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Overview on Strokes

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Abstract

Stroke is sudden death of brain cells due to lack of oxygen due to blood supply blockage or rupture of arteries of the brain. WHO indicates Stroke as the second leading cause for global mortality. Stroke is categorised into subtypes based on aetiology, assisting treatment evaluation.

Risk factors for stroke are age, race, heredity, hypertension, diabetes, smoking, alcohol consumption, obesity, cholesterol. Prevention methods involve lifestyle modifications, low cholesterol diet, physical activity, minimising risk factors like cigarette smoking and alcohol consumption.

Pharmacological treatments for hypertension, diabetes and interventional procedures are suggested. The prognosis depends on type extent, severity, duration of stroke and co-morbid risk factors.

Timely management of stroke, pre-hospital stroke care minimise mortality rate and enhances survival rates. Life style modifications, decrease the recurrence, thereby decrease the economic burden of stroke.

Keywords: Stroke, Pathophysiology of Stroke, Classification of Stroke, Risk Factors of Stroke, Treatment of Stroke.

1. Introduction

Stroke is focal neurological deficit, due to vascular lesion, for more than 24 hours. The blood vessel ruptures or blocked by clot, thereby the oxygen, nutrient supply is cut, causing damage to the brain tissue. The symptoms of stroke include numbness of parts or one half of the body, fainting, loss of balance, difficulty in walking, seeing, speaking or understanding and headache with no known cause. Depending on severity and part of brain affected, stroke can lead to sudden death [1].

Stroke with 5 million deaths a year (second cause of death); 15 million people suffer stroke annually, of whom one third suffer morbidity. Stroke is biggest cause of disability in United Kingdom, WHO estimates stroke events due to demographic changes in Iceland, Norway, and Switzerland to increase by 0.4 million/year(by 2025) from the present 1.1 million/year (2000). Globally stroke burden is predicted to rise from 38 million DALYs (Disability-adjusted life years) in 1990 to 61 million DALYs in thirty years. The incidence of stroke declined in developing countries due to control of risk factors like blood pressure and reduced levels of smoking; whereas absolute number of strokes rise, due to an aging population [2–5].

2. Pathophysiology

2.1 Types of Stroke

There are different types of stroke depending on pathophysiology of the stroke.

Ischemic strokes: due to occlusion of a major cerebral artery, most commonly middle cerebral artery, by thrombus or embolism; hypotension, haemorrhage resulting from burst of blood vessel either within or on the brain's surface.

Chronic infections: Clinical research and epidemiological studies suggest multiple exposures affecting carotid arteries are associated with risk of stroke, pathogenesis atherosclerosis and progression to plaque thrombosis and rupture [8].

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Deposition of atherosclerotic plaque and its subsequent rupture result in ischemia. Plaques with more lipids, localised eccentrically in the intima, are prone to rupture. The macrophages by depositing enzymes and toxic metabolites facilitate rupture. Subsequently plaque area is prone to thrombus formation by platelets activation. Further the release of vasoactive substances, increase myocardial oxygen demand; arterial spasm contributes to thrombotic occlusion leading to ischemia. As a result of thrombotic occlusion lacunar infracts are formed contribute to stroke depending on other risk factors like diabetes, hypertension and ethnicity [9, 10].

2.2 Embolic Stroke

Emboli result from atheromatous plaque (carotid, vertebrobasilar arteries), or cardiac mural thrombi resulting from myocardial infarction or atrial fibrillation. These result in embolic stroke [1].

Air embolization occurs in procedures during neurosurgy, otolaryngology, anesthesia, central venous catheterization or from injuries and in case of divers [10].

2.3 Hypotensive Stroke

Occurs due to decrease in arterial pressure or regional haemodynamic changes, due to vessel stenosis. The areas/arteries affected to the with less or marginal blood supply are parietal-temporal-occipital triangle at the junction of the anterior, middle and posterior cerebral arteries, Watershed infarcts make up approximately 10% of all ischemic strokes, majority, around 40% of these occur in patients with carotid stenosis or occlusion [10].

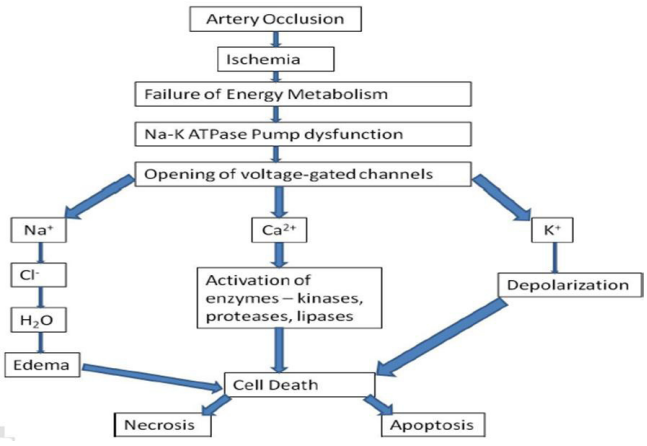

Figure 1. Pathophysiology of stroke, events leading to cell death are shown in the flow chart. [14]

Rare causes of stroke: changes in blood coagulability, vasospasm, vasculitis or artery dissection [1, 6, 7].

3. Risk Factors

Risk factors can be categorised as modifiable and non modifiable risk factors.

3.1 Non modifiable Risk Factors

These risk factors cannot be modified but aids treatment in identifying those with greatest risk. The non modifiable risk factors include Age, Gender, Race, Ethnicity [1, 10–12].

Age: Is the prime, single risk factor. The stroke rate doubles for every successive age of 10 years after age 55 in both sexes; while stroke incidence are more predominant in males; the mortality rate in male per year is more than female population, as women tend to live longer than males [1, 10–12].

Heredity: Offspring analysis study revealed that both the maternal and paternal histories of stroke are associated with increased risk of stroke [1, 10–12].

Race: The mortality and incidence rates for stroke vary in different racial groups. National Health and Nutrition Examination Survey in USA revealed that the mortality rates are twice in Black Americans compared to White Americans; in age [45–55] is as much as four times higher and differences decreases as age progresses. Epidemiological studies indicate stroke death rates were similar in Hispanics and whites less than 65, but lower in those above 65. Also among the age group of 45 to 65, half of the stroke risk racial disparity is attributed to traditional risk factors like systolic blood pressure and socioeconomic factors. The incidence rates of stroke are comparatively high in Asian population (China and Japan) [1, 10–13].

3.2 Modifiable Risk Factors

Atrial fibrillation, while hypertension, Diabetes Mellitus, hyperlipedemia, smoking are major risk factors for thromboembolic stroke.

The major modifiable risk factors for stroke include Hypertension, diabetes mellitus, factors (physical activity, obesity, diet,) oral contraceptives, homocystiene, Haemostatic and Inflammatory Factors, Asymptomatic Carotid Stenosis, Transient Ischemic Attacks, Risk Factors for Recurrent Ischemia, Factors for Intracerebral and Subarachnoid Haemorrhage, Multiple risk factors. cigarette smoking, hyperlipidaemia, Cardiac Disease, alcohol, illicit

drug use, life style. The impact of these risk factors are summarised as follows [1, 11].

Hypertension: Hypertension is considered the most important single modifiable risk factor for ischemic stroke. It is a potent risk factor for Intracerebral haemorrhagic stroke (15) Relative Risk [RR] for stroke increases- from 0.5 to 4-with level of Hypertension [HTN] increasing from normal to moderate and severe HTN.

Cardiac Diseases: Cardiac diseases like Atrial fibrillation [AF], cardiac valve abnormalities (Mitral valve stenosis, mitral annular calcification) are predominant risk factors. Valvular strands are risk factors for ischemic stroke, Left atrial enlargement, cardiac structural abnormalities(patent foramen ovale (PFO) and atrial septal aneurysm (ASA) increase the riskfor embolic stroke.

Diabetes: Diabetes increases risk of ischaemic stroke and all other subtypes of stroke but has a minimal effect on Intracerebral haemorrhagic stroke. Hyperinsulinemia and insulin resistance are factors for stroke for people with normal levels of glucose [11, 15].

Smoking: Smoking cigarettes doubles the relative risk of ischemic stroke. Response in association with number of cigarettes smoked per day was more for Ischemic stroke than intercerebral haemmoragic stroke [11, 15].

Illicit Drug Use: Illicit substances abuse like Cocaine, heroin, amphetamines, Lysergic acid diethylamide, Phencyclidine, Pentazocine, tripelennamine, and marijuana are associated with stroke [11].

Alcohol: Increase in consumption of alcohol causes brain haemorrhage. Moderate consumption leads to reduced risk of stroke. Consumption of alcohol has a J-shaped association with ischemic stroke [11, 15].

In a Case control study involving 22 countries across the world, among middle and low income, suggests at least ten factors associated with 90%, the risk of stroke. This study also indicated that a targeted intervention of reducible risk factors like blood pressure, smoking, promotion of physical activity and a healthy diet, could substantially decrease the resulting economic burden due to stroke [15].

Classification and analysis of subtypes of stroke is essential for evaluation of prognosis of patients, their clinical treatment, and clinical studies, this subtype classification assists in evaluating recent therapeutic strategies, and evolving concepts of stroke definitions and mechanisms [16–18].

4. Classifications

4.1 TOAST Classification

The aetiology of ischemic stroke affects its prognosis, outcome and assists in management. A methodology for classification of subtypes of ischemic stroke mainly based on etiology has been developed for the Trial of Org 10172 in Acute Stroke Treatment (TOAST). Subtypes according to this classification are five subtypes of ischemic stroke that are: Large-artery atherosclerosis (LAA), cardioembolism (CE), Small-vessel/arteryocclusion (SAO), Stroke of other determined etiology (OC), and Stroke of undetermined etiology (UND) [16, 17].

4.2 ASCO Phenotypic Classification

The ASCO Classification categorises Stroke into four phenotypes using different grades for different stroke subtypes. The different Phenotypes according to ASCO include atherosclerosis (A), small vessel disease (S), cardiac source (C), and other cause (O). The different grades assigned are 1 when the potential cause of index stroke is definite, 2 for uncertain casuality, 3 when presence of phenotype and uncertain casuality 0 when disease is absent completely, 9 when there is no possibility of grading due to insufficient work up. The scores obtained by this system are based on levels of diagnostic evidence-: A-direct demonstration by gold standard diagnostic tests, B-indirect evidence or less sensitive specific tests, C- weak or absence of specific tests [18].

5. Current Prevention Methods

The primary stroke is the initial stroke and the secondary stroke is the subsequent strokes. Transient ischemic stroke [TIA] is a risk factors for secondary stroke.

Primary stroke prevention includes lowering blood pressure, anti-diabetic therapy, antiplatelet therapy, antithrombotic therapy for atrial fibrillation, life style modification (increasing physical activity, cessation of alcohol and cigarette smoking), Diet modification for lowering lipids.

Secondary stroke prevention includes lowering blood pressure, anti-diabetic therapy, treatment with an angiotensin-converting enzyme inhibitor (ACEI) , angiotensin receptor blocker (ARB)), antiplatelet therapy (aspirin, clopidogrel, and aspirin plus extended-release dipyridamole (ER-DP) are used in antiplatelet therapy), antithrombotic therapy in cardio embolic strokes, life style modification (increasing physical activity, cessation of alcohol and

cigarette smoking), Diet modification for lowering lipids, Endovascular or surgical treatment in extracranial or intracranial carotid or vertebral artery disease. Warfarin is used to treat patients with cardio embolic stroke with Atrial fibrillation [19–22].

6. Treatment Methods

6.1 Non-interventional Approaches

Time management is crucial in treatment of stroke. Pre-hospital and in-hospital time delays in evaluation and treatment of stroke are to be minimised. Early notification would reduce inter-hospital delays, diagnostic or imaging procedural times. A possible suggestion to reduce pre-hospital delays is a aetiology specific treatment is to be followed at the emergency site. The first inline effective treatments is administering thrombolytic agent [tissue plasminogen activator (t-PA)], this reduces the brain tissue damage and has to be given within first few hours after stroke. A structured pre-hospital stroke care approach followed prior to hospitalisation after onset of stroke ensures survival rate, and through this structured approach prioritisation of shifting patients to specialised stroke care units will minimise in-hospital delay times. A thorough synchronisation of various professionals involved (paramedics, dispatchers, nurses, emergency physicians) for effective treatment of stroke can reduce the economic burden of stroke [23–27].

6.2 Interventional Approaches

In patients with recent non-disabling strokes or TIA (Transient Ischemic Attacks) and a very high grade of stenosis carotid endarterectomy was found to be beneficial and would reduce the risk of subsequent ipsilateral cerebral ischemia and this technique requires exceptional surgical skills to avoid the risk factors involved [28–31].

7. Antihypertensive Therapy

Hypertension is the prime risk factor for stroke. Pharmacological treatment of hypertension and life style modification would prevent strokes and recurrence of TIA. The proposed drug regimen include thiazide diuretics, BBs, ACEIs, and ARBs, β-adrenergic receptor blockers, and calcium channel blockers, Nitrendipine, are beneficial in reducing cardiovascular events and stroke incidence in patients with hypertension and diabetes. Thiazide diuretics were found to be more effective in antihypertensive therapy [32–35].

7.1 Lipid/cholesterol Lowering Therapy

Along with diet and life style modifications the recommended drug therapy is use of statins proved effective in treatment of patients with known Coronary Heart Diseases. Niacin, gemfibrozil reduces incidence of stroke in men with known Coronary Heart Diseases and low HDL/LDL cholesterol [36, 37].

Obesity: Prospective studies indicated weight reduction and maintaining BMI between 18.5 and 24.9 kg/m^2 and a waist circumference of <35 for women and <40 for men is recommended for overweight Ischemic patients and patients with TIA to prevent recurrence of stroke [38, 39].

7.2 Physical Activity

Physical activity decreases incidence of stroke and other coronary heart diseases. Life style modification activities like increasing physical activity will minimise pharmacological and medical interventions. Physical activity will reduce weight, blood pressure, improves glucose tolerance and enhances vasodilation [40–44].

Anticoagulants: In patients with Ischemic stroke or TIA with paroxysmal (intermittent) AF, anticoagulation with adjusted-dose warfarin and for the patients who cannot take oral anticoagulants aspirin is recommended [45–47].

7.3 Antiplatelet Therapy

In Patients with ischemic stroke or TIA with mitral valve prolapse antiplatelet therapy is reasonable. For patients who develop Intra Cerebral Haemorrhage, SubArachanoid Haemorrhage, or subdural hematoma, all anticoagulants and antiplatelet should be discontinued during the acute period for at least 1 to 2 weeks after the haemorrhage, and the anticoagulant effect should be reversed immediately with appropriate agents. For patients who require anticoagulation soon after a cerebral haemorrhage, intravenous heparin may be safer than oral anticoagulation. Oral anticoagulants may be resumed after 3 to 4 weeks, with rigorous monitoring [33, 48–53].

In patients with extra cranial vertebral artery stenosis and recurrent vertebrobasilar TIA and strokes occurring in spite of pharmacological therapy, Surgical revascularisation procedures are performed [32, 33].

8. Prognosis

Ischemic strokes have better survival rates than haemorrhagic strokes, but the recovery time is more in haemorrhagic strokes than ischemic strokes, the severity and outcome of stroke depends on extent and location of damage on the brain, duration and severity of stroke [54].

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