Relation Between Hospital Primary Angioplasty Volume and Mortality for Patients With Acute MI Treated With Primary Angioplasty vs Thrombolytic Therapy

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Reperfusion therapy with either primary angioplasty or thrombolytic therapy reduces mortality for eligible patients with acute myocardial infarction (AMI). Several randomized clinical trials conducted at selected medical centers have demonstrated lower mortality for patients with AMI who received primary angioplasty, compared with those who received thrombolytic therapy. In contrast, some large community-based observational studies found no survival benefit for patients who received primary angioplasty, compared with those who received thrombolytic therapy. These divergent study results may reflect the fact that the randomized trials were conducted at medical centers highly experienced in performing primary angioplasty, whereas the observational studies were conducted at an unselected group of hospitals having varying levels of experience with primary angioplasty.

The American College of Cardiology (ACC) and American Heart Association (AHA) recommend that "primary angioplasty should be used as an alternative to thrombolytic therapy only if performed in a timely fashion by individuals skilled in the procedure and supported by experienced personnel in high-volume centers." Despite the inherent logic in the ACC/AHA guidelines, we are aware of no large studies that have directly compared outcomes of primary angioplasty vs thrombo-

Context Institutional experience with primary angioplasty has been suggested as a factor in selecting a reperfusion strategy for patients with acute myocardial infarction (AMI). However, no large studies have directly compared outcomes of primary angioplasty vs thrombolytic therapy as a function of institutional experience.

Objective To compare outcomes among patients with AMI who were treated with primary angioplasty vs thrombolytic therapy at hospitals with different volumes of primary angioplasty.

Design Retrospective cohort.

Setting A total of 446 acute care hospitals with 112 classified as low volume (≤16 procedures), 223 as intermediate volume (17-48 procedures), and 111 as high volume (≥49 procedures) based on their annual primary angioplasty volume.

Patients A total of 62,299 patients with AMI treated with primary angioplasty or thrombolytic therapy from June 1, 1994, through July 31, 1999.

Main Outcome Measure In-hospital mortality.

Results Mortality was lower among patients who received primary angioplasty compared with those who received thrombolysis at hospitals with intermediate volumes (4.5% vs 5.9%; P < .001) and high volumes (3.4% vs 5.4%; P < .001) of primary angioplasty. At low-volume hospitals, there was no significant difference in mortality between patients treated with primary angioplasty vs those treated with thrombolysis (6.2% vs 5.9%; P = .58). Adjusting for differences in demographic, medical history, clinical presentation, treatment, and hospital characteristics did not significantly alter these findings.

Conclusions In this study, patients with AMI treated at hospitals with high or intermediate volumes of primary angioplasty had lower mortality with primary angioplasty than with thrombolysis, whereas patients with AMI treated at hospitals with low angioplasty volumes had similar mortality outcomes with primary angioplasty or thrombolysis.

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lytic therapy as a function of hospital primary angioplasty volume.

To address this issue, we examined the association between hospital-specific primary angioplasty volume and short-term mortality for patients with AMI treated with primary angioplasty vs thrombolytic therapy. We hypothesized that the higher the volume of cases of primary angioplasty performed at an institution, the lower the relative risk of death during hospitalization among patients with AMI receiving primary angioplasty compared with similar patients receiving thrombolytic therapy.

### METHODS

#### Data Sources

The National Registry of Myocardial Infarction (NRMI) is a voluntary, prospective, observational database that collects data on patients admitted with AMI throughout the United States. Characteristics of the NRMI registry, data gathering procedures, and reliability have been previously described.15-17 For this study, we used data for patients enrolled in the registry from June 1, 1994, through July 31, 1999.

#### Hospitals

Hospitals were eligible for this study if they performed 5 or more primary angioplasty and 5 or more intravenous thrombolysis procedures per year. Prior studies have noted that patients initially treated with thrombolytic therapy are more likely to be subsequently transferred to another facility than patients initially treated with primary angioplasty.16 To reduce the potential bias associated with differential patient transfer, we excluded hospitals with patient transfer rates exceeding 15%. We also excluded hospitals that did not regularly report data to the NRMI registry and those that had participated in the registry for fewer than 6 months, because of concerns regarding the completeness of data from these hospitals.

#### Hospital Primary Angioplasty Procedural Volume

We classified hospitals into primary angioplasty volume quartiles based on the annual number of procedures each had performed. Hospitals in the lowest quartile were defined as the low-volume group (≤16 procedures per year), whereas hospitals in the highest quartile were defined as the high-volume group (≥49 procedures per year). Because the unadjusted and adjusted mortality rates for both angioplasty and thrombolysis were similar for patients in the middle 2 quartiles, and were distinctly different from those in the lowest and highest quartiles, we combined the middle 2 quartiles into a single intermediate-volume group (17-48 procedures per year).

#### Patients

The following clinical criteria were used to identify patients with AMI who were optimal candidates for both thrombolytic therapy and primary angioplasty: (1) arrival at the hospital within 12 hours of AMI symptom onset; (2) initial electrocardiogram demonstrating ST-segment elevation or left bundle-branch block; (3) absence of cardiogenic shock; and (4) no contraindications to thrombolytic therapy.13,14 We excluded patients who did not complete their hospital stay at a single hospital because data on baseline characteristics, clinical outcomes, or both were not consistently available for these patients.

#### Data Analysis

The study population was divided into 2 cohorts based on whether the patients received intravenous thrombolysis or primary angioplasty. Complete data were available for more than 96% of patients for all baseline demographic, medical history, clinical presentation, medical therapy, and hospital variables.

The primary outcome for this study was in-hospital mortality. Secondary outcomes included nonfatal stroke (both hemorrhagic and thromboembolic), other major bleeding following reperfusion therapy (defined as bleeding other than intracranial that resulted in substantial hemodynamic compromise), and subsequent revascularization during the index hospitalization (defined as coronary artery bypass graft surgery or angioplasty that was performed for reasons other than as the initial reperfusion strategy). Process of care measures included the time to treatment, defined as the time from hospital arrival to the initiation of thrombolytic therapy for patients receiving intravenous thrombolysis and as the time from hospital arrival to first balloon inflation for patients undergoing primary angioplasty.

For this study the unit of analysis was the individual patient. For each patient we included a variable for the total number of primary angioplasty procedures performed at the admitting hospital. We used the generalized estimating equation (GEE) for risk modeling to adjust for the effects of within hospital clustering.18,19 Separate models were constructed for each of the primary angioplasty volume strata (low, intermediate, and high). The outcome variable for all risk models was in-hospital mortality. An indicator variable with thrombolytic therapy as the referent group was included in the models to assess the relation of reperfusion modality with hospital mortality. All patient and hospital variables listed in Tables 1, 2, and 3 were included as covariates in the risk models. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for all covariates in the models.

We developed additional regression models to test for an interaction between hospital primary angioplasty volume and reperfusion modality. The initial model included terms for reperfusion modality, hospital-specific primary angioplasty volume, and the interaction between reperfusion modality and primary angioplasty volume. Subsequent models adjusted for all baseline patient and hospital characteristics. In separate analyses, primary angioplasty volume was coded as a categorical and as a continuous variable.

We performed several subgroup analyses. To evaluate potential selection bias associated with different patient transfer rates, we repeated our analysis assuming that all transferred patients survived. To test for possible referral bias resulting from the influence of patient clinical status on the physi-
cian’s choice of reperfusion strategy, we performed an analysis that included only patients classified as high risk using the definition of the Primary Angioplasty in Myocardial Infarction (PAMI) trial, ie, those with either an anterior location of infarct, age older than 70 years, or heart rate greater than 100/min. The relationship between primary angioplasty volume and outcomes of reperfusion therapy also was assessed in patient cohorts stratified by sex, age older than or younger than 65 years, and in the subset of patients treated with primary angioplasty with coronary stent placement. Additional subgroup analyses were conducted for patient groups stratified by total hospital AMI volume (≤ or >300 AMI patients per year) and total hospital thrombolysis volume (≤ or >65 patients per year).

### RESULTS

#### Study Population

Of the 1799 hospitals reporting data to NRMI during the study period, we identified 616 hospitals that provided thrombolytic therapy and primary angioplasty. We excluded hospitals that had participated in the registry for fewer than 6 months (43), those that did not regularly report data to the registry (91), and institutions with patient transfer rates exceeding 15% (36). Overall, 446 hospitals met the criteria for the study; there were 112 low-volume, 223 intermediate-volume, and 111 high-volume primary angioplasty hospitals.

A total of 488,738 patients with AMI were treated at the 446 eligible hospitals during the 62-month study period. We excluded 187,141 patients because they did not complete their hospital stay at a single hospital. Of the remaining 301,617 patients, 87,873 were optimal candidates, by our criteria, for thrombolytic therapy or primary angioplasty. A total of 62,299 (70.9%) of these patients received reperfusion therapy. The final study population included 21,973 in the primary angioplasty group and 40,326 in the thrombolytic therapy group.

#### Baseline Characteristics

The thrombolytic therapy and primary angioplasty groups were similar with regard to age, sex, and race/ethnicity (Table 1). Given the large patient sample size, most baseline comparisons between the 2 cohorts were statistically different at the P<.01 level. Baseline characteristics with relative differences of 10% or more between the 2 cohorts are reported below.

Patients in the group receiving thrombolytic therapy were more likely to have a history of myocardial infarction (MI), heart failure, and coronary artery bypass graft surgery, but less likely to have had a prior angioplasty procedure. Patients treated with thrombolytic therapy arrived at the hospital sooner after onset of symptoms and were less likely to present with an anterior MI (Table 2).

Treatment with thrombolytic therapy was evenly distributed during the day, evening, and night, whereas treatment with primary angioplasty was more common during the daytime. Compared with patients who received primary angioplasty, patients who received thrombolysis were more likely to have been given aspirin and β-blockers and less likely to have received angiotensin-converting enzyme inhibitors during the first 24 hours of hospitalization. Treatment with primary angioplasty was more common in teaching hospitals and during the later years of the study (Table 3).

### Table 1. Patient Characteristics by Reperfusion Strategy at Low-, Intermediate-, and High-Volume Primary Angioplasty Hospitals

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Low-Volume (n = 10,144)</th>
<th>Intermediate-Volume (n = 14,323)</th>
<th>High-Volume (n = 8,817)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean, y</td>
<td>61.9</td>
<td>60.3</td>
<td>60.9</td>
</tr>
<tr>
<td>Men</td>
<td>69.2</td>
<td>71.6</td>
<td>71.8</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>84.7</td>
<td>82.4</td>
<td>83.9</td>
</tr>
<tr>
<td>Black</td>
<td>7.1</td>
<td>7.1</td>
<td>6.5</td>
</tr>
<tr>
<td>Other</td>
<td>8.1</td>
<td>10.6</td>
<td>10.5</td>
</tr>
<tr>
<td>Diabetes</td>
<td>19.3</td>
<td>18.8</td>
<td>18.7</td>
</tr>
<tr>
<td>Hypertension</td>
<td>45.7</td>
<td>45.5</td>
<td>45.6</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>29.0</td>
<td>30.4</td>
<td>32.2</td>
</tr>
<tr>
<td>Current smoker</td>
<td>38.3</td>
<td>36.6</td>
<td>39.6</td>
</tr>
<tr>
<td>Prior angina</td>
<td>11.3</td>
<td>11.1</td>
<td>12.9</td>
</tr>
<tr>
<td>Prior CHF</td>
<td>4.2</td>
<td>2.6</td>
<td>3.5</td>
</tr>
<tr>
<td>Prior MI</td>
<td>19.1</td>
<td>17.4</td>
<td>18.6</td>
</tr>
<tr>
<td>Prior stroke</td>
<td>3.4</td>
<td>3.3</td>
<td>3.1</td>
</tr>
<tr>
<td>Prior angioplasty</td>
<td>7.7</td>
<td>11.5</td>
<td>9.3</td>
</tr>
<tr>
<td>Prior CABG surgery</td>
<td>7.3</td>
<td>6.2</td>
<td>7.5</td>
</tr>
</tbody>
</table>

*Values are percentages unless otherwise indicated. Percentages do not always total 100 because of rounding. P values are not reported because, given the large number of patients, assessing whether differences are statistically significant is not informative. See Methods section for definition of low-, intermediate-, and high-volume categories. CHF indicates congestive heart failure; MI, myocardial infarction, and CABG, coronary artery bypass graft.

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In-Hospital Mortality by Primary Angioplasty Volume

For patients receiving care at low-volume primary angioplasty centers, unadjusted in-hospital case fatality rates were similar for the primary angioplasty and thrombolytic therapy groups (6.2% vs 5.9%, respectively; *P* = .58) (FIGURE). In the separate GEE regression models that adjusted for all baseline demographic, medical history, clinical presentation, medical therapy, and hospital characteristics (TABLE 4), there was no association between reperfusion strategy and in-hospital mortality in low-volume institutions (OR, 1.06; 95% CI, 0.80-1.40).

At intermediate-volume primary angioplasty centers, patients treated with primary angioplasty had significantly lower unadjusted mortality rates during hospitalization than those treated with thrombolysis (4.5% vs 5.9%; *P*<.001). The survival advantage of primary angioplasty compared with thrombolysis persisted after adjusting for all baseline patient and hospital characteristics (OR, 0.65; 95% CI, 0.57-0.75).

At high-volume primary angioplasty centers, unadjusted in-hospital mortality rates were also lower for patients treated with primary angioplasty than those for patients treated with thrombolysis (3.4% vs 5.4%, *P*<.001). The association between treatment with primary angioplasty and lower in-hospital

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Low-Volume</th>
<th>Intermediate-Volume</th>
<th>High-Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time from onset of MI symptoms to hospital arrival, h</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2</td>
<td>59.7</td>
<td>60.4</td>
<td>60.3</td>
</tr>
<tr>
<td>2-6</td>
<td>33.1</td>
<td>33.1</td>
<td>33.3</td>
</tr>
<tr>
<td>7-12</td>
<td>7.2</td>
<td>6.4</td>
<td>6.4</td>
</tr>
<tr>
<td>Time of hospital arrival Day (8 AM-4 PM)</td>
<td>39.3</td>
<td>36.0</td>
<td>31.4</td>
</tr>
<tr>
<td>Evening (4 PM-midnight)</td>
<td>33.7</td>
<td>35.6</td>
<td>24.3</td>
</tr>
<tr>
<td>Night (midnight − 8 AM)</td>
<td>27.0</td>
<td>28.5</td>
<td>20.2</td>
</tr>
<tr>
<td>Chest pain at presentation</td>
<td>96.2</td>
<td>96.6</td>
<td>96.6</td>
</tr>
<tr>
<td>Pulse &gt;100/min</td>
<td>10.9</td>
<td>10.8</td>
<td>10.3</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>3.6</td>
<td>3.5</td>
<td>3.4</td>
</tr>
<tr>
<td>&lt;90</td>
<td>9.0</td>
<td>4.1</td>
<td>3.4</td>
</tr>
<tr>
<td>90-120</td>
<td>22.9</td>
<td>22.4</td>
<td>22.5</td>
</tr>
<tr>
<td>&gt;120</td>
<td>73.5</td>
<td>74.1</td>
<td>73.1</td>
</tr>
<tr>
<td>Killip class</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I (no heart failure)</td>
<td>88.6</td>
<td>89.4</td>
<td>89.0</td>
</tr>
<tr>
<td>II (heart failure)</td>
<td>9.5</td>
<td>8.6</td>
<td>8.6</td>
</tr>
<tr>
<td>III (pulmonary edema)</td>
<td>1.9</td>
<td>2.0</td>
<td>2.5</td>
</tr>
<tr>
<td>Initial ECG findings</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST-segment elevation</td>
<td>99.4</td>
<td>99.5</td>
<td>99.6</td>
</tr>
<tr>
<td>ST-segment depression</td>
<td>38.2</td>
<td>45.5</td>
<td>44.0</td>
</tr>
<tr>
<td>Nonspecific ST-segment or T-wave changes</td>
<td>3.6</td>
<td>3.3</td>
<td>2.5</td>
</tr>
<tr>
<td>Q waves</td>
<td>12.0</td>
<td>14.8</td>
<td>4.6</td>
</tr>
<tr>
<td>LBBB</td>
<td>1.6</td>
<td>1.6</td>
<td>1.4</td>
</tr>
<tr>
<td>RBBB</td>
<td>3.4</td>
<td>3.3</td>
<td>6.0</td>
</tr>
<tr>
<td>Anterior location of infarct</td>
<td>34.8</td>
<td>33.6</td>
<td>40.4</td>
</tr>
<tr>
<td>Admission diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MI or rule-out MI</td>
<td>98.2</td>
<td>98.8</td>
<td>98.4</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>0.9</td>
<td>0.8</td>
<td>1.0</td>
</tr>
<tr>
<td>Other</td>
<td>0.8</td>
<td>0.4</td>
<td>0.6</td>
</tr>
<tr>
<td>Medication within 24 h</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>94.2</td>
<td>94.3</td>
<td>94.3</td>
</tr>
<tr>
<td>β-Blocker</td>
<td>56.7</td>
<td>58.0</td>
<td>59.3</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>13.7</td>
<td>16.4</td>
<td>12.6</td>
</tr>
</tbody>
</table>

*Values are percentages unless otherwise indicated. Percentages do not always total 100 because of rounding. *P* values are not reported because, given the large number of patients, assessing whether differences are statistically significant is not informative. See Methods section for definition of low-, intermediate-, and high-volume categories. MI indicates myocardial infarction; ECG, electrocardiogram; LBBB, left bundle-branch block; RBBB, right bundle-branch block; and ACE, angiotensin-converting enzyme.
mortality remained significant in a regression analysis that adjusted for all patient and hospital characteristics (OR, 0.61; 95% CI, 0.52-0.72).

The difference in crude hospital mortality rates between the primary angioplasty group and the thrombolysis group increased as hospital primary angioplasty volume increased (Figure; \( P < .001 \) for the overall interaction between hospital primary angioplasty volume and reperfusion modality). The interaction between primary angioplasty volume and reperfusion modality was also significant in analyses in which primary angioplasty was coded as a continuous variable (\( P < .01 \)) and in analyses that adjusted for all baseline patient and hospital characteristics (\( P < .01 \)).

The time to treatment for patients who received thrombolytic therapy (the time from hospital arrival to delivery of intravenous thrombolysis) was shorter than the comparable time to treatment for patients who received primary angioplasty (the time from hospital arrival to balloon inflation) (TABLE 5). Although the time to treatment for thrombolytic therapy was relatively constant across hospital volume strata, the time to treatment for primary angioplasty decreased as the hospital primary angioplasty volume increased. After adding the time to treatment variable to our regression model, the association between primary angioplasty volume and mortality was slightly attenuated (approximately 7% of the mortality reduction at higher-volume hospitals was explained by differences in time to reperfusion).

### Secondary Outcomes During Hospitalization and Subgroup Analyses

Overall, patients treated with thrombolytic therapy were more likely to have a nonfatal stroke than patients treated with primary angioplasty (1.1% vs 0.8%).

The interaction between reperfusion strategy and primary angioplasty volume was significant (\( P < .001 \)). There were 112 low-volume (≤16 procedures per year), 223 intermediate-volume (17-48 procedures per year) and 111 high-volume hospitals (≥49 procedures per year).
0.4%; \( P < .001 \). There was no significant difference in the rates of major bleeding between the 2 treatment groups (4.0% in the thrombolysis group vs 3.7% in the primary angioplasty group; \( P = .10 \)). These findings were consistent across primary angioplasty volume strata (Table 5) and persisted after adjustment for all baseline patient and hospital characteristics.

The incidence of subsequent revascularization was higher for patients treated with thrombolysis than for those treated with primary angioplasty (overall incidence, 59.0% vs 15.0%; \( P < .001 \)). For patients treated with primary angioplasty, the incidence of subsequent revascularization decreased as the hospital primary angioplasty volume increased (\( P < .001 \)). These findings persisted after adjusting for all baseline patient and hospital characteristics.

More patients treated with thrombolysis (3.6%) than those treated with primary angioplasty (1.4%) were excluded from the primary analysis because they were transferred from the initial hospital to a second hospital. To assess the potential for bias resulting from differential patient transfer rates, we repeated the analysis assuming that all transfer patients survived. In this analysis, the adjusted risk of death among patients who received primary angioplasty compared with that of those who received thrombolysis was similar to the adjusted risk found in the primary analysis (low-volume centers: OR, 1.10; 95% CI, 0.87-1.38; intermediate-volume centers: OR, 0.66; 95% CI, 0.58-0.76; high-volume centers: OR, 0.61; 95% CI, 0.52-0.73).

To test for selection bias in the physicians' choice of reperfusion strategy, we also performed a subgroup analysis that included only high-risk patients as defined in the PAMI trial. In this analysis, the adjusted risk of death among patients who received primary angioplasty compared with that of those who received thrombolysis was similar to the adjusted risk found in the primary analysis (low-volume centers: OR, 1.10; 95% CI, 0.87-1.38; intermediate-volume centers: OR, 0.66; 95% CI, 0.58-0.76; high-volume centers: OR, 0.61; 95% CI, 0.52-0.73).

### COMMENT

In this study, we compared outcomes among patients with AMI treated with primary angioplasty vs thrombolytic therapy at hospitals having varying levels of experience with primary angioplasty. At intermediate- and high-volume hospitals, we found that mortality was lower among patients who received primary angioplasty compared with those who received thrombolytic therapy. In contrast, the risk of death among patients treated with primary angioplasty and thrombolysis at low-volume hospitals was similar. Adjusting for differences in patient and clinical variables did not significantly alter these findings. Results were also similar in age, sex, and high-risk subgroups. Patients treated with primary angioplasty were less likely to have a nonfatal stroke or to undergo subsequent revascularization than patients treated with thrombolysis.

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**Table 4.** Association Between Reperfusion Strategy and Risk of Death During Hospitalization for 3 Volume Groups, and the Effect of Adding Covariates

<table>
<thead>
<tr>
<th>Model†</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
<td>Low-Volume</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>1.07 (0.85-1.35)</td>
</tr>
<tr>
<td>Adjusted for demographics</td>
<td>1.18 (0.92-1.50)</td>
</tr>
<tr>
<td>Adjusted for demographics, medical history, and clinical factors</td>
<td>1.10 (0.84-1.43)</td>
</tr>
<tr>
<td>Adjusted for demographics, medical history, clinical factors, and treatments</td>
<td>1.01 (0.77-1.33)</td>
</tr>
<tr>
<td>Adjusted for demographics, medical history, clinical factors, treatments, hospital factors, and event year</td>
<td>1.06 (0.80-1.40)</td>
</tr>
</tbody>
</table>

*CI indicates odds ratio; CI, confidence interval.†The unadjusted model included reperfusion strategy with thrombolytic therapy as the referent group. Covariates for the adjusted models are listed in Tables 1, 2, and 3.

**Table 5.** Reperfusion Treatment Time and Secondary Outcomes by Reperfusion Strategy at Low-, Intermediate-, and High-Volume Primary Angioplasty Hospitals

<table>
<thead>
<tr>
<th>Secondary Outcomes</th>
<th>Low-Volume</th>
<th>Intermediate-Volume</th>
<th>High-Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reperfusion treatment time, mean, min</td>
<td>48</td>
<td>49</td>
<td>51</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>3.2</td>
<td>4.3</td>
<td>4.0</td>
</tr>
<tr>
<td>Nonfatal stroke</td>
<td>1.1</td>
<td>1.0</td>
<td>0.9</td>
</tr>
<tr>
<td>Subsequent revascularization</td>
<td>54.3</td>
<td>60.8</td>
<td>59.7</td>
</tr>
</tbody>
</table>

*Values are percentages unless otherwise indicated. See Methods section for definition of low-, intermediate-, and high-volume categories.
There was no significant difference in rates of other major bleeding between the 2 cohorts.

By using the NRMI registry we were able to assess AMI outcomes at geographically diverse hospitals with a wide range of primary angioplasty experience. An additional strength was the availability of extensive clinical and demographic data that allowed for adjustment of patient and hospital differences (including overall hospital MI volume)\(^{21}\) that might influence short-term mortality.

This study may provide an explanation for the discordant results of previous studies comparing primary angioplasty with thrombolytic therapy. Our finding of improved outcomes for primary angioplasty at higher-volume centers is consistent with previous clinical trials, mostly conducted at experienced centers.\(^{5-8}\) However, our finding of no difference in outcomes by reperfusion strategy at low-volume centers is consistent with previous community-based studies that included institutions with low primary angioplasty volumes.\(^{9,12}\)

We noted a progressive decline in mortality associated with primary angioplasty at hospitals with higher procedural volume. This finding supports the ACC/AHA guideline recommendations and is consistent with prior studies documenting an inverse association between hospital procedural volume and outcomes following coronary artery bypass graft surgery, elective angioplasty, and primary angioplasty.\(^{13,14,22-32}\)

Since primary angioplasty is a complex procedure, improved organizational performance may contribute to superior outcomes at high-volume centers. Our finding of shorter times between hospital arrival and balloon inflation at higher-volume centers is consistent with this hypothesis. High-volume centers also may experience more favorable outcomes because they have more experienced operators or perform more total procedures (including elective angioplasty procedures). However, since the NRMI registry does not contain data on physician procedure volume or total hospital angioplasty volume, we were not able to assess the degree to which these factors contributed to our findings.

Another possible explanation for our finding of lower mortality with primary angioplasty at higher-volume centers might be that physicians at these centers selected lower-risk patients for primary angioplasty. However, patients who received primary angioplasty and thrombolytic therapy were similar with regard to baseline factors. If anything, the primary angioplasty cohort may have been at greater risk of death given their significantly larger proportion of anterior MIs and longer time from onset of symptoms to hospital arrival. The lower mortality observed for primary angioplasty at higher-volume centers persisted after adjustment for important clinical predictors of mortality and was also noted in subgroup analyses stratified by mortality risk.

Two prior studies found no relationship between primary angioplasty volume and the relative outcomes of primary angioplasty and thrombolytic therapy. In a subgroup analysis of patients in the Myocardial Infarction Triage Intervention study, Every et al\(^{9}\) noted no difference in outcome by reperfusion strategy for 995 patients treated at 3 high-volume primary angioplasty centers compared with 1394 patients treated at 9 low-volume centers. Similarly, Danchin et al,\(^{11}\) in a cohort of 721 patients, found no difference in relative mortality between hospitals that performed more than 4 primary angioplasty procedures per month and those that performed 3 or fewer procedures per month. However, the relatively small number of hospitals and patients in these studies limited the investigators’ ability to assess the influence of primary angioplasty volume on mortality.

Several potential limitations of our study should be acknowledged. Most important, patients were not randomly assigned to undergo primary angioplasty or receive thrombolytic therapy. To minimize patient selection bias we restricted our analysis to patients who were optimal candidates for both thrombolytic therapy and primary angioplasty. Although the results did not significantly change after adjustment for known baseline differences in the 2 study cohorts, there may be residual bias from unmeasured differences between the 2 groups.

In addition, the NRMI registry does not include long-term follow-up; therefore, we cannot be certain that the mortality differences observed in this study will persist. In the Gusto IIB trial,\(^{33}\) an early mortality benefit of primary angioplasty over thrombolyis was not evident at 6-month follow-up. However, in a more recent study, Zijlstra et al\(^{34}\) reported a survival benefit among patients treated with primary angioplasty that was sustained for 5 years.

Most US medical centers do not have the facilities and staff to provide primary angioplasty.\(^{13,14}\) Our findings do not support a policy of routine patient transfer from hospitals offering only thrombolyis to high-volume interventional hospitals, because potential benefits from primary angioplasty may well be offset by delays in achieving reperfusion.\(^{13,14}\) Alternatively, emergency medical service systems may consider out-of-hospital triage of eligible AMI patients to high-volume primary angioplasty centers if triage can be accomplished without significant delays to reperfusion. Since only 71% of eligible AMI patients received reperfusion therapy in this study, efforts also should be made to increase reperfusion rates for eligible patients.

Our study may be relevant for hospitals contemplating offering primary angioplasty as a reperfusion option. Our findings suggest that, at hospitals that perform higher volumes of primary angioplasty procedures, patients with AMI who are eligible for reperfusion may experience reduced mortality from the use of primary angioplasty compared with thrombolyis. In contrast, hospitals that perform low volumes of primary angi-
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compared with alteplase (recombinant tissue-type
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