Polyvascular Disease and Long-Term Cardiovascular Outcomes in Older Patients With Non–ST-Segment–Elevation Myocardial Infarction

Sumeet Subherwal, MD, MBA; Deepak L. Bhatt, MD, MPH; Shuang Li, MHS; Tracy Y. Wang, MD, MHS; Laine Thomas, PhD; Karen P. Alexander, MD; Manesh R. Patel, MD; E. Magnus Ohman, MD; W. Brian Gibler, MD; Eric D. Peterson, MD, MPH; Matthew T. Roe, MD, MHS

Background—The impact of polyvascular disease (peripheral arterial disease [PAD] and cerebrovascular disease [CVD]) on long-term cardiovascular outcomes among older patients with acute myocardial infarction has not been well studied.

Methods and Results—Patients with non–ST-segment–elevation myocardial infarction aged ≥65 years from the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines) registry who survived to hospital discharge were linked to longitudinal data from the Centers for Medicare & Medicaid Services (n=34,205). All patients were presumed to have coronary artery disease (CAD) and were classified into the following 4 groups: 10.7% with prior CVD (CAD+CVD group); 11.5% with prior PAD (CAD+PAD); 3.1% with prior PAD and CVD (CAD+PAD+CVD); and 74.7% with no polyvascular disease (CAD alone). Cox proportional hazards modeling was used to examine the hazard of long-term mortality and composite of death or readmission for myocardial infarction or stroke (median follow-up, 35 months; interquartile range, 17–49 months). Compared with the CAD alone group, patients with polyvascular disease had greater comorbidities, were less likely to undergo revascularization, and received less often recommended discharge interventions. Three-year mortality rates increased with number of arterial bed involvement as follows: 33% for CAD alone, 49% for CAD+PAD, 52% for CAD+CVD, and 59% for CAD+PAD+CVD. Relative to the CAD alone group, patients with all 3 arterial beds involved had the highest risk of long-term mortality (adjusted hazard ratio [95% CI], 1.49 [1.38–1.61]; CAD+CVD, 1.38 [1.31–1.44]; CAD+PAD, 1.29 [1.23–1.35]). Similarly, the risk of long-term composite ischemic events was highest among patients in the CAD+PAD+CVD group.

Conclusions—Among older patients with non–ST-segment–elevation myocardial infarction, those with polyvascular disease have substantially higher long-term risk for recurrent events or death. Future studies targeting greater adherence to secondary prevention strategies and novel therapies are needed to help to reduce long-term cardiovascular events in this vulnerable population.

Key Words: myocardial infarction ■ peripheral vascular disease ■ coronary diseaese ■ rebrovascular disorders ■ aged

Atherosclerotic involvement of extracardiac vascular beds (ie, peripheral arterial disease [PAD] and cerebrovascular disease [CVD]) is prevalent among older patients with acute myocardial infarction (MI). Furthermore, there appears to be a gradation of risk with the number of affected arterial beds such that patients with atherosclerotic involvement of all 3 arterial beds have worse short-term and intermediate-term outcomes compared with those with dual-bed involvement, whereas those with coronary bed involvement alone have the lowest risk. Despite these findings, the influence of polyvascular disease on the long-term outcomes of patients after MI has...
WHAT IS KNOWN

- Prior studies have shown that patients with non–ST-segment–elevation myocardial infarction and polyvascular disease (prior peripheral arterial disease, cerebrovascular disease, or both in addition to coronary artery disease) have worse in-hospital and intermediate-term (6–12 months) outcomes following their acute myocardial infarction.
- There appears to be a gradation of risk with the number of affected arterial beds such that patients with atherosclerotic involvement of all 3 arterial beds have worse short-term and intermediate-term outcomes compared with those with dual-bed involvement, whereas those with coronary bed involvement alone have the lowest risk.

WHAT THE STUDY ADDS

- The present analysis extends findings of prior studies to the long-term setting by demonstrating in a contemporary cohort that older patients with non–ST-segment–elevation myocardial infarction and polyvascular disease have very high rates of mortality (>50% at 3 years) and composite ischemic end points compared with patients without polyvascular disease.
- The risk of long-term outcomes increases incrementally with increasing number of arterial beds involved.
- Despite increased long-term risk associated with polyvascular disease, the use of guidelines-based recommended therapies is modest.

Methods

The CRUSADE Quality Improvement Initiative comprised a database of patients with high-risk unstable angina and NSTEMI admitted to US hospitals from November 2001 through December 2006. Inclusion criteria were chest pain or anginal equivalent at rest of at least 10 minutes in duration and occurring <24 hours before presentation and at least one of the following: (1) ischemic ECG changes (ST-segment depression or transient ST-segment elevation) or (2) elevated levels of biomarkers of myocardial necrosis (creatine kinase-MB or troponin) above the upper limits of normal of local laboratory assays. Patients were ineligible if they were transferred into a participating hospital >24 hours after the last episode of ischemic symptoms. Approximately 8800 patients with STEMI were also included in the CRUSADE registry from 2003 to 2006. A detailed process of care and in-hospital outcomes were collected through retrospective chart review using a standardized data collection form. The institutional review board of each center approved participation in CRUSADE. Because data were collected anonymously, informed consent was not required.

Study Population

This analysis focused on patients with NSTEMI aged ≥65 years who were discharged alive from 514 CRUSADE hospitals between February 2003 and December 2006 and who had detailed clinical data linked to CMS longitudinal administrative data through 2008 using indirect identifiers, including site, age, admission date, discharge date, and sex. Of the 48,479 patients enrolled in the CRUSADE registry and linked to the CMS administrative data set during this time period, we excluded the following: patients with STEMI (n=2619) because of the small sample size of this population (the variable was added in a later time period, and sites were not mandated to include all patients with STEMI), patients whose CMS records did not match for sex (n=538), patients who were ineligible for fee for service during the CMS discharge month (n=2143) because their NSTEMI hospitalizations could not be matched with the CMS data, patients with inconsistent death dates (n=27), patients who died during the index hospitalization (n=2526 overall), patients with inconsistent stroke or MI readmission dates (n=8), patients transferred out of the original CRUSADE hospital (n=4020) because in-hospital and discharge treatments could not be fully profiled in these patients, and patients with missing PAD or stroke information (n=3721) on the case report form. We also excluded nonindex admissions for patients with multiple admissions (n=1402), keeping only the index admission. The final analysis population thus comprised 34,205 patients.

Data Definitions

Prior PAD was defined as a history of any of the following conditions: claudication (either with exertion or at rest), amputation for arterial insufficiency, vascular reconstruction, bypass surgery or percutaneous intervention to the extremities, documented aortic aneurysm, or a positive noninvasive test (eg, ankle brachial index <0.8). Prior CVD was defined as a history of stroke. Given that the analysis was performed in an NSTEMI population, all patients were considered to have current CAD.

Consequently, all these patients with CAD were initially divided into the following 4 groups based on history of extracardiac vascular bed involvement (ie, whether they had a history of PAD, CVD, both, or neither): (1) CAD+PAD, (2) CAD+CVD, (3) CAD+PAD+CVD, and (4) CAD alone (no history of PAD or CVD). Polyvascular disease was defined as having any additional extracardiac vascular bed involvement (history of PAD, CVD, or both).

End Point Definitions

The primary end point of interest was all-cause death and a composite of all-cause death, readmission for MI, or readmission for ischemic stroke. Long-term, all-cause mortality was available through CMS linkage data. Readmission for MI was defined as hospitalization for MI captured through the CMS linkage data defined using International Classification of Diseases, Ninth Revision, primary discharge diagnosis code 410.x1. Readmission for ischemic stroke was defined using the primary discharge diagnosis codes 434.x1, 436, or 433.x1.

Statistical Analysis

Baseline demographics, clinical presentation, in-hospital procedures, and discharge medications were described among the 4 groups. Continuous variables were summarized using medians with interquartile ranges and compared with Kruskal-Wallis tests, whereas categorical variables were summarized using percentages and compared with Pearson χ² tests.

The primary outcome of interest was death and the composite end point (death, readmission for MI, or readmission for ischemic...
stroke). Event rates and time-to-event distributions among the 4 groups were displayed using Kaplan-Meier analyses and compared with the log-rank test. Cox proportional hazards modeling was used to examine the post-NSTEMI hazard of long-term mortality and the hazard of the composite end point among patients with polyvascular disease (CAD+PAD, CAD+CVD, CAD+PAD+CVD) relative to patients without polyvascular disease (those with isolated CAD), after adjustment for variables in the CRUSADE–CMS long-term mortality model. The previously published long-term mortality model identifies variables associated with long-term mortality among admitted patients with NSTEMI (c-index=0.75). The variables in the model for risk adjustment included the following: age, initial serum creatinine level, initial systolic blood pressure, signs of heart failure on presentation, initial heart rate, weight, prior heart failure, hyperlipidemia, initial hematocrit level (with knot at 35%), initial troponin ratio (with two knots at 5 and 50), diabetes mellitus, male sex, family history of CAD, prior MI, current or recent smoking, prior percutaneous coronary intervention, race, ECG changes (transient ST elevation, both [versus neither]), hypertension, and prior coronary artery bypass graft.

All comparisons were 2 tailed, and P<0.05 was considered statistically significant. All analyses were performed using SAS version 9.2 (SAS Institute) statistical software.

### Results

#### Baseline Characteristics

Baseline demographics and clinical presentations of the 4 subgroups are presented in Table 1. Overall, patients with polyvascular disease had a higher prevalence of most ischemic risk factors (diabetes mellitus, hypertension, prior MI, prior coronary artery bypass graft, and renal insufficiency) compared with patients without polyvascular disease. There was an increasing trend of prevalence of these risk factors going from 2–arterial bed involvement (CAD+CVD or CAD+PAD) to 3–arterial bed involvement (CAD+PAD+CVD).

#### In-Hospital Cardiac Procedures

Rates of early invasive management (catheterization within 48 hours) and in-hospital cardiac catheterization were lower overall among patients with polyvascular disease, with less use among those with CAD+PAD+CVD than among those with CAD+PAD or CAD+CVD; those with single–arterial
bed involvement (CAD alone) had higher rates of invasive management (Table 2). Patients with polyvascular disease also had a greater number of diseased coronary vessels, with patients with 3-arterial bed involvement having the greatest rates of 3-vessel CAD. Similar findings were demonstrated for the use of revascularization procedures.

### Discharge Therapies

Use of guidelines-recommended medications at discharge were modest for all groups (Table 3). Given that discharge on warfarin therapy may influence prescription of clopidogrel on discharge, the online-only Data Supplement Table shows rates of warfarin at discharge among patients not discharged on clopidogrel. Lifestyle modification interventions were used less frequently among patients with polyvascular disease, particularly among those with CAD+PAD+CVD (Table 3).

### Long-Term Outcomes

The individual components and composite outcome at 1, 2, and 3 years after the index NSTEMI event are shown in Figure 1. The presence of polyvascular disease among patients with NSTEMI was associated with 3-year mortality rates >50%, with the highest 3-year mortality rate among those with CAD+PAD+CVD (58.7%) followed by those with CAD+CVD (52.1%) and CAD+PAD (49.2%). Patients without prior extracardiac vascular disease had the lowest 3-year mortality rate at 33.2%. Similar findings were demonstrated for readmission for MI, readmission for ischemic stroke, and the composite outcome.

The Kaplan-Meier mortality analyses demonstrate an early and sustained separation of the curves, with the highest long-term mortality rates observed in the CAD+PAD+CVD group and similar observed long-term mortality rates in the CAD+PAD and CAD+CVD groups (Figure 2). Similar findings were seen with the composite outcome (Figure 3).

The adjusted risk of long-term mortality was higher among patients with 2 arterial beds involved (CAD+PAD and CAD+CVD groups) than among those in the CAD alone group.

### Table 2. In-Hospital Cardiac Procedures

<table>
<thead>
<tr>
<th>No Polyvascular Disease (CAD Alone) (n=25,537)</th>
<th>CAD+CVD (n=3652)</th>
<th>CAD+PAD (n=3946)</th>
<th>CAD+PAD+CVD (n=1070)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac catheterization</td>
<td>68.8</td>
<td>48.4</td>
<td>60.4</td>
<td>49.7</td>
</tr>
<tr>
<td>Catheterization &lt;48 hours of arrival</td>
<td>52.2</td>
<td>32.1</td>
<td>41.3</td>
<td>33.1</td>
</tr>
<tr>
<td>No. diseased vessels*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>9.9</td>
<td>9.7</td>
<td>6.9</td>
<td>6.0</td>
</tr>
<tr>
<td>One</td>
<td>28.0</td>
<td>24.1</td>
<td>20.3</td>
<td>16.5</td>
</tr>
<tr>
<td>Two</td>
<td>28.0</td>
<td>27.8</td>
<td>26.8</td>
<td>25.6</td>
</tr>
<tr>
<td>Three</td>
<td>34.2</td>
<td>38.4</td>
<td>46.0</td>
<td>51.9</td>
</tr>
<tr>
<td>Revascularization procedures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCI</td>
<td>39.2</td>
<td>25.6</td>
<td>31.6</td>
<td>22.9</td>
</tr>
<tr>
<td>CABG</td>
<td>10.5</td>
<td>5.9</td>
<td>8.5</td>
<td>6.5</td>
</tr>
</tbody>
</table>

Data are presented as %. CAD indicates coronary artery disease; CVD, cerebrovascular disease; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft.

*Defined by sites as lesions >50% on angiogram in each of the 3 major coronary vessels.

### Table 3. Discharge Medications and Interventions*

<table>
<thead>
<tr>
<th>Discharge medications</th>
<th>No Polyvascular Disease (CAD Alone)</th>
<th>CAD+CVD</th>
<th>CAD+PAD</th>
<th>CAD+PAD+CVD</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>94.3</td>
<td>92.6</td>
<td>93.6</td>
<td>93.1</td>
<td>0.002</td>
</tr>
<tr>
<td>β-blocker</td>
<td>91.9</td>
<td>92.1</td>
<td>93.6</td>
<td>92.1</td>
<td>0.008</td>
</tr>
<tr>
<td>Statin</td>
<td>76.2</td>
<td>72.9</td>
<td>77.8</td>
<td>76.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ACE inhibitor or ARB</td>
<td>67.8</td>
<td>69.1</td>
<td>67.7</td>
<td>69.3</td>
<td>0.396</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>68.9</td>
<td>68.2</td>
<td>70.1</td>
<td>71.9</td>
<td>0.107</td>
</tr>
</tbody>
</table>

Discharge interventions

| Smoking cessation counseling | 78.0 | 73.6 | 77.0 | 64.8 | 0.0006 |
| Cardiac rehabilitation referral | 61.2 | 56.4 | 60.0 | 59.3 | 0.0002 |
| Dietary counseling          | 80.4 | 76.7 | 80.4 | 77.1 | <0.0001|

Data are presented as %. CAD indicates coronary artery disease; CVD, cerebrovascular disease; PAD, peripheral arterial disease; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker.

*Defined for each medication class and intervention for patients without listed contraindications.
group (Table 4). Meanwhile, patients with 3 arterial beds involved (CAD+PAD+CVD) had the highest adjusted risk of long-term mortality (adjusted hazard ratio, 1.49; 95% CI, 1.38–1.61). Similar findings were demonstrated with the composite outcome. Additionally, in a sensitivity analysis of patients who died in the hospital (CAD alone, 5.2%; CAD+PAD, 7.1%; CAD+CVD, 7.9%; CAD+PAD+CVD, 9.0%), we found very similar results among the groups with respect to adjusted risk of long-term mortality and composite outcomes.

![Figure 1](http://circoutcomes.ahajournals.org/content/545/545/Figure1)

**Figure 1.** Long-term outcomes after non–ST-segment–elevation myocardial infarction by previous vascular bed involvement. A, Mortality. B, Readmission rates for ischemic stroke. C, Readmission for myocardial infarction. D, Composite of death, readmission for myocardial infarction, or readmission for stroke. Event rates estimated using Kaplan-Meier methods, which allow for variable patient follow-up and censoring. CAD indicates coronary artery disease; CVD, cerebrovascular disease; PAD, peripheral arterial disease.

![Figure 2](http://circoutcomes.ahajournals.org/content/545/545/Figure2)

**Figure 2.** Kaplan-Meier estimates of mortality after non–ST-segment–elevation myocardial infarction by previous vascular bed involvement. CAD indicates coronary artery disease; CVD, cerebrovascular disease; PAD, peripheral arterial disease.
Discussion

To our knowledge, this study is the largest analysis of the impact of polyvascular disease on long-term outcomes in older patients with NSTEMI and yielded several important findings. First, we demonstrated very high rates of long-term mortality and composite cardiovascular outcomes among older patients with polyvascular disease. Second, the risk of long-term outcomes appears to increase incrementally with increasing number of arterial beds involved (3 versus 2 extracardiac vascular beds). Finally, guidelines-recommended therapies and procedures are used less frequently in higher-risk patients with polyvascular disease.

Association of Polyvascular Disease with Short- and Intermediate-Term Risk

Prior analyses have demonstrated that patients with acute coronary syndrome (ACS) and a history of polyvascular disease are at increased risk of short-term and intermediate-term mortality. This increased mortality may be related to an increased severity of coronary atherosclerotic burden among patients with polyvascular disease because extracardiac arterial bed involvement is likely a marker for more-diffuse atherosclerosis.8,13,19 Additionally, these earlier analyses demonstrated a graded response of in-hospital ischemic events with increasing vascular bed involvement such that patients with 3–arterial bed involvement are at highest risk of in-hospital mortality. Analyses from the GRACE (Global Registry of Acute Coronary Events) registry; the PAMISCA (Prevalence of Peripheral Arterial Disease in Patients with Acute Coronary Syndrome) registry; and the Worcester, Massachusetts, registry extended these observations to intermediate-term outcomes (6–12 months).12,14,20 In comparison, the 6 months to 12 months Kaplan-Meier estimates of ischemic events from the present study of older patients with NSTEMI are much higher than those of these other registries (eg, our analysis demonstrates a near-30% rate of 6-month composite outcome versus 21% in GRACE among patients with 3–arterial bed involvement). Similarly, analyses from clinical trial databases have demonstrated an increased risk of short-term ischemic outcomes among patients with ACS who have polyvascular disease.10,21 Thus, polyvascular disease has been determined to be an independent predictor of risk among patients with ACS through at least 1 year of follow-up.

Association of Polyvascular Disease With Long-Term Risk

Although the aforementioned analyses described short- and intermediate-term outcomes, studies exploring the association between a history of polyvascular disease and long-term outcomes among patients with ACS have been limited. Prior analyses of long-term outcomes among patients with polyvascular disease have included only patients with stable CAD or those undergoing coronary bypass surgery or were published before coronary stents were routinely used for percutaneous coronary intervention procedures.20,22-24 By comparison, the present study is, to our knowledge, the largest contemporary long-term analysis of the risk associated with

Table 4. Adjusted Risk of Long-Term Outcomes After NSTEMI by Previous Vascular Bed Involvement

<table>
<thead>
<tr>
<th>End Point</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-term mortality*</td>
<td></td>
</tr>
<tr>
<td>CAD+PAD+CVD</td>
<td>1.49 (1.38–1.61)</td>
</tr>
<tr>
<td>CAD+CVD</td>
<td>1.38 (1.31–1.44)</td>
</tr>
<tr>
<td>CAD+PAD</td>
<td>1.29 (1.23–1.35)</td>
</tr>
<tr>
<td>Long-term composite of death, MI readmission, or stroke readmission*</td>
<td></td>
</tr>
<tr>
<td>CAD+PAD+CVD</td>
<td>1.44 (1.34–1.55)</td>
</tr>
<tr>
<td>CAD+CVD</td>
<td>1.35 (1.30–1.42)</td>
</tr>
<tr>
<td>CAD+PAD</td>
<td>1.25 (1.20–1.31)</td>
</tr>
</tbody>
</table>

CAD+PAD indicates patients with NSTEMI with history of PAD; CAD+CVD, patients with NSTEMI with history of CVD; CAD+PAD+CVD, patients with NSTEMI with history of PAD and CVD. NSTEMI indicates non–ST-segment-elevation myocardial infarction; HR, hazard ratio; CAD, coronary artery disease; PAD, peripheral arterial disease; CVD, cerebrovascular disease; MI, myocardial infarction.

*Adjusted for Centers for Medicare & Medicaid Services long-term mortality model.18 Reference group is the CAD alone group.
polyvascular disease among patients with ACS. We have demonstrated that patients with NSTEMI without polyvascular disease had the lowest long-term mortality and composite ischemic rates followed by patients with 2–arterial bed involvement (CAD+PVD or CAD+CVD), whereas those with 3–arterial bed involvement (CAD+PVD+CVD) had the highest mortality and composite ischemic rates. Importantly, we have demonstrated 3-year mortality rates of 50% among older patients with NSTEMI and polyvascular disease, with a gradation of risk for 3– versus 2–vascular bed involvement after adjustment. These findings indicate that not only does polyvascular disease increase long-term risk, but also there is a gradation of long-term risk associated with increasing burden of atherosclerosis (eg, increasing number of arterial beds involved).

**Underuse of Guidelines-Recommended Treatments**

Although both the unstable angina and NSTEMI guidelines and the PAD guidelines highlight the importance of secondary prevention with antiplatelet therapy, hypertension control, and statin therapy, we found that the use of these cardioprotective agents was suboptimal not only among patients with a history of polyvascular disease, but also among the entire older NSTEMI population. Further, although aspirin and β-blocker prescription rates on discharge were relatively high, roughly 25% to 30% of all eligible patients (those with and without extracardiac vascular disease) were not discharged on statins, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, or clopidogrel.

The suboptimal use of clopidogrel at discharge could partly be explained by the fact that 22% to 28% of patients with polyvascular disease not discharged on clopidogrel were treated with warfarin, but a large percentage of patients who could have benefited from clopidogrel therapy remains. Similar findings were demonstrated with the use of lifestyle modification interventions, such as smoking cessation counseling, diet modification counseling, and cardiac rehabilitation referral. This modest use of evidence-based therapies among eligible patients becomes even more notable given the high long-term mortality, particularly among patients with 3–arterial bed involvement. Increased use of these life-saving therapies has the potential to reduce long-term ischemic events.

Additionally, although guidelines recommend an early invasive approach to treat the high-risk NSTEMI population, we found that compared with patients without extracardiac vascular disease, eligible patients with polyvascular disease were less likely to undergo catheterization within 48 hours of arrival. Furthermore, patients with polyvascular disease had lower rates of any in-hospital revascularization (percutaneous coronary intervention and coronary artery bypass graft combined) than those without extracardiac vascular disease, with the patients with 3–arterial bed involvement having the lowest revascularization rates of all groups. The more-conservative lower rates of revascularization may reflect that patients with polyvascular disease may have advanced, nonrevascularizable vascular disease, and this may contribute to higher mortality rates among those with polyvascular disease. Furthermore, patients with polyvascular disease or their clinicians may favor a medical management approach given the additional comorbidities and decreased quality of life associated with stroke and advanced PAD.

**Limitations**

The present analysis was an observational study limited to patients aged >65 years. The long-term association between history of extracardiac vascular disease and ischemic outcomes needs to be confirmed in a younger cohort; however, it must be noted that PAD is more prevalent in elderly persons, with a mean age of 65 to 70 years in most real-world registries. The present analysis was limited to in-hospital survivors. Other studies have demonstrated an association between polyvascular disease and in-hospital mortality among patients post ACS. The findings expand earlier observations with long-term follow-up. With the registry design, we could not confirm diagnosis of PAD with repeat noninvasive testing. Similarly, we could not stratify based on symptomatic versus asymptomatic PAD status, even though these entities have different rates of ischemic outcomes.

Additionally, among patients with a history of MI, percutaneous coronary intervention, or coronary artery bypass graft, we could not determine age at the time of their initial CAD diagnosis. It is possible that polyvascular disease represents a global atherosclerotic process and, consequently, is more likely present among patients who have had CAD longer. Regardless, the findings are applicable in that patients with polyvascular disease, particularly those with all vascular beds involved, are at the highest risk; therefore, greater attention is needed to optimize in-hospital and secondary prevention.

Another limitation to definition and identification of patients relates to those with prior CVD. We did not include patients with documented carotid artery disease without a prior stroke and may have included patients without actual atherosclerotic disease (eg, hemorrhagic or thromboembolic stroke). We identified stroke and MI with linkage to the CMS database; consequently, these end points were not adjudicated and relied solely on billing data. However, the positive predictive value of patients with MI and stroke by Medicare claims-based definition is high. Adjustments for covariates in the present study were limited to those in the data collection form. Further, the analysis was limited to patients with NSTEMI only because the CRUSADE database included a small sample of patients with unstable angina and STEMI.

Importantly, it is possible that our rate of use of evidence-based therapies, including early invasive strategy, revascularization, or discharge therapies, was relatively low because of increased comorbidities among patients with polyvascular disease (advanced and nonintervenable coronary disease, other medical comorbidities such as malignancy or kidney disease, hospice care, etc). The database was limited to specific patient characteristics captured by the data collection form. To limit selection bias of therapies, data abstractors were instructed to note contraindications on the collection form if patients did not receive these evidence-based therapies;
subsequently, the data on use of therapies reported here likely represent rates of use among patients without contraindications. Finally, we did not have information on long-term medication adherence. Thus, we were unable to determine whether patients were taking the cardioprotective medications throughout the follow-up time period.

**Conclusions**

We found that older patients with NSTEMI and polyvascular disease have very high rates of mortality and composite ischemic end points compared with patients without polyvascular disease, in this largest contemporary analysis with the longest follow-up to our knowledge. We found a gradient of increasing risk based on the number of arterial beds involved. Despite the increased long-term risk associated with polyvascular disease, the use of guidelines-recommended therapies at discharge was modest among all patients with NSTEMI (with and without polyvascular disease), and patients with polyvascular disease were less likely to undergo early invasive therapy and revascularization. Given the high rate of mortality in older patients with NSTEMI and polyvascular disease, future studies targeting better use of secondary prevention strategies and novel therapies are needed to help to reduce long-term cardiovascular events in this vulnerable population.

**Acknowledgments**

We thank Amanda McMillan, MPH, MA, and Morgan deBlecourt for their editorial contributions to this manuscript. Ms McMillan and Ms deBlecourt did not receive compensation for their contributions apart from their employment at the institution where this study was conducted, for their editorial contributions to this manuscript. Ms McMillan did not receive compensation for her contributions apart from her employment at the institution where this study was conducted.

**Sources of Funding**

CRUSADE was funded by the Schering-Plough Corporation. A Bristol-Myers Squibb/sanofi Pharmaceuticals partnership provided additional funding support. Millennium Pharmaceuticals Inc also funded this work. This work was supported in part by a grant from the National Institute on Aging (R01 AG025312-01A1) to Dr Peterson, principal investigator.

**Disclosures**

Dr Bhatt has received research grants from Amarin, AstraZeneca, Bristol-Myers Squibb, Eisai, Ethicon, Medtronic, Sanofi-aventis, and The Medicines Company. Dr Wang has received research grants to the Duke Clinical Research Institute from a Bristol-Myers Squibb/sanofi Pharmaceuticals partnership, Schering-Plough (now Merck), The Medicines Company, Canyon Pharmaceuticals, Heartscapes, and an Eli Lilly/Daiichi Sankyo partnership and has consulted for or received honoraria from KAI Pharmaceuticals, Bristol-Myers Squibb, sanofi-aventis, Merck, Orexigen, Helsinn Pharmaceuticals, AstraZeneca, and Regeneron. All conflicts of interest for Drs Wang, Patel Ohman, Peterson, and Roe are listed at www.cdc.gov.

**References**


Polyvascular Disease and Long-Term Cardiovascular Outcomes in Older Patients With Non–ST-Segment–Elevation Myocardial Infarction
Sumeet Subherwal, Deepak L. Bhatt, Shuang Li, Tracy Y. Wang, Laine Thomas, Karen P. Alexander, Manesh R. Patel, E. Magnus Ohman, W. Brian Gibler, Eric D. Peterson and Matthew T. Roe

Circ Cardiovasc Qual Outcomes. 2012;5:541-549; originally published online June 19, 2012; doi: 10.1161/CIRCOUMOTES.111.964379
Circulation: Cardiovascular Quality and Outcomes is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-7705. Online ISSN: 1941-7713

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circoutcomes.ahajournals.org/content/5/4/541

Data Supplement (unedited) at:
http://circoutcomes.ahajournals.org/content/suppl/2012/07/12/CIRCOUTCOMES.111.964379.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Quality and Outcomes can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Quality and Outcomes is online at:
http://circoutcomes.ahajournals.org//subscriptions/
Supplemental Material

Table. Discharge rates on warfarin among patients not discharged on clopidogrel (n=9,106)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Discharge on Warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAD alone (n=6,930)</td>
<td>18.0%</td>
</tr>
<tr>
<td>CAD + PAD (n=989)</td>
<td>22.4%</td>
</tr>
<tr>
<td>CAD + CVD (n=941)</td>
<td>24.8%</td>
</tr>
<tr>
<td>CAD + PAD + CVD (n=246)</td>
<td>28.1%</td>
</tr>
</tbody>
</table>