Preventing Ischemic Stroke in Patients With Prior Stroke and Transient Ischemic Attack

A Statement for Healthcare Professionals From the Stroke Council of the American Heart Association

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stroke, the third leading cause of death in the United States, is a leading cause of adult neurological disability and accounts for the greatest number of hospitalizations for neurological disease. Although treatment of acute stroke has the potential of reducing death and disability, it is likely that prevention will more effectively reduce the ravages of stroke. The patient who is recovering from a mild stroke or who has had a recent transient ischemic attack (TIA) is at high risk of stroke recurrence, physical and intellectual disability, long-term institutionalization, and death.

There is substantial evidence from observational epidemiological studies and clinical trials that recurrent ischemic stroke can be prevented (Table 1). Control of risk factors is important for prevention of a first stroke and is practical after ischemic stroke and TIA have occurred. Identification of the specific ischemic stroke mechanism, eg, TIA or minor stroke ipsilateral to a moderate or severe internal carotid stenosis, guides decision making with regard to recurrent stroke prevention (Table 2). A patient with symptomatic cerebrovascular disease is likely to have other cardiovascular diseases or is predisposed to develop them. Preventive measures should complement reduction in risk of atherothrombotic events in the coronary arteries and other arterial territories. Certain nonmodifiable characteristics identify persons at high risk of stroke and stroke recurrence. These include advancing age, male sex, and black and Hispanic race-ethnic backgrounds. Some risk factors, however, such as elevated blood pressure, cigarette smoking, obesity, impaired glucose tolerance, and physical inactivity, are modifiable. Other conditions, ie, prior cardiovascular diseases such as coronary heart disease with angina or prior myocardial infarction, valvular heart disease, congestive heart failure, atrial fibrillation, increased left ventricular mass, and certain other echocardiographic abnormalities, identify persons at increased risk who may be treated with antithrombotic therapy. More recently, other modifiable risk factors for stroke have been identified. These are elevated total and low-density lipoprotein (LDL) cholesterol in patients with prior coronary heart disease and elevated plasma homocysteine levels.

Prevention

There are 3 treatment strategies to prevent recurrent stroke in patients with TIA or mild ischemic stroke. For patients with atrial fibrillation, dose-adjusted warfarin sodium is administered (international normalized ratio [INR] in the 2 to 3 range; target 2.5) unless there is a specific contraindication for that medication. In the latter case, the patient should be treated with aspirin 50 to 325 mg/d.

In patients with TIA or mild stroke and symptoms referable to severe (70% to 99%) carotid artery stenosis (or to moderate [50% to 69%] stenosis in a patient with significant risk factors), the treatment of choice is carotid endarterectomy by a surgeon with a low complication rate (morbidity and mortality <6%). For patients with TIA or mild stroke who do not have atrial fibrillation or moderate-to-severe carotid stenosis, treatment with a daily dose of 50 to 325 mg of aspirin is of demonstrated benefit. Although previous studies used doses of aspirin up to 1300 mg/d, the lower dose range is currently recommended. Other antiplatelet agents, including clopidogrel, extended-release dipyridamole plus aspirin, and ticlopidine, may be used. Recent retrospective postmarketing surveillance suggests that the use of ticlopidine with aspirin after coronary angioplasty and stenting was complicated by thrombotic thrombocytopenic purpura approximately once in every 4184 patients and was fatal in 20% of cases. In light of these findings, the use of ticlopidine must be reassessed.

Likelihood and Consequences of Stroke Recurrence

Stroke recurrence is an important public health concern. The decline in stroke mortality and the increase in life expectancy of the US population will undoubtedly increase the number of persons at risk for recurrent stroke, stroke-related disability, and the cost of medical care. The long-term stroke recurrence rates range from 4% to 14% annually. In the Framingham Study, the 5-year cumulative recurrence rate for athero-

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thrombotic brain infarction was 42% for men and 24% for women. In Rochester, Minn, the 5-year cumulative recurrence rate was 29%, with no sex difference. Recurrences were generally of the same type as the initial stroke. In the Northern Manhattan Stroke Study, the 5-year stroke recurrence rate was 25%. Overall, stroke recurrence is highest in the first 30 days after the initial event; 30% of recurrences occur within this time frame. However, there may be differences in recurrence rates by stroke subtype. Lacunar infarction may have the lowest recurrence rate, atherothrombotic infarction the highest, and infarction of unknown cause and cardioembolic stroke intermediate rates. Cardiovascular risk factors such as hypertension, glycemic control, cardiac disease, and heavy alcohol consumption may be potentially modifiable predictors of stroke recurrence.

More than 50% of stroke survivors have significant residual physical disability and functional impairment. Stroke recurrence not only may add to physical impairment and disability but may also increase mortality and length of hospital stay. In addition, stroke recurrence may lead to vascular dementia or may be an important trigger for dementia in the elderly. Because some first and recurrent strokes are preceded by transient ischemic attacks (TIA), we also present a guide to the risk reduction of patients with TIA or stroke (Table 1).

### Table 1. Guide to Risk Reduction for Patients With Ischemic Cerebrovascular Disease (Patients Who Have Already Had Their First TIA or Stroke): General Risk-Factor-Specific Recommendations

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Goal</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>SBP &lt;140 mm Hg and DBP &lt;90 mm Hg; SBP &lt;135 mm Hg and DBP &lt;85 mm Hg</td>
<td>Lifestyle modification and antihypertensive medications</td>
</tr>
<tr>
<td>Smoking</td>
<td>Cessation</td>
<td>Strongly encourage patient and family to stop smoking</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Glucose &lt;126 mg/dL (6.99 mmol/L)</td>
<td>Diet, oral hypoglycemics, insulin</td>
</tr>
<tr>
<td>Lipids</td>
<td>LDL &lt;100 mg/dL (2.59 mmol/L)</td>
<td>Start AHA Step II diet</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Moderate consumption (≤2 drinks/d)</td>
<td>Strongly encourage patient and family to stop excessive drinking or provide formal alcohol cessation program</td>
</tr>
<tr>
<td>Physical activity</td>
<td>30–60 minutes of activity at least 3–4 times/wk</td>
<td>Moderate exercise (eg, brisk walking, jogging, cycling, or other aerobic activity)</td>
</tr>
<tr>
<td>Weight</td>
<td>≤120% of ideal body weight for height</td>
<td>Diet and exercise</td>
</tr>
</tbody>
</table>

SBP indicates systolic blood pressure; DBP, diastolic blood pressure; AHA, American Heart Association; HDL, high-density lipoproteins; TC, total cholesterol; and TG, triglycerides.

### Table 2. Guide to Risk Reduction for Patients With Ischemic Cerebrovascular Disease (Patients Who Have Already Had Their First TIA or Stroke): Additional Subtype-Specific Recommendations

<table>
<thead>
<tr>
<th>Ischemic Stroke Subtype</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Atherosclerotic carotid disease</strong></td>
<td></td>
</tr>
<tr>
<td>≥70% stenosis</td>
<td>Carotid endarterectomy of definite benefit if done with acceptable morbidity and mortality</td>
</tr>
<tr>
<td></td>
<td>Antiplatelet agents</td>
</tr>
<tr>
<td></td>
<td>Angioplasty with stent undergoing evaluation</td>
</tr>
<tr>
<td>50–69% stenosis</td>
<td>Carotid endarterectomy of potential benefit depending on risk factors</td>
</tr>
<tr>
<td></td>
<td>Antiplatelet agents</td>
</tr>
<tr>
<td>&lt;50% stenosis</td>
<td>Carotid endarterectomy of no benefit</td>
</tr>
<tr>
<td></td>
<td>Antiplatelet agents</td>
</tr>
<tr>
<td><strong>Cardiac embolism</strong></td>
<td></td>
</tr>
<tr>
<td>Definite source:</td>
<td>Oral anticoagulation (unless contraindicated):</td>
</tr>
<tr>
<td>Nonvalvular AF</td>
<td>INR 2–3 (target 2.5) lifelong therapy</td>
</tr>
<tr>
<td>LV thrombus, recent MI</td>
<td>INR 2–3 (target 2.5) 6-month therapy</td>
</tr>
<tr>
<td>Prosthetic VHD</td>
<td>INR 3–4 (target 3.5) lifelong therapy</td>
</tr>
<tr>
<td>Possible source</td>
<td>Antiplatelet agents (oral anticoagulation undergoing evaluation)</td>
</tr>
<tr>
<td>Other infarct subtypes including:</td>
<td></td>
</tr>
<tr>
<td>small-vessel lacunar disease and cryptogenic stroke</td>
<td>Antiplatelet agents (aspirin, clopidogrel, extended-release dipyridamole plus aspirin, ticlopidine) (oral anticoagulation undergoing evaluation)</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; LV, left ventricular; MI, myocardial infarction; and VHD, valvular heart disease.
strokes are preventable, vascular-associated causes of cognitive impairment might be prevented by appropriate risk-prevention measures.

**Prevention of Other Cardiovascular Outcomes in Cerebrovascular Patients**

Patients with stroke and TIA are also at risk for myocardial infarction and cardiovascular death. That is, they often have generalized atherosclerosis and are at risk for thrombosis in multiple vascular territories. The present report has emphasized the treatment of atherosclerotic risk factors for stroke prevention, eg, cessation of smoking, reduction of high blood pressure, control of body weight and blood glucose, and use of antithrombotic drugs. These treatments are also effective in reducing the risk of coronary artery events.

The reduction of LDL cholesterol with 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (“statins”) prevents coronary events in patients with coronary artery disease (CAD), especially when LDL cholesterol is elevated. Consequently, stroke patients with known CAD and elevated LDL cholesterol are often prescribed a statin. The value of reducing high blood LDL cholesterol for stroke prevention has been less clear. However, recent trials in patients with CAD have shown treatment with statins prevents stroke as well. Because many stroke patients have clinical CAD, statin use is indicated. Statin use in stroke patients without prior CAD may also reduce the risk of stroke recurrence, as well as myocardial infarction and other vascular disease, but this has not been demonstrated. Additional studies of statins in stroke patients without clinical CAD are in progress.

**Educational Aspects**

The synthesis of epidemiological and clinical trial data is only the first step in preventing stroke recurrence. New data must be disseminated to healthcare providers and gaps identified between current and “best” practice. Therapeutic decisions based on the best available evidence need to be incorporated into routine clinical practice, and the impact of treatments on patient outcomes should be systematically monitored. These problems are not trivial, because dissemination of preventive guidelines lags behind clinical trial and consensus statement results. For example, ≈2 years after the results of randomized trials became available indicating that endarterectomy was efficacious in selected symptomatic patients with high-grade carotid artery stenosis, the operation was reported as being always or often recommended by only about half of internists and noninterventional primary care physicians in the United States for patients with newly symptomatic disease. Less than 33% of the latter physicians indicated that they were considering or expecting to alter their practices. Although there are several possible explanations for this finding, targeted dissemination of clinical trial results might help address this apparent “knowledge gap” and be an important vehicle for change.

In contrast, the majority of physicians in the United States are knowledgeable regarding the use of anticoagulants in the prevention of cardiogenic embolism in patients with atrial fibrillation. Yet several recent studies show that anticoagulants are prescribed to only ≈50% of individuals in the United States with atrial fibrillation who are candidates for such therapy. In this case, there is a discrepancy between knowledge and practice that is unlikely to be addressed by reiterating the results of clinical trials. As illustrated by these examples, the optimal methods of translating evidence into effective clinical practice may differ depending on a variety of factors. Systematic study of these factors and the careful assessment of the impact of possible solutions on both the process of care and patient outcomes will be increasingly required in the future. Overall, healthcare organizations need to develop systems that ensure that patients at high risk for stroke are identified, screened, and treated appropriately.

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