INTRODUCTION

Studies of the epidemiology of stroke have greatly improved over the past 20 years because of 1) the development of new technology that improved classification of specific types of stroke (1), 2) better therapies that have reduced case fatality (1), 3) prevention of stroke (i.e., antihypertensive drug therapy) (1), and 4) health insurance, especially Medicare. Stroke cases can now be classified in epidemiology studies by type. For example, in the Framingham Study, for men aged 55–84 years, 45 percent of strokes were classified as atherosclerotic, 19 percent as cerebral embolism, 5 percent as intracerebral hemorrhage, 4 percent as subarachnoid hemorrhage, 19 percent as transient ischemic attacks (TIAs), and 2 percent as other (2). Stroke cases can also be classified by whether the vascular disease is extracerebral, intercranial, or intracerebral.

DESCRIPTIVE EPIDEMIOLOGY

The reduction in stroke death rates has been one of the major contributions to the reduction in mortality during the last half of the 20th century (1, 3). The age-adjusted stroke mortality rate in the United States fell from 88.8 in 1950 to 26.6/100,000 from 1993–1995. The decline in stroke mortality affected all age, race, and sex groups in the United States (3). There has also been a very substantial decline in stroke mortality in other countries (4). The reasons for the decline in stroke mortality have not been explained fully by changes in risk factor effectiveness of treatment (i.e., the introduction of antihypertensive therapy) or decreased case fatality after a stroke. The decline in the United States began in the 1930s, prior to the introduction of antihypertensive therapy. The decline in stroke mortality has tended to flatten in recent years (3). The trends in incidence of stroke over time are difficult to evaluate because of the introduction of new diagnostic methods such as computerized tomography and magnetic resonance imaging (MRI). There has been an apparent decline in stroke incidence (6).

Mortality rates from stroke are much higher for Blacks than for Whites in United States, especially in younger age groups (7). The higher prevalence of hypertension and less effective use of drug therapy for hypertension probably accounts for much of the excess stroke mortality among Blacks. In the United States, stroke death rates are very strongly and inversely related to measures of socioeconomic class for both Blacks and Whites (7).


Increased potassium intake may have accounted in part for this decline in stroke mortality, possibly because of the greater availability of fruits and vegetables in the diet (9). An increase in animal protein and a decrease in salt intake may also be contributing to the decline in stroke mortality (10). A very low serum cholesterol level has been associated with an increased risk of stroke, both in Japan and in the United States (11, 12). In Japan, the low serum cholesterol levels were a strong risk factor for large intracerebral hemorrhage. Over time, the incidence of large intracerebral hemorrhage has declined in Japan, and the association of low cholesterol with stroke is also diminishing (12). Another possible, but also unproven, suggested association is that the increased use of antibiotic therapy has reduced the extent of kidney disease and associated risks of hypertensive disease and stroke. In the United States, there is still an inverse association between cholesterol levels and intracerebral hemorrhage and a direct association...
between serum cholesterol levels and cerebral infarction (13). The very low serum cholesterol levels may be a reflection of very low animal protein or inflammation rather than a part of the causal pathway in the risk of stroke. Reduction of blood cholesterol levels by drug therapies, such as statins, decreases the risk of stroke (14).

The sex difference in the risk of stroke (men compared with women) is much smaller than that for coronary artery disease (5, 8). Stroke rates appear to be higher in men in the younger age groups, but in older age groups, the incidence is about the same in men and women. The pathology of stroke includes disease in different vascular beds, such as intracranial and intracellular vessels. The sex difference in vascular pathology in these different beds is much less than that for atherosclerosis of the coronary arteries (15).

There is little or no increased risk of stroke among women taking current lower-dose oral contraceptives (16). Hormone replacement therapy does not appreciably reduce the risk of stroke among postmenopausal women. There is little increased risk of stroke during pregnancy (17). However, the risk of stroke is substantially increased during the immediate postpartum period, both by cerebral infarction and, especially, by cerebral hemorrhage. Young women (ages 18–44 years) with lupus have an increased risk of stroke compared with young women without lupus (18). Thrombosis related to antiphospholipid antibodies and small vessel disease may contribute to the higher risk of stroke (19).

In the United States, there have been consistently higher rates of stroke in the southeastern states since the 1930s (9). Studies in the 1960s documented that the differences among areas were not an artifact due to death certification practices. The incidence of stroke was also higher in the southeastern United States. The specific risk factors that explain this geographic variation have not been identified (20).

**RISK FACTORS**

Elevated blood pressure is the most important determinant of the risk of stroke due to hemorrhage and infarction. The risk is almost linear from relatively low levels of systolic and diastolic blood pressures (21). Factors that are associated with higher blood pressure, such as obesity, increased waist circumference, higher alcohol intake, greater sodium intake, etc., will be risk factors for stroke.

The decrease in blood pressure with drug therapy, rather than any specific type of antihypertensive drug therapy, appears to be the major determinant for reduction in the risk of stroke (22). Diabetes mellitus is a major risk factor for stroke. It is still not certain whether there is a linear relation between blood glucose or insulin levels and the risk of stroke (23). The combination of hypertension and diabetes, especially in older individuals, is associated with very high risk of stroke. Clinical trials have shown that reduction of blood pressure and lipid lowering will reduce the risk of stroke, but there is no evidence that reduction of blood glucose (by insulin or other drugs) reduces the risk of stroke (24). Cigarette smoking is also an important determinant of risk of stroke (25).

There is strong familial aggregation of stroke (26). The familial aggregation can be due to genetic or environmental factors related to stroke risk factors or to unique genetic determinants of stroke or cerebral vascular disease. There are genetic animal models of an increased risk of stroke that are not primarily due to elevated blood pressure or other risk factors (26).

The newer, noninvasive methods of measuring atherosclerosis have provided another approach to evaluating the risk of stroke (27). Increased carotid intima medial wall thickness and stenosis are associated with increased risks of both stroke and myocardial infarction, independent of traditional cardiovascular risk factors (28). Ankle brachial blood pressure (another measure of atherosclerosis) is also associated with an increased risk of stroke (29). Surgical therapy and endarterectomy for severe stenotic lesions in the carotid arteries reduce the risk of stroke (30).

A higher percentage of all nonhemorrhagic strokes than previously believed may be due to embolism (31). Potential sources of emboli include atherosclerotic plaques in the ascending aorta and the arch of the aorta. Thrombi in the left ventricle after a myocardial infarction may also be an important source of emboli. Individuals who have had a myocardial infarction have a higher risk of stroke, especially shortly after the myocardial infarction (1).

Individuals with atrial fibrillation are at very high risk of stroke, especially if they also have associated left ventricular hypertrophy, congestive heart failure, or hypertension. Treatment to prevent embolization, including both aspirin and other antiplatelet aggregating agents and anticoagulants, has been very effective in reducing the risk of stroke among patients with atrial fibrillation (32, 33).

TIAs are temporary focal brain defects that are caused by vascular disease and that clear completely within 24 hours. Most TIAs last less than 1 hour. Atherosclerosis of the arteries supplying the brain is believed to be the most common cause of TIA. Microembolization may also be a cause. TIAs occur before a stroke in approximately 25–50 percent of atherothrombotic strokes. The risk factors for TIA are similar to those for atherosclerosis-related stroke.

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Individuals who have TIAs have a much higher risk of subsequent stroke. This risk is especially high in the first month or so after the onset of a TIA. About one quarter of the participants with TIA will develop a stroke over the next 5 years—about a sevenfold increased risk compared with those without TIA (34).

Specific medical therapies will reduce the risk of stroke among patients with TIA. These include aspirin and other antiplatelet aggregating agents and anticoagulants, as well as surgical therapy for carotid stenosis (34).

Epidemiologic studies are continuing to evaluate whether levels of specific clotting factors, clotting, thrombotic and fibrinolytic factors in the blood, and measures of inflammation, adhesion molecules, etc., are independent risk factors for stroke. Several of these risk factors have been associated with increased risk of stroke. There is, however, no evidence that modifying these risk factors will reduce the risk of stroke. Tissue plasminogen activator increases fibrinolysis and, if given intravenously within a few hours after a stroke, has been associated with a reduction in stroke morbidity (35).

SILENT CEREBRAL INFARCTION AND VASCULAR DISEASE AND DEMENTIA

The association of vascular disease and dementia has been evolving with the introduction of MRI and computerized tomography of the brain. Silent cerebral infarction and white matter grade changes of likely vascular origin may be important determinants of cognitive decline and dementia (36–38).

In the Cardiovascular Health Study, 36 percent of 3,660 participants had infarct-like lesions on their MRI (39). The prevalence of infarcts were found in 72 percent of the participants with and 28 percent without a history of stroke. Infarct-like lesions are strongly related to risk factors for clinical stroke and to measures of clinical and subclinical cardiovascular disease. There are many more individuals with subclinical compared with clinical stroke, especially in the older populations. The risk of clinical stroke among individuals who have subclinical infarction or high white matter grade abnormalities on MRI is currently being evaluated in several studies.

Approximately 20 percent of the individuals who have clinical strokes may develop dementia. The interrelations between the silent cerebral infarctions, subclinical vascular disease, and Alzheimer’s disease are currently an important area of research (40).

THE FUTURE

A major challenge to epidemiology and prevention research in the 21st century will be “protection of the brain,” especially reducing the risks of dementia, mild cognitive impairments, and focal neurologic damage directly related to stroke.

Vascular disease is the second leading cause of dementia and probably also contributes to the progression of Alzheimer’s disease. The ability to image the brain using MRI and new functional measurements provides a better method of quantifying the effects of risk factors, such as blood pressure level, on brain morphology.

The development of new cognitive testing that can be used in epidemiologic studies will provide an “exercise test” of the brain. It is likely that these approaches will demonstrate a continuum of pathology and functional abnormalities with blood pressure levels. There will also be positive interactions with other risk factors, such as diabetes mellitus and hyperlipidemia. These risk factors may be the primary determinants of the subclinical vascular pathology in the brain.

Individual risk of cerebral vascular pathophysiology and functional changes will also be determined by host susceptibility, i.e., selected genetic attributes, as well as by other risk factors, such as vitamins, folic acid, vitamin B12, antioxidants, and inflammatory factors. The goal will therefore be to identify the specific environmental, i.e., lifestyle, factors and their interaction with host genetic characteristics in order to prevent both subclinical and overt vascular disease and cognitive changes.

The development of more efficacious antihypertensive drug therapies will continue to have a major impact on the risk of stroke. Clearly, however, the most important challenge of the new century will be the prevention of elevated blood pressure. The optimal blood pressure is a systolic pressure of less than 120 and a diastolic pressure of less than 80. If most of the population could maintain such blood pressure levels through their life spans, it is likely that stroke would no longer be a major public health issue. A much better application of current knowledge of the etiology of elevated blood pressure and stroke, as well as the possible identification of new risk factors and genetic host susceptibility, will be major challenges for the 21st century.

CONCLUSION

The epidemiologic study of stroke and its application to preventive therapies have been a great success. Stroke incidence and mortality are still far too high, especially among Blacks. The prevalence of stroke will increase because of the aging of the population and decreased case-fatality percentage. Stroke is a preventable disease (41).
REFERENCES


