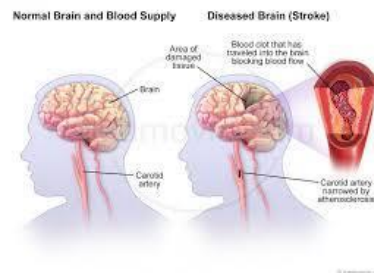


CVA

Introduction

Definition & Overview

A stroke occurs when the blood supply to part of the brain is interrupted. Consequently, brain cells die rapidly. There are two types: ischemic stroke, which is caused by a blood clot blocking a vessel; and hemorrhagic stroke, caused by a rupture in a blood vessel. Also, there is a transient ischemic attack, a temporary blockage, often called a "mini stroke," which increases future risk. That therefore means that immediate treatment is very essential for survival and recovery

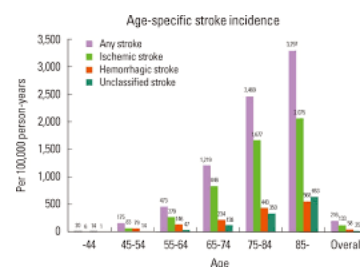


Historical Context:

Although doctors understand strokes today, this wasn't always so. Hippocrates first recognized strokes over 2400 years ago and called them apoplexy, which means "struck down by violence". In the 1600s, Jacob Wepfer determined that disrupted blood supply caused apoplexy and identified bleeding and blocked arteries. Medical science progressed, and eventually, apoplexy was divided into categories, then finally termed stroke and cerebrovascular accident, or CVA. Now doctors differentiate two main kinds of stroke: ischemic, if provoked by blood clots, and hemorrhagic, if a rupture of a blood vessel caused the problem. Stroke is the fifth principal cause of death in the U.S., but about 7 million Americans have managed to survive a stroke.

Epidemiology

Epidemiologic studies on stroke define the natural history of the disease, identify risk and prognostic factors, and reveal markers for disease mechanisms. The studies also point out that some persons, groups, or areas are at increased risk for the disease or have poorer outcomes, thus guiding further research. They also provide information about public health strategies so as to develop effective programs for stroke risk, mortality, and disability reduction. Stroke is one of the



most common causes of chronic disability, dementia, and death. In the United States, for example, that is about 3% of adults. Stroke rates appear to occur 800,000 times every year. The majority are of the ischemic type; primary hemorrhages are more common worldwide. The incidence doubles each decade after age 55 years. Modest declines in developed countries are attributed to better vascular risk factor control; future increases may be seen with aging populations. Even more confusing to the statistics of strokes are TIAs, the definition of which means that the symptoms are temporary and usually go unreported, yet they increase the risk of future strokes manifold

Etiology

Causes & Risk Factors

The stroke essentially results from either blocked or leaking/burst blood vessels in the brain. The most common types of strokes are those caused due to the narrowing or blockage of blood vessels by deposits of fatty substances, blood clots, or any other particles—this is called an ischemic stroke. This may be caused by high blood pressure, blood thinners, aneurysms, head trauma, and cerebral amyloid angiopathy. Transient ischemic attacks are transient disruptions of circulation and therefore fail to harm the target organs. However, it is a high alert of a stroke because of some of these risk factors: obesity, physical inactivity, heavy drinking, use of drugs, high blood pressure, smoking, and high cholesterol. Other contributing conditions to its development include diabetes, sleep apnea, and cardiovascular disease. Age, race/gender, and hormone therapies are also risk determinants of stroke. Those who are over 55 years of age, African American, Hispanic, male, and those using estrogen therapies are at higher risk. TIA requires urgent treatment.

Genetic & Environmental influences

Strokes also tend to run in the family, and 15-52% of all stroke patients report a family history. Genetics play their part in increasing the risk of strokes in many ways including genetic disorders that can cause strokes, disorders where stroke is a complication of the disorders, genetic mutations that enhance the risk of strokes, and mutations leading to risk factors of stroke like hypertension or diabetes. Other causes are those genetic conditions that involve strokes, such as CADASIL, CARASIL, and familial amyloid angiopathy. It may also be increased by a person's being born with a genetic disorder, like sickle cell anemia, metabolic

disorders, and environmental risk factors, including air pollution, high altitude, noise pollution, and exposure to persistent organic pollutants. This may further be impacted by seasonal factors like flu season and cold weather or some very rare events like snake bites.

Clinical Features

Signs & Symptoms

Strokes are time-critical emergencies. Fast action is the key to recovery. The FAST test will help you to know the symptoms of strokes: ****F**** stands for Face—check if one side droops, ****A**** for Arms—to see if one arm drifts down, ****S**** for Speech—to look for slurred or strange speech, and ****T**** for Time—call 911 immediately and note when the symptoms started. The BE FAST test adds ****B**** for Balance (loss of balance) and ****E**** for Eyes (sudden vision loss). Other symptoms: Sudden numbness, confusion, dizziness, or trouble walking. Women also experience hiccups, nausea, or chest pain. Repeated symptoms may be of different degrees or character. A transient ischemic attack, or TIA, also has the same symptoms but goes away in just minutes; however, it should also be treated as urgent to prevent a full stroke.

Complications

Common complications of stroke include brain edema, pneumonia from difficulty in swallowing and immobility, urinary tract infections relating to catheter use, and seizures, especially after major strokes. Depression follows, which is furthered by the emotional and physical impacts of the stroke. Other problems include pressure ulcers from long-term immobility, contracture of limbs from not being used, spasticity leading to muscle stiffness, shoulder pain from weak support of the arm, and deep-vein thrombosis due to reduced movement.

Diagnosis

Diagnostic Criteria

The diagnosis of stroke is made on clinical criteria, indicating a focal or general disturbance of cerebral function lasting more than 24 hours, with the exclusion of those cases of sudden death or surgical intervention. These may also present with features of subarachnoid hemorrhage, intracerebral hemorrhage, and cerebral

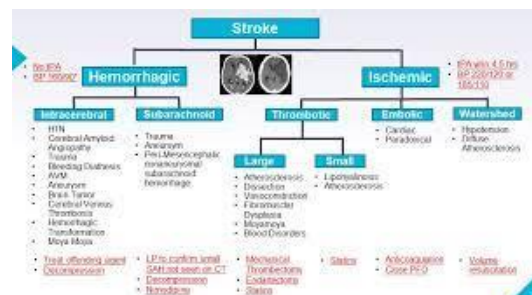
ischemic necrosis. Definite strokes are thus far diagnosed based on unilateral or bilateral motor and sensory disturbances, aphasia, hemianopia, diplopia, forced gaze, dysphagia, apraxia, ataxia, and perception deficits of acute onset. Other symptoms, such as dizziness, headache, and impaired cognitive function, are not pathognomonic symptoms and signs of stroke and therefore cannot establish a diagnosis by themselves. The cases could be classified into the definite stroke, not stroke, or insufficient data where the evidence is not enough to prevail, for example, in sudden death without autopsy or when there is overlapping in symptoms with diseases.

Diagnostic tests & procedures

A stroke is diagnosed by professionals after a physical and neurological examination, including blood pressure and heart function tests. Blood tests may be done for clotting times, blood sugar, and infection. More important would be imaging tests: CT scan reveals the bleeding or tumors, while MRI detects damage to brain tissue and hemorrhages. Carotid ultrasound measures plaque build-up in the neck arteries; a cerebral angiogram gives detailed views of the brain arteries using a catheter and dye. An echocardiogram involves the use of sound waves to identify clots in the heart, which may have caused the stroke.

Differential Diagnosis

Differential diagnosis of stroke is initiated by a detailed history and physical examination that describes the size, shape, and location of the abnormality and suggests possible etiologies. CT scan is necessary to differentiate it from other conditions and identify hemorrhage. If CT is not available,



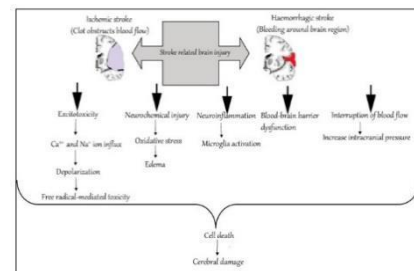
then radioisotope brain scan or lumbar puncture may be done, though they have a lower sensitivity. Although arteriography is useful in estimating the extracranial circulation, it is risky and usually reserved for patients who have had transient ischemic attacks. The initial investigations must include CBC, platelet count, urine analysis, and other blood tests to provide baseline and differential data. An EEG is essential to rule out seizures or postictal paralysis. Other tests are based on the patient's clinical presentation—for instance, sickle cell screening in young Black patients, echocardiography in those with heart murmurs. Prothrombin time and partial thromboplastin time are of the essence to bleeding and clotting, in particular in hemorrhage or anticoagulant therapy. Electrolyte levels must be monitored, as these continue to change over time. Management of blood sugar

levels is crucial for avoiding non-ketotic hyperosmolar syndrome or hypoglycemia with devastating neurological sequelae.

Pathophysiology

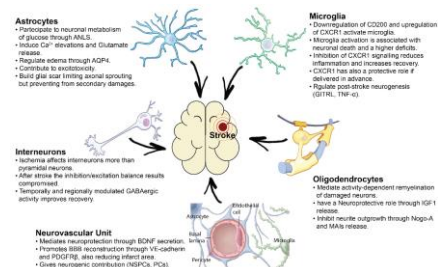
Mechanisms of Disease Development:

A stroke is defined as a sudden neurological event originating from a reduction in blood supply to the brain. Blood supply to the brain is provided by two internal carotid arteries anteriorly and two vertebral arteries that form the circle of Willis. There are two main types of strokes: hemorrhagic and ischemic ones. Stroke, specifically ischemic stroke, accounts for about 85%, depending on the reason for blood and oxygen level reduction as a consequence of clots in the atherosclerotic arteries or embolic blockage. This has caused cell death or dysfunction through necrosis and assorted pathophysiologic processes including inflammation and oxidative stress. About 10-15% are hemorrhagic strokes, which occur because of a rupture of the blood vessel due to stress or an injury, most likely to result in intracerebral or subarachnoid bleeding. Hypertension or use of anticoagulants is usually responsible for intracerebral hemorrhage. As for subarachnoid hemorrhage, normally head trauma or aneurysms are considered to be the cause.



Cellular & Molecular changes

Stroke is one of the major health concerns in the world; on average, 17 million people succumb to this disorder every year. Broadly speaking, it can be divided into two major categories: ischemic and hemorrhagic. Ischemic strokes are caused by the occlusion of cerebral arteries by thrombus or emboli, while hemorrhagic ones are due to either intracerebral or subarachnoid bleeding, often related to chronic hypertension. Only 5% of patients qualify for acute treatments that are comprised of recombinant tissue plasminogen activator and mechanical clot retrieval. This results in diffuse damage to the brain, leading to significant disabilities or death. Several studies are currently targeting



downstream mechanisms that control cell death and inflammation, which exacerbate brain injury further through the apoptotic, necrotic, and autophagic pathways.

Impact on body

A stroke is a condition whereby the blood supply to the brain gets partly blocked, thereby starving the cells of oxygen and hence causing damage. Immediate caring for medical care after a stroke is important to minimize damage and maximize prospects of recovery. The effects of a stroke depend on which areas of the brain have been affected and include respiratory problems, numbness, vision loss, and muscle weakness; it also increases future cardiovascular risk. Treatments vary according to the type of stroke: tPA for ischemic and thrombectomy; in some cases, clipping aneurysm or surgical intervention works for hemorrhagic strokes. Early treatment, however, is the requirement for better outcomes.

Management & Treatment

Medical & Surgical treatment

The kind of treatment that an individual will be subjected to in case of stroke depends on whether it is an ischemic or hemorrhagic stroke. For an ischemic stroke, tissue plasminogen activator is used in dissolving clots. Anticoagulants may also be of importance in preventing further clotting. Restoring blood flow by thrombectomy would be the next, together with angioplasty with stenting, and lastly carotid endarterectomy. In hemorrhagic strokes, blood pressure is managed, anticoagulants are withdrawn, and surgical procedures such as aneurysm clipping or coil embolization are sometimes indicated. Other treatments may include suction of pooled blood or removal of excess fluid. Radiation treatment may be necessary in the case of AVMs. In both, early interventions are necessary if there is to be any hope of recovery.

Lifestyle & Dietary Modification

The sooner, the better in making life changes and dietary risk factor limitations for stroke. At least 150 minutes of moderate aerobic physical activity a week should be done, including no smoking, moderate alcohol use, controlled weight, controlled cholesterol and blood pressure, and a heart-healthy diet. Emphasize a heart-healthy pattern of high intake of fruits, vegetables, whole grains, lean protein, and healthy fats while maintaining low intake of foods that are processed, have added sugars, and excess salt. In case of a history of stroke, adapt diets for

dysphagia; maintain or gain weight with calorie-dense foods and smoothies, especially those that are very nutrient-dense. Treat hypertension with a reduced intake of sodium, which can be replaced with herbs and spices to add flavor. Follow-up visits with your healthcare provider for stroke survivors are very important for individual guidance.

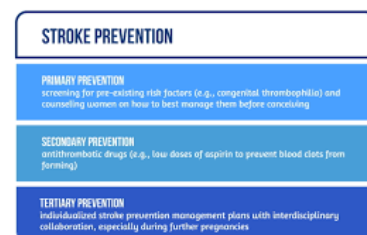
Supportive Care & Rehabilitation

It means being supportive to the stroke survivor by listening to his or her special needs, providing support emotionally, and guiding in rehabilitation exercises while promoting independence. Keep in touch—call them or send small surprises. Celebrate small victories by their side and help adapt the environment with mobility aids. Communicate with them in the easiest way possible, and also support the caregivers by sharing some tasks with them and providing emotional support. The rehabilitation process consists of the relearning of skills and neuromuscular stimulation itself involving neuroplasticity with spontaneous continued improvement. Inpatient rehabilitation should be started as early as possible and has to be as active as possible both for the patient and the support network.

Prevention & Control

primary secondary and tertiary prevention

Primary prevention of stroke is achieved by preventing its risk factors, which include smoking, obesity, poor diet, and lack of exercise. Secondary prevention includes those people with risk factors of stroke to prevent stroke with lifestyle modifications and medical treatments. This includes control of hypertension, diabetes, and high cholesterol. Tertiary prevention is hence related to caring for those who already had a stroke, preventing further strokes, and minimizing disability by offering rehabilitation and follow-up support. Evidence has shown that recurrent strokes are generally associated with poorer outcomes and higher long-term costs than a first stroke.



public health intervention

Stroke is the second worldwide leading cause of death and one of the major causes of long-term disability. Stroke is the fifth-ranked cause of death in the United States. It kills nearly 800,000 people each year in the country. The significant declines in stroke mortality over the last five decades were attributed to the treatment of risk factors like hypertension and smoking and increased anticoagulant use. Despite these advances, it is estimated that 80% of strokes can still be prevented if people better controlled risk factors such as hypertension, diabetes, and cholesterol. Hypertension represents the largest modifiable risk factor for stroke; it has affected up to 29.3 percent of adults in the United States. Besides, lifetime stroke risk is higher in women than in men. It has certain risk factors in women, which include conditions related to pregnancy and hormonal changes. One should have a well-integrated, effective stroke care system provided within the delivery of care and delivered in an effective and timely manner for treatments across settings and coordinating care. This work was supported by CDC's Paul Coverdell National Acute Stroke Program and the National Institutes of Health. This underscores the need for both clinically based and community-based interventions to improve stroke prevention, treatment, and recovery.

Vaccination & Screening program

A recently published study estimated the risk for stroke in Medicare beneficiaries aged 65 and older after COVID-19 bivalent vaccines and influenza vaccines. There were no significant increased risks of stroke with either brand of the COVID-19 bivalent vaccine alone. Combinations of COVID-19 and high-dose or adjuvanted influenza vaccines did show significant associations with stroke risk; results were specific to vaccine type and stroke subtypes. Stroke dominates as one of the most common causes of death and disability globally. The major cause is ischemic strokes due to blockage in blood flow and hemorrhagic strokes due to the rupture of blood vessels. A person above 45 years with a number of risk factors should take ample screening. It consists of an overall evaluation through various tests and consultations that will evaluate the risk of stroke.

Prognosis

Outcomes & Survival ratesThe stroke care performance measures are designed by the Joint Commission and AHA/ASA to

Time after initial stroke	Chance of survival	Chance of having another stroke
3 months	79.4%	7.8%
1 year	73%	11%
5 years	52.8%	19.8%
10 years	36.4%	26.8%

evaluate Michigan Medicine against best practices and benchmarks. Another important measure in this case was that 60 percent of eligible patients who received mechanical thrombectomy within 6 hours of last known well—a symptom onset time—met or exceeded AHA's goals, thus beating the 50 percent goal. Stroke ranks as the fifth leading cause of death in the United States; approximately 795,000 cases occur annually. Although there is no defined number of strokes that a person can tolerate, it is obvious that every stroke causes further brain damage and increases the risk of death. Very early treatment significantly enhances the chances of survival. Repeated strokes increase the likelihood of having subsequent strokes and decrease life expectancy. Survival rate varies by age group and ethnicity, with older people and minority groups having higher risks. Other factors that will increase the possibility of serious consequences include atherosclerosis, irregular heartbeat, and diabetes.

Measure	American Heart Association Goal	Michigan Medicine	National Benchmark 2022	Michigan Benchmark 2022
Percentage of eligible patients treated within 60 minutes of arrival	85%	95%	86.4%	84.8%
Percentage of eligible patients treated within 45 minutes of arrival	75%	93.3%	65.0%	60.8%
Percentage of eligible patients treated within 30 minutes of arrival	50%	75.0%	31.5%	22.8%

Factors that affect prognosis

A stroke is caused by the interruption of blood supply to the brain, eventually leading to the death of brain cells and even death. It moved from the 4th leading cause of death to the 5th leading cause of death in the U.S. with improved diagnostic, therapeutic, and preventive measures. Hypertension, high cholesterol, diabetes, and smoking predispose to stroke by damaging the arteries. Improved risk factor management and prompt treatment within the first 3 hours following a stroke improved survival rate and reduced disability.

Quality of life

One key outcome with respect to quality of life (QOL) after stroke is the potential reduction in recreational and social activity engagement of the affected survivor, independent of their recovery in physical function. Quality-of-life measurement instruments have been designed to measure multi-dimensional aspects using, for example, the Stroke Impact Scale, SF-36, and Quality of Well-Being-A [QWB]

with measures of physical, mental, and social health. While the Stroke Impact Scale has been shown to work and be used for mild and moderate conditions, its application for conditions of severe magnitude requires the performance of additional research. Additionally, the validity and practicality of proxy testing should also be researched for severe conditions. Finally, the SF-36, being a widely used and validated tool, might not cover all the requisite outcomes and might be challenging to interpret due to the presence of floor and ceiling effects. Alternative methods such as item response theory offer aspects of it that are promising with exciting developments by giving a continuous scale for fine-tuning the measurement and interpretation.

Current research & future directions

Recent discoveries

There are nearly 800,000 new or recurrent strokes annually; the bulk are ischemic with the remainder being intracranial hemorrhages and subarachnoid hemorrhages. The incidence of stroke has been declining over the past three decades, but the total number of cases of stroke is projected to increase strikingly by 2030. The evolution in the management of AIS, in particular with EVT, has vastly improved outcomes. Other advantages of EVT, with improved devices and treatment protocols, exist for posterior circulation strokes and large strokes. After all this progress, there are still ongoing challenges, such as identifying the best outcome measures for stroke and assessment of new thrombolytic therapies like Tenecteplase. In all the trials, EVT had superior functional outcomes when compared to standard medical management, thereby establishing its real efficacy in treating anterior circulation strokes with proximal, large-vessel occlusions.

Ongoing Clinical Trials

The ARCH study will determine whether warfarin or the combination of aspirin and clopidogrel is more appropriate for preventing further vascular events in patients with a significant atheroma of the aortic arch after a stroke or systemic arterial embolism. Patients will be monitored for four months for a variety of outcome measures, including recurrent ischemic stroke and vascular death. The BASC is investigating the association of changes in blood pressure during acute stroke and outcome and is also conducting an individual patient data meta-analysis of trials of vasoactive agents to determine whether such an approach to blood pressure management is beneficial. The CAVATAS trial compares the

risks and benefits of carotid and vertebral artery angioplasty versus carotid endarterectomy in patients with cerebrovascular disease, both symptomatic and asymptomatic.

Future Research needed

Dr. Nestor Gonzalez, MD, at Cedars-Sinai, is pioneering some of the newest research in innovative care for stroke, with a particular interest in ICAD. His work on the application of the EDAS procedure, pioneered for the treatment of pediatric Moyamoya disease, holds great promise for significantly reducing secondary stroke rates in patients with ICAD compared to traditional medical management. The research by Gonzalez is moving forward into a multicenter clinical trial to further assess EDAS. He is also following trends in stroke care that include the expansion of endovascular therapies and increasing stroke awareness among health professionals as well as the general public. The Cedars-Sinai Stroke Program is dedicated to fast action and quality care; it is Comprehensive Stroke Center certified.

Case Study

This is an acute onset 61-year-old senior partner with a law firm who presented with slurred speech, left facial droop, and left upper and lower limb weakness while he was eating breakfast. His wife dialed 911 immediately, and he was treated within an hour and 54 minutes of symptom onset with intravenous tPA. He was rushed for an MRI, which was followed by cerebral angiography. The diagnosis was confirmed to be an acute ischemic stroke due to the occlusion of the right middle cerebral artery and right internal carotid artery because of a thrombus. He underwent endovascular thrombectomy at 4 hours 19 minutes from the time of symptom onset. Subsequently, Michael was admitted to the Acute Stroke Unit for 24-hour monitoring and initiation of referral in occupational therapy, speech-language therapy, and physiotherapy.