Management of stroke

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Abstract

Stroke continues to be associated with high mortality and disability rates, posing a great burden on society.

Recognition and modulation of stroke risk factors have allowed its management to evolve from rehabilitation to prevention.

Maximizing the benefit of acute thrombolysis imposes a more efficient practice. Multiple studies have addressed the role of decompressive craniectomy, revascularization, recanalization, carotid stenosis treatment, haematoma evacuation, the role of intraventricular thrombolysis and the use of minimally invasive techniques in stroke treatment. Although some techniques have been proven beneficial, others are still in need of properly designed trials to assess their impact in stroke outcomes.

Keywords Craniectomy; endarterectomy; haemorrhagic; ischaemic; stroke

Introduction

Incidence and burden

Cardiovascular disease continues to rank highest in population-based mortality indicators on the impact on society of any specific disease. Performances such as *years of life lost* measured in the UK in 2010, where stroke ranked third only to ischaemic heart disease and lung cancer, reflect the magnitude of the burden of this preventable disease.[1]

The Global Burden of Diseases, Injuries and Risk Factors Study 2010 found stroke to be the world's second most common cause of death. From 1990 to 2010, the age-standardized incidence of stroke significantly decreased by 12% in high-income countries and appears to have shown an increasing trend in low-income countries. In 2010, the absolute number of people with a first stroke (16.9 million), stroke survivors (33 million), stroke-related deaths (5.9 million) and *disability adjusted life-years* lost (102 million) had significantly increased since 1990, with most of the burden originating from low-income and middle-income countries.[2]

Stroke units

'Time Is Brain':

> *"Compared with the normal rate of neuron loss in the ageing brain, the ischemic brain ages 3.6 years each hour without treatment."*[3]

Multidisciplinary care within dedicated stroke units is known to reduce mortality and disability independently of age, sex and stroke severity.

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With the introduction of reperfusion therapy, stroke management has evolved from rehabilitation to emergent, posing greater attention on shortening pre-hospital delay. Accurate clinical recognition reinforcing public awareness and medical staff training, rapid means of transport to designated stroke centres and bridging therapies initiated on site with a mobile stroke unit concept could significantly increase the dismaying only 8% of patients who are currently eligible for intravenous thrombolytic treatment.

A New York state-wide large observational study comparing mortality for patients admitted with acute ischaemic stroke at designated stroke centres and non-designated hospitals, found the former carried lower 30-day all-cause mortality, reduced 1-day and 1-year follow-up stroke-specific mortality and allowed for a higher rate of thrombolytic therapy.[4]

In 2010, a metropolitan, centralized model with a small number of high-volume specialist centres for acute stroke management capable of providing hyper-acute care in the first 72 hours was introduced in London. This concept appears to have increased the rate of intravenous thrombolysis treatment from 5% to 12% of all stroke patients, reduced fatality while decreasing the 90-day cost per patient, predominantly as a result of shorter length of hospital stay.[5]

Primary prevention

Modifiable risk factors

Ischaemic stroke is a known preventable cause of disability and death.

Realizing that three-quarters of all strokes are first-time events, understanding the natural history of such devastating disease and appreciating the entailed individual and global public health burden reinforce primary prevention with modulation of risk factors. Risk factor assessment tools predictive of stroke have been developed, and although consensually helpful, none are without inherent limitations in predicting the multivariate influence of contributors. Ageing, black ethnicity and genetic influence are accountable for non-modifiable factors contributing to cerebrovascular events. Transient ischaemic attack is widely regarded as a sign of impending stroke; as such, its occurrence must be regarded as an opportunity for stroke prevention.

On the other hand, lifestyle modification with physical activity and a healthy diet have acknowledged direct benefit and are recommended to all individuals; weight reduction is indicated when body mass index (BMI) is above 25 kg/m^2.

In 2010, the two leading risk factors for global disease burden were high blood pressure and tobacco smoking. In hypertensive patients medication should target blood pressure values to under 140/90 mmHg, an aim which holds true amongst diabetics. Smoking should be strongly discouraged and alcohol consumption should be eliminated or reduced; drug abuse, particularly cocaine and amphetamines, should be ceased and its addiction treated accordingly.

Asymptomatic stenosis

The prevalence of severe asymptomatic carotid stenosis may be as high as 3%.[6]

Multiple studies have established the relationship between atherosclerotic disease of the extracranial internal carotid,

carotid bulb and vertebral arteries and both transient cerebrovascular ischaemia and stroke.

Not forgetful of the protective roles of intracranial collateral circulation through a fully developed circle of Willis and the presence of leptomeningeal supply, contributive mechanisms of carotid atherosclerotic disease to ischaemic events include: artery-to-artery embolism of thrombus originated within the plaque; plaque rupture with acute occlusion; atheroembolism of crystals; and the recognition of a degree of stenosis beyond which there is a pressure drop, a flow reduction, or both, with resulting reduced cerebral perfusion; stenosis 60% or higher are estimated to carry such haemodynamic burden.

Currently there is no indication to screen the general population. There are even those who argue against identifying carotid stenosis in those with no prior history of anterior territory transient attack or stroke.

Management

Carotid endarterectomy: although preceded by many retrospective and observational studies, the existing guidelines on management of asymptomatic carotid artery stenosis arose originally from the *Asymptomatic Carotid Atherosclerosis Study* (ACAS) published in 1995. This controlled clinical trial randomly assigned patients with asymptomatic carotid stenosis of 60% or higher (NASCET method) to either the association of aspirin (the role of newer antiplatelet drugs was not yet proven) and risk factor control (limited to blood pressure and diabetes) or the above in association with carotid endarterectomy (CEA). The end points were perioperative stroke or death and ipsilateral ischaemia thereafter. The trial ended before completion with an advantage of the CEA group, yielding an aggregate risk over 5 years for ipsilateral stroke and any perioperative stroke or death, estimated in 5.1% in the surgical versus 11% in the medically only treated group (RR reduction of 53%). The calculated perioperative stroke morbidity and overall mortality was 2.3%.[7]

Published in 2004, the Medical Research Council of Great Britain *Asymptomatic Carotid Surgery Trial* (ACST) randomized asymptomatic patients with carotid artery stenosis of 70% or higher to immediate CEA versus indefinite deferral of the procedure. Primary outcomes were perioperative stroke, myocardial infarct or death and non-perioperative stroke. Perioperative stroke or death in either group was 3.1%. The 5-year risk was calculated in 6.4% for the immediate surgery group and almost doubled (11.8%) in the deferred CEA group for any stroke or peri-operative death.[8]

Interestingly, although the ACST overall supported the ACAS results despite its more inclusive end points, neither study was able to show an increase in surgical benefit with greater degrees of stenosis within the range of 60–99%.

Carotid stenting: the meta-analysis of short-term and long-term outcomes of carotid artery stenting (CAS) versus CEA published in 2011 pooled outcomes of several randomized trials in asymptomatic and symptomatic carotid disease. The inclusion of SPACE,[9] CREST,[10] CAVATAS[11] and EVA-3S[12] showed significantly less frequent long-term stroke events after CEA. Although confirming a higher risk for peri-procedural cranial nerve injury and myocardial infarction, the outcomes of CEA seemed superior to CAS, although in certain younger patient subgroups might be equivalent.

Types of stroke and their management

Cerebral

Ischaemic: stroke should be considered in the presence of an acute neurologic deficit or altered level of consciousness. Common clinical presentation may course with nausea, vomiting or headache and include abrupt onset of facial, mono- or hemiparesis, hemisensory deficit, mono- or bi-nocular visual loss, visual field defect, aphasia or dysarthria.

Physical examination aims to: detect extracranial causes of stroke symptoms; distinguish stroke from stroke mimics (found in 19–30%); document degree of deficit for adequate follow-up commonly using the National Institutes of Health Stroke Scale (NIHSS); establish a topographic diagnosis; identify comorbidities such as polycythaemia rubra vera, thrombotic thrombocytopenic purpura, coagulopathies, heavy protein diseases, and any conditions that may influence treatment decisions.

In 1991, the *Oxfordshire Community Stroke Project* (OCSP) proposed a classification into four subtypes of cerebral infarction capable of predicting prognosis, based solely on presenting signs and symptoms.[13] The *Trial of Org 10172 in Acute Stroke Treatment* (TOAST) method was develop to classify ischaemic stroke into specific subtypes based on the mechanism of infarction[14] – Table 1.

Emergent non-contrast CT scan is essential when considering the diagnosis of stroke and to rule out the presence of haemorrhage.

Ischaemic stroke courses with focal cerebral hypoperfusion of the affected vascular territory. Most importantly, perfusion parameters can be used to differentiate irreversible, infarct core from ischaemic penumbra, an area with enough hypoperfusion to cause neuronal dysfunction but still salvageable if blood supply is promptly restored with targeted treatment. Currently, CT perfusion (CTP) and MR perfusion (MRP) are two perfusion approaches with good application, with the former holding the advantage of rapidity and accessibility in the emergency setting. Perfusion-weighted image (PWI) was thought to represent ischaemic penumbra, whereas DWI-lesions identified the ischaemic core, with the resulting PWI/DWI mismatch representing salvageable tissue. There are now sufficient data to support paradigm shift with insights that the mismatch does not optimally define penumbra and visible zone of perfusion abnormality overestimates penumbra by including regions of benign oligaemia.

Technological advances have allowed for determination of cerebral blood flow (CBF) with Xe-CT, infrared spectroscopy MRI in response to acetazolamide challenge test or positron emission tomography scan to measure oxygen extraction fraction.[15]

Management

Medical

'Time Is Brain':

"The typical patient loses 1.9 million neurons each minute in which stroke is untreated."[3]

Salvage of penumbra is known to significantly reduce fatality rates and proportion of dependants at 3–6 months after stroke. Intravenous thrombolytic therapy with recombinant tissue

