From the Society for Clinical Vascular Society

Preoperative inflammatory status as a predictor of primary patency after femoropopliteal stent implantation

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ABSTRACT

Objective: The purpose of this study was to evaluate the impact of preoperative inflammatory status, as determined by complete blood count test parameters, on 12- and 24-month patency of femoropopliteal stenting for peripheral arterial disease.

Methods: We retrospectively analyzed baseline clinical and angiographic data among 138 patients (median age, 73 years; 46% female) from 2005 to 2014 at our institution with preoperative complete blood count test values and information of patency for at least 12 months after first-time femoropopliteal stenting. Patients were stratified into tertiles on the basis of preoperative blood counts to evaluate associations with in-stent restenosis (ISR) leading to loss of primary patency, defined by a Doppler velocity ratio ≥2.5:1, computed tomography angiography demonstrating ≥50% luminal narrowing within the stent, or reintervention.

Results: Univariate analysis determined that the 81 patients (59%) who experienced ISR within 12 months had significantly higher preoperative white blood cell (WBC), platelet, neutrophil, and lymphocyte counts than the 57 patients (41%) whose stents remained patent for longer than 12 months (8.7 vs 6.7 [$P < .001$], 246 vs 184 [$P < .001$], 5.7 vs 4.7 [$P = .001$], and 1.8 vs 1.2 [$P = .004$], respectively). Compared with patients in the lower WBC tertile (n = 45) who had a median patency of 19.4 months, those in the upper WBC tertile (n = 44) had a median patency of only 7.0 months and a 3.3-fold increased risk for ISR after adjusting for age, sex, lesion type, TransAtlantic Inter-Society Consensus II score, tibial vessel runoff, antiplatelet therapy, presence of diabetes, critical limb ischemia, adjunct procedures, hyperlipidemia, and end-stage renal disease in multivariate analysis ($P < .001$). Compared with patients in the lower platelet tertile (n = 45) who had a median patency of 16.9 months, those in the upper platelet tertile (n = 47) had a median patency of 7.1 months and a 2.7-fold increased adjusted risk ($P = .001$). Compared with patients in the lower neutrophil tertile (n = 33) who had a median patency of 14.3 months, those in the upper neutrophil tertile (n = 33) had a median patency of 6.2 months and a 3.2-fold increased adjusted risk ($P = .001$). After adjusting for covariates, patients divided into tertiles by lymphocyte counts exhibited no significant differences for ISR.

Conclusions: Routine preoperative tests that determine baseline inflammatory status may provide strong clinical utility in assessing potential risk stratification of patients for ISR after femoropopliteal stenting. Circulating WBCs, platelets, and neutrophils may be important inflammatory mediators of ISR. (J Vasc Surg 2017;■:1-9.)

Peripheral arterial disease (PAD) is a widespread vascular problem of significant consequence, affecting >8.5 million Americans older than 40 years and contributing to claudication and critical limb ischemia.[1] Throughout the years, endovascular revascularization through stenting has emerged as a common primary procedure for treating infrainguinal PAD. However, neointimal hyperplasia leading to in-stent restenosis (ISR) continues to be a major limitation that prevents long-term patency. Loss of primary patency from ISR after superficial femoral artery stenting has been documented as high as 47% within 12 months.[2] Subsequently, ISR often requires secondary endovascular or open surgical reinterventions, adding to the burden of patients with PAD. Identifying key mediators involved in the pathophysiologic mechanism of ISR is crucial for guiding decision-making in the management of PAD and improving the long-term patency of peripheral stents.

Although ISR is a complex and multifactorial process, there is well-established evidence that inflammation plays a critical role in contributing to neointimal hyperplasia. Several studies from the coronary artery literature have indeed demonstrated associations between inflammatory biomarkers and ISR, suggesting that certain patients may be predisposed to higher risk of restenosis

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Author conflict of interest: none.

Presented at the Forty-fourth Annual Symposium of the Society for Clinical Vascular Society, Las Vegas, Nev, March 12-16, 2016.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214

http://dx.doi.org/10.1016/j.jvs.2017.01.031

on the basis of simple hematologic parameters.[3-5] However, in the context of infrainguinal arterial interventions, particularly stenting, these relationships have not yet been extensively studied. Thus, this study aimed to evaluate the impact of baseline inflammatory status, as determined by preoperative complete blood count (CBC) values, on primary patency of femoropopliteal stenting.

METHODS

Study design. We conducted a retrospective assessment of clinical and angiographic records from January 2005 to October 2014 of all patients who underwent first-time stenting of femoral or above-the-knee popliteal arterial occlusive disease at the Mount Sinai Hospital (New York). Our study population included only patients with available preoperative CBC test results and information of patency for at least 12 months after operation. Patients with a history of prior interventions for lower limb revascularization, cancer, human immunodeficiency virus infection, transplants, or other autoimmune diseases were excluded. Subjects were also excluded if they experienced any other recent significant medical events (ie, myocardial infarction, stroke, major surgical procedure, or active infection) within 30 days before the index operation. Information about patient demographics, PAD risk factors, comorbid conditions, procedural characteristics, and discharge medications was noted and systematically reviewed from the patients' electronic hospital records. Diagnoses of comorbid conditions, such as hyperlipidemia and diabetes, were recorded if they were clearly noted in the charts, instead of examining actual cholesterol, glucose, and hemoglobin A_{1c} levels. Institutional Review Board approval was obtained for this study and conducted in accordance with the Health Insurance Portability and Accountability Act and the prevailing ethical principles governing research. Informed consent of the patient was waived.

Hematologic parameters. Patients can receive either a simple CBC or CBC with differential. The CBC provides absolute white blood cell (WBC), red blood cell, and platelet counts as well as mean platelet volume, hemoglobin concentration, hematocrit, mean corpuscular volume, and red cell distribution width. The CBC with differential also records additional information about neutrophil, lymphocyte, monocyte, eosinophil, and basophil counts.

For this study, the first preoperative CBC test recorded on admission was used to determine the patient's baseline inflammatory status. If a preoperative CBC test was not performed during admission, we used the most recent CBC within 30 days before intervention. All CBC tests were conducted at our institution within a few hours after initial blood sample collection using a Coulter LH755 or LH785 automated machine with SlideMaker and SlideStainer (Beckman Coulter Inc, Brea, Calif).

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective single-center cohort study
- **Take Home Message:** Femoropopliteal stent patency is strongly and negatively associated with elevated preoperative white blood cell, platelet, and neutrophil counts.
- **Recommendation:** The authors suggest that elevated levels of white blood cells, platelets, and neutrophils result in poor primary patency after femoropopliteal artery stenting.

Interventions. Experienced vascular interventionalists (vascular surgeons or interventional radiologists) performed all procedures using fixed fluoroscopic equipment (Siemens, Munich, Germany) or a portable imaging fluoroscopic C-arm (OEC 9800; GE Medical Systems, Milwaukee, Wisc), following standard techniques as previously described.[6,7] Computed tomography angiography, hemodynamic studies, or digital subtraction angiography was used to preoperatively evaluate lesion severity and anatomy. Lesions were classified as chronic total occlusions or stenotic (50%-99% stenosis) and were further categorized according to TransAtlantic Inter-Society Consensus II (TASC II) classification.[8] Angioplasty with a non-drug-coated balloon was uniformly performed, and if there was >30% residual stenosis or flow-limiting dissection, a self-expanding nitinol stent was deployed. None of the patients in this series received drug-eluting stents, covered stents, or adjunct atherectomy. Stent dimensions were chosen at the discretion of the interventionist. Completion angiography was performed to determine patency and tibial vessel runoff. Primary technical success was defined as a residual stenosis of <30% within the stent according to the final angiogram. All patients were discharged on aspirin (81 or 325 mg), clopidogrel (300 to 450 mg given immediately after intervention with maintenance dose of 75 mg for at least 30 days), or both antiplatelet medications.

Study end point. The primary study end point was ISR within 24 months after the procedure. ISR, which was considered loss of primary patency, was defined by a peak systolic velocity ratio ≥2.5:1 within the stent or computed tomography angiography demonstrating ≥50% in-stent luminal narrowing. Peak systolic velocity was determined by duplex ultrasound with color Doppler interrogation performed at routine follow-ups at a minimum of 3, 6, 9, 12, and 24 months postoperatively.

Statistical analysis. Patients were dichotomized into two cohorts: patients with vs patients without ISR