including aggressive risk factor control, was associated with a lower recurrence risk (Level B).

Anticoagulation is indicated in patients with definite cardioembolic sources of stroke, such as mechanical valves or atrial fibrillation. In embolic strokes caused by atrial fibrillation, anticoagulation with warfarin was superior to aspirin, with a relative risk reduction of about 68% (Level A). Recommended options for secondary prevention among patients with atrial fibrillation now include warfarin with an INR between 2.0 and 3.0, or use of one of the newer antithrombotic agents, such as dabigatran, rivaroxaban, edoxaban, or apixaban (Level A). For patients who cannot tolerate anticoagulants because of a risk of ICH or bleeding elsewhere, newer treatment modalities, including interventions to exclude the left atrial appendage from the circulation using devices or cinching procedures, show promise in early trials, though they are not yet approved (Level B).

Other causes of cardiogenic emboli require different treatments. Infected prosthetic valves need replacement if emboli persist on antibiotics, or if patients develop heart failure. Emboli from myxomatous tumors of the atria frequently require surgical removal of tumor. The need for anticoagulation among patients with less well-established sources of emboli, such as paradoxical embolism through a patent foramen ovale or aortic arch embolization, is unproven, and current guidelines do not support its use in this setting (Level A). Closure of patent foramen ovale using umbrella-like devices may reduce the risk of recurrent stroke in selected patients (younger patients without other stroke risk factors), though recent trials have not proven this effect; further trials in highly selected patients are ongoing.

All patients with ischemic stroke without a definite indication for anticoagulation, and in whom no contraindication is present, should receive long-term antiplatelet therapy, which reduces the risk of recurrence by 20% to 25% (Level A). Agents currently approved for this purpose include aspirin, dipyridamole, and clopidogrel, a thienopyridine derivative ADP receptor inhibitor. Head-to-head trials have failed to demonstrate a benefit of one of these agents over another; the combination of aspirin and dipyridamole was more effective than either agent alone, but long-term treatment with the combination of aspirin and clopidogrel was no more effective than aspirin alone and increased the risk of significant bleeding. A more recent trial in China suggested that there may be benefit to the combination of aspirin and clopidogrel when used for the short term after stroke or TIA, and a similar study is ongoing in the United States. Aspirin doses as low as 30 mg daily appear effective and have fewer side effects, such as gastrointestinal bleeding, than higher doses. The FDA recommends doses between 50 and 325 mg daily for stroke prevention.

Clinical trials provide evidence for increased use of antihypertensive agents in patients with stroke and TIA. There are theoretical concerns about lowering blood pressure in patients with existing cerebrovascular disease due to the possibility that in patients with arterial disease of cerebral vessels and reduced autoregulation, a reduction in blood pressure could worsen perfusion and precipitate clinical events or affect cognition. Randomized trials like PROGRESS provide evidence, however, that blood pressure reduction among patients with cerebrovascular disease reduces risks of recurrent stroke by 28% independently of a history of hypertension (Level A). Guidelines currently focus on the use of blood pressure agents to achieve recommended target blood pressure levels, rather than on specific agents, which should be individualized depending on a patient's comorbidities.

Trials using HMG-CoA reductase inhibitors, or statins, among cardiac and other vascular disease high-risk patients have demonstrated benefits in stroke risk reduction. The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial provides more direct evidence of the benefit of statin therapy in secondary prevention of stroke among patients presenting with stroke or TIA (Level A). SPARCL randomized patients with recent stroke or TIA to atorvastatin 80 mg daily or placebo. Over 5 years, atorvastatin reduced the risk of the primary outcome, recurrent stroke, from 13.1% to 11.2%, an absolute risk reduction of about 2%.

Among those with diabetes, diet and exercise, oral hypoglycemic drugs, and insulin are recommended to obtain glycemic control. While glycemic control reduces risks of microvascular complications, the benefit in reducing macrovascular complications is less certain. In one trial, tight glycemic control of a prospective cohort of newly diagnosed diabetics was not found to significantly reduce stroke risk. Ongoing trials are addressing the use of newer agents in secondary stroke prevention among those with insulin resistance.

Behavioral risk factors are difficult to control, but are important. Smoking is addictive, and cessation may necessitate psychologic counseling and medical aids, such as nicotine patches or varenicline. Physical activity should be encouraged, as a sedentary lifestyle is associated with elevations in blood pressure and stroke risk. Alcohol consumption in excess of 2 drinks daily should be discouraged, though there is evidence that moderate alcohol consumption may have protective effects against stroke risk. It should be noted, however, that there is only Level B evidence that control of these risk factors reduces recurrent stroke risk.

PROGNOSIS

The immediate period after an ischemic stroke carries the greatest risk of death, with fatality rates ranging from 8% to 20% in the first 30 days. Age and stroke severity are the most important predictors of prognosis. Case fatality rates are worse for hemorrhagic strokes, ranging from 30% to 80% for intracerebral hemorrhage and 20% to 50% for subarachnoid hemorrhage.

Stroke survivors continue to have a three to fivefold increased risk of death, compared with the age-matched general population. Annual aggregate estimates of death have been 5% for minor stroke and 8% for major stroke. Survival is influenced by age, hypertension, cardiac disease, and diabetes. Patients with lacunar infarcts appear to have a better long-term survival than do those with the other infarct subtypes.

Recurrent stroke is frequent. The immediate period after a stroke carries the greatest risk for early recurrence; rates range from 3% to 10% during the first 30 days. Thirty-day recurrence risks vary by infarct subtypes; the greatest rates are in patients with atherosclerotic infarction and the lowest rates in patients with lacunes. After the early phase, the risk of stroke recurrence continues to threaten the quality of life of a stroke survivor.