Long-Term Outcomes After Invasive Management for Older Patients With Non–ST-Segment Elevation Myocardial Infarction

Matthew T. Roe, MD, MHS; Shuang Li, MS; Laine Thomas, PhD; Tracy Y. Wang, MD, MHS; Karen P. Alexander, MD; E. Magnus Ohman, MD; Eric D. Peterson, MD, MPH

Background—Early invasive management is recommended for patients with non–ST-segment elevation myocardial infarction (MI), but the incidence of long-term outcomes after early catheterization among older patients and the relationship of revascularization procedures with outcomes in this population have not been described.

Methods and Results—Using data from the Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the American College of Cardiology/American Heart Association Guidelines (CRUSADE) registry, we linked 19,336 older patients (≥65 years) with non–ST-segment elevation MI found to have significant coronary disease during catheterization and who survived through 30 days posthospital discharge to Medicare/Medicaid data. All-cause mortality, readmission for MI, readmission for stroke, and use of repeat revascularization procedures were tracked for a median of 1181 days. Outcome comparisons were stratified by use of percutaneous coronary intervention (PCI; n=11,766, 60.8%) or coronary artery bypass grafting (n=3515, 18.2%) performed during the index hospitalization and through 30 days postdischarge, as well as by medical management without revascularization (n=4055, 21.0%). During follow-up, ≈17% of patients underwent PCI (most commonly in patients initially treated with PCI), and only 3% of patients underwent coronary artery bypass grafting. Compared with an unadjusted long-term mortality cumulative incidence through 5 years of 50% in the medical management group, mortality was lower in the PCI group (33.5%; adjusted hazard ratio, 0.75; 95% confidence interval, 0.70–0.79) and lowest in the coronary artery bypass grafting group (24.2%; adjusted hazard ratio, 0.52; 95% confidence interval, 0.47–0.57; P<0.001 for 3-way comparisons). The unadjusted cumulative incidence of the composite of death, readmission for MI, or readmission for stroke at 5 years was 62.4%, 44.9%, and 33.0% for medical management, PCI, and coronary artery bypass grafting, respectively.

Conclusions—Older patients with non–ST-segment elevation MI with significant coronary disease face high long-term risks for mortality and nonfatal cardiovascular outcomes after early catheterization that differ by type of revascularization procedure performed. These findings can help guide the design of studies evaluating long-term therapies among elderly post-MI patients. (Circ Cardiovasc Qual Outcomes. 2013;6:323-332.)

Key Words: coronary disease ■ long-term outcomes ■ myocardial infarction ■ NSTEMI ■ revascularization

The use of an early invasive management strategy (early cardiac catheterization within 48–72 hours of presentation, with provisional revascularization determined by angiographic results) is designated as a class IA recommendation by practice guidelines for high-risk patients with unstable angina (UA)/non–ST-segment elevation myocardial infarction (NSTEMI). This recommendation is based on results from numerous randomized clinical trials that have shown improved short- and intermediate-term outcomes among high-risk patients with UA/NSTEMI randomized to an early invasive management strategy versus a conservative strategy (in which cardiac catheterization is reserved for patients who fail an initial strategy of medical management). The Fragmin and Fast Revascularization During Instability in Coronary Artery Disease (FRISC II), Randomized Intervention Trial of Unstable Angina (RITA-3), and Invasive Versus Conservative Treatment in Unstable Coronary Syndromes (ICTUS) trials have reported outcomes through 5 years of follow-up and have demonstrated long-term mortality rates ranging from 10% to 15%, with no significant differences by randomized treatment assignment (invasive versus conservative management). However, results from the ICTUS trial demonstrated that the use of in-hospital revascularization procedures as compared with a conservative strategy of medical management alone was associated with lower 4-year mortality rates (4.8% versus 10.0%), although...
WHAT IS KNOWN

- The long-term risks of adverse outcomes after invasive management (coronary angiography) for patients with non–ST-elevation myocardial infarction stratified by the use and type of postangiography revascularization procedures have been delineated from previous randomized clinical trials but have not been described for the unselected population of patients treated in routine practice.

WHAT THE STUDY ADDS

- Among a large sample of unselected, older patients with non–ST-elevation myocardial infarction from the CRUSADE registry linked to longitudinal Medicare data who were found to have significant coronary artery disease during in-hospital angiography, the cumulative incidence of mortality starting 30 days after the index hospitalization date through 5 years was ≈35% in the overall population.
- The cumulative incidence of mortality through 5 years was highest among those patients who were medically managed without revascularization after angiography (50%), intermediate among patients who underwent percutaneous coronary intervention (34%), and lowest among patients who underwent coronary artery bypass grafting (24%).
- Similar findings were observed for the cumulative incidence of the composite outcome of death, readmission for myocardial infarction, and readmission for ischemic stroke.
- This analysis provides a benchmark for event rate considerations for future studies evaluating long-term therapies for patients with invasively managed non–ST-elevation myocardial infarction with consideration to include a significant proportion of older patients to enhance event rates.

this was a post hoc analysis that was strongly influenced by postrandomization crossover rates and selection biases. Therefore, the provisional use of revascularization procedures after early catheterization for UA/NSTEMI may be directed by postrandomization crossover rates and selection biases. This was a post hoc analysis that was strongly influenced by postrandomization crossover rates and selection biases.

Methods

Patient Inclusion Criteria and Data Collection

A total of 195,240 patients with UA and NSTEMI were previously included in the CRUSADE registry from 2001 through 2006 at 568 hospitals in the United States. Patients with UA/NSTEMI were included in CRUSADE if they presented with ischemic chest pain lasting ≥10 minutes within the previous 24 hours and were found to have either positive local laboratory cardiac markers (either creatine kinase-MB or troponin levels above the upper limit of normal, which is designated as NSTEMI) or ischemic ST-segment changes on ECG (either ST-segment depression or transient ST-segment elevation, which is designated as UA in the absence of positive cardiac markers). Between 2003 and 2006, ≈8800 patients with STEMI were also included. Institutions that participated in CRUSADE received approval from their local institutional review boards before starting data collection and submission. In-hospital data were collected anonymously without patient-informed consent; therefore, direct patient identifiers were not collected. For patients who underwent in-hospital angiography, the collection of angiographic data was limited to the designation of a ≥50% stenosis in a major coronary vessel (left main, left anterior descending, left circumflex, or right coronary artery) or a bypass graft.

Matching to Longitudinal Administrative Data

From the original sample of 115,541 patients aged ≥65 years with NSTEMI and STEMI who were included in CRUSADE from 2001 through 2006, a total of 76,279 (66%) patients included from 514 hospitals were matched to CMS longitudinal administrative data through the end of 2008, with indirect identifiers including site, age, admission date, discharge date, and sex. The process of matching CRUSADE data to CMS data and the clinical characteristics of the overall elderly (age ≥65 years) versus matched elderly populations has been detailed in a separate article.

Analysis Population

We limited the population for this analysis to the interval of 2003 to 2006 because this period had more complete baseline clinical and lab data that were used to derive the CRUSADE long-term mortality model used in this analysis. From the matched sample of 48,479 patients included in CRUSADE from February 15, 2003, through December 31, 2006, we excluded 2619 patients with STEMI because they were not the focus of this analysis, 538 patients linked to CMS data who did not match on sex, 2143 patients not eligible for fee-for-service (CMS Part A and B) during their discharge month, 27 patients who died but were listed as being discharged on a later date in CMS data, 4811 patients who died during the index hospitalization or within 30 days of discharge, and 107 patients who were censored before 30 days after discharge. Additionally, we excluded 7904 patients from hospitals that did not have percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) capabilities (to limit biases related to patients who were transferred to other hospitals as data collection ended at the time of interhospital transfer), 8239 patients who did not undergo cardiac catheterization; 1991 patients who underwent cardiac catheterization but in whom all recorded coronary lesions showed ≤50% stenosis; 390 patients who were transferred to another facility (and for whom in-hospital data were thus incomplete), and 374 nonindex admissions (ie, patients from the original matched sample who had repeated admissions in the CRUSADE database were evaluated only once starting with their index admission; subsequent admissions were not analyzed). The final patient sample for this analysis, thus, consisted of 19,336 patients with NSTEMI from 313 hospitals who were included in CRUSADE from February 15, 2003, through December 31, 2006, and who survived through 30 days after hospital discharge.
Assignment of Patients to a Treatment Strategy Group

Initial analyses showed that the median time from hospital discharge to subsequent CABG procedures was ≈30 days among patients who were treated solely with a medical management strategy during the index hospitalization. We believe this finding indicated that a proportion of patients with multivessel disease, who were determined to need surgical revascularization based on in-hospital angiographic findings, were discharged from the index hospitalization to recover further before undergoing semielective CABG within the first month after discharge. Given that the primary objective of this analysis was to characterize the long-term outcomes associated with the actual use and choice of revascularization procedures after in-hospital cardiac catheterization, we chose to start the analysis 30 days after hospital discharge to account for near-term revascularization procedures that were performed soon after hospital discharge and likely were planned before discharge. Based on this strategy, we assigned patients to a treatment strategy group in a hierarchical manner: Patients who had CABG performed from the time of the index cardiac catheterization through 30 days postdischarge were assigned to the CABG group even if they also underwent PCI, whereas patients who had only PCI performed during this same time period were assigned to the PCI group. The remaining patients who did not undergo either CABG or PCI during the same time period were assigned to the medical management group.

Outcomes Assessment

We assessed long-term, all-cause mortality as the primary outcome measurement. Additional outcomes assessed included readmission for myocardial infarction (MI); readmission for ischemic stroke; a composite of death, readmission for MI, or readmission for ischemic stroke; and revascularization procedures (PCI, CABG, and both). Readmissions within the CMS longitudinal data set were classified as attributable to MI using the International Classification of Diseases, Ninth Revision (ICD-9) diagnosis code 410.x1. Readmissions were classified as attributable to ischemic stroke using the following primary ICD-9 diagnosis codes: 433.x1, 434.x1, or 436. The incidence of PCI during hospital readmission was calculated using the ICD-9 procedure codes of 00.66 or 36.01-09, whereas the incidence of CABG during hospital readmission was calculated using the ICD-9 procedure codes of 36.10-19, 36.2, 36.30, 36.33 to 39, 36.91, or 36.99.

Statistical Analysis

Baseline clinical and presentation characteristics as well as discharge medication use were compared across the 3 treatment groups using Pearson χ² tests for categorical variables and the Kruskal–Wallis test for continuous and ordinal categorical variables. Median and interquartile ranges (IQRs) were summarized for continuous variables, and percentages were used for categorical variables.

Kaplan–Meier methods were used to determine long-term, all-cause, unadjusted cumulative incidence of mortality for the 3 treatment groups starting at 30 days after hospital discharge; these incidences were compared using the log-rank test.

Unadjusted cumulative incidence of nonfatal outcomes (readmission for MI; readmission for ischemic stroke, PCI, or CABG; and total revascularization) was calculated to account for the competing risks with long-term mortality; these were compared across treatment groups. Unadjusted cumulative incidence of the composite of death, readmission for MI, or readmission for ischemic stroke was calculated using the product-limited Kaplan–Meier method and compared across treatment groups using the log-rank test.

To account for early deaths that may have occurred before planned revascularization procedures could be performed, as well as deaths that occurred during the index hospitalization after a revascularization procedure, we performed a sensitivity analysis to account for all patients (n=20906) who were found to have significant coronary artery disease during cardiac catheterization. A total of 662 patients who were found to have significant coronary artery disease during catheterization but died during the index hospitalization were added to the analysis population. For this sensitivity analysis, we focused on characterizing the unadjusted cumulative incidences of mortality and the composite of death, readmission for MI, or readmission for ischemic stroke from the time of the catheterization through 5 years by actual revascularization procedures performed only during the index hospitalization. For this sensitivity analysis, patients were assigned to the CABG group if they had CABG performed during the index hospitalization, even if they also underwent PCI because CABG was considered to be the procedure with the greatest periprocedural mortality risk that would be accounted for in the sensitivity analysis. Accordingly, patients who had only PCI performed during the index hospitalization were assigned to the PCI group. The remaining patients who did not undergo either CABG or PCI during the index hospitalization were assigned to the management group.

All comparisons were 2-tailed, and a P value of <0.05 was considered statistically significant. The entire analysis was performed with SAS software (version 9.2, SAS Institute) and R software (version 2.13.1).

Results

Treatment Groups

Among 19336 patients with NSTEMI in the analysis population, 11766 (60.8%) patients underwent only PCI from the time of hospital presentation until 30 days after discharge, 3515 (18.2%) underwent CABG during this period, and 4055 (21.0%) were treated solely with a medical management strategy and did not undergo PCI or CABG.

Baseline Clinical Characteristics

Clinical characteristics of the 3 treatment groups are shown in Table 1. The median age was 74 years for patients in the CABG group, 75 years for those in the PCI group, and 76 years for those in the medical management group. Patients in the CABG group were least likely to be women; least commonly had a history of previous MI, previous revascularization, previous heart failure, and previous stroke; and had the highest median creatinine clearance value among the 3 groups.

Procedural Details

The median time to cardiac catheterization from hospital presentation was longer in the medical management group (Table 2). The frequency of single-vessel disease was highest in the PCI group and lowest in the CABG group, whereas the distribution of the frequency of 3-vessel disease was the opposite. Approximately 73% of patients in the medical management group and 63% of patients in the PCI group had 2- or 3-vessel disease. The proportion of patients with moderate or severe left ventricular systolic dysfunction was higher in the medical management and CABG groups compared with the PCI group.

Among patients in the PCI group, 97.5% underwent PCI during the index hospitalization, with a median time to PCI of 27 hours (IQR, 13–55 hours), whereas 2.5% underwent PCI within 30 days after hospital discharge, with a median time to PCI from discharge of 16 days (IQR, 9–24 days). Among patients assigned to the CABG group, 92.0% underwent CABG during the index hospitalization, with a median time to CABG of 83 hours (IQR, 46–132 hours), whereas 8.0% underwent CABG within 30 days after hospital discharge,
with a median time to CABG from discharge of 16 days (IQR, 10–25 days).

**Discharge Care Processes**

The use of guideline-recommended discharge medications and interventions is shown in Table 3. Medications were most likely to be used in the PCI-treated patients and least likely to be used in the CABG-treated patients, whereas discharge lifestyle modification interventions were most likely to be used in the CABG group.

**Follow-up**

The median follow-up for the 19336 patients in the overall population, starting from 30 days after hospital discharge, was 1181 days (3.2 years; IQR, 840–1516 days), with a maximum follow-up of 2026 days (5.6 years). Among patients who
survived during the entire analysis period, median follow-up was 1328 days (3.6 years; IQR, 1035–1596 days).

### Unadjusted Mortality Cumulative Incidence
The long-term mortality cumulative incidence at 5 years was 50.0% in the medical management group, 33.5% in the PCI group, and 24.2% in the CABG group ($P < 0.0001$ for across-group comparisons). The Kaplan–Meier mortality curve for the medical management group diverged early from the curves for the PCI and CABG groups, whereas curves for these 2 latter groups seemed to diverge only after 6 months (Figure 1).

The median time to death was 506 days (IQR, 191–884 days) in the medical management group, 629 days (IQR, 266–1018 days) in the PCI group, and 705 days (IQR, 238–1068 days) in the CABG group.

### Nonfatal and Composite Outcomes
The cumulative incidence of readmission for MI through 5 years was distributed in a fashion similar to that of mortality rates across the 3 treatment groups, but the cumulative incidence curves for the 3 groups diverged early with no overlap (Figure 2A). The cumulative incidence of readmission for ischemic stroke through 5 years was highest in the medical management group, and the cumulative incidence curve for the medical management group diverged early, but the curves seemed to overlap for the PCI and CABG groups (Figure 2B).

### Table 2. In-Hospital Cardiac Catheterization Details by Treatment Group

<table>
<thead>
<tr>
<th>Catheterization Details</th>
<th>Overall (n=19,336)</th>
<th>Medical Management (n=4,055)</th>
<th>PCI (n=11,766)</th>
<th>CABG (n=3,515)</th>
<th>PValue*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure timing, h</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to catheterization, median (25th–75th percentiles)</td>
<td>27 (14–54)</td>
<td>39 (20–70)</td>
<td>25 (12–49)</td>
<td>26 (13–50)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. of diseased vessels†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>29.2</td>
<td>27.2</td>
<td>37.0</td>
<td>4.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>30.7</td>
<td>26.4</td>
<td>34.3</td>
<td>23.4</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>40.2</td>
<td>46.4</td>
<td>28.7</td>
<td>71.8</td>
<td></td>
</tr>
<tr>
<td>LVEF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measured in hospital</td>
<td>90.5</td>
<td>91.7</td>
<td>88.5</td>
<td>95.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEF results, %‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;50</td>
<td>52.5</td>
<td>46.9</td>
<td>55.7</td>
<td>48.9</td>
<td></td>
</tr>
<tr>
<td>41 to 50</td>
<td>23.2</td>
<td>20.4</td>
<td>23.4</td>
<td>25.8</td>
<td></td>
</tr>
<tr>
<td>25 to 40</td>
<td>18.8</td>
<td>23.2</td>
<td>16.8</td>
<td>20.5</td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>5.2</td>
<td>9.3</td>
<td>3.9</td>
<td>4.6</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as percentages unless otherwise indicated. CABG indicates coronary artery bypass grafting; LVEF, left ventricular ejection fraction; and PCI, percutaneous coronary intervention.

*P values represent 3-way comparisons across treatment groups.
†Significant lesions $\geq 50\%$ denoted on the case report form in each major epicardial vessel.
‡Among patients with LVEF measured in hospital.

### Table 3. Discharge Medications and Interventions by Treatment Group

<table>
<thead>
<tr>
<th>Variables</th>
<th>Overall (n=19,336)</th>
<th>Medical Management (n=4,055)</th>
<th>PCI (n=11,766)</th>
<th>CABG (n=3,515)</th>
<th>PValue*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discharge medications</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>96.4</td>
<td>94.0</td>
<td>97.5</td>
<td>95.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>78.8</td>
<td>60.0</td>
<td>96.4</td>
<td>29.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>β-Blocker</td>
<td>93.1</td>
<td>93.8</td>
<td>93.3</td>
<td>91.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ACE inhibitor or ARB†</td>
<td>69.2</td>
<td>71.6</td>
<td>72.5</td>
<td>54.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lipid-lowering agent‡</td>
<td>89.1</td>
<td>88.4</td>
<td>91.2</td>
<td>83.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Discharge interventions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking cessation counseling</td>
<td>82.6</td>
<td>76.5</td>
<td>83.6</td>
<td>86.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiac rehabilitation referral</td>
<td>69.5</td>
<td>57.2</td>
<td>68.7</td>
<td>85.3</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are presented as percentages. Medication use at the time of hospital discharge reported for patients without a recorded contraindication to each medication class. ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CABG, coronary artery bypass grafting; CRUSADE, Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the American College of Cardiology/American Heart Association Guidelines registry; and PCI, percutaneous coronary intervention.

*P values represent 3-way comparisons across treatment groups.
†Calculated only for patients with an ejection fraction $<40\%$, heart failure, diabetes mellitus, or hypertension per practice guideline recommendations during the time of patient recruitment for CRUSADE.
‡Calculated only for patients with a history of hyperlipidemia or with a measured low-density lipoprotein $>100$ mg/dL per practice guideline recommendations during the time of patient recruitment for CRUSADE.
The cumulative incidence of the composite outcome of death, readmission for MI, or readmission for ischemic stroke at 5 years was highest in the medical management group (62.4%), followed by the PCI group (44.9%) and then the CABG group (33.0%) (Figure 2C). The Kaplan–Meier curve for the medical management group diverged early from the curves for the PCI and CABG groups, whereas the curves for these 2 latter groups seemed to diverge only after 3 months. The median time to the first event of the composite outcome was 388 days (IQR, 126–740 days) in the medical management group, 483 days (IQR, 189–893 days) in the PCI group, and 558 days (IQR, 187–970 days) in the CABG group.

Use of Subsequent/Repeat Revascularization Procedures

The cumulative incidence of subsequent/repeat revascularization procedures performed during the follow-up period is shown in Table 4. The cumulative incidence of subsequent/repeat PCI at 5 years was highest in the PCI treatment group and lowest in the CABG treatment group. The cumulative incidence of total revascularization (PCI or CABG) at 5 years was highest in the PCI treatment group (23.7%) compared with the medical management group (15.0%) and the CABG treatment group (8.6%).

Sensitivity Analysis

When all 20,096 patients who were found to have significant coronary artery disease during cardiac catheterization were accounted for in the sensitivity analysis, similar long-term outcomes were demonstrated by revascularization strategy. The long-term mortality cumulative incidence at 5 years starting from the time of catheterization was 53.3% in the medical management group, 34.4% in the PCI group, and 28.4% in the CABG group (P<0.0001 for across-group comparisons). However, the risk of mortality was initially higher in CABG-treated patients compared with PCI-treated patients through 1 to 2 years of follow-up and thereafter remained higher in PCI-treated patients (Figure 3A). The cumulative incidence of the composite outcome of death, readmission for MI, or readmission for ischemic stroke during this same time period was highest in the medical management group (64.4%), followed by the PCI group (46.7%) and then the CABG group (37.2%; P<0.0001 for across-group comparisons). Similar findings were demonstrated with an initial higher incidence of composite outcomes in CABG-treated patients compared with PCI-treated patients that changed after 1 year of follow-up (Figure 3B).

Discussion

We have demonstrated high cumulative incidence of long-term mortality and composite adverse cardiovascular outcomes in a contemporary sample of older patients with NSTEMI treated with early invasive management in routine practice who were found to have significant coronary artery disease during in-hospital cardiac catheterization and who survived initially for 30 days after discharge. The baseline clinical characteristics of patients by revascularization strategy were significantly different, and the long-term risk of adverse outcomes was highest among patients treated with a medical management strategy without revascularization and lowest among patients who underwent CABG. These findings demonstrate the high long-term risk for patients with NSTEMI treated with an invasive management strategy in routine practice, provide a benchmark for event rate considerations for future studies evaluating long-term therapies in the elderly post-MI population, and highlight how selection biases related to the use and choice of revascularization procedures relate to long-term, postdischarge outcomes in this population.

We have also demonstrated a number of important findings regarding use of early invasive management in an older, unselected population of patients with NSTEMI treated in routine practice. First, we have shown a much higher 5-year...
Figure 2. Kaplan–Meier curves showing cumulative incidence of readmission and mortality from 30 days after hospital discharge through 5 years for patients stratified by treatment group: medical management vs percutaneous coronary intervention (PCI) vs coronary artery bypass grafting (CABG)—(A) cumulative incidence of readmission for myocardial infarction (MI), P<0.0001 for 3-way comparisons across groups; (B) cumulative incidence of readmission for ischemic stroke, P=0.002 for 3-way comparisons across groups; and (C) cumulative incidence of the composite outcome of death, readmission for MI, or readmission for ischemic stroke, P<0.0001 for 3-way comparisons across groups.
mortality rate (35%) in an invasively managed population of older patients from CRUSADE compared with 10% to 15% from the patients randomized to an invasive strategy in previous clinical trials, despite censoring deaths within 30 days of hospital discharge in our primary analysis.4–6 Additionally, we have shown an early and sustained divergence in the cumulative incidence of reinfarction among the 3 treatment groups—a novel finding that deserves further study with respect to treatment considerations in the elderly population.

Second, we have observed that patients with NSTEMI who undergo CABG within 30 days of hospital discharge and survive for that period have a consistently lower risk of subsequent long-term mortality compared with PCI-treated patients despite less commonly receiving evidence-based medications at hospital discharge. These findings contrast with a previous analysis from the Superior Yield of the New Strategy of Enoxaparin, Revascularization, and Glycoprotein IIb/IIIa Inhibitors (SYNERGY) trial that demonstrated an increased 1-year mortality risk for patients with UA/NSTEMI treated with CABG compared with those treated with PCI.11 These contrasting results are likely explained by the fact that we censored patients who died within 30 days of hospital discharge from our primary analysis; when these patients were accounted for in a sensitivity analysis, the mortality risk associated with CABG was higher than that with PCI for the first 1 to 2 years. These results not only confirm the initial risks associated with surgical versus percutaneous revascularization in this population, but also highlight the selection biases related to the choice of revascularization procedure for older patients with NSTEMI with multivessel disease who did not have a recent MI.12 Thus, the use and choice of revascularization procedures for patients with NSTEMI seem to be strongly associated with the risk of long-term outcomes, but a causal relationship cannot be determined without a prospective randomized trial in this setting.

Finally, the results from this analysis highlight important differences among patients treated in routine practice versus those included in randomized clinical trials. Recently conducted trials that have focused on invasively managed patients with UA/NSTEMI have demonstrated 1- to 2-year mortality rates between 4% and 8% and composite event rates of ≈10% to 15% despite use of enrichment criteria designed to enhance event rates.13,14 However, relatively few older patients were enrolled in these trials (median age was 62–64 years in each trial), and trial sample sizes of 10,000 to 20,000 patients were needed to accumulate the requisite number of events to ensure adequate power to address the studies’ objectives. The results of our analysis provide a benchmark for event rate considerations for future studies evaluating long-term therapies for invasively managed patients with UA/NSTEMI, and they suggest that these types of studies can be designed with much smaller sample sizes if a significant proportion of older patients are included to enhance event rates.

### Limitations

Our analysis has a number of limitations. First, we chose to evaluate long-term outcomes starting 30 days after hospital discharge to account for near-term, postdischarge revascularization procedures that had likely been planned based on the initial, in-hospital angiographic findings—an approach that may be more commonly used in older compared with younger patients with NSTEMI. This analytic approach did not account for adverse outcomes and deaths related to periprocedural complications, and those that occurred before planned procedures could be performed, so we performed a sensitivity analysis to account for all patients, and similar long-term results by treatment group were demonstrated. Second, we ascertained PCI among propensity-matched, stable, older patients with multivessel disease who did not have a recent MI.12 Thus, the use and choice of revascularization procedures for patients with NSTEMI seem to be strongly associated with the risk of long-term outcomes, but a causal relationship cannot be determined without a prospective randomized trial in this setting.

### Table 4. Cumulative Incidence of Subsequent/Repeat Revascularization Procedures Through 5 Years

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Overall (n=19,336)</th>
<th>Medical Management (n=4055)</th>
<th>PCI (n=11,766)</th>
<th>CABG (n=3,515)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCI, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>7.8</td>
<td>4.8</td>
<td>10.2</td>
<td>3.3</td>
</tr>
<tr>
<td>2</td>
<td>11.2</td>
<td>7.7</td>
<td>14.4</td>
<td>5.2</td>
</tr>
<tr>
<td>3</td>
<td>13.6</td>
<td>9.5</td>
<td>17.1</td>
<td>6.6</td>
</tr>
<tr>
<td>4</td>
<td>15.3</td>
<td>10.6</td>
<td>19.3</td>
<td>7.5</td>
</tr>
<tr>
<td>5</td>
<td>16.7</td>
<td>11.2</td>
<td>21.2</td>
<td>8.4</td>
</tr>
<tr>
<td>CABG, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.6</td>
<td>3.1</td>
<td>1.6</td>
<td>0.1</td>
</tr>
<tr>
<td>2</td>
<td>2.2</td>
<td>3.7</td>
<td>2.3</td>
<td>0.1</td>
</tr>
<tr>
<td>3</td>
<td>2.6</td>
<td>4.1</td>
<td>2.7</td>
<td>0.2</td>
</tr>
<tr>
<td>4</td>
<td>3.0</td>
<td>4.6</td>
<td>3.2</td>
<td>0.2</td>
</tr>
<tr>
<td>5</td>
<td>3.2</td>
<td>4.8</td>
<td>3.6</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Data are presented as percentages. For patients initially treated with PCI and CABG, these are repeat revascularization procedures after the index procedures performed within 30 d of hospital discharge that were used to classify patients into the treatment groups. CABG indicates coronary artery bypass grafting; and PCI, percutaneous coronary intervention.
nonfatal cardiovascular outcomes (ie, readmissions for MI and ischemic stroke) based solely on administrative billing codes without independent reporting by the treating physician and independent event adjudication (as in a clinical trial) because this was the only approach suitable for the CMS database. Therefore, the cumulative incidence rates of readmission for MI and stroke cannot be directly compared with incidence of MI and stroke from NSTEMI clinical trial databases. Third, because we did not have access to CMS Part D data on long-term medication use, we could only profile hospital discharge medication use. Because we began outcomes ascertainment 30 days after discharge, hospital discharge medication use may not accurately reflect medication use and adherence starting 30 days after hospitalization. Fourth, we were unable to determine how or why the treating physician chose to treat individual patients after cardiac catheterization (medical management versus PCI versus CABG). Thus, we cannot comment on the suitability of decision making regarding revascularization for the 3 treatment groups analyzed. Fifth, we evaluated patients who underwent in-hospital cardiac catheterization rather than restricting the population to only those patients who underwent catheterization within the first 48 hours because a recent analysis from the FRISC-2, ICTUS, and RITA-3 trials demonstrated no difference in long-term outcomes based on the timing of angiography for patients who were randomized to an early invasive strategy. Sixth and finally, this analysis was not designed or intended to be a comparative effectiveness analysis, but rather is a descriptive, epidemiological study. Hence,
our results should not be interpreted to conclude that CABG is a more effective or better treatment option for patients with NSTEMI compared with medical management or PCI.

Conclusions
Among older patients with NSTEMI with significant coronary disease identified during in-hospital catheterization, the long-term risk of adverse outcomes starting 30 days after discharge through 5 years is substantial and seems to be differentiated by the use and type of postangiography revascularization procedures. The findings of this analysis suggest that the inclusion of a significant proportion of older patients in future studies targeting invasively managed patients with UA/NSTEMI will enhance event rates and may, thus, help to better evaluate new strategies designed to mitigate the high risks of adverse outcomes in this population.

Sources of Funding
CRUSADE was funded by the Schering-Plough Corporation, Bristol-Myers Squibb/Sanofi-Aventis Pharmaceuticals Partnership provided additional funding support. Millennium Pharmaceuticals, Inc also funded this work.

Disclosures
Dr. Roe has received research funding from Eli Lilly, Roche, Bristol-Myers Squibb, American College of Cardiology, and American Heart Association; consulting or honoraria from KAI Pharmaceuticals, Bristol-Myers Squibb, Sanofi-Aventis, Daiichi-Sankyo, Merck, Helsinn Pharmaceuticals, Astra Zeneca, and Regeneron. All conflicts of interest are listed at www.dcri.org. Dr. Wang has received funding from Bristol-Myers Squibb, Daiichi-Sankyo, Lilly, Heartscap Technologies, Sanofi-Aventis, Schering-Plough Corporation, and The Medicines Company, and personal royalties from Lilly. Dr. Ohman has received funding from Daiichi-Sankyo, Datascope, and Lilly, and consults for AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead Sciences, Liposcience, Merck, Pozen, Sanofi-Aventis, The Medicines Company, and WebMD. Dr. Peterson has received funding from Lilly, Ortho-McNeil-Janssen Pharmaceuticals, the Society of Thoracic Surgeons, the American Heart Association, and the American College of Cardiology, and consults for Merck, Ortho-McNeil-Janssen Pharmaceuticals, Pfizer, Sanofi-Aventis, and WebMD. The other authors report no conflicts.

References
Long-Term Outcomes After Invasive Management for Older Patients With Non–ST-Segment Elevation Myocardial Infarction
Matthew T. Roe, Shuang Li, Laine Thomas, Tracy Y. Wang, Karen P. Alexander, E. Magnus Ohman and Eric D. Peterson

Circ Cardiovasc Qual Outcomes. 2013;6:323-332; originally published online May 7, 2013; doi: 10.1161/CIRCOUTCOMES.113.000120
Circulation: Cardiovascular Quality and Outcomes is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2013 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/6/3/323

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/