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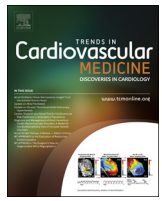

Acute stroke therapy: A review

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ABSTRACT

This review summarizes the modern early diagnosis and acute phase treatment of acute stroke. The guidelines for treatment of acute ischemic stroke underwent major changes in 2015 and endovascular therapy (catheter-based mechanical thrombectomy with a stent retriever) became the class IA indication for patients presenting within less than 6 h from symptom onset who have proven occlusion of large intracerebral artery in anterior circulation. Acute stroke care organization should enable to perform effective revascularization therapy as soon as possible after the initial brain imaging whenever this examination provides indication for the procedure.

Key words: Acute stroke, Intravenous thrombolysis, Mechanical thrombectomy, Stent retriever.

Introduction

Despite significant progress in the treatment strategies in the past 2 decades, stroke still remains the most common cause of disability worldwide and is responsible for the third largest number of deaths. Even with improving care and better stroke organization, a proportion of patients die or are left with significant neurological and cognitive disability.

This review aims to summarize the treatment approach to acute stroke patients mostly dealing with acute pharmacotherapy and/or surgery. An important note is devoted to mechanical thrombectomy for acute ischemic stroke with large artery occlusion.

Epidemiology

According to the recent data from European countries (including post–soviet republics), stroke is responsible for more than 1 million deaths annually and, of those, 15% prematurely, before age of 65 years [1]. Stroke mortality rate decreased in the world from 1990 to 2010 by 37% in high-income countries and by 22% in low-income countries. Globally, in 2010, the incidence-to-mortality ratio was 0.35 [2]. Incidence of ischemic stroke is higher in men in all age bands, though this difference tends to even out after the age of 75 years. There was also very little sex difference for stroke detected in the age band up to 35 years due to a specific combination of risk factors in young women. In contrast, subarachnoid hemorrhage more frequently afflicts women, although this difference is not statistically significant. Most population studies did not find a significant sex difference in intracerebral hemorrhage incidence.

Risk factors

Systematic evaluation in the general population determined the impact of major risk factors on stroke occurrence [3]. Arterial hypertension represents an odds ratio (OR) of 1.6–4.2 in dependence on sex and age. Permanently increased blood pressure impacts remodeling of vessel walls that results in atherosclerosis in large arteries and arteriosclerosis and lipohyalinosis in small cerebral vessels. Consequent arterial

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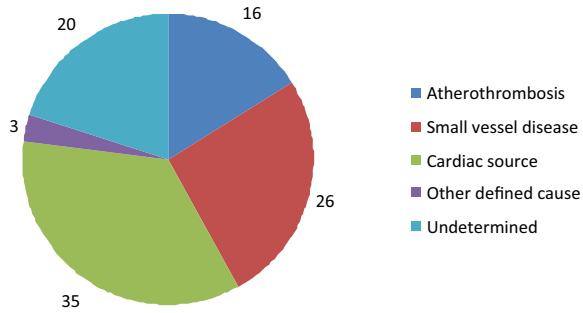
stiffness impairs autoregulation of cerebral hemodynamics. Diabetes (OR = 1.7–2.8) promotes endothelial dysfunction and thus also affects cerebro-vascular autoregulation. Hyperlipidemia (OR = 1.2–1.6) and smoking (OR = 1.7–2.6) are involved in formation of atherosclerotic changes. Atrial fibrillation (AF) is an independent risk factor for ischemic stroke and is being recognized more and more frequently as the main risk factor. Its relative risk depends on the $CHADS_2$ score. Besides, 30–35% of ischemic stroke patients with known AF, an additional 10–20% of cryptogenic stroke patients may suffer from paroxysmal AF as an etiologic factor. Observational trials clearly demonstrated that the chance of paroxysmal AF detection increases with the duration of ECG monitoring [4,5].

The specific combination of smoking, migraine, and oral contraception gives rise to a 35-fold increase of ischemic stroke incidence among young women. Elevated fasting homocysteine increases risk of stroke onset, supplementation by folic acid reduces the risk of stroke occurrence among hypertensive patients [6]. Prothrombotic conditions like antiphosphopholipid syndrome or mutation of Leiden's factor may explain the onset of ischemic stroke in young individuals. Several genes have been identified to associate with specific stroke subtypes (e.g., CADASIL, Fabry disease, and MELAS) or interfere with the vascular risk factors. However, apart from the abovementioned monogenic disorders, the current genomic technology is unlikely to improve assessment of stroke risk profile [7].

Pathophysiology of stroke

In cerebral ischemia, inadequate cerebral perfusion results in irreversible structural changes in a specific vascular territory. Hypoperfusion is usually a consequence of supplying artery obliteration. A less frequent pathogenetic mechanism is hemodynamic stroke with insufficient perfusion in the distal part of the cerebral vascular tree (watershed infarcts) due to insufficient collateral flow in proximal artery occlusion or due to systemic circulation collapse. In the zone referred as the ischemic core where the flow is lower than 10 ml/100 g of tissue/min, cellular metabolic breakdown leads to influx of calcium ions and intracellular increase of water content. This is called cytotoxic edema and occurs very early in cerebral ischemia. Neurons, as well as supporting glial cells, subsequently undergo necrosis. Ischemic disruption of the blood–brain barrier enables protein and water to flood into the extracellular space, which leads to vasogenic edema. The surrounded area where the flow is lower than 25 ml/100 g tissue/min called penumbra is potentially salvageable if sufficient perfusion is restored in a timely manner. Ischemic stroke is a heterogeneous disorder with various clinical symptoms and different causes. The Graph shows the proportion of main stroke subtypes [8]. Most frequently, the blood clot in the intracerebral artery is of embolic origin—(1) either cardiac embolization (atrial fibrillation or flutter, valvular disease including prosthetic valves, infective endocarditis, left ventricular thrombi, atrial septal aneurysms, paradoxical embolization in atrial septal defect or patent foramen ovale, etc.) or (2) distal embolization from ulcerated plaque in carotid or vertebral arteries or in the thoracic aorta. Less frequently, ischemic stroke is caused by intracerebral



Graph – Proportion of ischemic stroke subtypes (in %) according to the etiology.

atherosclerotic stenosis with in situ thrombosis or by arterial dissection. In up to one-third of ischemic strokes, despite extensive and sophisticated examinations, no cause is found.

Acute stroke care organization

Experience with the revascularization procedures emphasizes time as a principal factor for the prediction of clinical outcome. Organizing prehospitalization care is essential to minimize the delay of therapy initiation. Transport to the closest primary stroke center or comprehensive stroke center should be immediate and rapid. It may even involve air medical transport. Implementation of the guidelines for acute care organization shortens the course of procedures in the acute phase of stroke and may improve the patient's outcome (Table 1) [9]. In patients with moderate or severe clinical deficit (NIHSS > 8), performing of vascular intracerebral imaging is advocated to select the subjects with large-vessel occlusion. In such instances, it is recommended to transfer the patient to a center where it is feasible to carry out endovascular treatment. The secondary transport should not postpone the administration of fibrinolysis.

Initial acute clinical examination by a trained neurologist evaluates the level of consciousness and looks for focal neurologic signs. Assessment of the neurological-deficit degree using the National Institute of Health Stroke Scale (NIHSS) scale correlates with the site of arterial obliteration. Patients with occlusion of main intracerebral artery only very rarely present a deficit with NIHSS lower than 10 points. Reliability of the clinical diagnosis of vascular territory (carotid versus vertebrobasilar) is only moderate [10]. Oculomotor and visual symptoms are the most sensitive indicators of posterior circulation stroke. Clinical examination is insensitive to distinguish between ischemic and hemorrhagic stroke, though the latter initially presents more frequently headache, signs of intracranial hypertension, and sudden impairment of consciousness.

Neuroimaging

CT scan is, since the institution of thrombolytic reperfusion therapy, an integral component of acute stroke diagnostics. It is widely available, fast, and has excellent sensitivity for the detection of acute intracranial hemorrhage. Brain CT is also useful for the detection of early ischemic changes (EIC). These