

Hypercholesteremia, Hypertension, and Antiplatelet Therapy in PAD

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Medical management of cardiovascular (CV) risk factors, such as hypercholesteremia, hypertension (HTN), and the use of antiplatelet therapy may improve patient outcomes for peripheral artery disease (PAD). Michael R. Jaff, DO, Massachusetts General Hospital, Boston, Massachusetts, USA, discussed optimized medical therapy for patients with PAD.

In 2010, CV disease (CVD) was estimated to be present in 10.7% of women and 12.8% of men across the world [Lozano R et al. *Lancet* 2012]. Risk factors for PAD, such as hypertension, tobacco smoking, high fasting plasma glucose, and high total cholesterol levels represent a major reason why the burden of atherosclerosis remains significant throughout the world [Lim SS et al. *Lancet* 2012]. The top three pharmacologic interventions that can be undertaken include the use of antiplatelet therapy and treatment for hypercholesterolemia and hypertension.

Dr. Jaff summarized the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III that had previously recommended patients with high to very high risk of coronary heart disease (CHD) have a low-density lipoprotein cholesterol (LDL-C) goal of <70 mg/dL to 100 mg/dL. The recently released American College of Cardiology (ACC)/American Heart Association (AHA) cholesterol guideline statement [Stone NJ et al. *J Am Coll Cardiol* 2013] no longer recommends treatment toward a goal LDL-C target. A new calculator to determine an individual patient's CV risk has been included in this new document. In addition to the calculator, these new guidelines identify two groups of primary and secondary prevention patient types in whom physicians should choose the appropriate intensity of statin therapy in order to achieve percent reductions in LDL-C as defined below:

1. Individuals with clinical atherosclerotic CVD
2. Individuals with LDL-C levels ≥ 190 mg/dL, such as those with familial hypercholesterolemia
3. Individuals with diabetes aged 40 to 75 years old with LDL-C levels between 70 and 189 mg/dL and without evidence of atherosclerotic CVD
4. Individuals without evidence of CVD or diabetes but who have LDL-C levels between 70 and 189 mg/dL and a 10-year risk of atherosclerotic CVD $\geq 7.5\%$

Groups 1 and 2 should be treated with a high-intensity statin (defined as a statin that reduces LDL-C by at least 50%) and Groups 3 and 4 should be treated with a moderate intensity statin to achieve an LDL-C reduction of 30% to 49%.

The AIM HIGH trial, which evaluated the addition of niacin to statin therapy in order to raise high-density lipoprotein (HDL) levels, demonstrated no significant difference (log-rank $p=0.79$) in a composite of CHD-associated death, nonfatal myocardial infarction, ischemic stroke, acute coronary syndrome (ACS), and hospitalization due to ACS or other coronary or cerebrovascular reasons [Boden WE et al. *N Engl J Med* 2011]. Therefore, the addition of HDL-raising agents to the routine medical management of hypercholesterolemia is not recommended at this time. Ongoing trials of CETP inhibitors have the opportunity to provide definite evidence for the value of HDL-raising therapies.

In the National Health and Nutrition Examination Surveys database, 50% of the 13,375 patients with HTN had uncontrolled HTN, and most were taking one to two antihypertensive therapies per day [Egan BM et al. *Circulation* 2011]. A systolic/diastolic blood pressure (BP) of $\geq 140/90$ mm Hg is considered to be Stage 1 HTN, with 160 to 179/100 to 109 mm Hg considered Stage 2, and $\geq 180/110$ mm Hg considered Stage 3 HTN [Chobanian AV et al. *Hypertension* 2003]. Lifestyle interventions for HTN include weight reduction, diet modification including sodium reduction, increased physical activity, and limiting alcohol consumption. If lifestyle modification does not improve BP to the goal of <140/90 mm Hg, then Stage 1 HTN patients may receive thiazide-type diuretics or angiotensin-converting enzyme (ACE) inhibitor, angiotensin II receptor blocker (ARB), calcium channel antagonist (CCA), or β -blocker. Stage 2 HTN patients may require a two-drug combination of these agents. Dose optimization and additional agents may be required for patients who do not achieve their BP goal.

Antiplatelet therapy includes oral agents such as aspirin, clopidogrel, and ticagrelor. In patients with asymptomatic PAD, aspirin is recommended, while patients with symptomatic PAD are recommended to receive aspirin or clopidogrel, and patients with claudication may also be treated with cilostazol [Alonso-Coello P et al. *Chest* 2012].

Dr. Jaff concluded by suggesting that intervention of PAD risk factors by prescribing 1) statins for hypercholesterolemia, 2) antihypertensive therapy using a diuretic with or without ACE inhibitors, ARB, CCA, or β -blocker, and 3) aspirin or clopidogrel for PAD may be able to reduce CV events.