Missed Opportunities to Treat Atherosclerosis in Patients Undergoing Peripheral Vascular Interventions
Insights From the University of Michigan Peripheral Vascular Disease Quality Improvement Initiative (PVD-QI)²

Debabrata Mukherjee, MD; Prasanth Lingam, BS; Stanley Chetcuti, MD; P. Michael Grossman, MD; Mauro Moscucci, MD; Ann E. Luciano, RN; Kim A. Eagle, MD

Background—Peripheral vascular disease is a manifestation of systemic atherosclerosis and is associated with an increased risk of cardiovascular morbidity and mortality.

Methods and Results—We examined clinical outcomes in 66 consecutive patients undergoing peripheral vascular interventions at our institution between January 2001 and October 2001. At hospital discharge and at 6 months, lifestyle modifications and use of evidence-based therapy was suboptimal. At 6 months, a significant proportion continued to smoke (22.7%) and only half of the patients exercised, controlled their weight, or modified their diet for lipid control. The use of antiplatelet therapy was 77.2%; of angiotensin-converting enzyme, 35.9%; of β-blockers, 42.5%; and of statins, 50%. Twelve of the 66 patients (18.2%) had a clinical event of death, myocardial infarction, or stroke. An appropriateness algorithm for use of secondary prevention measures was created with the use of evidence-based therapy guidelines, and a composite appropriateness variable was also created. The use of evidence-based therapy was associated with a significant reduction of the composite of death, myocardial infarction, and stroke at 6 months (OR 0.02, 95% CI 0.01 to 0.44, \( P=0.01 \)).

Conclusions—Atherosclerosis risk factors are very prevalent in patients with peripheral vascular disease, but these patients receive less than optimal treatment after a predominantly technical vascular intervention. Effective secondary prevention with appropriate lifestyle interventions and evidence-based medical therapy needs to be strongly encouraged and implemented in these patients. (Circulation. 2002;106:1909-1912.)

Key Words: hypertension ■ peripheral vascular disease ■ atherosclerosis ■ risk factors

Atherosclerosis is the most common cause of peripheral vascular disease (PVD). PVD affects a large segment of the adult population, with an age-adjusted prevalence of 12% to 20%.² Several studies have demonstrated that patients with PVD have a 3- to 5-fold increased risk of cardiovascular mortality compared with age-matched controls.³ ⁶ A recent study demonstrated that atherosclerotic risk factors are very prevalent in patients with PVD, but these patients are treated less intensively with lipid-lowering agents, antiplatelet therapy, or antihypertensives.⁷

We assessed the intensity of risk factor modification and the use of evidence-based medical therapy in consecutive patients undergoing peripheral vascular intervention at our institution. We also examined predictors of clinical outcomes in these patients.

Methods

Data Collection

The Institutional Review Board of the University of Michigan approved the study. The study cohort consisted of 66 consecutive patients undergoing peripheral vascular interventions between January 2001 and October 2001 on the cardiology interventional service. Clinical, procedural, and in-hospital outcome data were collected prospectively by trained abstractors with the use of a standardized data collection form. Follow-up data on lifestyle interventions, compliance, evidence-based medical therapy, and clinical outcomes were collected by a dedicated clinical research nurse at 6 months after index intervention with telephone call interviews and review of medical records. Myocardial infarction (MI) was a clinical diagnosis based on the history of chest discomfort with elevated cardiac enzyme levels (CK-MB or troponin) requiring hospitalization, or new Q waves on the ECG in ≥2 contiguous leads documented in the medical record. Complete follow-up data were available for all subjects.

Appropriateness Algorithm

An appropriateness algorithm for the use of each of the various secondary prevention strategies was created with evidence-based clinical practice guidelines from the American College of Cardiology (ACC) and the American Heart Association (AHA).⁸ ¹¹ Class I recommendations from ACC/AHA guidelines were used to develop the appropriateness algorithm. On the basis of this information,
patients were considered candidates for lipid-lowering therapy if they had known hyperlipidemia. Hyperlipidemia was defined if it met any of the following criteria: total cholesterol ≥240 mg/dL, LDL ≥160 mg/dL, triglycerides ≥200 mg/dL, total cholesterol/HDL ratio ≥5.0, or past/present use of lipid-lowering agents. Angiotensin-converting enzyme (ACE) inhibitors were judged indicated for patients with any of the following conditions: hypertension, heart failure, MI, or a documented ejection fraction <30%. Similarly, β-blockers were judged indicated for patients with any of the following conditions: patients with prior MI, ejection fraction <30%, heart failure, and/or known coronary artery disease. Coronary artery disease was identified on the basis of history of angina, prior MI, PCI, or CABG. All patients with PVD were considered candidates for antiplatelet therapy, dietary modification, exercise training, and complete cessation from smoking. The percentage of patients on appropriate evidence-based therapy among those considered eligible was then calculated at hospital discharge and at 6 months. For each patient there were 4 possible recommended drugs: antiplatelet agents, lipid-lowering therapy, ACE inhibitors, and β-blockers. A composite appropriateness score was calculated for each patient on the basis of the number of the drugs used divided by the number of the drugs indicated, expressed as a percentage.

Statistical Analysis
Baseline characteristics were summarized with the use of frequencies and percentages for categorical factors and means and SD for continuous factors. A multivariable logistic regression model for the study cohort was performed for the composite of death, MI, and/or stroke at 6 months after the peripheral intervention. The following covariates were evaluated in the multivariable models: age, diabetes, and the composite appropriateness variable. Both a C index (measure of model discrimination) and Hosmer-Lemeshow test (measure of model calibration) were used to determine the performance of the multivariate models. All analyses were performed with the use of SAS version 8.2 (SAS Institute, Cary).

Results
The baseline characteristics of this cohort are shown in Table 1. The type of procedure performed in the cohort is listed in Table 2. According to the appropriateness algorithm discussed above, effective secondary prevention modalities were underutilized both at hospital discharge and at 6-month follow-up. At a mean follow-up of 6.4±7.1 months, a significant proportion continued to smoke (22.7%) compared with 27.3% before the procedure. Thus, >80% of smokers continued to smoke at 6-month follow-up. At follow-up, only half of the patients exercised, controlled their weight, or modified their diet for lipid control. Among eligible patients, the use of antiplatelet therapy was 77.2%; of ACE inhibitors, 35.9%; and of lipid lowering, only 50%. The composite appropriateness variable was 65.9±22% at discharge (Table 3).

Twelve of the 66 patients (18.2%) had a clinical event of death, MI, and/or stroke. There were 4 deaths (6%), 8 myocardial infarctions (12.1%), and one stroke (1.5%). The use of evidence-based therapy on the basis of the composite appropriateness variable was associated with a reduction of the composite end point of death, MI, and stroke at 6 months (OR 0.02, 95% CI 0.01 to 0.44, P=0.01). Older age and known diabetes mellitus were associated with a trend for worse clinical outcomes (Table 4). The C index was 0.77, suggesting good model discrimination, and the Hosmer-Lemeshow test statistic was 0.40, suggesting adequate model calibration and goodness of fit.

Discussion
As expected, we have shown that atherosclerotic risk factors are common in patients with PVD. However, the intensity of lifestyle modification and the use of evidence-based medical therapy in this high-risk cohort remain suboptimal. Another

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**TABLE 1. Baseline Characteristics of the Cohort Undergoing Peripheral Vascular Interventions (n=66)**

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Mean age, y (SD)</th>
<th>Male</th>
<th>Diabetic</th>
<th>Current smoker</th>
<th>Hypertension</th>
<th>Hypercholesterolemia</th>
<th>Renal insufficiency*</th>
<th>Coronary artery disease</th>
<th>Ejection fraction &lt;30%</th>
<th>Previous events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y (SD)</td>
<td>64.6 (10.4)</td>
<td>50.0</td>
<td>22.7</td>
<td>27.3</td>
<td>92.4</td>
<td>42.4</td>
<td>10.6</td>
<td>66.6</td>
<td>7.5</td>
<td>30.3</td>
</tr>
</tbody>
</table>

**TABLE 2. Types of Peripheral Interventional Procedure Performed**

<table>
<thead>
<tr>
<th>Type of Peripheral Interventional Procedure Performed</th>
<th>At Discharge (% of Patients)</th>
<th>At 6 Months (% of Patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subclavian artery</td>
<td>5 (7.5)</td>
<td></td>
</tr>
<tr>
<td>Renal artery</td>
<td>35 (53.1)</td>
<td></td>
</tr>
<tr>
<td>Common iliac artery</td>
<td>18 (27.2)</td>
<td></td>
</tr>
<tr>
<td>External iliac artery</td>
<td>5 (7.5)</td>
<td></td>
</tr>
<tr>
<td>Common femoral artery</td>
<td>2 (3.1)</td>
<td></td>
</tr>
<tr>
<td>Popliteal artery</td>
<td>1 (1.6)</td>
<td></td>
</tr>
</tbody>
</table>

**TABLE 3. Evidence-Based Therapy at Baseline and at 6-Month Follow-Up in Patients Undergoing Peripheral Vascular Interventions With the Use of an Appropriateness Algorithm**

<table>
<thead>
<tr>
<th>Evidence-Based Lifestyle and Medical Therapy</th>
<th>At Discharge (% of Patients)</th>
<th>At 6 Months (% of Patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continues tobacco use</td>
<td>27.2</td>
<td>22.7</td>
</tr>
<tr>
<td>Compliance with all medications</td>
<td>100</td>
<td>77.2</td>
</tr>
<tr>
<td>Exercise program</td>
<td>NA</td>
<td>54.5</td>
</tr>
<tr>
<td>Weight control</td>
<td>NA</td>
<td>54.5</td>
</tr>
<tr>
<td>Low-fat diet</td>
<td>42.4</td>
<td>57.5</td>
</tr>
<tr>
<td>Antiplatelet therapy</td>
<td>89.3</td>
<td>77.2</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>42.2</td>
<td>35.9</td>
</tr>
<tr>
<td>Lipid-lowering therapy</td>
<td>57.2</td>
<td>50</td>
</tr>
<tr>
<td>β-Blocker use</td>
<td>57.5</td>
<td>42.5</td>
</tr>
<tr>
<td>Composite appropriateness variable</td>
<td>65.9</td>
<td>48.4</td>
</tr>
</tbody>
</table>

NA indicates not applicable.

Percentages reflect use among patients considered eligible for each therapy.
important issue is that of patient noncompliance with medications. There is a significant opportunity, we believe, to improve the appropriate use of secondary preventive therapy in these high-risk patients and improve patient compliance with education and empowerment. Continuous quality-improvement initiatives such as the American College of Cardiology Guidelines Applied in Practice (GAP) project may be particularly relevant in this high-risk population.

Statin therapy has been shown to be beneficial in patients undergoing percutaneous coronary interventions. Statins lower lipids and have salutary effects on platelet adhesion, thrombosis, endothelial function, inflammation, and plaque stability. However, minimal data exist on the effectiveness of statins in patients undergoing vascular interventions. One meta-analysis of randomized trials described 698 patients with PVD and demonstrated a trend for a reduction in mortality. The Heart Protection Study demonstrated that statins produce substantial clinical benefits for a wide range of high-risk patients with coronary and vascular diseases.

Both aspirin and clopidogrel have been demonstrated to be beneficial in patients with PVD. Moreover, a study that examined pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention (Clopidogrel in Unstable angina to prevent Recurrent ischemic Events in patients undergoing Percutaneous Coronary Intervention [PCI-CURE]) demonstrated significant benefit of the combination of aspirin and clopidogrel. Chew et al had similarly demonstrated that pretreatment with clopidogrel was associated with a substantial reduction in 30-day death or MI in individuals undergoing coronary interventions.

The Heart Outcomes Prevention Evaluation study demonstrated that ramipril, an ACE inhibitor, significantly reduced the rate of cardiovascular death, MI, and stroke in patients at high risk of cardiovascular events. Of the 9297 patients in this study, 4051 had PVD, and these patients had a similar reduction in the primary end point when compared with those without peripheral vascular disease. Ellis et al recently demonstrated the benefit of ACE inhibitors in patients undergoing coronary stenting.

Thus, drugs such as statins, clopidogrel, and ACE inhibitors have been associated with significantly improved outcomes in patients undergoing coronary interventions. However, data on the efficacy of these agents in patients undergoing peripheral interventions is not available. In this pilot study, we have shown significant beneficial effects of the evidence-based use of antiplatelet therapy, statins, ACE inhibitors, and β-blockers in patients undergoing peripheral vascular interventions with an improvement in clinical outcomes at 6-month follow-up.

There are several potential limitations of the present study, including the small sample size. Thus, this analysis should be considered hypothesis generating. The appropriateness assessment for evidence-based therapy was based on ACC/AHA Class I guidelines by retrospective review. If patients had previously experienced untoward reactions or contraindications to therapy, this may have been underrepresented with our sampling methodology. This might overestimate the potential opportunity to improve secondary preventive measures.

Patients undergoing peripheral vascular interventions represent an important cohort in which secondary vascular disease prevention is likely to be particularly effective and cost-effective. Cardiologists are doing an increasing share of peripheral vascular interventions, and there is an opportunity to have a far-reaching impact by focusing beyond the intervention. Cardiovascular specialists have an opportunity not only to provide high-quality and appropriate vascular interventions, but also to seize the periprocedural moment in aggressively treating the underlying atherosclerotic process through lifestyle modifications and effective pharmacological therapies. Ultimately, we suspect that attention to these disease management opportunities is more likely to affect both quality and quantity of life than the procedures themselves. This pilot experience has galvanized a more disciplined approach to atherosclerosis management after peripheral vascular intervention in our cardiology interventional program.

Acknowledgment
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