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Start a statin prior to vascular surgery

Rather than increasing cardiac complications, as previously feared, the perioperative use of statins appears to lower the risk.

PRACTICE CHANGER

HMG-CoA reductase inhibitors (statins), initiated 30 days before noncardiac vascular surgery, reduce the incidence of postoperative cardiac complications, including fatal myocardial infarction.[1,2]

STRENGTH OF RECOMMENDATION

A: 1 new randomized controlled trial (RCT), and 1 smaller, older RCT.

Schouten O, Boersma E, Hoeks S, et al. Fluvastatin and perioperative events in patients undergoing vascular surgery. *N Engl J Med.* 2009;361:980-989.

Durazzo AE, Machado FS, Ikeoka DT, et al. Reduction in cardiovascular events after vascular surgery with atorvastatin: a randomized trial. *J Vasc Surg.* 2004;39:967-975.

ILLUSTRATIVE CASE

A 67-year-old man with recurrent transient ischemic attacks comes in for a preoperative evaluation for carotid endarterectomy. The patient's total cholesterol is 207 mg/dL and his low-density lipoprotein cholesterol (LDL-C) is 109 mg/dL. He takes metoprolol and lisinopril for hypertension.

Should you start him on a statin before surgery?

Nearly 25% of patients with peripheral vascular disease suffer from a cardiac event within 72 hours of elective, noncardiac vascular surgery.[3] While most of these "complications" have minimal clinical impact and are detected by biochemical markers alone, some patients experience serious cardiac complications—including fatal myocardial infarction (MI).

That's not surprising, given that most patients who require noncardiac vascular surgery suffer from severe coronary vascular disease.[4] What is surprising is that most candidates for noncardiac vascular surgery are not put on statins prior to undergoing surgery.[1,2,5]

Statins were thought to increase —not prevent—complications

Until recently, taking statins during the perioperative period was believed to increase complications, including statin-associated myopathy. Indeed, guidelines from the American Heart Association (AHA), American College of Cardiology (ACC), and National Heart, Lung and Blood Institute (NHLBI) suggest that it is prudent to withhold statins during hospitalization for major surgery.[6]

1 small study hinted at value of perioperative statins

A small Brazilian trial conducted in 2004 called the AHA/ACC/NHLBI guidelines into question. The researchers studied 100 patients slated for noncardiac vascular surgery who were randomized to receive either 20 mg atorvastatin (Lipitor) or placebo preoperatively —and monitored them for cardiac events 6 months postoperatively. They found that the incidence of cardiac events (cardiac death, nonfatal MI, stroke, or unstable angina) was more than 3 times higher in the placebo group compared with patients receiving atorvastatin

(26% vs 8%, number needed to treat [NNT]=5.6; *P*=.031).[2]

The results of this small single study, although suggestive, were not sufficiently convincing to change recommendations about the preoperative use of statins, however. A more comprehensive study was needed to alter standard practice, and the Schouten study that we report on below fits the bill.[1]

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STUDY SUMMARY

Preoperative statin use cuts risk in half

Schouten et al followed 500 patients, who were randomized to receive either 80 mg extended-release fluvastatin (Lescol XL) or placebo for a median of 37 days prior to surgery.[1] All enrollees were older than 40 years of age and were scheduled for noncardiac vascular surgery. The reasons for the surgery were abdominal aortic aneurysm repair (47.5%), lower limb arterial reconstruction (38.6%), or carotid artery endarterectomy (13.9%). Patients who were taking long-term beta-blocker therapy were continued on it; otherwise, bisoprolol 2.5 mg was initiated at the screening visit. Patients who were already taking statins (<50% of potential subjects) were excluded. Other exclusions were a contraindication to statin therapy; emergent surgery; and a repeat procedure within the last 29 days. Patients with unstable coronary artery disease or extensive stress-induced ischemia consistent with left main artery disease (or its equivalent) were also excluded.

The primary study outcome was myocardial ischemia, determined by continuous electrocardiogram (EKG) monitoring in the first 48 hours postsurgery and by 12-lead EKG recordings on days 3, 7, and 30. Troponin T levels were measured on postoperative days 1, 3, 7, and 30, as well. The principal secondary end point was either death from cardiovascular causes or nonfatal MI. MI was diagnosed by characteristic ischemic symptoms, with EKG evidence of ischemia or positive troponin T with characteristic rising and falling values.

To gauge fluvastatin's effect on biomarkers, lipids, high-sensitivity C-reactive protein, and interleukin-6 were measured upon initiation of the medication and on the day of admission for surgery. Serum creatine kinase, alanine aminotransferase (ALT) levels, clinical myopathy, and rhabdomyolysis were monitored as safety measures, with levels measured prior to randomization, on the day of admission, and on postoperative days 1, 3, 7, and 30.

Both groups were similar in age (mean of 66 years), total serum cholesterol levels, risk factors for cardiac events, and medication use. About 75% of the enrollees were men. At baseline, 51% of the participants had a total cholesterol <213 mg/dL, and 39% had an LDL-C <116 mg/dL. Within 30 days after surgery, 27 (10.8%) of those in the fluvastatin group and 47 (19%) of patients in the placebo group had evidence of myocardial ischemia (hazard ratio=0.55; 95% confidence interval [CI], 0.34-0.88; *P*=.01). The NNT to prevent 1 patient from experiencing myocardial ischemia was 12.

Statin users had fewer MIs. A total of 6 patients receiving fluvastatin died, with 4 deaths attributed to cardiovascular causes. In the placebo group, 12 patients died, 8 of which were ascribed to cardiovascular causes. Eight patients in the fluvastatin group experienced nonfatal MIs, compared with 17 patients in the placebo group (NNT=19 to prevent 1 nonfatal MI or cardiac death (hazard ratio= 0.47; 95% CI, 0.24-0.94; *P*=.03).

Effects of statins were evident preoperatively. At the time of surgery, patients in the fluvastatin group had, on average, a 20% reduction in their total cholesterol and a 24% reduction in LDL-C; in the placebo group, total cholesterol had fallen by 4% and LDL-C, by 3%.

Patients receiving fluvastatin had an average 21% decrease in C-reactive protein, compared with a 3% increase for the placebo group. Interleukin-6 levels also were reduced far more in the fluvastatin group (33% vs a 4% reduction in the placebo group [*P*<.001]).

The medication was well tolerated. Overall, 6.8% of participants discontinued the study because of side effects, including 16 (6.4%) patients in the fluvastatin group and 18 (7.3%) in the placebo group. (After surgery, 115 [23.1%] of patients in the statin group temporarily dis-

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INSTANT POLL QUESTION

Do you initiate statin therapy for patients at least 30 days prior to noncardiac vascular surgery?

- ❑ *Yes, unless there are contraindications*
- ❑ *No, I am not convinced of the value of doing so*
- ❑ *It depends on the patient*
- ❑ *Other* _____

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continued the drug because of an inability to take oral medications for a median of 2 days.)

Rates of increase in creatine kinase of >10× the upper limit of normal (ULN) were similar between the fluvastatin and placebo groups (4% vs 3.2%, respectively). Increases in ALT to >3× ULN were more frequent in the placebo group compared with the fluvastatin group (5.3%, placebo; 3.2%, fluvastatin). No cases of myopathy or rhabdomyolysis were observed in either group.

WHAT'S NEW

Preop statins can be a lifesaver

The initiation of fluvastatin prior to vascular surgery reduced the incidence of cardiovascular events by 50%—a remarkable result. While patients at the highest risk were excluded from the study, those with lower cardiac risk nonetheless benefited from statin therapy. Experts have not typically recommended statins in the perioperative period for this patient population. The results of this study make it clear that they should.

Starting patients on statin therapy prior to vascular surgery reduced the incidence of cardiovascular events by half.

CAVEATS

Extended-release formulation may have affected outcome

The statin used in this study was a long-acting formulation, which may have protected patients who were unable to take oral medicines postoperatively. While we don't know if the extended-release formulation made a difference in this study, we do know that atorvastatin was effective in the Brazilian study discussed earlier.

CHALLENGES TO IMPLEMENTATION

Preop statins may be overlooked

Not all patients see a primary care physician prior to undergoing vascular surgery. This means that it will sometimes be left to surgeons or other specialists to initiate statin therapy prior to surgery, and they may or may not do so.

Optimal timing is unknown. It is not clear how little time a patient scheduled for vascular surgery could spend on a statin and still reap these benefits. Nor do we know if the benefits would extend to patients undergoing other types of surgery; in a large study of patients undergoing all kinds of major noncardiac surgery, no benefits of perioperative statins were found.[7]

Adherence to the medication regimen presents another challenge, at least for some patients. In this case, however, we think the prospect of preventing major cardiac events postoperatively simply by taking statins for a month should be compelling enough to convince patients to take their medicine. **JFP**

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