thrombotic deposits and atherosclerotic plaque from the lumen of the common and internal carotid arteries. The vessel lumen is then irrigated with a saline solution containing heparin. Once the surgeon is satisfied that the necessary manipulations are complete, the incision in the artery is sutured closed.

In 1991, the findings of two major randomized controlled trials were reported to investigate the efficacy of carotid endarterectomy (CEA) in managing carotid artery stenosis among patients with symptomatic disease. CEA has been demonstrated to decrease the risk of subsequent stroke and is now extensively utilized to prevent stroke in individuals with symptomatic carotid stenosis.

In the same year, the first major clinical studies were initiated to investigate the management of asymptomatic carotid artery stenosis. The Study of Asymptomatic Carotid Artery Stenosis-1 (ACST-1) and its parallel North American Asymptomatic Carotid Atherosclerosis Study collectively enrolled over 5,000 patients with carotid stenosis but no history of stroke or transient ischemic attack in the prior 6 months. The primary objective of ACST-1 was to compare the outcomes of immediate surgical intervention versus conservative management. The findings demonstrated that carotid endarterectomy (CEA), when compared to non-operative care, was associated with a significantly lower risk of perioperative stroke or mortality(~ 3% vs. ~ 12%). Moreover, long-term follow-up over 5 years revealed that the risk of stroke was also comparatively reduced in the surgical treatment group(~ 6% vs ~12%).

Carotid artery stenting is an emerging therapeutic approach for managing carotid artery stenosis. This minimally invasive procedure involves accessing the target vessels through remote arterial routes, without the need for direct surgical intervention on the carotid artery itself. Typically, the procedure is initiated by inserting a catheter into the femoral artery and navigating it through the aorta until it reaches the narrowed segment of the carotid artery. A stent is then deployed and expanded within the affected arterial region, using an inflatable balloon mechanism, to restore vascular patency and improve blood flow. Finally, the catheter and balloon are withdrawn, leaving the stent in place to maintain the integrity of the carotid artery.

Compared to carotid endarterectomy (CEA), carotid artery stenting (CAS) is associated with reduced postoperative discomfort, is often performed under local anesthesia, may shorten hospital stay, and may be more acceptable to patients. However, there is significant uncertainty regarding the short-term risks and long-term durability of CAS compared to CEA, even when both procedures are conducted by experienced clinicians. During the stenting procedure, with an "unstable" atherosclerotic plaque, there is a risk of cerebral artery embolism, potentially resulting in partial or complete blockage of blood flow to areas of the brain and causing either a "minor" or "major" stroke. Longer-term, there is also a higher rate of in-stent restenosis with carotid artery stenting compared to endarterectomy, necessitating close imaging surveillance and potential reintervention

According to data from the Agency for Healthcare Research and Quality in the USA, carotid endarterectomy was the predominant intervention for carotid artery stenosis during the period from 1993 to 2014 (Figure 6). However, in more recent years, there has been a noteworthy increase in the utilization of carotid artery stenting as an alternative treatment approach.

**Figure 6.** Quantitative indicator of carotid endarterectomy and carotid stenting (USA, 1993-2014).



**Source:** Nationwide Inpatient Sample, Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality.42

According to estimates from the Healthcare Cost and Utilization Project (HCUP) and the National Heart, Lung, and Blood Institute (NHLBI) registry, 86,000 carotid endarterectomy (CEA) procedures were performed in hospital settings across the United States in 2014. CEA is the most widely utilized surgical intervention for stroke prevention. Between 2004 and 2014, following the introduction of carotid artery stenting (CAS), the number of CEA procedures declined. A comparative analysis using Medicare data revealed that the incidence of in-hospital stroke and mortality were comparable between CEA and CAS.43,44

Recent studies using the NIS (National Inpatient Sample) database have demonstrated significant improvements in periprocedural outcomes associated with carotid artery stenting over the past decade.45 Additionally, in the Medicare population, 30-day readmission rates and long-term adverse clinical outcomes were similar between carotid artery stenting and carotid endarterectomy.46,47

When evaluating the cost-effectiveness of the procedures, the expense of carotid artery stenting was comparable to that of carotid endarterectomy ($15,055 vs. $14,816).48 Additionally, the proportion of patients undergoing carotid endarterectomy within 2 weeks of stroke onset increased from 13% in 2007 to 47% in 2010.49

A meta-analysis of five randomized controlled trials evaluated the effectiveness of modern endovascular therapy for stroke and found compelling evidence supporting thrombectomy initiated within 6 hours, regardless of patient age, NIHSS score, or prior intravenous thrombolysis.50 In the study cohort of 234 eligible patients, 51% were transported for mechanical thrombectomy by ambulance and 49% by helicopter, with 27% ultimately undergoing the procedure. The average actual transfer time was 132 minutes.

Contemporary scientific research emphasizes the importance of early detection of pathological processes in the brain by neurologists, vascular specialists, and other relevant experts. This is crucial, as these early-stage abnormalities can potentially progress to irreversible brain damage if left unaddressed.51,52

Recurrent stenosis following prior carotid endarterectomy or stenting is infrequent (approximately 6% at 2 years).53 When restenosis occurs within the initial 2 years post-procedure, it is typically attributable to neointimal hyperplasia. Conversely, if restenosis manifests after 2 years have elapsed since the initial intervention, the more common underlying etiology is the development of a new atherosclerotic plaque. Additionally, the concept of residual stenosis exists, referring to stenosis detected within 30 days following a carotid intervention.

There is ongoing debate surrounding the optimal treatment strategy for this relatively uncommon condition.53 In numerous nations, pharmacological management is recommended for asymptomatic individuals due to the diminished risk of embolic stroke linked to neointimal hyperplasia. Revascularization procedures are reserved for symptomatic patients. The specific revascularization method employed is not dictated by a standardized protocol, but rather determined at the discretion of the treating physician.

In the United States, the prevailing guidance is to conduct carotid artery stenting for stenosis of ≥70% and ≥50%.54 Patients undergoing this procedure typically receive dual antiplatelet therapy for the initial 1 to 3 months, followed by monotherapy with aspirin for an indeterminate duration.55

Continuous patient monitoring, appropriate postoperative pharmacological management, oversight by a vascular specialist, perioperative nursing support, and control of vascular health using CVDS techniques collectively contribute to enhanced long-term treatment outcomes.56

**Involvement of vertebral arteries in the structure of ischemic stroke and approaches to treatment**

Ischemic stroke is primarily caused by atherosclerotic lesions in the arteries that provide blood supply to the brain, including the internal carotid and vertebral arteries. Despite the availability of treatments aimed at reducing lipid and cholesterol levels in patients, atherosclerosis remains the leading cause of disability and premature mortality globally.57 The vertebral and basilar arteries are responsible for perfusing the brainstem, cerebellum, thalamus, as well as the posterior temporal and occipital lobes in most individuals.58

Recent data indicates that 20-30% of all transient ischemic attacks and ischemic strokes are attributed to lesions in the vertebrobasilar region.59 While the management of carotid artery stenosis has been well-studied, some questions regarding vertebral artery stenosis remain unresolved. The treatment approaches for VA stenosis vary depending on the location of the atherosclerotic plaque, its extent, degree of narrowing, and the volume of damage to the vertebrobasilar area.

Current treatment methods for symptomatic extracranial vertebral artery stenosis require further in-depth study and research.

Surgical treatment of the vertebral and basilar arteries is technically challenging and carries a high risk of strokes, transient ischemic attacks, and perioperative mortality.60,61 Endovascular treatment using percutaneous transluminal balloon angioplasty alone does not yield sufficiently satisfactory results due to elastic recoil of the vessel and a high rate of restenosis, while there is a lack of well-designed randomized studies to evaluate the effectiveness and safety of this approach in both the short and long term.62,63 The use of bare metal stents provides favorable outcomes and low rates of periprocedural complications in the early period, but the results remain disappointing in the mid- and long-term, with a high incidence of restenosis and subsequent stent fractures associated with neointimal hyperplasia.64,65 Studies aimed at assessing the efficacy and safety of coronary drug-eluting stents for the prevention of in-stent restenosis are still ongoing and require additional evidence.66

There is also a conservative treatment method, the so-called “best medical treatment” (BMT) approach, including antithrombotic drugs, statins, treatment of concomitant pathologies and symptomatic treatment.

Proximal vertebral artery stenting demonstrated a high technical success rate of 99%, with a low mortality rate of 0.3% and a perioperative stroke rate of 1.3%. However, the procedure was associated with a restenosis rate of 25%, despite a relatively low recurrent stroke rate of 0.6%. In comparison, stenting and angioplasty of the distal VA were linked to a higher risk of mortality.67

Multiple studies have demonstrated a higher risk of perioperative stroke in patients undergoing intracranial VA interventions compared to extracranial VA interventions.68 However, there is a scarcity of randomized controlled trials evaluating the outcomes of treatment for vertebral artery stenosis (PsA), and the existing trials have insufficient patient numbers to meet the necessary inclusion criteria.

The CAVATAS study involved the randomization of only 16 patients with symptomatic extracranial VA stenoses, comparing the outcomes of percutaneous transluminal balloon angioplasty and best medical treatment.69 Additionally, the Vertebral Artery Stenting Trial (VAST) randomized 115 patients with symptomatic hemodynamically significant VA stenoses, both intra- and extracranial, with 57 patients undergoing stenting and 58 receiving aggressive drug treatment.68 Within the first 30 days, three patients in the stenting group experienced stroke, myocardial infarction, or death, compared to one in the BMT group. Over a 3-year follow-up, 12% of patients with VA stents suffered a stroke, while the rate was 7% in the BMT group.70 The VAST trial was prematurely terminated due to regulatory issues, but recent evidence suggests a high risk associated with intracranial VA stenting. Similar findings were reported in the SAMMPRIS trial, which compared stenting and BMT in 450 patients with symptomatic intracranial artery stenoses, 60 (13%) of whom had vertebral or basilar artery stenoses.71 Notably, basilar artery stenoses were particularly associated with an elevated risk of periprocedural ischemic stroke following stenting (21% versus 7% compared with other intracranial arteries).72

A systematic review conducted by Feng et al. examined the outcomes of 672 patients across four randomized controlled trials and six non-randomized studies between 2007 and 2015. The review compared the results of percutaneous transluminal balloon angioplasty (PTBA) plus best medical treatment (BMT) versus BMT alone. The findings did not reveal a significant advantage of either approach.73 It is noteworthy that this meta-analysis did not include the Vertebral Artery Stenting Trial (VIST), the results of which were presented at the 2016 European Stroke Organization conference.74 The VIST trial randomized 182 patients with symptomatic intra- and extracranial VA stenoses, with the primary objective of comparing BMT with PTBA with or without stenting. The trial was expected to recruit 540 patients, but it was prematurely halted due to slow enrollment and regulatory issues. Of the 91 patients randomized to the stenting group, the procedure was not performed in 30 patients, the primary reason being the finding of less than 50% stenosis on duplex angioscanning examination. The selection of patients before randomization was based on CT angiography or MR angiography. Out of the 61 patients in the stent group, 48 (79%) had extracranial stenosis, and 13 (21%) had intracranial stenosis. The average follow-up period for the study was 3.5 years.75

Ultrasound duplex vascular scanning is considered the gold standard for the primary diagnosis of arterial stenosis. However, as most cases of vertebral artery stenosis are asymptomatic, there is a need to identify biomarkers that can predict the progression of atherosclerotic plaque and the subsequent development of transient ischemic attacks and ischemic strokes. According to existing research, certain cytokines may serve as potential biomarkers for this purpose.76

**Methods of prevention and further management of patients who have undergone cerebral revascularization**

According to various research reports, patients who have undergone carotid artery revascularization without a prior history of stroke or transient ischemic attack (TIA) face an annual stroke risk of approximately 2-3%.77,78 However, if the patient has experienced a previous TIA or stroke, the risk increases significantly, approaching 10% per year.79

There is no clear consensus on the efficacy of monitoring policies in reducing 30-day death and stroke rates following carotid endarterectomy (CEA).80,81

During the perioperative period, the primary objective of monitoring is to maintain adequate cerebral blood flow, particularly when the carotid artery is clamped and during bypass grafting procedures. This can be accomplished through various methods, including transcranial Doppler imaging, performing carotid endarterectomy under locoregional anesthesia, measuring stump pressure, subjectively assessing internal carotid artery backflow after carotid artery clamping, and utilizing near-infrared spectroscopy. Additionally, brain electrical activity is evaluated using somatosensory evoked potentials and electroencephalography.

Quality control methods aim to alter operational strategies for preventing technical errors. These include identifying indirect signs of embolization during carotid artery dissection, diagnosing artery lumen conductivity after blood flow restoration, and diagnosing large intimal valves to assess residual stenosis.82 Evidence indicates that focused monitoring and management of cerebrovascular events may decrease perioperative mortality and stroke rates.83

Postoperative patients may undergo annual follow-up examinations related to their carotid artery revascularization procedures. However, annual surveillance is not universally recommended. The clinical assessment should involve a neurological examination to detect any new stroke-like symptoms. Diagnostic testing should include noninvasive methods, such as duplex ultrasound, to identify potential recurrent stenosis or development of stenosis in the ipsilateral and/or contralateral carotid artery. Additionally, patients receiving pharmacological management should not undergo routine annual revascularization due to the possibility of disease progression and increased stenosis. Combining neurological assessment with duplex ultrasound is a considered appropriate approach.84

Patients should be educated on the importance of actively managing risk factors for atherosclerosis, such as hypertension, hyperlipidemia, and smoking cessation. They should also be advised to maintain lifelong aspirin therapy.85

Substantial evidence indicates that population-level primary prevention interventions as well as individualized healthcare strategies have contributed to declining mortality trends. For instance, over a 10-year period, the World Health Organization's Multinational Monitoring of Morbidity and Mortality from Cardiovascular Diseases and Risk Factors program observed pronounced reductions in coronary heart disease mortality across many of the 38 populations it encompassed.86

**Conclusion**

Stroke persists as a critical global health concern due to its high incidence, significant mortality, and substantial long-term disability. Understanding the diverse risk factors and associated conditions, such as acute cerebrovascular disorders, atherosclerosis, and carotid artery stenosis, is essential for effective prevention and management strategies. Despite advancements in diagnostic techniques, surgical interventions like carotid endarterectomy and stenting, and pharmacological treatments, the burden of stroke continues to challenge healthcare systems globally, especially in low- and middle-income countries.

Ongoing research and innovation are crucial to developing more effective treatment approaches and improving patient outcomes. Efforts to raise public awareness and educate individuals on stroke prevention can significantly reduce the incidence and impact of this condition. By fostering collaboration among healthcare providers, policymakers, and researchers, we can enhance our understanding of stroke and implement strategies that will ultimately decrease its global burden, improve patient quality of life, and reduce healthcare costs.

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