Trends in Management and Outcomes of Patients With Acute Myocardial Infarction Complicated by Cardiogenic Shock

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Context Early mechanical revascularization in patients with acute myocardial infarction (AMI) complicated by cardiogenic shock is a therapeutic strategy that reduces mortality. It has been a class I recommendation in guidelines from the American College of Cardiology and the American Heart Association since 1999 for patients younger than 75 years. However, little is known about implementation of these guidelines in practice.

Objectives To assess trends in early revascularization and mortality for patients with cardiogenic shock complicating AMI and to determine whether the national guidelines affect revascularization rates.

Design, Setting, and Patients Prospective, observational study of 293,633 patients with ST-elevation myocardial infarction (25,311 [8.6%] had cardiogenic shock; 7,356 [29%] had cardiogenic shock at hospital presentation) enrolled in the National Registry of Myocardial Infarction (NRMI) from January 1995 to May 2004 at 775 US hospitals with revascularization capability (defined as the capability to perform cardiac catheterization, percutaneous coronary intervention [PCI], and open-heart surgery).

Main Outcome Measures Management patterns and in-hospital mortality rates.

Results There was an increase in primary PCI rates from 27.4% to 54.4% (P<.001) in hospitals with revascularization capability that paralleled the change in PCI for ST-elevation myocardial infarction. There was no significant change in rates of immediate coronary artery bypass graft surgery (from 2.1% to 3.2%). Propensity-adjusted multivariable analyses demonstrated that primary PCI was associated with a decreased odds of death during hospitalization (odds ratio, 0.46; 95% confidence interval, 0.40-0.53). There were no differences in the rates of change in revascularization rates based on the date when the guidelines were released regardless of patient age. Overall in-hospital cardiogenic shock mortality decreased from 60.3% in 1995 to 47.9% in 2004 (P<.001).

Conclusions The use of PCI for patients with cardiogenic shock was associated with improved survival in a large group of hospitals with revascularization capability. The American College of Cardiology and American Heart Association guidelines had no detectable temporal impact on revascularization rates. These findings support the need for increased adherence to these guidelines.
only from 8% to 12% and oral administration from 27% to 36%. Its use in recipients of intravenous fibrinolytic therapy 9 years later was 66.9%. Several recent studies have also reported that quality of care for patients with AMI was far from optimal, and compliance with guidelines from the ACC and the AHA was not satisfactory. The National Registry of Myocardial Infarction (NRMI) is a national database that has tracked practice patterns and outcomes of patients with AMI in the United States since 1990. We used the NRMI database to determine trends in the use of early mechanical revascularization for patients with AMI complicated by cardiogenic shock, and the relationship between mortality and the use of these procedures overall and among those younger or older than the cut point of 75 years specified in the guidelines from the ACC and the AHA. We also sought to determine the impact of the new guidelines on revascularization rates in patients with AMI complicated by cardiogenic shock managed in a non-protocol-directed clinical setting.

**METHODS**

The NRMI is a series of 5 industry-sponsored, prospective, observational studies of patients hospitalized with AMI throughout the United States. The data collection process and quality-control features of the NRMI have been described. Participation in the registry is voluntary. Registry hospitals tend to be larger than nonparticipating hospitals, are more likely to be certified by the Joint Commission on Accreditation of Healthcare Organizations, are more likely to be affiliated with a medical school, and are more likely to have available facilities for cardiac catheterization, coronary percutaneous coronary intervention (PCI), and cardiac surgery.

To be included in the NRMI, patients must have had a documented AMI according to local hospital criteria such as history, serial cardiac markers, and electrocardiographic findings. Concomitant medications, invasive procedures, transfer status, and adverse events are recorded if they occur at any time during hospitalization. Participating hospitals are encouraged to enter consecutive patients with AMI irrespective of treatment strategy and outcome.

A total of 293,633 nontransfer patients admitted with ST-elevation or left bundle-branch block AMI to a prospectively selected cohort of 775 hospitals with revascularization capability as defined as the capability to perform cardiac catheterization, PCI, and open-heart surgery were extracted from the 1.97 million AMI patients reported to the NRMI-2, NRMI-3, and NRMI-4 registries from June 1994 through May 2004. Of the 293,633 ST-elevation myocardial infarction (STEMI) patients, 25,311 (8.6%) were diagnosed with cardiogenic shock. Twenty-nine percent of these patients had shock at presentation (n=7356) and 71% (n=17,955) subsequently developed cardiogenic shock during hospitalization in 656 hospitals during the 10-year study period. We analyzed trends over time in baseline characteristics as well as management patterns, and in-hospital mortality rates in both STEMI patients and cardiogenic shock patients. A subset of hospitals were evaluated to determine whether the trends demonstrated for all hospitals were similar in this subset of core hospitals that consistently reported cardiogenic shock patients in the registry. Inclusion criteria for this core set of hospitals required that each hospital report at least 10 cardiogenic shock patients over the reporting life of NRMI-2, NRMI-3, and NRMI-4, with at least one of the cardiogenic shock cases discharged in each year of the 10-year analysis. We performed separate analyses for patients younger than 75 years and aged 75 years or older. The period showing the strongest effect in the patients younger than 75 years was then used to examine rate changes in the populations, including core hospitals and all STEMI patients. We also specifically considered the periods before and after the publication of the guidelines from the ACC and the AHA in September 1999.

The association between primary PCI use and mortality is well established even after adjusting for confounders; however, selection bias relating to procedure use can obscure this finding. Therefore, propensity scores were calculated using logistic regression for patients who received primary PCI and for those patients who did not receive primary PCI to identify patients who shared similar clinical and demographic characteristics. Independent variables were included in a forward logistic regression model and were used to model primary PCI as the dependent variable. The clinically relevant variables considered important in matching on patient characteristics between the 2 patient groups were demographics (patient age, sex, race, weight, payer), medical history (MI, angina, congestive heart failure, coronary artery bypass graft [CABG] surgery, stroke, diabetes, hypertension, current smoker, hypercholesterolemia, prior PCI), and clinical presentation (prehospital delay, chest pain, pulse, anterior MI, and year of discharge). The hospital characteristics of teaching hospital, annualized primary PCI volume, and US region also were considered to be important in generating the propensity score.

Using in-hospital mortality as the dependent variable, logistic regression models were constructed using successive blocks of relevant predictor fields.

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Primary PCI use was incorporated first into the model, followed by demographics (patient age, sex, race, weight, and payer), medical history (MI, angina, congestive heart failure, CABG surgery, stroke, diabetes, hypertension, current smoker, hypercholesterolemia, and prior PCI), clinical presentation (prehospital delay, chest pain, pulse, anterior MI, year of discharge, and treatment factors [IABP and immediate CABG surgery]), and propensity score. The adjusted odds ratios (AORs) and their 95% confidence intervals (CIs) were used to relate mortality to primary PCI by using successive blocks of predictors. To assess if any improvement in mortality occurred during the 10-year period, the 95% CIs and their AORs were generated and examined for the years 1995 through 2003, with reference to 2004. An AOR was considered statistically significant if its 95% CI did not include 1.0.

All statistical analyses were performed using SAS software version 8.2 (SAS Institute Inc, Cary, NC). All P values use 2-tailed tests of significance; P < .05 was considered significant.

RESULTS

Demographics, Clinical Characteristics, and Rate of Cardiogenic Shock

The rate of total shock (cardiogenic shock at presentation and/or clinical event shock, which was diagnosed after admission) in patients in the STEMI population (n = 293,633) was 8.6% (n = 25,311). Approximately 29% (n = 73,560) of total shock patients presented with cardiogenic shock, and the remaining 71% (n = 179,533) with total shock experienced shock only later during their stay (FIGURE 1). Patients younger than 75 years had cardiogenic shock at presentation less often (2.3%) than patients aged 75 years or older (3.1%). There was a slight but statistically significant upward trend in rates over time for those younger than 75 years (P < .001) but not for those aged 75 years or older (P = .14).

Demographics and clinical characteristics of the 73,560 patients with cardiogenic shock at presentation appear in TABLE 1. There were no differences over time in history of diabetes mellitus, congestive heart failure, stroke, and prior CABG surgery. There were fewer patients in recent years with history of MI, but more patients with prior PCI, hypertension, and dyslipidemia. Mean age and the proportion of women decreased over time. Time-related differences for several variables were statistically significant but small.

We evaluated rates of fibrinolytic therapy, IABP, diagnostic cardiac catheterization, PCI (total and primary), and CABG surgery (immediate and total). There was an increase in the rate of cardiac catheterization (from 51.5% to 74.4%), no change in IABP use (39.2%), and a reduction in the rates of fibrinolytic therapy (from 19.9% to 5.6%). We found an increase in rates of primary PCI (from 27.4% to 54.4%) and total PCI (from 34.3% to 64.1%), a decrease in overall CABG surgery rates (from 11.5% to 8.8%), and no significant change in immediate CABG surgery rates (FIGURE 2). Among the 73,560 patients with cardiogenic shock at presentation, 238 (3.24%) died prior to the median door-to-PCI time without having received PCI. For each year in the trend analysis, the median time was calculated using the set of nontransfer PCI patients. For cardiogenic shock patients, the median door-to-PCI times declined over time from 117 to 103 minutes (P = .001).

Mortality

Overall in-hospital mortality decreased from 60.3% in 1995 to 47.9% in 2004 (P < .001; TABLE 2). This paralleled the increasing use of revascularization. Furthermore, the mortality rate decreased over time for patients who underwent primary PCI for cardiogenic shock (TABLE 3). Multivariable analysis of in-hospital mortality adjusted for demographics, medical history, clinical presentation, hospital characteristics, year of discharge, and procedures demonstrated that primary PCI remained strongly independently associated with a lower in-hospital mortality rate (AOR, 0.46; 95% CI, 0.40-0.53 for confounding and pro-
Among the covariates in the model using all predictor blocks and propensity score, immediate CABG surgery during hospitalization was associated with lower mortality (AOR, 0.34; 95% CI, 0.25-0.47) in the full model including propensity score. A history of diabetes and a history of PCI were associated with increased mortality.

**Age, Management, and Mortality**

We found increases in primary PCI rates over time in patients younger than 75 years (from 31.4% to 63.7%; \( P < .001 \)) and aged 75 years or older (from 18.8% to 36.8%; \( P < .001 \)); **Figure 3**). Use rates of immediate CABG surgery remained low and did not show a time trend in patients younger than 75 years (from 2.4% to 3.6%; \( P = .87 \)) or in patients aged 75 years or older (from 1.3% to 2.6%; \( P = .46 \)).

Mortality rates decreased significantly over time in patients younger than 75 years and in patients aged 75 years or older (Table 2). After adjusting for demographics, previous medical history, and clinical and hospital characteristics, there was still a steady decrease in the likelihood of death with each increase in year. Primary PCI outcomes improved in patients younger than 75 years, with postprocedure mortality declining from 34.4% to 28.2% (\( P < .001 \)), but there was no significant change in mortality in patients aged 75 years or older (Table 3).

**Guidelines and Revascularization Rates**

We performed a multivariable analysis to assess if the revised guidelines from the ACC and the AHA published in September 1999 had a detectable impact on rates of early mechanical revascularization (primary PCI, immediate CABG surgery) in patients with cardiogenic shock.
In-Hospital Mortality and Patient Management

This large observational study of patients hospitalized with AMI suggests that over the last 10 years there has been a relatively stable rate of AMI complicated by cardiogenic shock, but there has been a decline in the associated inhospital mortality rate for hospitals with revascularization capability.

There was a significant increase in total and primary PCI rates. Primary PCI also was independently associated with a reduction in the odds of death during hospitalization even after adjustment with the propensity score. There were low and unchanging rates of IABP use, while fibrinolytic therapy use diminished over time. The association of increasing primary PCI rates for patients with cardiogenic shock and lower mortality rates is consistent with a benefit of early mechanical revascularization compared with initial medical stabilization and late or no revascularization that was shown in the SHOCK trial.2,3,12 The mortality rates were similar for those who underwent PCI in the SHOCK trial, SHOCK registry, and in the NRMI hospitals.2,3,6,7,12 This suggests that the randomized trial results are broadly applicable. The magnitude of the benefit of emergency revascularization is better estimated by the randomized SHOCK trial because selection bias is never fully accounted for even in a propensity analysis.

A notable difference between the SHOCK trial experience and the NRMI community experience is the marked difference in the use of CABG surgery. In the SHOCK trial, the protocol recommendation was for CABG surgery in sub-

### Table 2. In-Hospital Mortality Rates*

<table>
<thead>
<tr>
<th>Year</th>
<th>Total (%)</th>
<th>&lt;75 y (%)</th>
<th>≥75 y (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995</td>
<td>434 (60.3)</td>
<td>274 (55.8)</td>
<td>160 (69.9)</td>
</tr>
<tr>
<td>1996</td>
<td>510 (69.8)</td>
<td>290 (51.4)</td>
<td>220 (76.1)</td>
</tr>
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<td>1997</td>
<td>530 (60.7)</td>
<td>313 (53.3)</td>
<td>217 (75.9)</td>
</tr>
<tr>
<td>1998</td>
<td>413 (58.0)</td>
<td>225 (49.2)</td>
<td>188 (73.7)</td>
</tr>
<tr>
<td>1999</td>
<td>554 (65.9)</td>
<td>324 (60.3)</td>
<td>230 (66.3)</td>
</tr>
<tr>
<td>2000</td>
<td>475 (66.6)</td>
<td>258 (47.9)</td>
<td>217 (72.1)</td>
</tr>
<tr>
<td>2001</td>
<td>416 (62.1)</td>
<td>222 (43.9)</td>
<td>194 (66.4)</td>
</tr>
<tr>
<td>2002</td>
<td>339 (49.8)</td>
<td>187 (40.8)</td>
<td>152 (68.5)</td>
</tr>
<tr>
<td>2003</td>
<td>282 (51.3)</td>
<td>162 (44.7)</td>
<td>120 (63.8)</td>
</tr>
<tr>
<td>2004†</td>
<td>163 (47.9)</td>
<td>88 (39.5)</td>
<td>75 (64.1)</td>
</tr>
</tbody>
</table>

P value: .02. The Mantel-Haenszel *χ²* probability for the 2-sided alternative hypothesis that a linear association exists is presented.

<table>
<thead>
<tr>
<th>Year</th>
<th>Total (%)</th>
<th>&lt;75 y (%)</th>
<th>≥75 y (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995</td>
<td>89 (36.0)</td>
<td>70 (35.5)</td>
<td>53 (34.4)</td>
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<tr>
<td>1996</td>
<td>160 (42.7)</td>
<td>141 (47.6)</td>
<td>92 (40.5)</td>
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<td>1997</td>
<td>149 (40.8)</td>
<td>131 (44.0)</td>
<td>97 (41.1)</td>
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<tr>
<td>1998</td>
<td>134 (41.6)</td>
<td>106 (41.9)</td>
<td>65 (35.3)</td>
</tr>
<tr>
<td>1999</td>
<td>207 (41.3)</td>
<td>151 (40.6)</td>
<td>103 (38.3)</td>
</tr>
<tr>
<td>2000</td>
<td>182 (40.5)</td>
<td>135 (42.1)</td>
<td>89 (37.6)</td>
</tr>
<tr>
<td>2001</td>
<td>143 (35.8)</td>
<td>122 (35.0)</td>
<td>67 (37.7)</td>
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<tr>
<td>2002</td>
<td>116 (33.1)</td>
<td>104 (33.2)</td>
<td>62 (26.1)</td>
</tr>
<tr>
<td>2003</td>
<td>105 (34.3)</td>
<td>91 (36.4)</td>
<td>50 (28.3)</td>
</tr>
<tr>
<td>2004†</td>
<td>74 (33.9)</td>
<td>63 (34.1)</td>
<td>40 (28.2)</td>
</tr>
</tbody>
</table>

P value: .004. The Mantel-Haenszel *χ²* probability for the 2-sided alternative hypothesis that a linear association exists is presented.
sets with severe 3-vessel coronary artery disease (CAD) or left main CAD disease; more than two thirds had moderate or severe 3-vessel CAD and more than 20% had severe 3-vessel CAD. Cardiac surgeons were active SHOCK investigators, likely contributing to the finding that nearly 40% of those randomized to early revascularization had urgent early CABG surgery. In the current study, immediate and overall CABG surgery rates were low and unchanged over time.

**Guidelines and Age**

The Cooperative Cardiovascular Project demonstrates that implementation of guidelines into clinical practice in pilot states resulted in better performance on the defined quality indicators and reduced mortality. Furthermore, the Guidelines Applied in Practice initiative has shown that implementation of guidelines-based tools for AMI may facilitate quality improvement among a variety of institutions, patients, and caregivers.

Based on the SHOCK trial findings, the ACC and AHA revised guidelines elevated early mechanical revascularization for the management of AMI complicated by cardiogenic shock as a class I recommendation for patients younger than 75 years. Despite considerable investment in the development and dissemination of national guidelines for the management of AMI, several recent studies reported that quality of care for patients with AMI was far from optimal, with 30% of all reperfusion-eligible patients not receiving such therapy. The situation is even worse in patients aged 65 years or older, in which 80% of reperfusion-eligible patients did not receive this potentially life-saving therapy. We observed no difference in early mechanical revascularization use in all patients or in those younger than 75 years with AMI complicated by cardiogenic shock after publication of the guidelines. Fear of high PCI-associated mortality rates in states with public reporting of operator “scorecards” may lead to less intervention in high-risk patients as reported by Moscucci et al. Reluctance to perform PCI on high-risk patients with cardiogenic shock in New York state did not appear to explain our findings because only 1.65% of our cardiogenic shock cohort was from New York state hospitals. Analysis of the slope of primary PCI rates in cardiogenic shock patients demonstrated a significant increase in rates only late during the study period for any bimonthly interval in patients younger than 75 years. For the cardiogenic shock group (n = 7356), we saw a significant increase in rates only late during the period studied (around April 2003); this increase may be more a result of the overall increasing rates for all STEMI patients (n = 293 633), and may be related to the publication of reports favorable to primary PCI.

The SHOCK trial reported no apparent benefit of early revascularization for patients older than 75 years, but there were only 56 elderly patients in the co-

### Table 4. Association of Primary PCI and In-Hospital Mortality Among Patients With Cardiogenic Shock

<table>
<thead>
<tr>
<th></th>
<th>Odds of Death for Patients Receiving vs Not Receiving Primary PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>0.33 (0.30-0.36)</td>
</tr>
<tr>
<td>Adjusted for demographics, * medical history, † hospital characteristics, ‡ clinical presentation, § and discharge year</td>
<td></td>
</tr>
<tr>
<td>Plus procedures¶</td>
<td>0.46 (0.40-0.53)</td>
</tr>
<tr>
<td>Plus propensity score</td>
<td>0.46 (0.40-0.53)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; OR, odds ratio; PCI, percutaneous coronary intervention.

*Age, sex, race, weight, and payer status.
†Previous myocardial infarction, angina, congestive heart failure, coronary artery bypass graft surgery, stroke, diabetes, hypertension, current smoker, hypercholesterolemia, PCI.
‡Teaching, primary PCI volume, US region.
§Prehospital delay time, chest pain, pulse, systolic blood pressure, anterior location of myocardial infarction.
†Intra-aortic balloon pump counterpulsation or immediate coronary artery bypass graft surgery.

**Figure 3. Revascularization Rates in Patients With Cardiogenic Shock and All Patients With ST-Elevation Myocardial Infarction**

Asterisk indicates that there were 4830 cardiogenic shock patients and 211 929 ST-elevation myocardial infarction (STEMI) patients. Data are through May 2004. In 2004, there were 223 cardiogenic shock patients and 9428 STEMI patients. Dagger indicates that there were 2526 cardiogenic shock patients and 81 704 STEMI patients. Data are through May 2004. In 2004, there were 117 cardiogenic shock patients and 3698 STEMI patients.
hort and there were imbalances between the 2 treatment groups. The 1999 guidelines from the ACC and the AHA made no recommendation for the elderly. Recent analysis of the SHOCK trial registry demonstrated that early mechanical revascularization is associated with improved survival in patients aged 75 years or older or those who were clinically selected (approximately 20%) for early mechanical revascularization. Our study and other nonrandomized studies of elderly patients support the latter and demonstrate decreasing mortality in elderly patients in association with increasing PCI use in hospitals with revascularization capability. The 2004 guidelines on the management of AMI gave a class IIA recommendation for early revascularization in those older than 75 years who are suitable candidates (36.7% of the cohort in the NRMI registries).

**Limitations**

Approximately 15% of cardiogenic shock complicating AMI is due to mechanical complications, but the exact number is not known in this study because these data were not systematically collected. Even after adjusting for an estimated 15% of mechanical complications, emergency revascularization was underused for pump failure. The use of primary PCI was not examined in patients who were admitted to hospitals without revascularization capability.

In this registry, as in all registries, there was no independent review of source documents to confirm the diagnosis of cardiogenic shock. However, the rate of cardiogenic shock we found was similar to that found in other studies, supporting the validity of the diagnoses.

**Conclusions**

There was a general increase in the overall use of primary PCI and a parallel increase in the rate of primary PCI for shock in all age categories in hospitals with revascularization capability. This increase in PCI for shock patients was associated with improved survival, suggesting that the SHOCK trial results are applicable to a large group of hospitals with PCI and open heart surgery capability. The recommendation from the ACC and the AHA for early mechanical revascularization as a class I indication for treatment of patients with AMI complicated by cardiogenic shock had no detectable temporal impact on clinical management of these patients. Early CAGB surgery was underused in the NRMI compared with the SHOCK trial.

In accordance with guidelines from the ACC and the AHA, we recommend more aggressive use of early mechanical revascularization, including early CAGB surgery, in patients with AMI complicated by cardiogenic shock. The findings of our study support the need for efforts aimed at guideline adherence to improve survival of patients with cardiogenic shock.

**Author Contributions:** All of the authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Babaev, Hochman. Acquisition of data: Babaev, Sichrovsky. Analysis and interpretation of data: Babaev, Frederick, Pasta, Every, Sichrovsky, Hochman. Drafting of the manuscript: Babaev, Sichrovsky. Critical revision of the manuscript for important intellectual content: Babaev, Frederick, Pasta, Every, Hochman. Statistical analysis: Frederick, Pasta, Every. Obtained funding: Every. Administrative, technical, or material support: Babaev, Sichrovsky, Hochman. Study supervision: Hochman.

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**REFERENCES**