

(Jean-Louis Mas et al. *NEJM* 2006; 355:1660-1671)
The TACIT trial, currently under proposal, aims to directly compare medical therapy, endarterectomy and stenting.

Renal Failure Prevention

Progressive renal artery stenosis (RAS) is a problem, according to Chris White, MD, Chairman of the Department of Cardiology and Director of the Ochsner Heart & Vascular Institute in New Orleans, "I think it's actually quite dangerous to sit here and watch RAS progress." He adds that conservative medical therapy could lead to progression and eventually occlusion. Indeed, in the DRASTIC (Dutch Renal Artery STenosis Intervention Cooperative) trial, balloon angioplasty and medical therapy in RAS lead to 0% and 16% of patients suffering from occlusion, respectively. Finally, occlusion typically leads to renal failure. Renal artery stenosis has high prevalence in patients with coronary artery disease and confers additional mortality, making a case for screening high risk patients undergoing cardiac catheterization for presence of renal artery stenosis (White CJ et al. *Circulation* 2006; 114(17):1892-1895).

Patient selection is important for success in preventing RAS. Murray et al demonstrated that the more rapid the decline in renal function, the more likely the patient is to benefit from revascularization (Murray S et al. *Am J Kidney Dis* 2002; 39:60). Additionally, to avoid complications, embolic protection devices are recommended (though none of the devices are approved for use in renal arteries).

"Benign neglect of RAS is not benign," summarizes Dr. White, "you cannot treat patients with medical therapy and assume that because you are controlling the blood pressure you are not losing renal function."

Aortic Stenting and AAA Rupture Prevention

"Life really changed in September of 1999 when the FDA approved two graft prostheses," says Alan Lumsden, MD, Professor and Chief of the Division of Vascular Surgery at Baylor College of Medicine in Houston, when referring to the Guidant Bifurcated Endograft and the AneuRx Stent Graft System. Since then, many devices have emerged around the same concept and have shown significant promise.

In the US AneuRx trials, freedom from rupture was 98.4%, and freedom from aneurysm related death was 96.9%. The key to success, says Dr. Lumsden, is patient selection, with the single most important criteria being neck diameter (≤ 26 mm). Problems arise when a patient presents with a short, tapered neck. Therefore, pre-procedure planning involving a CT scan of the abdomen to calculate neck diameter, is critical.

"Good anatomy equals good results when you're treating patients with a stent graft," says Dr. Lumsden, adding, "We must understand and respect anatomical limits, practice careful follow-up, and understand the nuances of each device."

Improving Cardiovascular Risk Prediction in Women

Based on 2003 mortality data, 1 in 3 women are at risk for cardiovascular disease (CVD); this translates into more lives claimed by CVD than the next 5 leading causes of death combined. Currently, the best tool available for estimating a woman's risk factor is the Framingham risk score, yet most women under 70 years of age are classified as low risk using this method. These observations have prompted clinicians to incorporate other factors, such as family history and obesity (not

considered in the Framingham risk score), to predict overall risk. Additionally, there has been recent interest in identifying novel risk markers that improve traditional risk factor assessment in a cost effective way.

Exercise testing can improve risk reduction in asymptomatic women

Physical fitness has long been known to reduce all-cause mortality from a plethora of diseases, most notably CVD and cancer. Investigators sought to determine if fitness tests could predict heart disease in asymptomatic women. In a study of 2,994 North American asymptomatic women aged 30 to 80, exercise capacity and heart rate recovery (HRR) was tested and correlated with cardiovascular and all-cause mortality (Mora S. *JAMA* 2003; 290:1600). After age-adjustment, women who were below the mean for exercise capacity and HRR had a 3.5-fold increased risk of cardiovascular death compared to women who had above average values for both tests. This large increase in risk justifies the use of exercise testing and HRR in predicting CVD in asymptomatic women, combined with traditional risk factors.

Other non-traditional markers improve risk prediction in women

Recent data has suggested that plaque burden can be predictive of CAD risk. In a cohort of 10,377 asymptomatic women, calcium scores >1000 were 4.03 times more likely to experience CVD-related death as women whose calcium scores were <10 (Shaw LJ. *Radiology* 2003; 228:826). Additional factors demonstrating promising correlations with increased risk of CV events are levels of the inflammatory marker C-reactive protein, the ankle brachial index (measurements of blood pressure in the ankle and the arm) and carotid-artery media and intima thickness. The ongoing MESA trial (Multi-Ethnic Study of Atherosclerosis),

involving over 6,000 men and women between the ages of 45 and 84, will likely help us better understand the importance of sub-clinical disease measures in preventing CVD events, especially in women.

Cost considerations in CVD screening

The cost of CVD and stroke in the United States in 2006 is projected to be \$403.1 billion including direct and indirect costs, according to the Centers for Disease Control and Prevention. The use of screening tests to decrease this economic burden is therefore attractive, as long as the screening strategies succeed. Possible reasons why a screening strategy might fail are: clinicians do not act on screening results, available therapy may be ineffective, or real-world application of therapy may not yield expected results. Conversely, there is also the possibility that screening strategies may themselves improve adherence to clinical guidelines, observes Vera Bittner, MD, Professor of Medicine from the University of Alabama in Birmingham. Currently, however, there is insufficient data on the benefits of screening methods for CVD. In the future, studies must correlate screening tests not only to increases in risk, but to actual health benefits.

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What are the endogenous ligands of PPARs?

Finally, since most PPAR agonists were happened upon by chance, comments Jorge Plutzky, Assistant Professor at Harvard Medical School in Boston, MA, one way to better understand these synthetic agonists is to ask about the nature of the endogenous ligands. Dr. Plutzky's group found that endothelial lipase limits the expression of soluble adhesion molecules that are predictive of cardiovascular risk by hydrolyzing HDL and subsequently activating PPARalpha. Currently available PPAR-alpha agonists include fibrates such as fenofibrate. Construing these pathways could lead to the development of more effective and more physiologically relevant drugs.