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

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Abstract

A stroke is an emergency medical condition, commonly referred to as a cerebrovascular accident, occurs when the blood supply to the brain is interrupted, depriving brain tissue of oxygen and essential nutrients. This interruption can lead to rapid neurological impairment and, if not treated promptly, 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 lead in cause of disability and mortality, disproportion at early affecting low-and-middle - income countries. Efforts in stroke prevention emphasizes 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.

Introduction

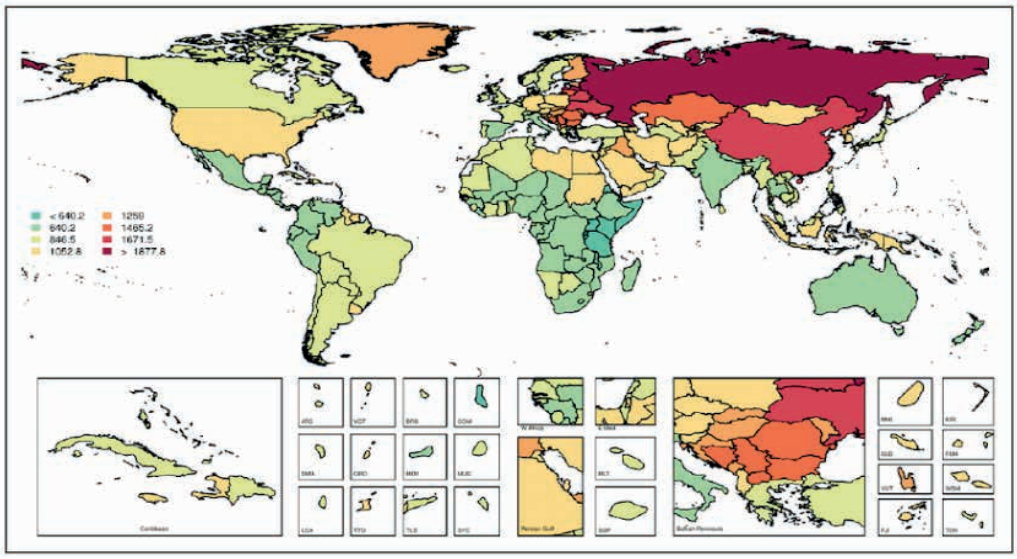
A stroke is an emergency medical condition, commonly referred to as a cerebrovascular accident, occurs when the blood supply to the brain is interrupted, depriving brain tissue of oxygen and essential nutrients. This disruption can precipitate the rapid onset of neurological impairments and, without 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 stroke. Acute ischemic stroke is a sudden reduction in blood flow to the brain, often resulting in transient ischemic attacks or more severe strokes. Athero-

sclerosis, the buildup of fatty deposits in the arterial walls, narrows and hardens the arteries, significantly increasing the risk of ischemic stroke.[2,3] Carotid artery stenosis, the narrowing of the carotid arteries that supply the brain, often results from atherosclerosis and poses a critical stroke risk by potentially reducing blood flow or causing embolism.[4] Understanding these conditions is critical to the prevention, early detection and treatment of stroke.

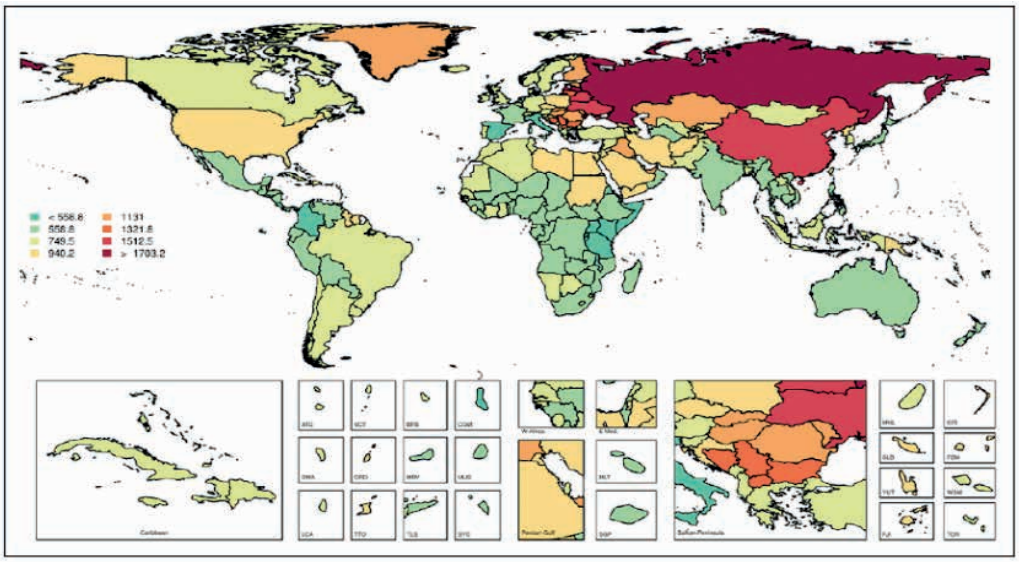
Stroke is the second leading cause of disability and mortality worldwide, with the greatest burden concentrated in low- and middle-income countries.[5] The 2016 GBD study used statistical models to report incidence, prevalence, mortality, and cause-specific mortality for 315 conditions in 195 countries. Globally, cerebrovascular disease affected 80.1 million people, with 67.6 million suffering ischemic stroke and 15.3 million suffering hemorrhagic stroke. From 1990 to 2016, the prevalence of ischemic stroke increased by 2.7%, while the prevalence of hemorrhagic stroke decreased by 6.8%. However, the more recent decrease from 2006 to 2016 was only 1.7%. The highest rates of cerebrovascular disease were found 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 2016, there were 5.5 million deaths from cerebrovascular disease worldwide. From 1990 to 2016, the absolute number of cerebrovascular deaths worldwide increased by 28.2%, while the age-standardized mortality rate decreased by 36.2%. From 2006 to 2016, the absolute number of cerebrovascular deaths worldwide increased by 5.1%, but the age-standardized mortality rate decreased by 21.0% over the 10-year period. Globally, 2.7 million people died from ischemic stroke and 2.8 million from hemorrhagic stroke.[6]

Despite the observed downward trend in cerebrovascular disease mortality in the Russian Federation, these conditions remain among the leading causes of death. In 2018-2023, between 430,000 and 470,000 strokes will be reported in Russia each year, with hospital mortality rates ranging from 17.6% in 2022 to 20.7% in 2020. According to Rosstat, stroke is a leading cause of death in the country, with a mortality rate more than double that of myocardial infarction.[7]

Stroke remains a major medical and societal concern worldwide, including in Kazakhstan, due to its high incidence, mortality and disability rates.[8]

In Kazakhstan, the incidence of cerebrovascular disease increased from 208.1 cases per 100,000 population in 2013 to 433.7 cases in 2020. Despite this increase, the mortality rate from stroke decreased from 71.90 cases per 100,000 population in 2013 to 66.57 cases in 2020.[9] A study from Kazakhstan also shows an almost twofold increase in all-cause mortality in the stroke population.[10]

In the 2016 GBD study, extensive work was done to calculate 1-year and 5-year recurrent stroke mortality rates with age, sex, and race distributions (Figure 3).

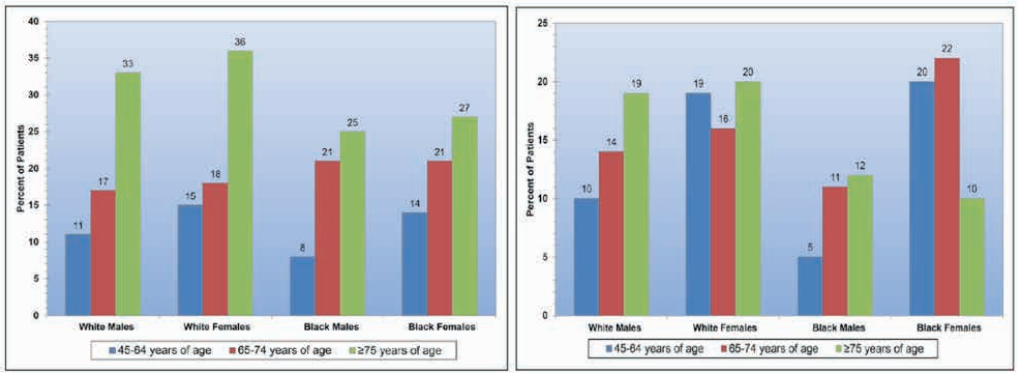


Figure 3.
Probability of stroke mortality within 1-year and 5-year

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.[11]

The aim of this study is to analyze recent advancements in the understanding and management of ischemic stroke, with a focus on the efficacy of various treatment modalities including carotid endarterectomy and carotid artery stenting (CAS). This study seeks to evaluate current trends in stroke prevention, identify gaps in treatment approaches, and assess the impact of emerging techniques on long-term patient outcomes.

Materials and methods

A comprehensive literature search was conducted using PubMed, Google Scholar, and the Cochrane Library databases. Keywords included stroke epidemiology, cerebrovascular disease, cardiovascular events, carotid artery stenosis, and carotid endarterectomy. Articles published between 2014 and 2024 were included. Both clinical and experimental studies were reviewed to provide a holistic understanding of stroke prevention and treatment methods. The review included a variety of article types, including clinical trials, observational studies, systematic reviews, and meta-analyses. Articles were selected

based on their relevance to stroke epidemiology, treatment methods such as carotid endarterectomy and stenting, and advances in prevention strategies. Articles were included if they contributed to the understanding of the effectiveness of different interventions, highlighted recent trends, or addressed gaps in current knowledge.

Etiopathogenetic aspects of the development of ischemic stroke

One of the key factors in the development of cerebral stroke is a disturbance in the regulation of cerebrovascular reactivity, characterized by an imbalance between vasoconstriction and vasodilation.[12] Accordingly, the assessment of cerebrovascular reactivity to carbon dioxide (CO2) can be used to predict the risk of stroke.[13] 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.[14] Atherosclerosis is the predominant vascular disease, characterized by the accumulation of lipid and cholesterol deposits in the vessels, resulting in arterial occlusion and/or inadequate perfusion of organs and tissues.

Atherosclerosis is the predominant vascular disease characterized by the accumulation of lipid and cholesterol deposits within blood vessels, resulting in arterial occlusion and/or inadequate perfusion of organs and tissues.[15] Consequently, atherosclerosis underlies the pathogenesis of several cardiovascular diseases, including myocardial infarction, coronary heart disease, stroke, and peripheral arterial disease.[16] 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.[17]

Recent scientific studies have shown that the pathogenesis of atherosclerosis is primarily associated with inflammatory responses involving both innate and adaptive immune cells.[18,19] Inflammation has been shown to play a pivotal role throughout the progression of atherosclerosis.[20] Early in the disease process, oxidized low-density lipoprotein (LDL) trapped in the vessel wall leads to endothelial dysfunction and increased expression of adhesion molecules, which promote leukocyte recruitment and migration into the subendothelial region. Macrophages and dendritic cells engulf lipids and transform into foam cells while producing various inflammatory cytokines.[21]

Current trends in the approach to cerebral revascularization

Prompt surgical revascularization of the brachiocephalic arteries has been shown to be an effective intervention for reducing the risk of cerebrovascular accidents in patients with lesions of the extracranial arteries.[25] The primary treatment modalities for carotid artery pathology include open surgical procedures such as carotid endarterectomy and carotid artery stenting. Timely surgical treatment of carotid artery disease has been shown to significantly reduce the incidence of acute ischemic cerebrovascular events and the severity of associated cognitive impairment.[26,27]

Carotid endarterectomy is a common reconstructive surgical procedure performed at the carotid bifurcation. The primary goal is to eliminate stenosis and restore patency to 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 heparinization, 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. Using specialized instruments, the surgeon removes any thrombotic debris and atherosclerotic plaque from the lumen of the common and internal carotid arteries. The lumen is then flushed with a saline solution containing heparin. Once the surgeon is satisfied that the necessary manipulations have been completed, the incision in the artery is sutured.

Carotid artery stenting is an emerging therapeutic approach for the treatment of 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 vessel 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 is associated with less postoperative discomfort, is often performed under local anesthesia, may shorten hospital stay, and may be more acceptable to patients. However, there is considerable uncertainty about the short-term risks and long-term durability of CAS compared with CEA, even when both procedures are performed by experienced physicians. During the stenting procedure, an "unstable" atherosclerotic plaque carries the risk of a cerebral artery embolism, which can lead to a partial or complete blockage of blood flow to areas of the brain and cause a "minor" or "major" stroke. In the longer term, there is also a higher rate of in-stent restenosis with carotid artery stenting compared to endarterectomy, requiring close imaging surveillance and possible reintervention.

According to the US Agency for Healthcare Research and Quality, carotid endarterectomy was the predominant intervention for carotid artery stenosis from 1993 to 2014 (Figure 4). However, in recent years, there has been a notable increase in the use of carotid stenting as an alternative treatment approach.

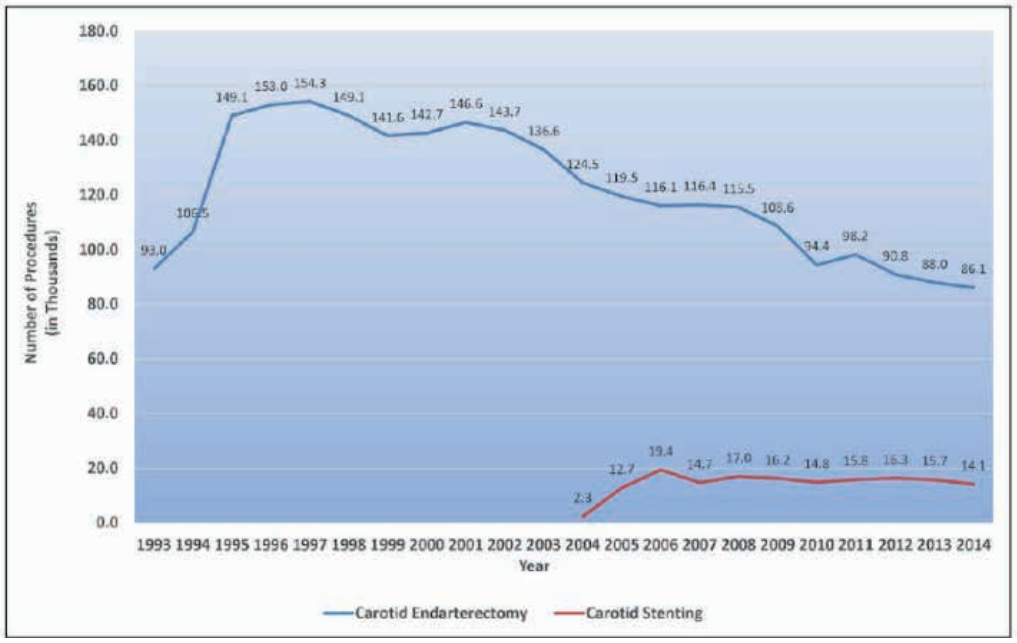


Figure 4.
Quantitative indicator of carotid endarterectomy and carotid stenting (USA, 1993-2014).

Source: Nationwide Inpatient Sample, Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality.[28]

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 procedures were performed in hospitals in the United States in 2014. CEA is the most commonly performed surgical procedure for stroke prevention. Between 2004 and 2014, the number of CEA procedures declined after the introduction of carotid stenting. A comparative analysis using Medicare data showed that the incidence of in-hospital stroke and mortality were comparable between CEA and CAS.[29]

Recent studies using the National Inpatient Sample (NIS) database have demonstrated significant improvements in periprocedural outcomes associated with carotid artery stenting over the past decade.[30] In addition, in the Medicare population, 30-day readmission

rates and long-term adverse clinical outcomes were similar between carotid artery stenting and carotid endarterectomy.[31]

A meta-analysis of five randomized controlled trials evaluated the effectiveness of modern endovascular therapy for stroke and found compelling evidence to support thrombectomy initiated within 6 hours, regardless of patient age, NIHSS score, or prior intravenous thrombolysis.[32] In the study cohort of 234 eligible patients, 51% were transported by ambulance and 49% by helicopter for mechanical thrombectomy, with 27% ultimately undergoing the procedure. The average actual transfer time was 132 minutes.

Current scientific research emphasizes the importance of early detection of pathological processes in the brain by neurologists, vascular specialists and other relevant experts. This is critical because these early abnormalities can potentially progress to irreversible brain damage if left untreated.[33,34]

Recurrent stenosis after previous carotid endarterectomy or stenting is rare (approximately 6% at 2 years).[35] When restenosis occurs within the first 2 years after the procedure, it is typically due to neointimal hyperplasia. Conversely, when restenosis occurs more than 2 years after the initial procedure, the more common underlying etiology is the development of new atherosclerotic plaque. In addition, there is the concept of residual stenosis, which refers to stenosis detected within 30 days of a carotid intervention.

The optimal treatment strategy for this relatively uncommon condition is still being debated. In many countries, pharmacological treatment is recommended for asymptomatic individuals because of the reduced risk of embolic stroke associated with neointimal hyperplasia. Revascularization procedures are reserved for symptomatic patients. The specific revascularization method used is not dictated by a standardized protocol, but is at the discretion of the treating physician.

In the United States, the prevailing guideline is to perform carotid artery stenting for stenoses of ⩾70% and ⩾50%. Patients undergoing this procedure typically receive dual antiplatelet therapy for the first 1 to 3 months, followed by aspirin monotherapy for an indeterminate duration.[36]

Continuous patient monitoring, appropriate postoperative pharmacologic management, vascular specialist oversight, perioperative nursing support, and vascular health monitoring using CVDS techniques all contribute to improved long-term outcomes.[37]

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

Ischemic stroke is primarily caused by atherosclerotic lesions in the arteries that supply blood to the brain, including the internal carotid and vertebral arteries. Despite the availability of treatments aimed at lowering lipid and cholesterol levels in patients, atherosclerosis remains the leading cause of disability and premature mortality worldwide.[38] The vertebral and basilar arteries are responsible for perfusing the brainstem, cerebellum, thalamus, and posterior temporal and occipital lobes in most people.[39]

Recent data suggest that 20% of all transient ischemic attacks and ischemic strokes are attributable to lesions in the vertebrobasilar region.[40] While the treatment of carotid artery stenosis has been well studied, some questions remain regarding vertebral artery stenosis. Treatment approaches for VA stenosis vary depending on the location of the atherosclerotic plaque, its extent, the degree of stenosis, and the volume of damage to the vertebrobasilar territory.

Current treatment modalities 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 stroke, transient ischemic attack, and perioperative mortality.[41] Endovascular treatment with percutaneous transluminal balloon angioplasty alone has not yielded satisfactory results due to elastic vessel recoil and a high rate of restenosis, while there is a lack of well-designed randomized trials to evaluate the efficacy and safety of this approach in the short and long term.[42,43] The use of bare-metal stents

provides favorable results and low rates of periprocedural complications in the early period, but results remain disappointing in the mid- and long-term, with a high incidence of restenosis and subsequent stent fracture associated with neointimal hyperplasia.[44] Trials evaluating the efficacy and safety of coronary drug-eluting stents for the prevention of in-stent restenosis are ongoing and require additional evidence.

There is also a conservative treatment approach, the so-called "best medical treatment" (BMT) approach, which includes antithrombotic drugs, statins, treatment of comorbidities and symptomatic treatment.

Several studies have demonstrated a higher risk of perioperative stroke in patients undergoing intracranial compared to extracranial interventions.[45] However, there is a paucity 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 trial randomized only 16 patients with symptomatic extracranial VA stenosis and compared the results of percutaneous transluminal balloon angioplasty with best medical therapy.[46] In addition, the Vertebral Artery Stenting Trial (VAST) randomized 115 patients with symptomatic hemodynamically significant VA stenosis, both intracranial and extracranial, with 57 patients receiving stenting and 58 receiving aggressive medical therapy.[47] 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 period, 12% of patients with VA stents had a stroke, compared with 7% in the BMT group.[48] The VAST trial was stopped early due to regulatory issues, but recent evidence suggests a high risk associated with intracranial VA stenting.

A systematic review by Feng et al. examined the outcomes of 672 patients in four randomized controlled trials and six nonrandomized trials between 2007 and 2015. The review compared the outcomes of percutaneous transluminal balloon angioplasty (PTBA) plus best medical therapy (BMT) versus BMT alone. The results did not show a significant advantage of either approach.[49] It is noteworthy that this meta-analysis did not include the Vertebral Artery Stenting Trial (VIST), the results of which were presented at the European Stroke Organization Conference in 2016.[50,51] The VIST trial randomized 182 patients with symptomatic intra- and extracranial VA stenosis, with the primary objective of comparing BMT with PTBA with or without stenting. The trial was expected to enroll 540 patients, but was stopped early due to slow enrollment and regulatory issues. Of the 91 patients randomized to stenting, 30 were not treated, primarily because of less than 50% stenosis on duplex angiography. Patients were selected prior to randomization based on CT angiography or MR angiography. Of the 61 patients in the stent group, 48 (79%) had extracranial stenosis and 13 (21%) had intracranial stenosis. The mean follow-up for the study was 3.5 years.[50,51]

Duplex ultrasonography is considered the gold standard for the primary diagnosis of arterial stenosis. However, because 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 stroke. According to existing research, certain cytokines may serve as potential biomarkers for this purpose.[52]

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

According to several research reports, patients who undergo necarotid artery revascularization have a 2.6% annual risk of stroke after carotid endarterectomy.[53]

There is no clear consensus on the effectiveness of surveillance strategies in reducing 30-day death and stroke rates after carotid endarterectomy.[54]

During the perioperative period, the primary goal of monitoring is to maintain adequate cerebral blood flow, especially when the carotid artery is clamped and during bypass grafting. This can be accomplished by several methods, including transcranial Doppler imaging, performing carotid endarterectomy un-

der local anesthesia, measuring stump pressure, subjectively assessing internal carotid artery reflux after carotid artery clamping, and using near-infrared spectroscopy. In addition, electrical brain activity is assessed using somatosensory evoked potentials and electroencephalography.

Quality control methods are aimed at modifying operational strategies to prevent technical errors. These include identification of indirect signs of embolization during carotid artery dissection, diagnosis of arterial lumen conductivity after restoration of blood flow, and diagnosis of large intimal valves to assess residual stenosis. Evidence suggests that targeted monitoring and management of cerebrovascular events may reduce perioperative mortality and stroke rates.[55]

Postoperative patients may undergo annual surveillance related to their carotid revascularization procedures. However, annual surveillance is not generally recommended. Clinical evaluation should include a neurological examination to detect any new stroke-like symptoms. Diagnostic testing should include noninvasive methods, such as duplex ultrasound, to detect potential recurrent stenosis or development of stenosis in the ipsilateral and/or contralateral carotid artery. In addition, patients on medical therapy should not undergo routine annual revascularization due to the possibility of disease progression and increased stenosis. The combination of neurological assessment with duplex ultrasound is considered an appropriate approach.[56]

Patients should be educated about the importance of active management of atherosclerotic risk factors such as hypertension, hyperlipidemia, and smoking cessation. They should also be advised to maintain lifelong aspirin therapy.[57]

Conclusion

Stroke remains a critical global health problem due to its high incidence, significant mortality and significant long-term disability. Understanding the multiple risk factors and associated conditions, such as acute cerebrovascular disease, atherosclerosis, and carotid artery stenosis, is essential for effective prevention and management strategies. Despite advances in diagnostic techniques, surgical interventions such as carotid endarterectomy and stenting, and pharmacological treatments, the burden of stroke continues to challenge healthcare systems worldwide, particularly in low- and middle-income countries.

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

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