

The Occurrence, Treatment, Prevention and Health Economics of Stroke

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Abstract

Stroke is a common and serious neurological condition that often leads to disability and death. Research on the occurrence, treatment, prevention, and health economics of stroke has provided important insights into the burden of the disease and strategies to reduce its impact. Primary and secondary prevention strategies, such as routine treatment of atrial fibrillation with anticoagulant drugs, have been shown to be effective in reducing the occurrence of stroke. Advances in acute and long-term stroke care have also improved patient outcomes. However, stroke remains a significant global health challenge, with ongoing efforts needed to better understand its determinants and reduce its burden. This study explores the occurrence, treatment, prevention and health economics of stroke in order to provide information to healthcare providers with the aim of reducing the burden on public health.

Keywords

Stroke, Pathophysiology of stroke, Health economics of stroke.

1. INTRODUCTION

Stroke is a disease characterized by local neurological deficits caused by impaired blood circulation in the brain. Stroke can be divided into hemorrhagic and ischemic according to the pathological nature, including cerebral hemorrhage, cerebral infarction, subarachnoid hemorrhage, etc. It is a common disease of middle-aged and elderly people. According to the statistics, Stroke is the third most frequent cause of death in developed countries, only next to heart attacks and cancers. In a global context, stroke has become more frequent and is the second most frequent cause of death.[1] The health and economic burden of stroke is a global issue. Many countries have used the results of health economics analyses as part of their clinical guidelines for stroke to assess the cost-effectiveness of stroke treatment. According to a population-based study of 32 countries worldwide, the economic burden of stroke was approximately US\$5.5 billion in 2017.[1] Their model showed that the economic impact and health losses of stroke for young adults in Australia were significant. The essay mainly focuses on the pathophysiology, treatment, prevention and health economic of the stroke.

2. RISK FACTORS

The risk factors of stroke are various. Age is the most obvious factor. The risk of stroke increases with age. According to Lindley's investigation, there is a nearly 10-fold increase in the risk of stroke from childhood to early adulthood and early adulthood and middle age and middle age to old age (as chart 1 reveals, on the next page).

Table 1. Incidence of stroke in different age bands

Age range (years)	Approximate incidence (strokes per 100,000 per year) per age group
All age groups	150–200
Childhood	2
16–44	5–20
45–54	50–100
55–64	200–300
65–74	500–1,000
75–84	1,000–2,000
≥85	2,000–3,000

Another common factor is family history, those people whose family members with a history of stroke usually have a higher risk than others. Ethnicity is also an essential factor. By Gulli's study (2016), the stroke incidence rate of the black race is higher than white race[2], which can indicate that coloured races have a higher risk of stroke. In addition, existing diseases and unhealthy lifestyles also increase the incidence rate of stroke. Hypertension is the most common inducement to stroke. Although high blood pressure cannot result in stroke directly, it can cause abnormalities in blood vessels, many related diseases might appear due to hypertension. Atrial fibrillation is also a risk factor, it might occasionally cause blood clots, if blood clots are pumped into the circulation and lodged in the blood supply to the brain, the stroke will occur. Diabetes mellitus is an independent risk factor for ischaemic stroke, and it also doubles the risk. In addition, the frequency of diabetes mellitus is increasing, so more attention should be paid. Another risk factor is obesity, and there is considerable overlap with other risk factors as people with obesity usually also have hypertension, diabetes, and high blood cholesterol. An unhealthy lifestyle also increases stroke risk, such as physical inactivity, smoking, drinking alcohol.[1]

3. PATHOPHYSIOLOGY

Ischemic stroke is a sudden neurological deficit caused by local cerebral ischemia and permanent cerebral infarction (such as positive on DWI). The large-vessel disease is the primary inducement in the last time; it is mainly caused by the complications of narrowing and occlusion of blood vessels damaged by atheroma. Hypertension, heart failure, and overfatigue can slow blood flow, increase blood viscosity, or build-up of abnormal arterial wall material, resulting in thrombosis and further develop into atheroma.[1] Small-vessel abnormal can also cause stroke, and it accounts for about 25% of all ischaemic strokes. Although small vessels can only provide a tiny amount of blood to the brain, severe stroke can also occur if small-vessel disease happens in a particular part of the brain. Small-vessel occlusion may be caused by micro-atheroma, arteriolosclerosis et al. [1]

Intracerebral haemorrhage accounts for about 10% to 15% of all stroke types. Intracerebral haemorrhage (previously called primary intracerebral haemorrhage), often referred as a haemorrhagic stroke. There are numerous causes of intracerebral haemorrhage. The most important mechanism is blood pressure too high. Long-period hypertension leads to the weakening of blood vessels. Some sharp bursts of very high blood pressure, such as severe stress, sexual intercourse, and illicit drugs, can cause haemorrhagic stroke. Smoking, obesity, diet, and alcohol can increase the risk level.[1] The second mechanism is that blood vessels

weaken or are damaged. Conditions that weaken blood vessels include small-vessel disease, amyloid angiopathy, and abnormalities including cerebral aneurysms, vascular abnormal, inflammation of the blood vessels (vasculitis), and trauma. Another mechanism is the bleeding tendency, which is highly related to blood factors. Anticoagulation, antiplatelet or thrombolytic therapy, leukaemia, thrombocytopenia, intracranial tumours, alcoholism, and sympathetic stimulants are all risk factors. The application of warfarin can also cause an intracerebral haemorrhage. Haemorrhagic stroke mortality is much higher than ischaemic stroke, and haemorrhagic stroke is more likely to happen at a younger age.

4. MANAGEMENT

In biochemical terms, the brain needs constant oxygen and nutrients from the arterial blood supply. If a stroke disrupts the blood supply, the capacity to survive will be severely limited. Under that condition, the brain cell starts to necrose within minutes of vascular occlusion or disruption. Stroke is now an eminently treatable medical emergency, but a quick first-aid is essential. [1]

5. MANAGEMENT OF ISCHAEMIC STROKE

As an arterial clot or embolus has caused the stroke, effective treatment requires quick removal of the clot. If this succeeds, some strokes can be reversed entirely. For acute management of ischaemic stroke, intravenous thrombolysis and endovascular thrombectomy are two standard operation methods.

Intravenous thrombolysis can be achieved with medical therapy. Recombinant human tissue plasminogen activator (alteplase) is one kind of medication widely used in intravenous thrombolysis. The mechanism of intravenous thrombolysis is the application of thrombolytic drugs such as plasminogen activator to directly or indirectly dissolve the fibrin in the thrombus, thereby recanalizing the blocked blood vessel. Alteplase is a new type of thrombolytic agent, which belongs to the gene recombinant thrombolytic drug line. Alteplase has become the first choice for the treatment of ACI in European and American countries.[5] It can recanalize blocked coronary arteries because it combines with fibrin after it enters the blood, then activates fibrinogen and promotes the degradation of plasma fibrinogen.

According to Wang's report, a Chinese study has revealed that thrombolysis with 0.9 mg/kg alteplase has significant advantages and does not increase the risk of intracranial haemorrhage. Previous research has also found that alteplase can inhibit the inflammatory response lowering the incidence of hemorrhagic transformation and reducing the risk of haemorrhage after thrombolysis.[5] Another research shows that if taking alteplase can effectively reduce the disability rate within three hours, if the treatment time is extended, it will cause the effectiveness decrease significantly. The conclusion is that the effectiveness of alteplase falls along with the extension of the treatment window although intravenous alteplase treatment can help improve the patient's prognostic function.[6]

Endovascular thrombectomy (ET) is another currently using method. According to Yarbrough's research, ET patients showed promising outcomes in 43.2% of patients, with an absolute risk reduction of 12.3% compared with the patient control group. Another outcome is that the motility of ET patients has dropped by 2.88%. The conclusion of this research suggests that older patients with good premorbid functional status may benefit from ET as well. Symptomatic ICH risk and mortality are similar between those who undergo ET and those who undergo standard therapy.[7] However, whether endovascular thrombectomy has a good effect on patients with severe irreversibly injure in the brain (especially ischaemic core) is still uncertain by now. One notable piece of data is that only approximately half of successful

endovascular thrombectomy patients with severe vessel occlusion can recover on independent function entirely. Whether to apply ET should be considered carefully before treatment.

6. MANAGEMENT OF INTRACEREBRAL HAEMORRHAGE

For acute management of haemorrhagic stroke, blood pressure-lowering is effective, that bleeds due to anticoagulation (blood-thinning treatment) need to be treated rapidly. That surgery has a role for selected patients. In the initial treatment stage, the only evidence-based treatment for intracerebral haemorrhage by lowering blood pressure is to control the blood pressure to nearly 140 mmHg. However, the blood pressure cannot be decreased lower than 140 mmHg due to renal adverse reaction potential risk.[4]

Except for surgical interventions, reversal of antithrombotic medications is another acute treatment for intracerebral haemorrhage. Vitamin K can correct INR by providing a substrate necessary for the synthesis of fat-soluble coagulation factors, and high doses (5-10 mg) of vitamin K can reverse INR faster and better. In addition, FFP can directly replace blood coagulation factors and is often used in combination with vitamin K to reverse the effects of warfarin in patients with ICH. Some blood clotting factors, such as activated Factor VII (aFVII), also affects antithrombotic treatment.[1] In one trial, treatment was associated with a better clinical outcome. Nevertheless, there was no apparent clinical benefit with treatment in another trial, called the FAST trial. So it can be supposed that aFVII does take effect, but its effect is perhaps not as strong as researchers estimated. A more and larger trial will be required to confirm these potentially promising initial results.[1]

7. ASPIRIN AND CLOPIDOGREL DUAL

Aspirin is an antiplatelet drug, which is widely used in stroke prevention and treatment. The mechanism of the antiplatelet drug is to inhibit cyclooxygenase in platelets, decrease the synthesis of thromboxane A₂, and inhibit platelet aggregation. It prevents thrombosis by this route. The role of antiplatelet therapy in the prevention of secondary stroke has been well established. Aspirin and clopidogrel can synergistically inhibit platelet aggregation; as Wang's research, for transient ischemic attack patients, stroke occurred in 8.2% of patients in the clopidogrel and aspirin combined group, which is 3.5% lower than only aspirin group. The research indicated that aspirin and clopidogrel dual antithrombotic therapy is superior to antithrombotic therapy that apply aspirin only.[3]

8. PREVENTION

The rate of stroke recurrence is very high. If the risk factors are not well controlled, a stroke will occur repeatedly. Excessive alcohol consumption will damage red blood cells and affect the adhesion of red blood cells, resulting in thrombosis.

There are three stages of stroke prevention, primordial prevention, primary prevention, and secondary prevention. Primordial prevention means reduce the incidence of risk factors. For an individual, change a lousy lifestyle like smoking, heavy drinking, a high-fat diet and long-term mental stress. If smokers quit or limit their tobacco consumption, drink in moderation and avoid excessive drinking. These measures all help reduce the risk of stroke.

There is primary prevention: once patients have figured out that they have risk factors related to stroke, they should actively treat and control it. For example, patients with high blood pressure should adjust their blood pressure below 140/90 mmHg. Patients with heart disease, hyperlipidemia, carotid artery stenosis, and obesity should also go to the hospital for treatment and control according to specialist recommendations and formulate prevention programs.

The secondary prevention of stroke is based on two preventions mentioned above, aspirin and statins such as pravastatin, simvastatin, and other lipid-lowering drugs also have a specific effect on preventing the onset of stroke.

9. SUMMARY

Stroke is a cerebrovascular disease, and it is a major factor causing death and disability in the world. The risk factors are various, but a healthy lifestyle can effectively prevent stroke since the indication of high-risk disease can be reduced. Ischaemic stroke is the most common stroke, and it is mainly caused by embolism. Intravenous thrombolysis and endovascular thrombectomy are the two primary therapies of this category. The most common pathogeny of intracerebral haemorrhage is sharp bursts of very high blood pressure. Long-term hypertension can increase the risk, for the management, lowering blood pressure and reversing antithrombotic medications are optional acute management. For stroke prevention, healthy living habits, proper drug therapy, and formulated prevention programs are all essential routes in every stage.

REFERENCES

- [1] Lindley RI. Stroke. Oxford: Oxford University Press, Incorporated; 2017.
- [2] Gulli G, Rutten-Jacobs L, Kalra L, Rudd AG, Wolfe CDA, Markus HS. Differences in the distribution of stroke subtypes in a UK black stroke population - final results from the South London Ethnicity and Stroke Study. *BMC medicine* 2016 May 20;14:77.
- [3] Wang Y, Wang Y, Zhao X, Liu L, Wang D, Wang C, Wang C, Li H, Meng X, Cui L, Jia J, Dong Q, Xu A, Zeng J, Li Y, Wang Z, Xia H, Johnston SC; CHANCE Investigators. Clopidogrel with aspirin in acute minor stroke or transient ischemic attack. *N Engl J Med.* 2013 Jul 4;369(1):11-9.
- [4] Prof Bruce C V Campbell PhD, Prof Pooja Khatri MD, Volume 396, Issue 10244, 11–17 July 2020, Pages 129-142.
- [5] Wang J, Fang X, Wang D, Xiao Y. Effect of intravenous thrombolysis with alteplase on clinical efficacy, inflammatory factors, and neurological function in patients with acute cerebral infarction. *Brazilian journal of medical and biological research.* 2021;54(5).
- [6] *N Engl J Med*, The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke 333 (1995), pp. 1581-1587.
- [7] Yarbrough CK, Ong CJ, Beyer AB, Lipsey K, Derdeyn CP. Endovascular Thrombectomy for Anterior Circulation Stroke: Systematic Review and Meta-Analysis. *Stroke* (1970). 2015;46(11):3177–83.