Prevention of Recurrent Ischemic Stroke

Written by Rita Buckley

Secondary Prevention After Ischemic Stroke or Transient Ischemic Attack

Every year 15 million people worldwide suffer a stroke. Nearly 6 million die and another 5 million are permanently disabled. Stroke is the second leading cause of disability, after dementia. Transient ischemic attacks (TIAs) are sometimes referred to as "warning strokes" as they may be an indication that a full, far more serious stroke is about to happen [http://www.world-heart-federation.org/cardiovascular-health/stroke].

In the United States, 795,000 people experience a new or recurrent stroke each year. Approximately 610,000 of these are first attacks, and 185,000 are recurrent attacks. Mortality data from 2008 indicate that stroke accounted for 1 of every 18 deaths [Roger VL et al. *Circulation* 2012]. Hussien H. Rizk, MD, Cairo University Medical School, Cairo, Egypt, discussed the prevention of recurrent ischemic stroke.

The INTERSTROKE study [O'Donnell MJ et al. *Lancet* 2010], a standardized case-control study in 22 countries worldwide, suggested that 10 risk factors are associated with 90% of the risk of stroke. The population-attributable risk for common risk factors range from 3.8% (99% CI, 0.9 to 14.4) for alcohol intake to 34.6% (99% CI, 30.4 to 39.1) for hypertension (Table 1).

Table 1. INTERSTROKE: Population-Attributable Risk for Common Risk Factors.

Risk factor	Population-attributable risk, % (99% CI)
Hypertension	34.6 (30.4–39.1)
Smoking	18.9 (15.3–23.1)
Waist-to-hip ratio (tertile 2 vs tertile 1)	26.5 (18.8–36.0)
Dietary risk score (tertile 2 vs tertile 1)	18.8 (11.2–29.7)
Regular physical activity	28.5 (14.5–48.5)
Diabetes	5.0 (2.6–9.5)
Alcohol intake	3.8 (0.9–14.4)
Cardiac causes	6.7 (4.8–9.1)
Ratio of apolipoprotein B to A1 (tertile 2 vs tertile 1)	24.9 (15.7–37.1)
Psychological factors	
Stress	4.6 (2.1–9.6)
Depression	5.2 (2.7–9.8)

For the protective factor of physical activity, the population-attributable risks are provided for individuals who do not participate in regular physical activity.

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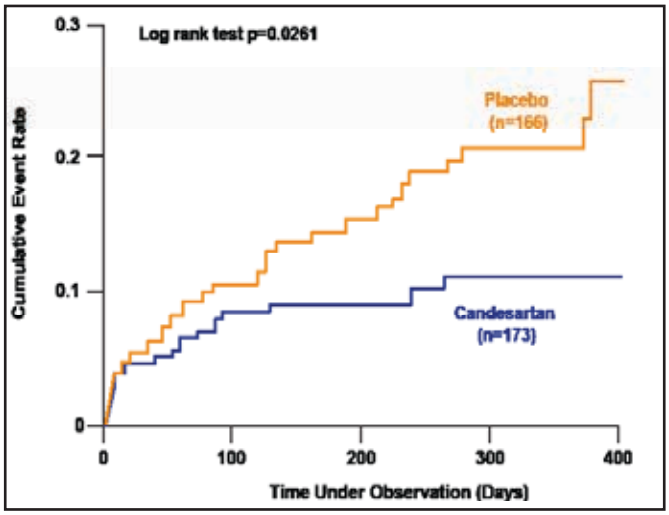
The Acute Candesartan Cilexetil Therapy in Stroke Survivors study [ACCESS; Schrader J et al. *Stroke* 2003] assessed the safety of modest blood pressure reduction by candesartan (an angiotensin receptor blocker) in the early treatment of stroke. Five hundred patients were recruited in a prospective, double-blind, placebo-controlled, randomized, multicenter Phase 2 safety study.

The trial was stopped prematurely when the cumulative 12-month mortality and number of vascular events differed significantly in favor of the candesartan group (OR, 0.48; 95% CI, 0.25 to 0.90). The cumulative event rates in patients receiving candesartan or placebo following an acute stroke are shown in Figure 1.

Figure 1. ACCESS: Cumulative Event Rate in Patients Receiving Candesartan or Placebo Following an Acute Stroke.



ACCESS=Acute Candesartan Cilexetil Therapy in Stroke Survivors.

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The Perindopril Protection Against Recurrent Stroke Study [PROGRESS] determined the effects of a blood pressure–lowering regimen in hypertensive and nonhypertensive patients with a history of stroke or TIA [PROGRESS Collaborative Group. *Lancet* 2001]. The primary outcome was total stroke (fatal or nonfatal).

A total of 6105 individuals from 172 centers in Asia, Australasia, and Europe were randomly assigned active treatment (n=3051) or placebo (n=3054). Active treatment was a flexible regimen based on the angiotensin-converting enzyme inhibitor perindopril (4 mg QD), with the addition of the diuretic indapamide at the discretion of treating physicians.

Over 4 years of follow-up, active treatment reduced blood pressure by 9/4 mm Hg on average. Combination therapy with perindopril plus indapamide reduced blood

pressure by 12/5 mm Hg and stroke risk by 43% (95% CI, 30 to 54). Single-drug therapy reduced blood pressure by 5/3 mm Hg and produced no discernible reduction in the risk of stroke.

Davis and Donnan [*N Engl J Med* 2012] noted that investigations (including brain imaging and arterial cardiac assessment) are warranted promptly after a TIA or stroke to determine cause and guide interventions to reduce subsequent risk. Physicians should routinely pay attention to lifestyle factors and prescribe blood pressure–lowering, statin, and antiplatelet drugs as indicated. Effective secondary-prevention strategies for selected patients include carotid revascularization for high-grade carotid stenosis and anticoagulation therapy for atrial fibrillation.

2012 European Guidelines on CVD Prevention in Clinical Practice

Written by Rita Buckley

Joep Perk, MD, Linnéuniversitetet, Kalmar, Sweden, presented a short summary with the main recommendations of the 2012 European Guidelines on cardiovascular disease (CVD) prevention in clinical practice. The Fifth Joint Task Force of the European Society of Cardiology and other societies on CVD prevention included representatives of 9 societies and invited experts [Perk J et al. *Atherosclerosis* 2012; *Eur Heart J* 2012].

According to Prof. Perk, the 2012 version is practical, shorter, and more adapted to clinical needs. It addresses 5 questions: 1) What is CVD prevention? 2) Why is it needed? 3) Who needs it? 4) How is it applied? and 5) Where should it be offered?

CVD prevention is needed because atherosclerotic CVD remains the leading cause of premature death worldwide. CVD affects both men and women. Of all deaths that occur before the age of 75 years in Europe, 42% are due to CVD in women and 38% in men. Prevention works. Over 50% of the reductions seen in CHD mortality relate to changes in risk factors and 40% to improved treatments [J Perk et al. *Eur Heart J* 2012].

One way this year's guidelines differ from earlier years is how recommendations are graded (strong or weak). Prior recommendations were based on graded evidence, giving randomized, controlled trials the greatest weight while undervaluing population studies, said Prof. Perk.

Risk age is a new way to drive home the importance of prevention to patients. For example, a 40-year-old male smoker with the same risk factors as a 60-year-old man with ideal risk factor levels has a risk age of 60 years.

Total risk estimation using multiple risk factors (eg, the Systematic Coronary Risk Evaluation Project [SCORE]) is recommended for all asymptomatic adults. Those at high risk can be identified by the presence of established CVD, type 1 or type 2 diabetes with end-organ damage, moderate to severe renal disease, or very high levels of individual risk factors (eg, a high SCORE risk; Table 1).

Table 1. Who Needs CVD Prevention?

Recommendations Regarding Risk Estimation	Class	Level	Grade
Total risk estimation using multiple risk factors (such as SCORE) is recommended for asymptomatic adults without evidence of CVD	I	C	Strong
High-risk individuals can be detected on the basis of established CVD, diabetes type 2 or type 1 with end-organ damage, moderate to severe renal disease, very high levels of individual risk factors, or a high SCORE risk	I	C	Strong

CVD=cardiovascular disease; SCORE=Systematic Coronary Risk Evaluation Project.

Major recommendations cover smoking, nutrition, physical activity, blood pressure, diabetes mellitus (Table 2), dyslipidemia (risk defined by low-density lipoprotein cholesterol level) with and without severe chronic kidney disease, patient adherence, and where and when CVD prevention programs should be offered.

Table 2. Recommendations on Diabetes Mellitus 2012.

Recommendations on Diabetes Mellitus	Class	Level	Grade
The target HbA1C for the prevention of CVD in diabetes of <7.0% (<53 mmol/mol) is recommended	I	A	Strong
Statins are recommended to reduce cardiovascular risk in diabetes	I	A	Strong
BP targets in diabetes are recommended to be <140/80 mm Hg	I	A	Strong

BP=blood pressure; CVD=cardiovascular disease.

Four key messages were emphaized:

- Risk-factor screening, including lipid profile, should be performed in adult men ≥40 years of age and women ≥50 years or postmenopausal.
- The physician in general practice is the key person to initiate, coordinate, and provide long-term follow-up for CVD prevention.
- The practicing cardiologist should be the advisor in cases where there is uncertainty over the use of preventive medication or when usual preventive options are difficult to apply.
- Patients with cardiac disease may participate in self-help programs to increase or maintain awareness of the need for risk factor management.