Stroke: Risk and Protective Factors

What We Know

› Stroke is a medical emergency that results from an alteration in the blood supply to the brain caused by either oxygen deprivation (ischemic stroke) or flooding with blood (hemorrhagic stroke). Both ischemic stroke and hemorrhagic stroke can result in permanent damage or death. (20) (For information regarding stroke, see the series of related Quick Lessons and Evidence-Based Care Sheets)

• Stroke is the fifth leading cause of death in the United States and a leading cause of disability. Approximately 795,000 persons experience stroke each year. Ischemic stroke is more prevalent than hemorrhagic stroke, accounting for 87% of stroke cases (6,7,12,20)

› Numerous factors have been identified that increase an individual’s risk for stroke; these include non-modifiable risk factors, modifiable lifestyle factors, cardiovascular and metabolic conditions, and certain biomarkers (4,7,12,20)

• Non-modifiable risk factors
  – Gender: Men are more likely to have a stroke than women. However, more women die as a result of stroke because they experience stroke at a later age than men (6,12,20)
  – Age: The risk for stroke doubles every 10 years after the age of 55; 34% of strokes occur in persons younger than 65 years and 20% of deaths after the age of 65 are attributed to stroke (2)
  – Ethnicity/race: Rates of stroke are higher in Blacks, Hispanics, and Native Americans than in Whites; this is linked to a greater incidence of diabetes mellitus and hypertension (12)

• Modifiable lifestyle factors
  – Tobacco use increases stroke risk by a factor of 2–4 (7,12,20)
  – Consuming a diet that is high in cholesterol, saturated fats, and sodium, as well as low in fruits and vegetables, increases the risk for stroke (7,12)
  – A randomized control trial including 7447 patients with increased risk of cardiovascular disease showed that the Mediterranean diet (plant-based diet with decreased dairy, fats and sugars) can decrease cardiovascular events including stroke, myocardial infarction and cardiovascular disease mortality (2,10)
  – Physical inactivity increases the risk for stroke by up to 30% (2,12)
  – Alcohol and drug abuse can increase blood pressure (BP), thereby increasing the risk for stroke (2)

• Cardiovascular and metabolic conditions
  – Hypertension increases the risk for stroke twofold; in patients with both diabetes mellitus and hypertension, stroke risk is increased approximately fourfold (7,12,16,20)
  – Diabetes mellitus increases stroke risk 1.8-fold in patients who are older than 75 years of age and 5.6-fold in those who are 30–44 years of age (7,20)
  – Obesity, usually defined by body mass index (BMI), is a risk factor for stroke. Stroke risk is increased by 18% for each 5 kg/m² higher BMI (4)
Individuals who have had a transient ischemic attack (TIA) or prior stroke have a 10–12% increased risk for stroke, especially within the first 90 days after the initial event\(^{(7,12)}\).

Cardiovascular conditions that increase stroke risk include coronary artery disease, history of myocardial infarction, left atrial enlargement, heart failure, carotid or peripheral artery disease, and atrial fibrillation\(^{(7)}\).

- Atrial fibrillation is the most common, sustained cardiac arrhythmia; untreated atrial fibrillation poses a significant risk for stroke\(^{(5)}\).
- Atrial fibrillation is responsible for ~ 20% of all strokes and increases stroke risk fivefold; coexisting chronic renal failure further increases stroke risk in patients with atrial fibrillation\(^{(7,12)}\).

Chagas disease—a parasitic infection transmitted by the triatomine bugs, known as “kissing bugs,” that often results in cardiomyopathy—is associated with a twofold increase in stroke risk\(^{(3)}\).

### Biomarkers for increased stroke risk

Abnormal cholesterol levels are associated with an increased risk for stroke, particularly ischemic stroke. Specifically, high levels of low-density lipoprotein cholesterol (LDL cholesterol, commonly referred to as “bad cholesterol”) and low levels of high-density lipoprotein cholesterol (HDL cholesterol, commonly referred to as “good cholesterol”) increase the risk for stroke\(^{(12)}\).

- Additional biomarkers that are associated with increased stroke risk include elevated C-reactive protein (CRP) levels and increased carotid intima-media thickness\(^{(12)}\).

### Other risk factors for stroke

- Sickle cell disease; use of hormone replacement therapy (HRT), which increases ischemic stroke risk by 44%\(^{(7,12)}\).

### Protective factors include medication and lifestyle modifications\(^{(6,7,9,12,16,19,20)}\)

- Treatment of high BP with antihypertensive medications (e.g., angiotensin-converting enzyme [ACE] inhibitors, angiotensin receptor antagonists), treatment of high cholesterol with statins (e.g., lovastatin), and treatment of coronary heart disease or atrial fibrillation with antithrombotic medications (e.g., clopidogrel [Plavix], warfarin [Coumadin]) are associated with a significant reduction in the risk for stroke\(^{(7,9,11,14,16,19,20)}\).

- Treatment of hypertension can reduce stroke risk by up to 50%\(^{(20)}\).

- Warfarin therapy is associated with a 64% decrease in stroke risk in patients with atrial fibrillation\(^{(19)}\).

- Although warfarin is highly effective, it has numerous limitations (e.g., narrow therapeutic window, drug-food interactions) that have led researchers to develop alternative agents for long-term oral anticoagulant therapy; oral direct thrombin inhibitors (e.g., dabigatran) and factor Xa inhibitors (e.g., rivaroxaban, apixaban) are alternatives to warfarin\(^{(2,9,11,12)}\).

- According to the National Institute for Health and Care Excellence (NICE) and the American Academy of Neurology, dabigatran, rivaroxaban, and apixaban are suitable alternatives to warfarin for stroke prophylaxis in patients with nonvalvular atrial fibrillation\(^{(1,13)}\).

- The authors of a meta-analysis concluded that risk of stroke is 22% lower in patients who received newer oral anticoagulants than in those receiving warfarin therapy; the authors reported that the newer oral anticoagulants had a more favorable safety profile\(^{(11)}\).

- In patients on long-term anticoagulation therapy, temporary interruptions of therapy are common and are associated with substantial risk of stroke and bleeding. Researchers in a recent randomized study including 4,692 patients with atrial fibrillation who experienced temporary interruption of therapy found that stroke and bleeding risks were similar in those treated with rivaroxaban or warfarin\(^{(15)}\).

- Aspirin and other antiplatelet agents (e.g., clopidogrel) reduce stroke risk by 22% and the addition of clopidogrel to aspirin therapy reduces stroke risk by an additional 28%\(^{(2)}\).

- Researchers in a meta-analysis of 30 trials found that cilastazol therapy produced a more significant reduction in the recurrent of fatal stroke when compared to aspirin in the Asian population\(^{(19)}\).

- Women who are pregnant and at high stroke risk should be carefully evaluated by their healthcare provider. Treatment with low-molecular-weight heparin (LMWH) or unfractionated heparin (UFH) might be considered. Breastfeeding women can be treated with warfarin, UFH, or LMWH\(^{(6,2)}\).
What We Can Do

› Learn more about stroke risk and protective factors so you can accurately assess your patients’ personal characteristics and health education needs; share this knowledge with your colleagues

› Educate your patients regarding stroke prevention strategies and encourage patients to
  • monitor BP comply with their medication regimen
  • avoid smoking tobacco and limit alcohol consumption to fewer than 2 drinks per day
  • exercise at least 30 minutes 3 times a week
  • eat a diet low in cholesterol, low in saturated, sodium, and trans fats that includes fruits, vegetables, and fish
  • talk with the treating clinician about HRT-related stroke risk, as appropriate for menopausal women

› Educate your patients that more information can be obtained from the American Stroke Association at http://www.strokeassociation.org, the Stroke Association at http://www.stroke.org.uk, and the World Stroke Organization at http://www.world-stroke.org

Coding Matrix

References are rated using the following codes, listed in order of strength:

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