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The association of statin therapy with the primary patency of femoral and popliteal artery stents

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ABSTRACT

Objective: It has long been known that hydroxymethylglutaryl-coenzyme A reductase inhibitors (statins) broadly reduce cardiovascular events in patients with peripheral vascular disease. It was the goal of this study to determine whether there is an association between statin therapy and primary patency after stenting of superficial femoral and popliteal arteries.

Methods: The records of all patients undergoing primary nitinol stenting of the femoral and popliteal arteries at a single institution and by a single surgeon during a 10-year period were reviewed. Demographic characteristics of the patients and risk factors were identified. TransAtlantic Inter-Society Consensus (TASC II) classifications were determined for all stented lesions. Analysis was performed to determine whether the use of statins at the time of stent placement was associated with a change in rates of primary patency. Loss of primary patency was said to have occurred when an intrastent occlusion or a ≥70% stenosis was identified by arterial duplex ultrasound or angiography. Kaplan-Meier survival curves were plotted, and differences between groups were tested by log-rank method.

Results: Between 2004 and 2014, primary femoral or popliteal stenting was performed on 308 limbs in 250 patients. At the time of intervention, 52.4% of these patients were being treated with statin therapy; 137 interventions were done for claudication and 113 for critical limb ischemia. Of the lesions treated, 165 were TASC A or B and 85 were TASC C or D. Primary patency rates for all stented lesions were 75%, 54%, and 35% at 12, 24, and 36 months. The patency rates at 12, 24, and 36 months, respectively, were 80%, 55%, and 40% for those taking statins and 68%, 49%, and 28% for those not taking statins ($P = .178$). Statin therapy demonstrated a trend toward an association with improved primary patency rates in TASC A/B lesions but had no association in TASC C/D lesions (TASC A/B, $P = .056$; TASC C/D, $P = .537$). Statin compliance was found to be 87% at a mean follow-up of 24.1 months.

Conclusions: Although the use of statins has been shown to reduce cardiovascular morbidity and mortality in patients with peripheral vascular disease, overall there is not an association of these drugs with improved primary patency after primary stenting of femoral and popliteal artery lesions. However, when limbs are stratified for severity, less severe (TASC A/B) lesions demonstrated a trend toward a significant association between statin use and improved primary patency. This finding was not seen in more severe (TASC C/D) disease. (J Vasc Surg 2017;■:1-8.)

The use of statins to reduce coronary vascular events is well established.[1-4] These findings, combined with the benefits of other lipid-lowering agents, propelled the American Heart Association (AHA) and American College of Cardiology (ACC) to incorporate risk reduction guidelines of low-density lipoprotein (LDL) levels <100 mg/dL for patients with coronary artery disease.[4,5]

In light of these findings, the benefits of statin therapy in peripheral arterial disease (PAD) have also been investigated.[6] In the randomized Scandinavian Simvastatin Survival Study (4S), statins significantly reduced the incidence of new intermittent claudication from 3.6% to 2.3% during a median period of 5.4 years in patients with known cardiovascular disease.[7] In addition, both simvastatin and atorvastatin have been shown to improve pain-free walking time in patients with known peripheral vascular disease.[8,9] Given the benefit of lipid-lowering agents in the treatment of PAD, the AHA and ACC have expanded the guidelines for risk reduction of LDL levels <100 mg/dL to include patients with PAD.[6,10] In higher risk patients, a target LDL level of <70 mg/dL is recommended.[6] Statin therapy has also been shown to improve outcomes related to major peripheral vascular surgery. Notably, this includes a reduction in major adverse cardiovascular events after vascular surgery,[11] improved patency after infrainguinal bypass surgery,[12] and improved outcomes after endovascular

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aortic aneurysm repair[13] and carotid artery stenting.[14] Despite this evidence and the recommendations of the AHA and ACC, optimal medical management in PAD has repeatedly been shown to be underused.[15-18]

The effect of periprocedural statin therapy in patients undergoing peripheral endovascular treatment is less clear. Although statins have been shown in some studies to be associated with superior clinical outcomes after endovascular treatment of critical limb ischemia (CLI),[15] their role in less severe PAD, including patients with claudication, remains unknown. In addition, these studies contained patients undergoing a variety of percutaneous interventions. The purpose of this study was to investigate the effects of statin therapy in patients suffering from both claudication and CLI specifically undergoing primary stenting of either the superficial femoral artery (SFA), popliteal artery (PA), or both.

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective, single-center, cohort study
- **Take Home Message:** Primary stenting of femoral and popliteal arteries in 250 patients (308 procedures) was performed, with 52.4% of patients receiving statins. Those with TransAtlantic Inter-Society Consensus (TASC) A and B lesions who were taking statins had a trend to improved primary stent patency up to 36 months.
- **Recommendation:** This study suggests that statin use may improve primary patency of stents of some lesions in the femoral and popliteal arteries.

METHODS

After approval was obtained from the Institutional Review Board, the records of all patients undergoing primary nitinol stenting of the SFA or PA during a 10-year period were reviewed. Because of the retrospective nature of the study, a waiver for informed consent was granted by the Institutional Review Board, and informed consent was not obtained before inclusion in the study. All procedures included in this study were performed at a single institution and by or under the direct supervision of one vascular surgeon (S.K.). During the study period, diseased segments involving the SFA and all segments of the PA were primarily treated with the same technique, using exclusively self-expanding nitinol stents after balloon angioplasty. As described previously,[19,20] no attempts were made to perform percutaneous intervention on patients with orificial or total occlusion of the SFA, PA, and proximal tibial arteries. These patients were preferentially treated with bypass surgery. The study excluded patients who were lost to follow-up before a repeated arterial duplex ultrasound scan was performed after stent placement and those who were taking lipid-lowering agents other than statins at the time of intervention. Data collected included demographics of the patients, comorbidities, and use of a statin drug at the time of intervention. Indication for procedure, location of lesion, and lesion severity were recorded on a per-limb basis. Statin compliance was monitored by reviewing the records of the study patients' primary care providers, which in large part included self-reported current medication regimens. Patients were considered to have been compliant with statin therapy if they continued statin therapy from the time of stent placement until last recorded follow-up.

Lesion severity was characterized using the TransAtlantic Inter-Society Consensus (TASC II) classification.[21] To reduce previously described interobserver variability with TASC II classification,[22] each angiogram was reviewed separately by at least two of the authors. Discrepancies in TASC II classification were resolved on joint review of the angiograms in question. For the purpose of data analysis, TASC A and B lesions were grouped together, as were TASC C and D lesions. TASC classifications were not evaluated on an individual basis to maintain more limbs in both the TASC A/B and TASC C/D groups as well as to allow expected interobserver bias.

All of the procedures were performed in an angiography suite with fixed imaging. Our methods of intervention have previously been described.[19,20] Stents were chosen on the basis of supply and the surgeon"s preference. Patients received clopidogrel (300 mg) and aspirin (325 mg) before their procedures. All patients received 5000 units of heparin before percutaneous transluminal angioplasty and stent placement. Anticoagulation was not reversed at the end of the procedure. After the intervention, all patients received a minimum of a 30-day course of clopidogrel (75 mg daily) and aspirin (81 mg). Successful intervention was defined as an angiographic residual stenosis $<30\%$ in the treated vessel.

Patients underwent arterial duplex ultrasound scans at 30 days after the intervention and at 6-month intervals thereafter. Loss of primary patency was defined as stent occlusion or development of a $\geq 70\%$ stenosis in the stented segment. A 70% stenosis was said to be present when a peak systolic velocity of at least 200 cm/s and a 3:1 velocity ratio were seen across the lesion, which in our vascular laboratory correlates with a hemodynamically significant stenosis of 70% on angiography.[23]

We analyzed 308 interventions consisting of 250 patients. To create an independent sample, a single intervention for each patient among those with multiple interventions was taken by simple random sampling methods, yielding an analytic data set of 250 distinct interventions or patients. The differences in characteristics of the patients, comorbidities, and characteristics of the lesions between the cohorts of statin users and nonstatin users were examined by Fisher exact test for categorical variables and *t*-test for continuous variables (age).