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Stroke mortality has decreased, in large part because of better prevention. There are several new treatment options for patients with atrial fibrillation. Reduction in cancer risk may be an additional benefit of aspirin. Aggressive lowering of blood pressure for secondary stroke prevention might be harmful. Changes in the organization of care enhance utilization of evidence-based therapies. Further reductions in stroke risk and mortality are anticipated.

In December 2010, the Centers for Disease Control and Prevention released 2008 data indicating that stroke declined from the third to the fourth leading cause of death in the United States, in part reflecting a steady decline in stroke-related mortality.[1] There were similar reductions in Western Europe.[2] Arguably, more effective prevention is the greatest contributor to the declines.[3] Declining stroke rates with medical therapy suggest that revascularization procedures for most persons with asymptomatic carotid artery stenosis may no longer be of value[4] and contributed to negative trials of angioplasty/stenting for intracranial steno-occlusive disease[5] and extracranial–intracranial bypass for carotid occlusion.[6] New research supports both novel and established therapies, and improved strategies for care delivery promise to add to the success of modern stroke prevention.

Studies consistently show a gap in the appropriate treatment of atrial fibrillation (AF). This partially may be related to the perceived bleeding risk associated with vitamin K antagonists, the required monitoring, and concern for drug and dietary interactions. Several stratification schemes identify patients with AF whose risk is low enough to obviate anticoagulation but can yield differing assessments. The $CHADS_2$ score is commonly used, but a considerable number of patients have "intermediate risk." This prompted a refinement, the CHA_2DS_2-VASc, having fewer intermediate risk classifications (15.1% vs 34.9%).[7]

Clinical trials support alternative therapies for AF patients. The RE-LY trial compared dabigatran, a direct thrombin inhibitor, with warfarin.[8] Randomization to dabigatran (150 mg twice daily) led to lower rates of stroke (including hemorrhagic stroke), but similar major bleeding (net benefit relative risk, 0.912; 95% CI, 0.82–1.00; $P=0.04$). Although having no food interactions, p-glycoprotein inhibitors increase dabigatran levels. Aside from dialysis, its effects cannot be emergently reversed. Although the aPTT may be prolonged, there is no rapid assay to measure its activity.

The AVERROES trial compared apixabam, a factor Xa inhibitor, to aspirin in patients with AF and 1 additional risk factor who were considered unsuitable for warfarin.[9] Apixabam lowered the risk of ischemic stroke/systemic embolization (hazard ratio, 0.45; 95% CI, 0.32–0.62), with lower rates of hemorrhagic stroke but similar rates of major and intracranial hemorrhages. As with dabigatran, there is no way of assessing drug activity and no antidote.

The ARISOTLE trial compared apixabam with warfarin in patients with AF and 1 additional risk factor.[10] Stroke or systemic embolization was reduced by 21% (hazard ratio, 0.79; 95% CI, 0.66–0.95; $P<0.001$ for noninferiority; $P=0.01$ for superiority). Both hemorrhagic and total strokes were lower, although there was no effect on ischemic or unknown-type strokes. Both intracranial and major hemorrhages were reduced (net benefit 3.2% vs 4.1%; $P<0.001$).

The ROCKET trial compared rivaroxabam, another Xa inhibitor, with warfarin in patients with AF.[11] Rivaroxabam was not inferior to warfarin in reducing stroke or systemic embolization (hazard ratio, 0.88; 95% CI, 0.74–1.03, $P<0.001$) but was not superior ($P=0.12$). Although major hemorrhage rates were similar, fatal and intracranial hemorrhages and hemorrhagic stroke rates were lower.

Aspirin remains the standard for prevention of vascular events in patients without AF. The PERFORM trial compared the selective thromboxane-prostaglandin receptor antagonist terutroban with aspirin in patients with recent transient ischemic attack or ischemic stroke.[12] PERFORM was stopped because of futility, with the primary end point occurring in 11% of subjects receiving either terutroban or aspirin (hazard ratio, 1.02; 95% CI, 0.94–1.12); there was no difference in major bleeding.

Adding to evidence that aspirin reduces colorectal cancer,[13] additional reports show it lowers the incidence and mortality of other cancers.[14,15] The effect of aspirin on cancer risk provides an additional indication for its use in primary prevention. Work is necessary to determine how this additional effect influences the overall risk of aspirin vs benefit.

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Blood pressure-lowering remains the most important primary stroke prevention medical intervention, but whether there is a level of blood pressure below which further treatment is ineffective or harmful remains controversial.[16] Exploratory analysis of PRoFESS trial data suggests increased stroke risk with systolic blood pressures <120 mm Hg in the secondary prevention setting.[17] Evidence showing harm for primary prevention is lacking, although there are little data from randomized trials assessing outcomes in otherwise healthy elderly patients with systolic blood pressures <160 mm Hg.

Effective implementation is necessary to optimize prevention. Quality-improvement programs lead to higher rates of compliance with evidence-based interventions.[18] Although up to one-third of stroke patients stop ≥1 secondary prevention medications within 1 year of hospital discharge, most do so based on health care professional recommendations.[19] Just as organized inpatient care is associated with improved ischemic and hemorrhagic stroke patient outcomes,[20,21] organized outpatient care also may be advantageous.[22] Continued advances in prevention and implementation should lead to further reductions in stroke incidence and mortality.

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