The Quality and Impact of Risk Factor Control in Patients With Stable Claudication Presenting for Peripheral Vascular Interventions

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Background—Peripheral arterial disease is a manifestation of systemic atherosclerosis and is predictive of future cardiovascular events. Clinical trial data have demonstrated that medical therapy can attenuate cardiovascular morbidity and mortality in patients with peripheral arterial disease. The utilization and impact of recommended medical therapy in a contemporary population of patients who undergo percutaneous interventions for lifestyle-limiting peripheral arterial disease is unknown.

Methods and Results—Using the Blue Cross Blue Shield of Michigan Cardiovascular Consortium Peripheral Vascular Intervention (BMC2 PVI) database, we identified 1357 peripheral vascular intervention encounters between January 2007 and December 2009 for the purpose of treating claudication. Before the intervention, 85% of these patients used aspirin, 76% used statin, 65% abstained from smoking, and 47% did all 3. There was no difference in cardiovascular events among those taking an aspirin and a statin on admission and those who were not. However, in both an unadjusted and a multivariable analysis, the odds of an adverse peripheral vascular outcome (repeat peripheral intervention, amputation, or limb salvage surgery) within 6 months decreased by more than half in patients receiving aspirin and statin therapy before peripheral vascular intervention as compared with those who received neither (odds ratio, 0.45; 95% CI, 0.29–0.71).

Conclusions—The fundamental elements of medical therapy in patients with lifestyle-limiting claudication are often underutilized before referral for revascularization. Appropriate medical therapy before percutaneous revascularization is associated with fewer peripheral vascular events at 6 months. (Circ Cardiovasc Interv. 2012;5:850–855.)

Key Words: claudication ■ peripheral vascular disease ■ percutaneous treatment ■ medical therapy ■ quality

Peripheral arterial disease (PAD) is a manifestation of systemic atherosclerosis and is predictive of future cardiovascular events. Despite ample evidence of risk, studies have shown that PAD patients commonly receive suboptimal medical therapy. Patients with lifestyle-limiting claudication are often referred for percutaneous revascularization to manage their symptoms. Current guidelines recommend revascularization in patients with vocational or lifestyle-limiting claudication who have had an inadequate response to exercise or pharmacological therapy. Percutaneous therapy is preferred in patients with focal aorto-iliac or femoropopliteal disease. Though revascularization and aggressive medical therapy have both been shown to reduce symptoms of claudication, only medical therapy has been shown to reduce morbidity and mortality related to vascular events.

The intention of this study is to assess the quality of medical therapy in patients who receive percutaneous interventions for the indication of lifestyle-limiting claudication and to quantify the association of preintervention medical therapy with clinical outcomes in the 6 months after the intervention.

Methods

Study Population

We used the Blue Cross Blue Shield of Michigan Cardiovascular Consortium Peripheral Vascular Intervention (BMC2 PVI) registry to identify patients who underwent percutaneous interventions for the treatment of stable claudication defined as leg pain attributable to poor arterial circulation that occurs during exercise and relieved with rest. The BMC2 PVI registry is a multicenter, multi-disciplinary, regional outcomes registry of consecutive patients who receive percutaneous, noncoronary, vascular interventions in the state of Michigan that was developed for the purposes of quality improvement. The data collection tool captures demographic, historical, clinical, and laboratory value elements along with intra-procedural variables. Peripheral disease specific data include symptoms, procedural indications and methods, and the validated Peripheral Artery Questionnaire. Follow-up data are collected by nurse coordinators via telephone interview at 30 days and 6 months. Data quality is controlled at 3 levels starting with stability of data, then reliability of data elements, and finally the validity of the data. The BMC2 PVI database is a repository of longitudinal data from consecutive patients undergoing vascular procedures, serving as an ongoing data resource for registry data quality improvement and outcomes research.

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WHAT IS KNOWN

- Patients with peripheral vascular disease are at high risk for developing coronary and cerebrovascular disease.
- Risk factor modification with use of statins and aspirin has been shown to reduce major adverse cardiovascular events in patients with peripheral vascular disease.
- Risk factors are often under treated in patients with peripheral vascular diseases.

WHAT THE STUDY ADDS

- Patients presenting for elective intervention for stable claudication often arrive on suboptimal medical therapy.
- Despite contact with a vascular specialist during the peripheral vascular intervention encounter patients are frequently discharged without statin therapy.
- Patients who present on a statin and aspirin before a peripheral vascular intervention have a lower odds of developing a peripheral vascular event in the six months after the intervention.

with manual review at the point of data entry to insure completeness and validity by trained nurse coordinators. A database manager confirms the quality of data entry and analyzes random samples of data for clinical consistency. Finally, twice a year a nurse coordinator from BMC2 PVI performs a site visit to audit all cases with severe complications and a random sample of 5% of cases. The BMC2 PVI registry has been approved by the Institutional Review Board of each participating site. The BMC2 PVI registry is based on the previously described PVD-QI database.7,16

The cohort included patients who received interventions in the aorto-iliac or femoropopliteal distributions. We excluded patients with rest symptoms or evidence of critical limb ischemia. Patients with a reported intolerance or contraindication to aspirin or cholesterol-lowering drugs were also excluded. Acceptable contraindications to medications are defined in the BMC2 PVI Definition Dictionary and confirmed at the point of data collection. Contraindications for aspirin included a history of hypersensitivity, concurrent warfarin therapy, and a history of coagulopathy. Acceptable contraindications for lipid-lowering drugs included a history of statin-induced myopathy or elevated liver function enzymes, or intolerance to statins as documented in the medical record. Data were prospectively collected from PVI procedures performed in 11 hospital sites from 2007 through 2009.

Definitions and Measures

Demographics and clinical data were collected before the PVI procedure and at discharge. Coronary artery disease (CAD) was defined as a history of myocardial infarction (MI), coronary artery bypass graft surgery, or percutaneous coronary intervention. Cerebrovascular disease was defined as having a history of stroke or transient ischemic attack. We defined minimal medical therapy before intervention as a combination of being on an aspirin, a statin, and being a nonsmoker. We defined minimal medical therapy at discharge as a combination of being prescribed an aspirin, a statin, and having documented tobacco cessation counseling before discharge or having been a nonsmoker at admission. These treatment elements are consistent with the recently published performance measures for adults with peripheral artery disease.17 Medication history was obtained from the medical record and confirmed with the patient before the procedure, at discharge and at each follow-up interval. We measured the outcomes of all-cause death, MI, stroke, amputation, repeat peripheral intervention, or

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All Patients 2007-2009
N = 10 483

Non-lower extremity interventions
N = 1463
Below the Knee interventions
N = 2168

Patients with Aorto-Iliac or Femoro-popliteal Interventions
N = 6837

Patients with Critical Limb Ischemia / Rest Symptoms
N = 2209

Patients with incomplete procedural data
N = 15

Patients with contraindication to Aspirin and/or Statin:
N = 559

Patients without 6 month follow-up data:
N = 2712

Final Patient Population
N = 1357

Figure 1. Flow chart of patient inclusion and exclusion.
Table 1. Patient Characteristics by Baseline Medication Use (n=1357)

<table>
<thead>
<tr>
<th>Demographics</th>
<th>On Both Aspirin and Statin (n=931)</th>
<th>Not on Both of Aspirin and Statin (n=426)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Median, y</td>
<td>68</td>
<td>67</td>
<td>0.52</td>
</tr>
<tr>
<td>Female, %</td>
<td>34.3</td>
<td>42.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Race (nonwhite), %</td>
<td>11.8</td>
<td>15.2</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Clinical history

| BMI, mean | 28.4                             | 27.0                                   | <0.01  |
| DM, %     | 42.0                             | 31.1                                   | <0.01  |
| HTN, %    | 90.3                             | 81.7                                   | <0.01  |
| COPD, %   | 26.9                             | 33.9                                   | <0.01  |
| Dialysis, % | 1.2                           | 1.0                                    | 0.69   |
| Current smoker, % | 31.9                        | 42.0                                   | <0.01  |
| Ever smoked, % | 91.7                        | 91.1                                   | 0.69   |
| CAD, %     | 71.7                             | 38.6                                   | <0.01  |
| Prior MI, % | 36.1                          | 17.6                                   | <0.01  |
| Prior CABG or PCI % | 61.1                       | 29.6                                   | <0.01  |
| Prior PCI % | 40.9                           | 17.2                                   | <0.01  |
| Prior CABG, % | 34.4                          | 18.5                                   | <0.01  |
| Atrial fibrillation, % | 9.9                        | 12.3                                   | 0.17   |
| Stroke or TIA, % | 29.1                           | 23.2                                   | 0.02   |
| Prior LE PVI, % | 47.7                          | 39.7                                   | <0.01  |
| Prior LE vascular surgery, % | 41.1                         | 35.4                                   | 0.05   |
| ABI, lowest recorded value | 0.6                           | 0.6                                    | 0.16   |

Location of intervention

| Aorto-iliac, % | 38.2                             | 39.0                                   | 0.80   |
| Femoropopliteal, % | 61.8                        | 61.0                                   | 0.80   |
| Bilateral intervention, % | 19.6                         | 17.8                                   | 0.46   |

BMI indicates body mass index; DM, diabetes mellitus; HTN, hypertension; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease defined as history of myocardial infarction, percutaneous coronary intervention or coronary artery bypass surgery; MI, myocardial infarction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; TIA, transient ischemic attack; LE, lower extremity; PVI, percutaneous peripheral vascular intervention; and ABI, ankle-brachial index.

Results

Patient Characteristics

There were 1357 PVI procedures included in the cohort. Our case selection process is described in Figure 1. Patient characteristics are shown in Table 1. Of the patients analyzed, 35 (2.6%) had missing data elements. Patients who were treated with aspirin and statin before PVI tended to have more comorbidities such as hypertension, diabetes mellitus, CAD, and stroke. These patients were also more likely to have undergone past coronary or peripheral revascularization procedures. Patients treated with aspirin and statins were also more likely to be on β-blockers (67.8% versus 40.4%; P<0.01) and angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (68.2% versus 49.1%; P<0.01).

Medical Therapy

Prescribed use of aspirin and statin increased from baseline to discharge (aspirin use increased from 85.3% to 91.6%, P<0.01; statin use increased from 75.8% to 81.2%, P<0.01). Aspirin and statin use together increased from 68.6% to 76.5% (P<0.01). Tobacco cessation counseling was provided to 76.7% of current smokers. At admission, 46.7% of patients were on aspirin, statin, and did not smoke; at discharge, 71.0% were on both drugs and either did not smoke at admission or did smoke and had tobacco cessation counseling (P<0.01).

Correlates of Medical Therapy at Baseline

Adjusted correlates of medical therapy at baseline are presented in Table 3. Nonwhite status and the presence of chronic obstructive pulmonary disease were associated with statistically lower utilization of medical therapy. Diabetes mellitus, CAD, and a history of previous peripheral revascularization were associated with statistically higher utilization of medical therapy at baseline. The relationship between age and baseline drug therapy was quadratic, with the very young and the elderly being less likely to arrive on treatment.

Association of Baseline Medical Therapy with Clinical Outcomes at 6 Months

Unadjusted results comparing drug therapy and outcomes are shown in Table 4. Users of both aspirin and statins had a lower incidence of peripheral events such as repeat peripheral intervention, limb salvage surgery, and amputation (7.3%
versus 15.8%; P<0.01). The incidence of major cardiovascular events such as death, MI, and stroke was not different between patients treated with aspirin and statin and patients receiving neither.

When adjustments were made for age, race, sex, current smoking, diabetes mellitus, prior cardiovascular events, previous peripheral vascular interventions, and renal failure requiring dialysis, baseline medical therapy remained associated with adverse peripheral outcomes at 6 months. Compared with patients admitted on neither aspirin nor a statin, the odds of an adverse peripheral vascular event were lower in patients admitted on 1 drug (either aspirin or statin; odds ratio, 0.67; 95% CI, 0.53–0.84) and lower still for patients admitted on both drugs (odds ratio, 0.45; 95% CI, 0.29–0.71; Figure 2).

## Discussion

Overall we have shown that patients presenting for elective invasive management of lifestyle-limiting PAD often do not receive the basic elements of medical therapy. The use of statin therapy only improves modestly at discharge. The application of medical therapy appears to be associated with both the patient’s clinical history and demographics. Notably, the use of aspirin and statin before intervention was associated with a reduced need for repeat interventions at 6 months. More than half of all patients fail to receive appropriate medical therapy and abstain from tobacco before PVI. Our multivariable model shows that patients with a history of CAD or prior peripheral revascularization tend to have a higher likelihood of being on medical therapy. This observation of more robust utilization of secondary prevention measures in patients with established CAD or CAD equivalents was also noted in the National Cardiovascular Data Registry and the National Health and Nutrition Examination Study.\(^2\)\(^{18}\)\(^{19}\) We also note a lower rate of medical therapy in nonwhite patients. This relationship between race and underutilization of medical therapy has been seen in both the Veterans Affairs health system and in the CRUSADE database of acute coronary syndrome patients.\(^2\)\(^{20}\)\(^{21}\) This finding warrants further investigation on the causes and solutions for disparate application of prevention strategies. Our model does not correct for socioeconomic, geographic, or payer differences and thus limited conclusions can be made about this finding.

In a follow-up window of only 6 months, we have demonstrated a significant clinical outcome difference in patients who present for PVI on appropriate medical therapy. After correcting for major comorbidities, we found a significantly lower rate of peripheral vascular adverse outcomes in patients who receive an aspirin and a statin before PVI. These findings suggest an association between preintervention medical therapy and intermediate term procedural outcome in this
high-risk population. Our population size and limited follow-up window preclude the ability to discern differences in hard cardiovascular outcomes. However, data from the Heart Protection Study suggest that use of statins reduces the rate of major cardiovascular events in patients with PAD.22

Our study is limited by the lack of data on lifestyle interventions such as supervised exercise programs. Though the positive impact of supervised exercise programs has been demonstrated in patients with intermittent claudication and is part of current treatment guidelines, the absence of payer support has limited real-world implementation of this intervention. Future studies should focus on the barriers to supervised exercise and possible methods to overcome them in this population. We are also unable to assess the adequacy of blood pressure control in patients with hypertension which may directly impact the outcome measures that we are evaluating. Though we are able to capture the number of patients treated with statin therapy we are unable to demonstrate the degree to which their lipids are controlled. Suboptimal lipid management may lead to an underestimation of the benefit of statin therapy. Finally, we did not have a sufficient number of patients to determine the association between an improvement in medication status and outcomes.

The modest improvement in statin prescription at discharge signifies a missed opportunity to provide a life-saving intervention for PAD patients. The prescription of secondary prevention medications in an in-hospital setting has been shown to improve long-term compliance in a CAD population.23 Using the procedural encounter as a springboard toward improved medical therapy may help patients and providers galvanize their approach to prevention. The relatively low risk of medical therapy combined with the established clinical benefits in patients with PAD speaks to the pressing need to bridge this quality gap. Although a considerable effort has been focused on the impact of guideline adherence in patients with MI and heart failure, there are currently no such national programs focused on patients with PAD.24 Strategies, such as collaborative continuous quality improvement programs, need to be explored and expanded, with the goal of improving the quality of medical therapy in this patient population. Further studies are warranted to elucidate and rectify the reasons for the dramatic underuse of medical therapy in this patient population and to establish effective solutions to this problem.

Our study has shown that appropriate medical therapy before elective PVI is associated with a lower rate of peripheral vascular events at 6 months. Future research should focus on identifying barriers to accessing care in this patient population. Efforts to improve the quality of medical therapy are needed in this high-risk patient population to reduce both peripheral and major cardiovascular clinical complications.

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Disclosures

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