Your first slide implied the lower the better. We see the cardiologists going from what used to be levels of 3 mmol/L down to 2 for LDL to now less than 2. Based on this data, what threshold would you recommend for trying to get a patient's LDL cholesterol to?

Dr Bulbulia. There should be no threshold for initiation of statin therapy. HPS was not a target-finding study, but results from some "more vs less" statin trials suggest that higher doses of statin therapy will reduce cardiac and noncardiac vascular events further. However, the question is whether the risks of side effects associated with statins, which are dose-dependent, justify this approach.

Dr Jacob Lustgarten (Chevy Chase, Md). Did you notice any morbidity and mortality benefits in patients who underwent surgery? Statins are increasingly associated with a plaque stabilization effect and a lower perioperative rate of adverse cardiac events, and even a lower stroke risk after carotid surgery. It seems almost like these patients should be on statins much the way β-blockers are used. You followed a large number of randomized patients. Did you look for this effect?

Dr Bulbulia. We have not performed such an analysis, but I am aware of the results of observational and smaller interventional studies suggesting improved outcomes with statin therapy in the perioperative period. However, our results clearly demonstrate that all these patients should be on a statin before, during, and after their operation.

INVITED COMMENTARY

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Current guidelines give a class I recommendation to lower low-density lipoprotein (LDL) cholesterol levels below 100 mg/dL in all patients with peripheral artery disease (PAD) and a class IIa recommendation to lower the LDL cholesterol level below 70 mg/dL in patients who are at "very high risk of ischemic events."[1] High-risk PAD would be defined as more than one vascular bed involved—eg, a clinical history of concomitant coronary or cerebral vascular disease. The primary evidence for these recommendations comes from the original publication of the Heart Protection Study that evaluated the benefits of simvastatin in over 20,000 high-risk patients.[2] There were 6748 patients with PAD reported in the original publication, and these patients had a reduction in fatal and nonfatal cardiovascular events with simvastatin similar to that in patients with other forms of atherosclerosis. A recent meta-analysis of statin therapy in a broad population of high-risk patients demonstrated that there was a consistent benefit in reduction of risk of cardiovascular events across a wide population of patients and a wide range of baseline LDL cholesterol levels.[3] Thus there is a broad consensus to treat all patients at risk with statin drugs, regardless of their baseline cholesterol level.

The publication of the Heart Protection Study Collaborative Group in the *Journal of Vascular Surgery* focuses on the benefits of statin therapy specifically in the PAD population. The major new finding was a significant reduction in noncoronary revascularizations. Confirmatory findings were the consistency of the benefit across all populations studied (including patients with PAD who had no pre-existing coronary artery disease) and benefit regardless of baseline LDL cholesterol level. There was no benefit of the statin in preventing amputations, perhaps reflecting the end-stage pathophysiology of patients who suffer limb loss.

The message is clear. All patients with PAD are at high risk and meet criteria for statin therapy. The benefit of statin therapy is primarily systemic (prevention of major cardiovascular events) but also local (reduction of the need for revascularization).

REFERENCES

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