SJHG Heartbeat

Number 109 **September 2006**

IN THE NEWS….

SPARCL: Sparks more support for high-dose statins to improve CV outcomes

The **S**troke **P**revention by **A**ggressive **R**eduction in **C**holesterol Levels (**SPARCL**) trial. SPARCL is the first and only trial to evaluate the effects of statin therapy in patients who previously had a stroke or transient ischemic attack (TIA) and who had no known cardiovascular disease (CVD).[1] SPARCL confirmed what many people had predicted; atorvastatin 80 mg/day significantly reduced the risk of stroke in these patients. These results support the initiation of atorvastatin 80 mg/day in patients with stroke or TIA soon after the event. The results of SPARCL should increase the proportion of stroke patients who get a statin from the very low level that it is now up to a much higher proportion.

For cardiologists it is just more support for intensive lipid-lowering treatment. It's like a primary prevention study in patients who have no known cardiovascular disease who have had a stroke or TIA and there was a 35% reduction in heart disease, which is quite extraordinary. This study comes on the heels other high dose atorvastatin studies showing significantly improved outcomes in the primary and secondary prevention of CVD in over 27,000 patients (Figure 1).

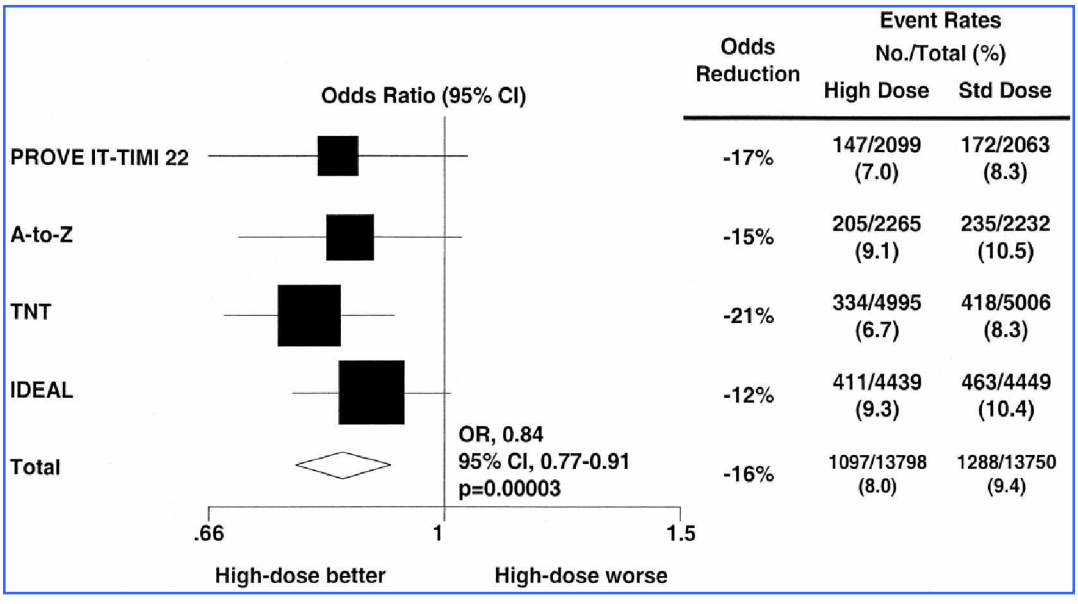

Figure 1. Reduction of events with high-dose atorvastatin treatment (*J Am Coll Cardiol* August 3 2006; 48:39-40).

Mean LDL-cholesterol at baseline in the SPARCL patients was 133 mg/dL. Mean on-atorvastatin-treatment LDL-C levels were 73 mg/dL (a 37% reduction) in this study of 4731 patients who were

randomized to placebo or atorvastatin 80mg with a mean 4.9-year follow-up. Most neurologists that I've talked to now believe that this treatment will become an established part of the way patients are managed after they've had a stroke or a TIA in addition, of course, to the rigorous control of blood pressure, and the use of antiplatelet medications. As well as bringing about a 16% reduction in the risk of stroke, the atorvastatin regimen also reduced the risk of major coronary events by 35%, coronary artery disease (CAD) events by 42 % and revascularization procedures by 45% in the SPARCL patients. A small increase in the incidence of hemorrhagic stroke was seen with atorvastatin, but the regimen of 80 mg/day of atorvastatin was well tolerated and the incidence of muscuskeletal adverse events was low.

Clinicians are currently advised to consider adding a statin in all stroke patients with a history of coronary events such as a myocardial infarction (MI), even when their LDL-cholesterol level is in the normal range. In patients with ischemic stroke and no history of a coronary event, however, no clear recommendations have been available prior to this study but **SPARCL provides clear evidence of the benefits of intensive statin therapy in the prevention of stroke in patients with cerebrovascular disease but no known CHD** and will expand the usage of this treatment. In this author's opinion the SPARCL trial is likely to add to the gathering momentum favoring the promotion of ischemic stroke to a "coronary heart disease risk equivalent," the adoption of statin therapy into guidelines for treatment of ischemic stroke, the enforcement of statin therapy on discharge after a stroke as a "quality indicator," and the inclusion of statins in preprinted stroke orders to improve adherence by physicians.

Lower Blood Pressure Better for Coronary Artery Disease Patients

The conclusion of a recent study in the August issue of JACC is that the most favorable rate of progression of coronary atherosclerosis is observed in those whose blood pressure (BP) falls within the "normal" JNC-7 category (i.e., systolic BP < 120mm Hg systolic and diastolic BP < 80mg Hg).[2] These findings point to a critical need to reassess the guidelines for managing BP in patients with coronary artery disease (CAD) just as has been done for heart failure and CKD with goal BPs of < 120/80.

The study evaluated the effects of normal BP, pre-hypertension (> 120/80 but < 140/90), and hypertension (> 140/90) on the progression of coronary atherosclerosis (as measured by intravascular ultrasound) in 274 patients taking part in a clinical trial. Both mean systolic BP and mean pulse pressure were significant predictors of change in atheroma volume in a multivariable analysis that controlled for lipid levels and other recognized coronary artery disease risk factors. The increase in adjusted atheroma volume was 12.0 mm for hypertensive patients and a non-significant 0.9 mm for pre-hypertensive subjects. Patients with normal BP experienced a decrease in atheroma volume of 4.6 mm over the 2-year study.

Patients who moved from pre-hypertensive to normal BP levels during the study had a decrease in atheroma volume (mean, 6.2 mm). Patients whose BP remained at pre-hypertensive levels had a mean 1.5-mm increase in atheroma volume. Thus, said Dr. Sipahi, the lead investigator, **BP levels below 120/80 mm Hg "are the best to slow progression of atherosclerosis."** These normal levels, he added, "were even associated with a strong trend for reversal of CAD." It is important to note that at this time it unknown whether this decrease in atheroma is associated with a reduction in cardiac events.

Two simple tests can reliably detect kidney disease in patients with CVD

An American Heart Association (AHA) science advisory recommends that all adult patients with (CVD) or cardiovascular risk factors be screened for kidney disease.[3] Chronic kidney disease (CKD) occurs commonly and is a major risk factor for progressive CVD, but appropriate intervention can lessen the progression. The main goal of this advisory is to give physicians the tools for reliably detecting kidney disease in these patients so that appropriate therapy can be instituted.

CKD, defined as structural or functional abnormalities in the kidney that persist for at least three months, is manifested by either kidney damage (detected as persistent albuminuria) or a decreased GFR. Up to 11% of American adults are affected. The writing group identifies two accurate, easy determinations to detect kidney disease: a test for estimated glomerular filtration rate (eGFR) that uses the Modification of Diet in Renal Disease (MDRD) equation, and a test for microalbuminuria.

The GFR is now calculated for us by most labs. This is necessary because when clinicians attempt to evaluate renal function relying on only serum creatinine values, results are misleading. Women and the elderly often have deceptively low serum creatinine levels, despite substantial reductions in GFR because of decreased muscle mass. Because the relationship between creatinine and GFR is inverse and nonlinear, small increases in creatinine can be mistakenly believed to be non-significant. The formula has built in multipliers for women (0.742) and blacks (1.21).

Screening for chronic kidney disease

Tests	Abnormal results
1. Measure serum creatinine and calculate eGFR using the MDRD study equation	<60 mL/min/1.73 m^2
2. In a random ("spot") urine sample, determine the albumin/creatinine ratio	>30 mg albumin/g creatinine

If either of the two screening tests is positive, it should be repeated at three months. If the test is still positive, the patient should be considered to have CKD and appropriate treatment should be initiated. If the tests are negative, they should be repeated annually. A patient with an extremely low GFR or a high urinary albumin/creatine ratio should be referred to a nephrologist.

The clear take home message here is **identify patients with CKD** because it is a major risk factor of progressive cardiovascular disease in patients with CVD or at high risk for CVD. Higher risk associated with **CKD is a signal for more aggressive treatment for CVD** with aspirin, statins, angiotensin blockade, blood pressure lowering and therapeutic lifestyle changes. Treat the patient accordingly.

Mario L Maiese DO, FACC, FACOI
Clinical Associate Professor of Medicine, UMDNJSOM Email: maiese1@comcast.net
Heartbeats online: www.sjhg.org

***Heartbeat* is a South Jersey Heart Group publication.**

[1] The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Investigators. High-dose atorvastatin after stroke or transient ischemic attack. *N Engl J* Med August 10 2006; 355: 549-559.

[2] Sipahi I et al. Effects of normal, pre-hypertensive, and hypertensive blood pressure levels on progression of coronary atherosclerosis. *J Am Coll Cardiol* August 15 2006; 48: 833-838.

[3] Brosius F C et al. Detection of chronic kidney disease in patients with or at increased risk of cardiovascular disease: A Science Advisory From the American Heart Association Kidney and Cardiovascular Disease Council; the Councils on High Blood Pressure Research, Cardiovascular Disease in the Young, and Epidemiology and Prevention; and the Quality of Care and Outcomes Research Interdisciplinary Working Group: Developed in Collaboration with the National Kidney Foundation. *Circulation* September 5 2006; 114: 1083-1087.