



**ORIGINAL RESEARCH PAPER**

**Medicine**

**"TIME IS BRAIN" AND "A STROKE IN TIME"**

**KEY WORDS:** Intracerebral Hemorrhage, Cerebral Small Vessel Diseases (cSVDs), Lacunar Infarction (LI), White-matter Lesions (WMLs), Angioplasty

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**ABSTRACT**

A stroke decrease in blood flow to the brain due to a clot or bleeding—is a medical emergency. And doctors often say “time is the brain”. Stroke is a ‘brain attack’. It is a sudden loss of brain function. An ischemic stroke which is an interruption of blood flow to the brain, usually as the result of a blood clot. Hemorrhagic stroke is the result of bleeding or a rupture of a blood vessel in the brain. The resulting leakage into surrounding brain tissue causes damage to nerve cells. Early warning signs of a stroke are clues that your body sends to indicate that your brain is not receiving enough oxygen and nutrients. If your brain does not receive oxygen and nutrients for a period of time, permanent damage (i.e., a stroke) can result. This deprivation of oxygen and nutrients can lead to the death of the brain cells. Paralysis is the loss of voluntary movement as a result of damage to nerve or muscle function. The brain controls the different muscles that are responsible for movement. When the brain is damaged, it can impair the function of the muscles. The damage can be lasting especially when the damage is within the area of the brain that controls the motor movements of the body. Balance and coordination are controlled by the brain. The vision can become blurry. Embolic stroke is a condition occurred when blood flow to a part of the brain stops. “Diabetes + Hypertension = Silent Stroke”. Women Recover Worse Than Men after a Stroke. Every two seconds someone has a stroke and one in six people will suffer a stroke in their lifetime. Stroke is the third leading cause of death worldwide, with over 6 million people dying from strokes each year. A sudden weakness or numbness of the face, arm or leg on one side of your body. Sudden dimness or loss of vision, particularly in one eye. Loss of speech, or trouble talking or understanding speech. Sudden severe headache. Unexplained dizziness (1) usually, hiccups are a minor nuisance. But when stroke affects the brain’s breathing center, it can trigger a sudden, protracted case of hiccups, more commonly in women.

**INTRODUCTION**

Stroke is an especially serious problem in Asia, which has more than 60% of the world’s population, and many of its countries are “developing” economies. Stroke mortality is higher in Asia than in Western Europe, the Americas or Australasia, except in the case of some countries such as Japan. (2)

Evidence-based approaches to organization and planning of stroke care and services require accurate ongoing data on stroke incidence, prevalence, and outcomes. (3) DM is suggested to adversely affect the outcome of AIS in Japanese patients. (4) Stroke is a leading cause of mortality worldwide, as well as a source of long-term disabilities and huge socioeconomic costs.(5) Ischemic stroke is a common disease with high mortality and morbidity worldwide. One of the important pathophysiological effects of ischemic stroke is apoptosis. (6) Intracerebral hemorrhage (ICH) and lacunar infarction (LI) are the major acute clinical manifestations of cerebral small vessel diseases (cSVDs). (7) Increased intake of the flavanone subclass was associated with a

reduction in the risk of ischemic stroke. Citrus fruit consumption may be associated with a reduction in stroke risk, and experimental data support these epidemiological associations that the flavanone content of citrus fruits may potentially be cardio protective. (8)

A healthy lifestyle and adherence to a Dietary Approaches to Stop Hypertension (DASH) style or Mediterranean diet, high in fruits, vegetables, and total flavonoids, are associated with reduced stroke risk (9, 10) Large and small cerebral vessel disease can trigger stroke and contribute to the vascular component of other forms of neurological dysfunction and degeneration.(11) To a great extent, stroke is a disease of the aged. The rate of vascular events including stroke increases markedly with age. (12,13) Disruption of mitochondrial function is a critical event hypoxia-ischemia (HI) and stroke.(14) Mitochondrial production of reactive oxygen species threatens neuronal survival by their ability to induce lipid peroxidation, protein oxidation, and DNA damage.(15,16) Cerebral white matter constitutes 50% of human

brain mass and contains abundant axons and oligodendrocytes. (17,18) The cerebral white matter is damaged by a variety of neurologic disorders including ischemic stroke, and white-matter lesions (WMLs) have been associated with cognitive impairment. (19)

The most common cause of disability according to the World Health Organization is the stroke, each year 15 million individuals suffer from a stroke in the world. Of these, 5 million succumb and an additional 5 million are permanently disabled. (20)

**HISTORY**

Episodes of stroke and familial stroke have been reported from the 2nd millennium BC onward in ancient Mesopotamia and Persia. (21) Hippocrates (460 to 370 BC) was first to describe the phenomenon of sudden paralysis that is often associated with ischemia. Apoplexy, from the Greek word meaning "struck down with violence", first appeared in Hippocratic writings to describe this phenomenon. (22, 23) The word stroke was used as a synonym for apoplectic seizure as early as 1599. (24) And is a fairly literal translation of the Greek term.

In 1658, in his Apoplexia, Johann Jacob Wepfer (1620–1695) identified the cause of hemorrhagic stroke when he suggested that people who had died of apoplexy had bleeding in their brains. (31) Wepfer also identified the main arteries supplying the brain, the vertebral and carotid arteries and identified the cause of a type of ischemic stroke known as a cerebral infarction when he suggested that apoplexy might be caused by a blockage to those vessels. Rudolf Virchow first described the mechanism of thromboembolism as a major factor. (25)

The term cerebrovascular accident was introduced in 1927, reflecting a "growing awareness and acceptance of vascular theories and recognition of the consequences of a sudden disruption in the vascular supply of the brain" (26) Its use is now discouraged by a number of neurology textbooks, reasoning that the connotation of fortuitousness carried by the word accident insufficiently highlights the modifiability of the underlying risk factors. (27, 28, 29) The cerebrovascular insult may be used interchangeably (30)

**MAJOR ADVANCES AND DISCOVERIES**

A stroke is often described as the brain equivalent of a heart attack; blood supply to part of the brain is cut off, leading to cell death and potentially life-threatening brain injury. The two main types of stroke are ischemic, where an artery to the brain is blocked, and hemorrhagic, when a blood vessel ruptures. Every two seconds someone has a stroke and one in six people will suffer a stroke in their lifetime. Stroke is the third leading cause of death worldwide, with over 6 million people dying from strokes each year. With an aging global population, the incidence of stroke is set to rise. These sobering statistics demonstrate its huge global impact and emphasize how essential it is that we continue to further our understanding of stroke, with the aim of better prevention, treatment, and management. (32) Microscopic channels that directly connect the skull marrow cavities with the meninges. Neutrophils originating from the skull marrow have a higher propensity to travel to the ischemic mouse brain than cells in the tibia. (33) In a recent study, rivaroxaban was not superior to aspirin for secondary prevention of stroke and systemic emboli after an initial embolic stroke of undetermined source (ESUS) but was associated with a higher risk of bleeding. (34)

But medical researchers are now warning that for certain high-risk individuals, a painful salon shampoo can be more than just a painful ordeal. It can bring on a life-threatening condition known as "beauty parlor stroke". If you are an adult with an arthritic neck, high blood pressure or high cholesterol, keeping your neck tilted backward at a sharp angle for long periods may be enough to seriously restrict blood flow to your brain and trigger a stroke. (35) 'Good fats' prevents strokes like Walnuts, soybean oil and canola oil contain alpha-linolenic acid. The more of this acid men have in their blood, the lower their stroke risk, according to a recent study at the University of California, San Francisco. Researchers found that Omega 3 fatty acids come from alpha-linolenic acids.

Omega 3 fatty acids keep blood clots from forming. The new study said that the more stearic acid you have in your blood, the higher your risk of stroke (36) Sex history of diabetes mellitus, hypertension, ischemic heart disease and smoking, presence of infarct in 7 brain areas, namely basal ganglia, brainstem, cerebellum, frontal lobe, parietal lobe, temporal lobe and occipital lobe and treatment of antiplatelet and lipid-lowering drugs were recorded as binary variables (37)

Stroke is a major health problem in South, East, and South-East Asia. With the majority of the world's population living in the developing countries of these regions, the global burden of stroke will have the largest contribution from Asia. In these countries, there are disparities in the health care provisions, and this will continue to pose a challenge to disease control. (38)

**WHERE THE RESEARCH GO NEXT?**

Angioplasty and stenting have begun to be looked at as possible viable options in the treatment of acute ischemic stroke. Intracranial stenting in symptomatic intracranial arterial stenosis, the rate of technical success (reduction to stenosis of <50%) ranged from 90-98%, and the rate of major peri-procedural complications ranged from 4-10%. The rates of restenosis and stroke following the treatment were also favorable. This data suggests that a randomized controlled trial is needed to more completely evaluate the possible therapeutic advantage of this preventative measure. (39) Neuroprotective agents including antioxidants which combat reactive oxygen species, or inhibit programmed cell death, or inhibit excitatory neurotransmitters have been shown experimentally to reduce tissue injury caused by ischemia. Until recently, human clinical trials with neuroprotective agents have failed, with the probable exception of deep barbiturate-induced coma. Disufenton sodium, the sulfonyl derivative of the radical-scavenging phenyl butyl nitron, was reported to be neuroprotective. (40) This agent is thought to work at the level of the blood vessel lining. So that the benefit of disufenton sodium is questionable. (41)

Hyperbaric oxygen therapy has been studied as a possible protective measure, but as of 2014, while the benefits of this have not been ruled out, further research is said to be needed. (42) Modulating microglial activation and polarization might mitigate hemorrhagic stroke injury and improve brain repair. (43)

**SIGNIFICANT GAP IN RESEARCH**

A sudden weakness or numbness of the face, arm or leg on one side of the body. Sudden dimness or loss of vision, particularly in one eye from the onset of stroke can have changes in vision. This is because the brain is no longer supplied with the appropriate amount of oxygen. Loss of speech, or trouble talking or understanding speech. Sudden severe headache. Unexplained dizziness, all of the vital functions of the body will no longer be functioning. This includes the eyes and the ears. Unsteadiness or sudden falls. When the brain is damaged due to the lack of oxygen supply. The nerves function slower than normal because of the shortage of necessary materials. This can cause the loss of balance and coordination.

**CURRENT DEBATE**

Dr. Diener presented the pro side, arguing that a fib increases the risk of stroke and while some microbleeds, such as with amyloid angiopathy, may be a contraindication, others are markers of small vessel disease. NOACs have a more favorable profile for ICH than warfarin and has been demonstrated to not increase microbleeds. Dr. Greenberg, however, iterated the dismal outcome of anticoagulation-related ICH (up to 50%), and pointed out that microbleeds lead to 5 ICH events/100 person-years. A decision analysis modeling the risk/benefit ratio of anticoagulation has previously identified an ICH risk of 1.4% as the tipping point where risk of anticoagulation outweighed benefits. (44) Both Dr. Dawson, who argued in favor of an early assessment, as well as Dr. Broderick, who argued in favor of a late assessment, used data from the MISTIE II and IMS III to support their points, which perhaps points to the true equipoise in this question. Dr. Dawson's point was that in general, the longer a trial is conducted, the more

confounders are introduced and often, additional time does not add information that significantly changes the interpretation of the results. Given the resources available, a better approach may be to recruit more patients within a shorter trial rather than follow fewer patients for a longer time frame. Dr. Broderick argued that especially with severe strokes, there are patients who recover later, and delayed follow up allows for better cost-effect analysis.(44) Stroke is a leading cause of long-term disability and death worldwide, ranking second to cardiac ischemia (45).

The antioxidant properties of alpha-lipoic acid (ALA) correlate with its ability to promote neuron proliferation. However, there have been no comprehensive studies examining the neurorestorative effects of ALA administration after the onset of ischemia (46)

Cerebral small vessel disease (SVD), one of the most prevalent neurological disorders, affects small arteries, arterioles, capillaries and small veins (47), and plays a key role in stroke (48), dementia (49) and aging. Ischaemic stroke is a major cause of neurological morbidity and mortality. Acute ischaemic stroke and its various aspects in a developing country like Pakistan, where resources are limited and the healthcare system is underdeveloped. (50) Epidemiologic studies on stroke help us to understand the natural history of the disease and to identify risks and prognostic factors that can lead to better knowledge of the markers for disease mechanisms (51)

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