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A Regional System to Provide Timely Access to Percutaneous Coronary Intervention for ST-Elevation Myocardial Infarction

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Background—Percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction (STEMI) is superior to fibrinolysis when performed in a timely manner in high-volume centers. Recent European trials suggest that transfer for PCI also may be superior to fibrinolysis and increase access to PCI. In the United States, transfer times are consistently long; therefore, many believe a transfer for PCI strategy for STEMI is not practical.

Methods and Results—We developed a standardized PCI-based treatment system for STEMI patients from 30 hospitals up to 210 miles from a PCI center. From March 2003 to November 2006, 1345 consecutive STEMI patients were treated, including 1048 patients transferred from non-PCI hospitals. The median first door-to-balloon time for patients <60 miles (zone 1) and 60 to 210 miles (zone 2) from the PCI center was 95 minutes (25th and 75th percentiles, 82 and 116 minutes) and 120 minutes (25th and 75th percentiles, 100 and 145 minutes), respectively. Despite the high-risk unselected patient population (cardiogenic shock, 12.3%; cardiac arrest, 10.8%; and elderly [≥80 years of age], 14.6%), in-hospital mortality was 4.2%, and median length of stay was 3 days.

Conclusions—Rapid transfer of STEMI patients from community hospitals up to 210 miles from a PCI center is safe and feasible using a standardized protocol with an integrated transfer system. (Circulation. 2007;116:721-728.)

Key Words: angioplasty myocardial infarction stents point-of-care systems

Primary percutaneous coronary intervention (PCI) is preferred over fibrinolysis for patients with ST-elevation myocardial infarction (STEMI) when it can be performed in a timely manner by experienced operators.1–4 PCI improves infarct artery patency and is associated with improved survival and lower rates of stroke, recurrent myocardial infarction, and ischemia compared with fibrinolytic therapy. Universal access is the major limitation of a PCI strategy for STEMI because PCI is available in only 25% of hospitals in the United States.5,6 In addition, the United States lacks both an organized system of care for STEMI patients and an integrated system for patient transfer.7–9

Recent trials have shown that a strategy of patient transfer for PCI yields superior outcomes compared with fibrinolysis at a non-PCI hospital.10–15 With 1 exception, these trials were performed in European countries with short transfer distances and organized transfer systems. The only randomized US trial had a first door-to-balloon time of 155 minutes, and the trial was stopped early because of slow enrollment.15 In the United States, the median first door-to-balloon time for patients transferred for PCI is 180 minutes.16 Only 4.2% of patients are treated within 90 minutes, the time recommended by the recent American College of Cardiology/American Heart Association (ACC/AHA) guidelines.1 This has led many to believe that a strategy of transfer for PCI in STEMI is not practical in the United States.

We developed a regional program for transfer of patients with STEMI for PCI from 30 community hospitals in Minnesota using a standardized protocol and an integrated transfer system. We describe the results in 1345 consecutive STEMI patients that demonstrate that transfer for PCI is both safe and feasible.
Methods

Our aim was to develop a standardized system of care for STEMI that included timely access to PCI for patients presenting to either the tertiary PCI center or the 30 referring non-PCI hospitals. The specific goals were (1) to standardize STEMI care throughout the system using hospital-specific protocols and orders; (2) to improve timely access to PCI with first door-to-balloon time of <120 minutes (ACC/AHA guidelines in 2002); (3) to establish a network for collection of data for STEMI patients who present to rural and community hospitals; (4) to implement STEMI quality improvement measures at each hospital, including immediate feedback to both emergency and primary care physicians; and (5) to improve cardiovascular outcomes in STEMI patients throughout the system.

The Minneapolis Heart Institute (MHI) is a group of 46 cardiovascular specialists at Abbott Northwestern Hospital (ANW), a 619-bed hospital (PCI center) in Minneapolis (Minn), which has referral relationships with community hospitals throughout Minnesota and Wisconsin. The MHI Level 1 Myocardial Infarction (MI) Program was initiated in 2002 and modeled on the trauma system concept. A level 1 Clinical Care Committee was formed to develop a standardized protocol for treatment of STEMI patients based on ACC/AHA guidelines with a consensus of local cardiovascular, emergency medicine, and primary care physicians. After an initial 9-month pilot program at a single community hospital, the standardized protocol was implemented in 5 community hospitals and the PCI center in March 2003. Currently, 11 hospitals <60 miles from the PCI center are designated zone 1 hospitals (Figure 1). After successful implementation in zone 1 hospitals, we developed a standardized facilitated PCI protocol to include hospitals 60 to 210 miles from the PCI center (zone 2). The decision to use a facilitated approach using reduced-dose fibrinolytics was based on the anticipated long-distance transfer times and a consensus of the MHI Level 1 MI Clinical Care Committee. After a pilot project in August 2003, the zone 2 protocol was implemented in 19 hospitals 60 to 210 miles from the PCI center (see online-only Data Supplement). The referral non-PCI hospital size ranged from 10 to 162 hospital beds, and none had 24-hour onsite cardiovascular consultation. Institutional Review Board approval was obtained for data collection, follow-up, and data analysis.

Inclusion/Exclusion Criteria

Patients with STEMI or new left bundle-branch block within 24 hours of symptom onset were included in the MHI Level 1 MI Program and database. No patients were excluded from the protocol unless the physician thought that reperfusion therapy was inappropriate because of an underlying condition such as advanced metastatic cancer or end-stage dementia. All patients, including those with advanced age, out-of-hospital cardiac arrest, cardiogenic shock, and initially nondiagnostic ECGs, were included in the data analysis.

MHI Level 1 Protocol

The diagnosis of STEMI was made by the emergency department (ED) physician directly caring for the patient in the community hospital who activated the system with a single phone call. A standardized protocol with preprinted standing orders was initiated at each hospital. The protocols for the PCI center and zone 1 and 2 hospitals were identical except that zone 2 patients received half-dose tenecteplase unless a contraindication to fibrinolysis was present. Extensive training was performed at each hospital for emergency medical services, nursing personnel, and ED and primary care physicians. Each hospital had a level 1 MI toolkit that included a protocol checklist, transfer forms, clinical data form, standing orders, adjunctive medications, and laboratory supplies. The clinical data form, ECG, and laboratory results were faxed to the PCI center cardiac catheterization laboratory. Transferred patients were taken directly to the cardiac catheterization laboratory for PCI without reevaluation in the ED. Backup protocols were in place for anticipated delays (such as inclement weather): zone 1, half-dose tenecteplase and facilitated PCI; and zone 2, full-dose tenecteplase. A comprehensive database with detailed treatment times, clinical and angiographic data, and in-hospital, 1-month, and yearly outcomes using ACC National Cardiovascular Data Registry defini-
A comprehensive feedback and quality assurance plan was developed for each hospital that included Joint Commission on Accreditation of Healthcare Organizations’ (JCAHO) STEMI indicators. Immediate feedback is provided to the ED physician and nursing supervisor for the community hospital. Aggregated quality data are reported to each hospital quarterly.17

**Statistical Analysis**

Three distinct groups of patients are described on the basis of the geographic location of initial presentation: the PCI center, zone 1 (<60 miles), and zone 2 (60 to 210 miles). Continuous data are presented as mean±SD and compared with 1-way ANOVA with 3 treatment groups. Time data are presented as median (25th and 75th percentiles) and compared via the nonparametric Kruskal-Wallis test. Proportions are compared via Pearson χ² test, with Fisher exact test used when the assumptions of the χ² test are not met. Monte Carlo approximations to Fisher exact test are used for test of proportions in r×3 tables (eg, for culprit artery) when computation of exact probability values is infeasible. Survival curves are generated by the Kaplan-Meier method and compared via the log-rank test. The analysis was performed on an intent-to-treat basis; baseline characteristics for all patients are included, regardless of whether they were subsequently determined not to have had a MI or whether they were entered into the backup protocol.

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

### Results

Between March 2003 and November 2006, 1345 consecutive patients with STE or new left bundle-branch block within 24 hours of symptom onset were treated, including 297 patients who presented to the PCI center, 627 patients transferred from zone 1 hospitals (<60 miles), and 421 patients transferred from zone 2 hospitals (60 to 210 miles). The baseline clinical characteristics (Table 1) are similar for all 3 groups, except zone 2 patients were older with more frequent renal insufficiency. High-risk clinical characteristics for all 3 groups also are shown in Table 1 and are similar between all 3 groups, except more frequent out-of-hospital arrest in zone 1 patients. High-risk characteristics were common and included age ≥80 years (14.6%), cardiogenic shock (12.3%), cardiac arrest before PCI (10.8%), and mechanical ventilation before PCI (6.9%). The mean Thrombolysis in Myocardial Infarction (TIMI) risk scores are shown in Table 1.19

Of the 1048 zone 1 and 2 patients, 70.5% were transported by helicopter and 29.5% by ground ambulance. As expected, zone 2 hospitals were more likely to use helicopters (93.6% versus 55.0% in zone 1; P<0.0001). In transferred patients, 54 patients (5.2%) required endotracheal intubation before transport and 7 (0.7%) during transport.

| TABLE 1. Baseline Characteristics | PCI Center | Zone 1 | Zone 2 | P
|-----------------------------------|-----------|-------|-------|---
| No.                              | 297       | 627   | 421   | . . .
| Age, y                           | 62.5±14.5 | 61.2±15.1 | 63.6±13.8 | 0.02
| Patients ≥75 y, n (%)             | 71 (24.9) | 146 (23.3) | 114 (27.1) | 0.38
| Male, n (%)                      | 213 (71.7) | 452 (72.1) | 299 (71.0) | 0.93
| Hyperlipidemia, n (%)             | 167 (56.2) | 322 (51.4) | 226 (53.7) | 0.37
| Hypertension, n (%)               | 170 (57.2) | 334 (53.3) | 227 (53.9) | 0.52
| Diabetes, n (%)                  | 49 (16.5) | 84 (13.4) | 67 (15.9) | 0.36
| Smoking, n (%)                   |           |       |       |   
| Ever                             | 176 (59.3) | 399 (63.6) | 272 (64.6) | 0.31
| Current                          | 102 (34.3) | 260 (41.5) | 168 (39.9) | 0.11
| BMI, kg/m²                       | 28.2±6.1 | 28.8±5.8 | 28.6±5.4 | 0.34
| Creatinine clearance <70 mL/min, n (%) | 105/285 (36.8) | 197/589 (33.4) | 169/395 (42.8) | 0.012
| History of MI, n (%)             | 62 (20.9) | 97 (15.5) | 77 (18.3) | 0.12
| History of CABG, n (%)           | 23 (7.7) | 40 (6.4) | 35 (8.3) | 0.47
| History of PCI, n (%)            | 64 (21.5) | 107 (17.1) | 74 (17.6) | 0.24
| High-risk clinical characteristics, n (%) |           |       |       |   
| Cardiogenic shock                | 45 (15.2) | 76 (12.1) | 44 (10.4) | 0.17
| Cardiac arrest before PCI        | 25 (8.4) | 81 (12.9) | 39 (9.3) | 0.06
| Out-of-hospital cardiac arrest   | 5 (1.7) | 31 (4.9) | 7 (1.6) | 0.003
| SBP <100 mm Hg at presentation   | 34 (11.4) | 61 (9.7) | 40 (9.5) | 0.65
| Heart rate >100 bpm at presentation | 37 (12.5) | 77 (12.3) | 54 (12.8) | 0.97
| Killip class 2–4                 | 52 (17.5) | 96 (15.3) | 57 (13.5) | 0.34
| Anterior MI                      | 111 (37.4) | 212 (33.8) | 137 (32.5) | 0.39
| LBBB                             | 4 (1.35) | 22 (3.5) | 14 (3.3) | 0.17
| Time to therapy >4 h             | 109 (36.7) | 247 (40.0) | 176 (43.0) | 0.24
| TIMI risk score                  | 3.5±2.5 (296) | 3.4±2.4 (617) | 3.6±2.6 (409) | 0.51

BMI indicates body mass index; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; and LBBB, left bundle-branch block.
The percentage of patients with door-to-balloon times <90 and <120 minutes for each patient cohort is shown in Figure 2. The “in-door” to “out-door” time at non-PCI hospitals was significantly greater in zone 2 patients because of time waiting for helicopter arrival, and as expected, zone 2 transport times were longer (Table 2).

A total of 1345 patients met Level 1 MI protocol criteria (Figure 3). Five patients died before angiography could be performed, including 4 patients who presented with out-of-hospital cardiac arrest. Angiography was canceled in 5 patients. Coronary angiography was performed in 1335 patients (99.2%). PCI was attempted in 1072 (80.3%) and was successful in 1065 (99.3%), 96.4% of whom received stent placement. The lesion could not be crossed in 5 patients, and suboptimal results occurred in 2 patients. Open heart surgery without PCI was performed in 48 patients (45 coronary artery bypass graft, 1 mitral valve, 1 aortic tumor, 1 myxoma removal; 3.6%). An additional 12 patients (0.9%) were referred for elective CAGB after successful PCI during the index hospitalization because of multivessel or left main disease. (In addition, 1 patient had mitral valve replacement for a ruptured papillary muscle, and 1 had a ventricular septal defect repaired.) Medical management without revascularization was the preferred treatment strategy in 37 patients (2.7%). No clear culprit artery could be identified in 187 patients (13.9%), but 31% of these patients had elevated cardiac biomarkers. The culprit artery was the left anterior descending artery in 31.5%, right coronary artery in 35.7%, left circumflex artery in 13.1%, left main artery 1.4%, and bypass graft artery in 2.9%. Preprocedural TIMI flow was significantly greater in zone 2 patients ($P<0.0001$) (Table 3).

Overall, 98.5% of patients received aspirin, 90.6% were given clopidogrel, 95.2% received β-blockers, and 96.3% took unfractionated heparin in the ED. Because of transfer delays, 31 patients (2.3%) received full-dose fibrinolysis. In patients with documented MI and successful PCI, 98.6% were discharged with aspirin, 97.0% with clopidogrel, 93.4% with β-blockers, 80.6% with angiotensin-converting enzyme inhibitors, and 88.8% with statins.

In-hospital and 30-day outcomes for the entire cohort are shown in Table 3. The median length of hospital stay was 3 days, with in-hospital mortality of 4.2% and 30-day mortality of 4.9%. There were no significant differences among groups with respect to in-hospital or 30-day mortality, but this study may have been underpowered to detect clinically relevant differences. For patients who underwent PCI, the in-hospital, 30-day, and 1-year mortality rates were 3.5%, 4.1%, and 6.4%, respectively. If patients with cardiogenic shock and out-of-hospital cardiac arrest are excluded, the in-hospital, 30-day, and 1-year mortality rates are 0.9%, 1.4%, and 3.3%, respectively. Zone 2 patients experienced less recurrent ischemia and reinfarction in-hospital and at day 30. No significant differences occurred with respect to stroke or TIMI major bleeding, although there was an increase in minor bleeding in zone 2 patients. Hemorrhagic stroke occurred in 2 patients, 1 each from zones 1 and 2. Both patients were discharged without disability. Overall mortality at 1 year based on Kaplan-Meier analysis was 7.2% (5.7% cardiovascular mortality), with no significant differences among treat-

### Table 2. Time-to-Treatment Intervals

<table>
<thead>
<tr>
<th></th>
<th>PCI Center (n=297), min</th>
<th>Zone 1 (n=620), min</th>
<th>Zone 2 (n=396), min</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sx to first door</td>
<td>100 (58, 226)</td>
<td>95 (50, 205)</td>
<td>85 (44, 185)</td>
<td>0.094</td>
</tr>
<tr>
<td>In door–out door</td>
<td>NA</td>
<td>49 (36, 66)</td>
<td>60 (48, 81)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Transport</td>
<td>NA</td>
<td>22 (15, 31)</td>
<td>34 (26, 49)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ANW to balloon</td>
<td>65 (47, 84)</td>
<td>21 (16, 28)</td>
<td>19 (15, 25)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CV lab to balloon</td>
<td>16 (11, 22)</td>
<td>14 (10, 20)</td>
<td>12 (9, 18)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>First door to Balloon</td>
<td>65 (47, 84)</td>
<td>95 (82, 116)</td>
<td>120 (100, 145)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total Sx to balloon</td>
<td>171 (118, 307)</td>
<td>203 (147, 325)</td>
<td>214 (167, 326)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Values in parentheses are 25th and 75th percentiles. Sx indicates symptom; CV lab, cardiovascular laboratory.
ment groups. Kaplan-Meier mortality curves for each of the 3 groups are shown in Figure 4.

**Discussion**

Both the ACC/AHA and European Society of Cardiology guidelines recommend PCI as the preferred method of reperfusion for STEMI if performed in a timely manner by experienced operators at high-volume centers. In the United States, the major limitations to a PCI strategy are universal access and the lack of an organized system of care for STEMI patients. Our experience demonstrates that a regional care system for STEMI, anchored by a timely PCI strategy, is feasible in the United States, yields outcomes similar to a PCI center, and therefore has the ability to provide the most effective therapy for STEMI to a large segment of the population. The key components of this system are (1) a regional network that unites a PCI center with non-PCI hospitals to focus on ideal patient care, (2) empowerment of ED physicians to activate treatment protocol with a single telephone call, (3) a standardized treatment protocol based on current AHA/ACC guidelines, (4) a coordinated hospital-specific transport plan, and (5) extensive initial training with comprehensive feedback and quality assurance that meets JCAHO criteria for STEMI.

### Transfer for PCI in STEMI

Recent randomized clinical trials have shown that transfer of STEMI patients for primary PCI compared with onsite fibrinolysis is both safe and effective. A meta-analysis of 3750 patients demonstrated a relative risk reduction of 42%...

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**TABLE 3. Outcomes**

<table>
<thead>
<tr>
<th>TIMI Flow</th>
<th>PCI Center</th>
<th>Zone 1</th>
<th>Zone 2</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIMI flow before PCI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>170 (57.2)</td>
<td>280 (45.1)</td>
<td>96 (23.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>1</td>
<td>18 (6.1)</td>
<td>27 (4.4)</td>
<td>22 (5.3)</td>
<td>...</td>
</tr>
<tr>
<td>2</td>
<td>44 (14.8)</td>
<td>120 (19.3)</td>
<td>105 (25.2)</td>
<td>...</td>
</tr>
<tr>
<td>3</td>
<td>65 (21.9)</td>
<td>194 (31.2)</td>
<td>194 (46.5)</td>
<td>...</td>
</tr>
<tr>
<td>TIMI flow after PCI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>8 (2.7)</td>
<td>5 (0.8)</td>
<td>11 (2.6)</td>
<td>0.11</td>
</tr>
<tr>
<td>1</td>
<td>0 (0.0)</td>
<td>3 (0.5)</td>
<td>0 (0.0)</td>
<td>...</td>
</tr>
<tr>
<td>2</td>
<td>4 (1.4)</td>
<td>10 (1.6)</td>
<td>7 (1.7)</td>
<td>...</td>
</tr>
<tr>
<td>3</td>
<td>285 (96.0)</td>
<td>603 (97.1)</td>
<td>399 (95.7)</td>
<td>...</td>
</tr>
<tr>
<td>In-hospital</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak CK, mean±SD, mg/dL</td>
<td>1477±1885</td>
<td>1338±1646</td>
<td>1363±3409</td>
<td>0.87</td>
</tr>
<tr>
<td>Length of stay, median (Q1, Q3), d</td>
<td>3 (2.5)</td>
<td>3 (2.4)</td>
<td>3 (2.4)</td>
<td>0.01</td>
</tr>
<tr>
<td>TIMI major bleeding, n (%)</td>
<td>0 (0.0)</td>
<td>5 (0.8)</td>
<td>2 (0.5)</td>
<td>0.3</td>
</tr>
<tr>
<td>Any bleeding, n (%)</td>
<td>8 (2.7)</td>
<td>17 (2.7)</td>
<td>21 (5.0)</td>
<td>0.03</td>
</tr>
<tr>
<td>Stroke, n (%)</td>
<td>4 (1.3)</td>
<td>6 (1.0)</td>
<td>5 (1.2)</td>
<td>0.84</td>
</tr>
<tr>
<td>Hemorrhagic stroke, n (%)</td>
<td>0 (0.0)</td>
<td>1 (0.2)</td>
<td>1 (0.2)</td>
<td>0.29</td>
</tr>
<tr>
<td>Reinfarction/ischemia, n (%) [95% CI]</td>
<td>7 (2.4) [0.6 to 4.1]</td>
<td>5 (0.8) [0.1 to 1.5]</td>
<td>1 (0.2) [0.01 to 1.5]</td>
<td>0.021</td>
</tr>
<tr>
<td>Mortality, n (%) [95% CI]</td>
<td>11 (3.7) [1.6 to 5.9]</td>
<td>24 (3.8) [2.3 to 5.3]</td>
<td>22 (5.2) [3.1 to 7.3]</td>
<td>0.48</td>
</tr>
<tr>
<td>At 30 d, n (%) [95% CI]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reinfarction/ischemia</td>
<td>13 (4.4) [2.1 to 6.7]</td>
<td>7 (1.1) [0.3 to 1.9]</td>
<td>0.0 (0.0) [0.01 to 1.5]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mortality</td>
<td>13 (4.4) [2.1 to 6.7]</td>
<td>29 (4.6) [3.0 to 6.3]</td>
<td>24 (5.7) [3.5 to 7.9]</td>
<td>0.65</td>
</tr>
</tbody>
</table>

CK indicates creatine kinase.
(95% CI, 29 to 53; P=0.001) in the combined end point of death, reinfarction, and stroke favoring transfer for PCI versus onsite fibrinolysis. Four of six studies included in this meta-analysis were from European centers with median door-to-balloon times of 82 to 109 minutes in contrast to 155 minutes in the only US study.15

On the basis of data from the National Registry of Myocardial Infarction (NRMI), most US patients transferred for primary PCI have door-to-balloon times exceeding the currently recommended 90-minute window, potentially negating the advantage of PCI over onsite fibrinolysis.16,20 This demonstrates a significant gap between currently recommended guidelines for STEMI and actual practice. Therefore, many believe a strategy that includes transfer for PCI is not practical in the United States.7,8,21

Timely Access to PCI

Barriers to timely access to primary PCI in the United States include the lack of a coordinated system of care for STEMI, including standardized guideline-based protocols; reimbursement policies that negatively affect non-PCI hospitals when STEMI patients are transferred; the lack of an efficient organized system for interfacility transfers; and physician and hospital capacity issues.17,21

Recently, the AHA AMI Advisory Working Group proposed strategies to develop coordinated systems of care for STEMI to increase the number of patients in the United States who could benefit from timely access to PCI and thereby decrease morbidity and mortality from this disease.7 Our experience in Minnesota provides 1 model of a regional system of care for STEMI.

Program Outcomes

The standardized protocol has been implemented successfully in 30 rural and community hospitals without onsite cardiovascular consultation. Despite distances up to 210 miles from the PCI center, 79% of patients in zone 1 and 49% of patients in zone 2 achieved door-to-balloon times <120 minutes compared with 16% of transferred patients and 65% of patients at PCI hospitals in recently reported NRMI data.16,22 We have established a network of rural and community hospitals with an extensive database to determine outcomes and to provide immediate quality feedback to each hospital, which will satisfy JCAHO requirements. These outcomes include a 3-day median length of stay, 30-day mortality of 4.9%, and 1-year mortality of 7.2% (5.7% cardiovascular). This likely reflects not only the improvement in time to treatment but also the high compliance with recommended medications on admission and discharge. These results are particularly notable because no patients were excluded from the analysis, including those with advanced age, cardiogenic shock, and out-of-hospital cardiac arrest. Recent data from the Global Registry of Acute Coronary Events (GRACE) demonstrate a significantly higher in-hospital mortality in patients who are eligible for but not enrolled in clinical trials and those who are ineligible.23 Despite a 30- and 55-minute-longer total ischemic time in zone 1 and 2 patients, respectively, there is no difference in in-hospital, 30-day, or 1-year mortality. Therefore, a regional PCI system can extend the benefits of PCI to hospitals up to 210 miles away.

Study Limitations

This study was not randomized and was not designed to test the effectiveness of a facilitated PCI approach in STEMI. However, recent experience indicates that it is challenging to enroll STEMI patients in randomized controlled trials in the United States, and a number of trials have stopped early as a result of poor enrollment.15,24–26 It is even more difficult to randomize STEMI patients in community and rural hospitals where there is limited or no research staff support. After the initial success in zone 1 hospitals, our goal was to improve the availability of PCI to hospitals even farther from the PCI center. In these distant non-PCI hospitals, transfer times were difficult to predict; therefore, we elected to use a facilitated...
approach based on available data. The decision to use half-dose tenecteplase was based on patency rates in TIMI 10A, which were similar to those in patients treated with 20 to 50 mg. The decision to use clodigorel instead of glycoprotein IIb/IIIa inhibitors was based on the anticipated time that it would take to initiate therapy in rural and community hospitals, which would lead to unacceptable delays. Facilitated PCI has subsequently become more controversial, but our zone 2 results combining aspirin, clodigorel, and half-dose fibrinolysis in patients transferred long distances resulted in an improvement in initial TIMI flow and outcomes similar to those achieved in the PCI hospital. Despite an efficient transfer system, 50% of patients were still treated >120 minutes after arrival at the zone 2 hospitals. The ideal reperfusion strategy for these patients remains controversial. Options include primary PCI with door-to-balloon times well outside current guidelines and full-dose thrombolytics with or without transfer, including rescue PCI or a facilitated PCI approach. This issue clearly deserves further study but is challenging from a clinical trial design standpoint.

Finally, our system model may not be effective in all regions of the United States. For example, hospital bed capacity, ED capacity, patient health insurance status, and urban or very remote locations can influence care choices.

Future Directions
A number of issues need to be considered before a strategy of regional centers for PCI in STEMI is adopted. The economic implications for non-PCI hospitals when patients are transferred directly from the ED need to be considered, and reimbursement policies may need to be adjusted to avoid a negative financial impact on these hospitals. From an overall economic standpoint, the potential increased costs of emergency transport and routine coronary angiography and intervention are countered by the decreased length of stay and potential improvement in outcomes, including mortality, recurrent ischemia, and preservation of left ventricular function. If successful, this could ultimately decrease the number of patients with congestive heart failure and the need for expensive therapies such as internal cardiac defibrillators. A formal cost-effectiveness analysis is needed to determine the overall economic impact of a regional transfer system.

Conclusions
Rapid transfer of STEMI patients from community hospitals up to 210 miles from a PCI center is safe and effective using a standardized protocol with an integrated transfer system. Outcomes for STEMI patients transferred from a community hospital to a regional center for PCI are similar to those who present to a PCI center directly. A standardized treatment approach to STEMI in the United States has the potential to provide the optimal treatment (primary PCI) to the greatest number of patients, which will translate into improvement in the long-term outcome of STEMI patients.

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**CLINICAL PERSPECTIVE**

Primary percutaneous coronary intervention (PCI) is the preferred method of reperfusion in patients with ST-elevation myocardial infarction (STEMI) if performed in a timely manner. Because only 25% of US hospitals have PCI capability, the major limitation of this strategy is availability. Transfer for primary PCI also has been shown to be superior to fibrinolytic therapy in selected European countries with organized transport systems and short transfer distances. Current US data indicate that <5% of patients transferred for primary PCI have door-to-balloon times of <90 minutes as recommended in the current American College of Cardiology/American Heart Association guidelines. We developed a regional system for transfer of STEMI patients from 30 community hospitals in Minnesota for primary PCI using a standardized protocol. The median first-door-to-balloon time for patients <60 miles (zone 1) and 60 to 210 miles (zone 2) from the PCI center was 95 and 120 minutes, respectively. Despite a high-risk unselected patient population, the in-hospital mortality was 4.2%, with a median length of stay of 3 days. Outcomes for STEMI patients transferred from community hospitals in both zones 1 and 2 were similar to those for patients who presented to the PCI center directly. These results indicate that a regional STEMI system can extend the benefits of primary PCI to hospitals up to 210 miles away from a PCI center. Although challenges exist in the rapid transfer of STEMI patients for primary PCI, our results indicate these issues are not insurmountable.