

Stroke: causes and clinical features

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Abstract

Stroke is a clinical syndrome rather than a specific disease. This article reviews risk factors for stroke, and the different pathologies that can cause stroke. Approximately 20% of strokes are due to cerebral haemorrhage, most of which is intracerebral, with a significant minority caused by subarachnoid haemorrhage. The remaining 80% are ischaemic, including large artery disease, cardioembolic and small vessel disease. Differentiation of cerebral ischaemia from haemorrhage is impossible without brain imaging. Assessment of a patient with ischaemic stroke requires knowledge of the cerebral arterial supply and cerebral anatomy to differentiate anterior and posterior territory involvement.

Keywords Brain imaging; cerebral haemorrhage; cerebral infarction; cerebrovascular disease; pathogenesis; risk factors; stroke; transient ischaemic attack

Introduction

Each year over 17 million people worldwide suffer a stroke, with 5 million left significantly disabled; an estimated 34 million people worldwide are living with the effects of stroke.¹ In the UK and USA, stroke is the third most common cause of death (>60,000 and 160,000 deaths per annum, respectively) and the leading cause of adult disability. Its incidence rises exponentially with age, and about 25% of men and 20% of women who live to 85 years of age can expect to suffer a stroke.

The incidence of stroke is falling in some developed countries (e.g. by 19% from 1990 to 2010 in the UK), but rising in less developed countries, and it is more common in the elderly, who comprise a higher portion of the population in developed countries. This means that the impact of stroke is increasing. A recent study on global burden of stroke between 1990 and 2010 reported a 25% increase in stroke in individuals aged 20–64 years, 113% rise in prevalence of stroke survivors, 70% increase in all strokes and 36% increase in number of deaths caused by stroke. Over 60% of global stroke occurs in people aged <75 years.

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Key points

- Stroke is a syndrome, not a specific disease
- It is caused by many different pathologies, some of which require specific treatment
- All result in usually sudden-onset focal loss of neurological function
- About 80% of strokes are caused by primary cerebral ischaemia, and 20% by cerebral haemorrhage
- A large number of risk factors, many modifiable, increase stroke risk

The National Audit Office report in 2005 found that stroke costs the UK National Health Service (NHS) and economy about £7 billion a year: £2.8 billion in direct costs to the NHS, £2.4 billion in informal care costs (e.g. costs of home nursing borne by patients' families) and £1.8 billion in income lost to productivity and disability.² Therefore preventive treatments with relative modest benefits in individual patients can have a major effect on public health and healthcare costs.

Stroke and cerebrovascular disease is the second leading cause of dementia, and there is increasing evidence that coexisting cerebrovascular increases the risk that someone with Alzheimer's disease pathology will develop clinical dementia. Stroke is also the most common cause of epilepsy in the elderly.

Definitions

Stroke

Stroke is a clinical syndrome characterized by the rapid onset of focal neurological signs, lasting >24 hours or leading to death, with a presumed vascular cause (infarction and/or haemorrhage). Stroke results from a number of different diseases and processes that all cause a sudden-onset disruption of blood supply to a particular part of the brain. About 80% are caused by primary cerebral ischaemia resulting in infarction, while 20% are due to cerebral haemorrhage with intracerebral haemorrhage being much more common than stroke due to subarachnoid haemorrhage (SAH). The subtypes of ischaemic stroke and intracerebral haemorrhage contain multiple pathologies, which may have different risk factor profiles and different treatments.

Transient ischaemic attack (TIA)

TIA has the same definition as stroke except that symptoms last <24 hours. Imaging studies show that patients with TIA frequently suffer cerebral infarction despite complete clinical recovery, particularly when symptoms last hours rather than minutes. This suggests a pathophysiological continuum with stroke, and there are calls for a change in the definition – either to exclude these patients and call this a stroke, or to reduce the duration of symptoms in the definition of a TIA.

Cerebrovascular disease

Cerebrovascular disease includes stroke and other diseases of the blood vessels of the brain, such as vascular dementia. It can be asymptomatic or subclinical (e.g. asymptomatic carotid stenosis or periventricular small vessel disease).

Risk factors

Most epidemiological studies, including prospective ones, which provide the most robust data, have been unable to differentiate risk factors for stroke caused by haemorrhage or infarction, let alone different ischaemic stroke subtypes. Most risk factor data therefore apply to the stroke syndrome as a whole.

Age

Age is the strongest risk factor for both cerebral infarction and primary intracerebral haemorrhage. The risk of stroke in people aged 75–84 years is 25 times the risk for age 45–54 years.

Sex

Male sex is a risk factor for stroke but, because of their greater life expectancy, more women suffer a stroke.

Blood pressure

Increasing blood pressure is a major risk factor for stroke and is strongly and independently associated with both ischaemic and haemorrhagic strokes. The relationship between diastolic blood pressure and subsequent stroke is log-linear throughout the normal range. There is no apparent threshold below which the risk of stroke becomes stable, at least not over the normal range of blood pressure. The increase in stroke risk almost doubles with each 7.5 mmHg increase in diastolic blood pressure. Systolic blood pressure is also a risk factor for stroke. The causal nature of the relationship is strongly supported by randomized controlled trials, demonstrating that stroke can be prevented by treating blood pressure, even at 'normal' blood pressure levels.

Smoking

Cigarette smoking doubles the risk of stroke.

Diabetes mellitus

Diabetes also doubles the risk of stroke. It is a risk factor for both carotid atherosclerosis and large vessel disease.

Cholesterol

Increased total cholesterol and low-density lipoprotein cholesterol are strong risk factors for ischaemic heart disease, but the relationship to stroke appears weaker. However, recent data have shown a relationship with ischaemic stroke, which may be partly obscured because of a negative association with intracerebral haemorrhage. Treatment trials have shown that statin therapy reduces recurrent stroke risk in patients with stroke or TIA.

Body mass index and physical exercises

Increased body mass index is a risk factor for stroke, partly because of its association with other risk factors such as hypertension and diabetes. Cohort and case-control studies have demonstrated that lack of exercise is associated with increased risk of stroke.

Alcohol

Heavy alcohol consumption is a risk factor for stroke, particularly intracerebral haemorrhage, possibly by increasing blood pressure and predisposing to atrial fibrillation. Moderate alcohol consumption may protect against both ischaemic heart disease and stroke although the evidence is not all consistent.

Ethnicity

There is an increased incidence of stroke in African-Caribbean individuals in the UK and African-Americans compared with white individuals. Intracerebral haemorrhage and small vessel ischaemic stroke are particularly increased, which may relate partly to the increased prevalence and severity of hypertension. In the UK, South-Asian populations have a higher stroke mortality than white individuals, perhaps partly due to increased central obesity, insulin resistance and diabetes mellitus. There are differences in the distribution of stroke subtypes between ethnic groups: for example, intracranial disease is more common in Chinese than white European stroke patients.

Homocysteine

Very high concentrations of serum homocysteine, associated with the autosomal recessive condition homocystinuria, are associated with an increased risk of stroke and other arterial thrombosis at a young age. Increasing evidence has recently suggested that a moderately elevated serum homocysteine concentration is associated with stroke on a population basis. Raised serum homocysteine has been associated with endothelial dysfunction. However, randomized trials using B vitamins and folic acid to reduce serum homocysteine have had negative results, although a secondary analysis of the VITATOPS (VITamins TO Prevent Stroke) study suggested a possible effect in lacunar stroke. A recent large Chinese primary prevention study found vitamins taken to lower homocysteine reduced stroke risk in hypertensive patients.

Vascular disease elsewhere

Many cases of stroke result directly or indirectly from atherosclerotic disease, which also causes ischaemic heart and peripheral vascular disease. It is not surprising that other evidence of cardiovascular disease is a risk factor for stroke. Furthermore, some risk factors, such as hypertension, are risk factors for both stroke and systemic atheroma. An increased risk of stroke has been associated with the presence of ischaemic heart disease, peripheral vascular disease, cardiac failure and atrial fibrillation. The latter is an important, and potentially preventable, cause of stroke. Elderly individuals with atrial fibrillation have an annual stroke risk of $\geq 5\%$.

Other risk factors

Migraine, particularly migraine with aura, and the oral contraceptive pill (particularly oestrogen-containing preparations) are risk factors for stroke. Hormone replacement therapy appears to increase the risk, particularly soon after its initiation, perhaps by a prothrombotic mechanism. There is a link between inflammation, infection and stroke. Chronic infection and inflammation can predispose to atherosclerosis and stroke. A number of studies suggest acute infections can cause stroke. There is a strong association between socioeconomic status and stroke risk,

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