Prevention and Health Services Delivery

Larry B. Goldstein, MD; Pierre Amarenco, MD

The American Heart Association continues to estimate that >700,000 Americans have a stroke each year.1 Stroke also continues to be a major health problem in Europe and Asia. Prevention and more effective delivery of established interventions remain major strategies for reducing this growing burden.

Current American Heart Association primary stroke prevention guidelines recommend a diet rich in fruits and vegetables.2 Cardiovascular and stroke risk-reduction benefits are thought to be at least in part related to the antioxidant vitamin content of these foods. However, last year, a meta-analysis of 7 randomized trials of vitamin E comprising 81,788 patients and 8 studies of beta carotene comprising 138,113 patients found neither had significant cardiovascular benefits.3 There was no reduction in stroke rates with either vitamin (3.6% with versus 3.5% without vitamin E, P=0.31; and 2.3% with versus 2.3% without beta carotene). The relationship between the intake of fruits and vegetables and the risk of ischemic stroke was investigated in a prospective cohort study of 54,506 Danish men and women.4 Total intakes of fruits and vegetables were obtained from a baseline questionnaire with rates of ischemic stroke obtained through a national registry and verified by record reviews. In contrast with the antioxidant vitamin studies, after adjustment for potential confounders (sex, total energy intake, smoking status, blood pressure, serum cholesterol, diabetes mellitus, body mass index, alcohol intake, intake of red meat and n-3 polyunsaturated fatty acids, physical activity, and education), persons in the top quintile of fruit and vegetable intake (median 673 g per d) had a 28% reduction in ischemic stroke risk (risk ratio [RR], 0.72; 95% CI, 0.47, 1.12) relative to persons in the bottom quintile of intake (median 147 g per day; P for trend=0.04). The relationship was most evident for fruit intake (top versus bottom quintile RR, 0.60; 95% CI, 0.38, 0.95; P for trend=0.02). Similar risk estimates were seen for most types of fruits and vegetables, but the risk reductions were significant only for citrus fruit. Although the study was observational rather than randomized and a “healthy user” effect cannot be excluded, the analysis further supports the recommendation for a diet rich in fruits and vegetables.

Treatment of hypertension remains a major preventive measure associated with a reduction in stroke risk. However, there is a paucity of data directly comparing different antihypertensive regimens. The Valsartan Antihypertensive Long-Term Use Evaluation trial randomized 15,245 patients >50 years old at high cardiovascular risk to angiotensin receptor blocker (valsartan) versus calcium channel blocker (amlodipine)–based treatment.5 The 2 strategies were similar based on the primary end point (cardiac mortality and morbidity, including heart failure) after 4.2 years (hazard ratio [HR], 1.04; 95% CI, 0.94 to 1.15; P=0.49). There was a 15% nonsignificant reduction in stroke with the amlodipine-based regimen (HR, 1.15; 95% CI, 0.98 to 1.35; P=0.08). Of note, blood pressure reduction was more pronounced with the calcium channel antagonist (average 4.0/2.1 mm Hg after 1 month and 1.5/1.3 mm Hg after 1 year; P<0.001). Thus, the marginal difference between the 2 regimens might be explained by a difference in the blood pressure–lowering effects of the drugs.

Several new studies have evaluated the effects of lipid lowering. Diabetics are among the patients at particular risk for stroke. The Collaborative Atorvastatin Diabetes Study (CARDS) trial randomized 2838 diabetic patients with normal baseline low-density lipoprotein cholesterol (LDL-C) and with no history of vascular events to placebo or a statin and found a 37% (95% CI, −52% to −17%; P=0.001) reduction for any vascular event and a 48% (−69 to −11%) reduction for stroke with treatment.6 The study supports the use of statins for primary stroke prevention in diabetics. The relationship between the degree of lipid lowering and benefit in high-risk patients has not been entirely clear. The Reversal of Atherosclerosis With Aggressive Lipid Lowering (REVERSAL) trial showed that reducing LDL-C from a mean of 150 mg/dL to an average of 79 mg/dL compared with 110 mg/dL in patients with coronary atherosclerosis led to a lower rate of disease progression as reflected in atheromata volume (P=0.02).7 The number of clinical events was too small for reliable analysis. However, the Pravastatin or Atorvastatin Evaluation and Infection Therapy (PROVE-IT) trial showed that lowering LDL-C in patients with acute coronary syndromes from a median of 106 mg/dL to a median of 62 mg/dL was more effective in reducing cardiovascular
events than lowering to a median LDL-C of 95 mg/dL.8 Consistent with these observations, a meta-analysis of >90,000 patients included in the large statin trials (primarily patients with coronary heart disease or major coronary heart disease risk) showed that the reduction in stroke (odds ratio [OR], 0.79; 95% CI, 0.73 to 0.85; \( P=0.0001 \); \( P=0.35 \) for heterogeneity between trials) was closely correlated with the degree of LDL-C reduction (reduction of LDL-C explained 33% to 80% of the benefit).9 A report from a group of National Cholesterol Education Program (NCEP) III writers endorsed a target of LDL-C <70 mg/dL in very high-risk patients.10

The Heart Protection Study reported an overall 25% (95% CI, 15% to 34%) relative risk reduction (RRR) for stroke among patients at high cardiovascular risk treated with a statin and a 20% RRR (95% CI, 8% to 29%) for major vascular events among patients with stroke and no coronary heart disease at entry.11 This benefit was present regardless of baseline LDL-C levels. However, there was no reduction in the rate of recurrent stroke among those having a history of stroke at baseline. A possible explanation for this lack of benefit could be the low stroke event rate related to the long delay (mean 4.3 years) between the index event and randomization. Whether early treatment of stroke patients without coronary heart disease with a statin leads to a reduction in recurrent stroke awaits the results of an ongoing study.12

The Management of Atherothrombosis With Clopidogrel in High-Risk Patients (MATCH) trial was designed to include high-risk patients with recent stroke or transient ischemic attack (TIA) to assess the benefit/RR of antiplatelet treatment with clopidogrel plus aspirin versus clopidogrel alone.13 Overall, there was a nonsignificant RRR of 6.4% (95% CI, −4.6% to 16.3%) for ischemic events but an absolute increase of 1.3% (95% CI, 0.6% to 1.9%) in major bleeding events. On the basis of these results, the combination should not be given to patients with stroke or TIA.

The body of knowledge related to interventions for extracranial carotid artery stenosis has been enhanced by reports of 2 major trials. The Asymptomatic Carotid Surgery Trial (ACST) was performed between 1993 and 2003 and randomized 3120 patients with >60% mainly asymptomatic carotid stenosis to immediate endarterectomy plus medical treatment versus medical treatment alone or until the operation became necessary.14 Supporting and extending the findings of the earlier Asymptomatic Carotid Atherosclerosis Study (ACAS) trial,15 ACST found similar absolute reductions in the 5-year risk with surgery (5.3%; 95% CI, 3.0% to 7.8% for ACST versus 5.1%; 95% CI, 0.9% to 9.1% for ACAS) despite a higher rate of perioperative stroke and death (3.0%; 95% CI, 2.1% to 4.0% in ACST versus 1.5%; 95% CI, 0.6% to 2.4% in ACAS; \( P=0.04 \)). Similar to ACAS, ACST found no significant increase in benefit with increasing degrees of stenosis in the 60% to 99% range as assessed by ultrasonography. ACST also reported a 2.5% (95% CI, 0.8% to 4.3%; \( P=0.004 \) absolute reduction in disabling or fatal stroke. However, it should also be noted that there was no benefit if stroke and all-cause mortality (31.2% with immediate versus 28.9% with deferred surgery; \( P=0.172 \)) or major stroke and all-cause mortality (25.5% versus 25.3%, respectively; \( P=0.242 \)) are considered. As previously, careful patient selection is critical when deciding whether to recommend the operation for asymptomatic disease with complication rates in the community often well in excess of those reported in these trials.16

Carotid angioplasty with stenting has been available for several years, but clinical studies showing that it is equivalent or superior to carotid endarterectomy have been limited. The Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial found that this procedure was not inferior (within 3%; \( P=0.004 \)) to carotid endarterectomy (based on a composite of stroke, death, or myocardial infarction [MI] within 30 days or death or ipsilateral stroke between 31 days and 1 year) in a cohort of patients considered at high risk for the operation.17 Approximately 70% of patients had asymptomatic stenoses with rates of stroke, MI, or death of 5.4% for stenting versus 10.2% for endarterectomy at 30 days and 9.9% versus 21.5% at 1 year. Because these rates include MI (including those defined by cardiac enzyme elevations in the absence of electrocardiographic changes), the results are not directly comparable to ACAS or ACST. The implications of the study results for patient care will likely be the subject of extensive discussion and debate pending completion of the Carotid Revascularization Endarterectomy Versus Stent Trial (CREST) comparing the 2 techniques in nonhigh-risk symptomatic patients.18

TIAs provide unique opportunities to reduce the risk of completed strokes. Recent population-based studies support the need for an expedited evaluation because the greatest risk is soon after the index TIA. Strokes occur in 4% to 9.5% at 90 days, with a risk of stroke, MI, or death of 21.8% at 1 year.19,20 In the Oxford Vascular Study, 7-day and 30-day stroke risks were 8.6% and 12%, respectively.21 Carried out with considerable effort and cost, the impact of community-based stroke screening programs on prevention practices is largely unknown. One study assessed the effect of a stroke screening event on stroke knowledge and actions taken as a result of the program 3 months later.22 Those attending the screenings and completing the study surveys undoubtedly represent a self-selected, motivated population. Knowledge of stroke warning signs increased from 59% to 94% immediately after screening but decreased to 77% at 3 months. At 3 months, 73% had done nothing to change their health practices. Therefore, only modest effects were observed and their impact on clinical outcomes unknown. More studies of this type are necessary to rationally decide how to allocate limited community-based stroke prevention resources.

Research often focuses on developing new treatment modalities, but optimizing the delivery of proven primary and secondary preventive therapies is a critical goal. The use of care maps is a method commonly used to improve hospital-based acute care and the consistent application of secondary preventive strategies. Also known as clinical pathways, critical pathways, or care paths, care maps provide a clear plan for the management of specific conditions. However, there is a paucity of data evaluating the usefulness of care maps for stroke. A systematic review of stroke care maps was performed based on 3 randomized trials and 7 nonrandomized
studies. There was no significant difference in death, dependency, discharge destination, or duration of hospitalization depending on whether a care map was used. However, stroke patients managed using a care map were less likely to have a urinary tract infection (OR, 0.38; CI, 0.18 to 0.79), less likely to be readmitted to hospital (OR, 0.11; CI, 0.03 to 0.39), and more likely to have a computed tomography brain scan (OR, 3.66; CI, 1.45 to 9.27) or carotid duplex study (OR, 2.45; CI, 1.3 to 4.61). Surprisingly, patient satisfaction (P=0.02) and quality of life (P=0.005) were lower in the care pathway group. The authors appropriately indicate that these results need to be interpreted with caution because the inclusion of nonrandomized studies may introduce important biases. Clearly, more high-quality work is needed in this area.

The use of web-based data systems to monitor the delivery of hospital initiated secondary preventive measures is a new approach to improving the use of established preventive therapies. Initial data for the American Heart Association Get With the Guidelines program for coronary heart disease is promising. Among 24 participating hospitals, compared with baseline, after 10 to 12 months, there were notable increases in smoking cessation counseling (48%; 95% CI, 37% to 58% increased to 87%; 95% CI, 73% to 100%), lipid treatment (54%; 95% CI, 47% to 70% increased to 79%; 95% CI, 70% to 88%), lipid measurement (59%; 95% CI, 52% to 66% increased to 81%; 95% CI, 72% to 90%), and cardiac rehabilitation referral (34%; 95% CI, 26%, to 40% increased to 68%; 95% CI, 60% to 76%). High baseline use was maintained for aspirin, β-blockers, and angiotensin-converting enzyme inhibitors. It is hoped, but not proven, that these improvements will lead to a reduced incidence of further cardiovascular events. A similar program is being evaluated for stroke.

References


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