Hospital Delays in Reperfusion for ST-Elevation Myocardial Infarction
Implications When Selecting a Reperfusion Strategy

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Background—It has been suggested that the survival benefit associated with primary percutaneous coronary intervention (PPCI) in ST-segment elevation myocardial infarction may be attenuated if door-to-balloon (DB) time is delayed by >1 hour beyond door-to-needle (DN) times for fibrinolytic therapy. Whereas DB times are rapid in randomized trials, they are often prolonged in routine practice. We hypothesized that in clinical practice, longer DB-DN times would be associated with higher mortality rates and reduced PPCI survival advantage. We also hypothesized that in addition to PPCI delays, patient risk factors would significantly modulate the relative survival advantage of PPCI over fibrinolysis.

Methods and Results—DB-DN times were calculated by subtracting median DN time from median DB time at a hospital using data from 192,509 patients at 645 National Registry of Myocardial Infarction hospitals. Hierarchical models that adjusted simultaneously for both patient-level risk factors and hospital-level covariates were used to evaluate the relationship between PCI-related delay, patient risk factors, and in-hospital mortality. Longer DB-DN times were associated with increased mortality (P<0.0001). The DB-DN time at which mortality rates with PPCI were no better than that of fibrinolysis varied considerably depending on patient age, symptom duration, and infarct location.

Conclusions—As DB-DN times increase, the mortality advantage of PPCI over fibrinolysis declines, and this advantage varies considerably depending on patient characteristics. As indicated in the American College of Cardiology/American Heart Association guidelines, both the hospital-based PCI-related delay (DB-DN time) and patient characteristics should be considered when a reperfusion strategy is selected. (Circulation. 2006;114:2019-2025.)

Key Words: myocardial infarction ■ angioplasty ■ fibrinolysis ■ survival ■ plasminogen activators

The goal of reperfusion therapy in ST-elevation myocardial infarction (STEMI) is to achieve early, full, and sustained coronary blood flow in the infarct artery. Both primary percutaneous coronary intervention (PPCI) and fibrinolytic therapy fulfill some but not all of these goals. An advantage of fibrinolytic therapy is the rapid initiation of therapy, but normal Thrombolysis In Myocardial Infarction (TIMI) grade 3 flow is restored in only 50% to 60% of arteries.1,2 Conversely, PPCI achieves better rates of TIMI grade 3 flow than fibrinolytic therapy, but there are often delays in restoring successful reperfusion.3,4 Other advantages of fibrinolytic therapy include the ease and consistent performance of administration. In contrast, performance of PPCI is more complex and can be logistically challenging. Finally, although PPCI is associated with favorable outcomes when performed rapidly, few hospitals in the United States consistently perform PPCI rapidly on a full-time, emergency basis.5,6 As a result, door-to-balloon (DB) times in routine clinical practice are often longer than in randomized, controlled trials, and many patients are transferred for PPCI, which further delays reperfusion. Indeed, transfer patients often experience long delays in the performance of PPCI, and as a consequence, <5% of transfer patients meet American College of Cardiology/American Heart Association (ACC/AHA) guidelines for timely implementation.7

Editorial p 2002
Clinical Perspective p 2025

The relative mortality benefit of PPCI over fibrinolytic therapy may be time-dependent. Mortality rates increase both
as DB times increase and as symptom-to-balloon times increase. Furthermore, when the percutaneous coronary intervention (PCI)-related delay (DB—door-to-needle [DN] time) exceeded 60 minutes in randomized studies, the mortality advantage of PPCI compared with fibrinolytic therapy was negated. Although the impact of PCI-related delay has been evaluated in the setting of randomized, controlled trials in which DB times are relatively rapid, in clinical practice, DB times are far more variable and prolonged. Evaluation of registry data affords the opportunity to evaluate the relative survival advantage of PPCI and fibrinolytic therapy in a more heterogeneous population than in randomized, controlled trials.

The ACC/AHA STEMI guidelines suggest that reperfusion strategy selection take into account both patient-based risk factors and hospital-based factors such as the PCI-related delay. Consistent with the approach advocated in the guidelines, the goal of the present study was to integrate the impact of hospital- and patient-based factors on selection of the optimal reperfusion strategy for STEMI.

The first hypothesis was that the survival advantage associated with PPCI compared with fibrinolytic therapy would decline as DB-DN time increased in clinical practice, in which interhospital transfer and DB times are more prolonged than in randomized, controlled trials. The second hypothesis was that the association between PCI-related delays and mortality would be significantly modulated by patient characteristics.

**Methods**

National Registry of Myocardial Infarction (NRMI) 2, 3, and 4 were voluntary, prospective registries that collected data from June 1994 to August 2003 on consecutive patients admitted to participating hospitals with documented acute myocardial infarction (MI). Characteristics of the NRMI data-gathering procedures, reliability, and hospital- and patient-level covariates have been described previously. The NRMI data-gathering procedures were approved by the institutional review board of each participating hospital, if required. These selection criteria yielded 192 509 patients and 645 hospitals eligible for analysis (Figure 1).

A given hospital’s PCI-related delay, or its median time delay in performing PPCI compared with administering fibrinolytic therapy, was calculated by subtracting the median DN time from the median DB time at each hospital. As suggested by the ACC/AHA Task Force on Performance Measures, median treatment times were selected because mean times can be unduly skewed by outlier times. For transfer patients, the point of reference to calculate DB and DN times was the first hospital arrival date/time. On the basis of previously described categories for analysis of DB times in NRMI, hospitals were divided into 4 categories of increasing PCI-related delay (<60, 60 to 89, 90 to 120, and >120 minutes). Then, the mean time delay within each of these 4 categories was calculated with the median PCI-related delay at each hospital, which yielded a mean-of-medians DB-DN time for each of the 4 time-delay categories.

**Statistical Methods**

After we computed the DB-DN time in reperfusion for each hospital, the PCI-related mortality advantage (difference in mortality rate for patients treated with PPCI and the rate for those treated with fibrinolytic therapy) was assessed. For continuous data, linear regression analysis was used to test whether the slope of the regression or trend differed significantly from zero. For categorical data, the Cochran-Mantel-Haenszel statistic was used as the measure of trend. All probability values used 2-tailed tests, and a P<0.05 was considered significant.

To capitalize on the patient-level data within NRMI and to provide better estimates of the true effects of covariates, generalized estimating equations that used the GENMOD procedure in SAS 9.1 (SAS Institute, Inc, Cary, NC) were used to assess the relationship between median DB-DN time (a hospital-level variable), the administered reperfusion strategy, and in-hospital mortality, with adjustment for both patient- and hospital-level characteristics. PROC GENMOD was used with the following patient covariates as correlates of mortality: treatment type (PPCI or fibrinolysis), age, gender, race, diabetes mellitus, hypertension, angina, Killip class 2/3, Killip class 4, previous infarction, current smoking, stroke, pulse, systolic blood pressure, payer, prehospital delay, and discharge year. Hospital covariates included STEMI volume, PPCI volume, transfer-in rate, rural location, and status as a teaching hospital.
Results

Baseline patient- and hospital-level characteristics are reported in Table 1, stratified by hospital PCI-related delays. Given the large size of the data set, statistically significant but clinically modest differences were observed in many covariates (Table 1). PPCI was performed in 65 600 patients, and fibrinolytic therapy was administered to 126 909 patients. More than 65% of patients (n=125 737) presented within 2 hours of symptom onset. Fibrin-specific agents were administered in 92% (n=117 256) of patients administered fibrinolytic therapy. The mean hospital-related DB-DN time was 77.8±23.5 minutes. Patients transferred to an NRMI-reporting hospital (transfer-in patients) for PPCI or fibrinolysis accounted for 35.7% (n=68 716) of the population. Overall, the mean TIMI risk score for STEMI did not differ in patients as the DB-DN time increased (P=0.12). Longer DB-DN times at a hospital were associated with a higher proportion anterior MI, % 36.2 36.4 37.1 39.6 0.004
Proportion of STEMI patients treated with PPCI, % 46.2 37.9 27.6 22.1 0.001
STEMI volume per year (n=SD) 118±74 140±80 140±83 127±82 0.12
TIMI risk score of STEMI patients (mean=SD) 2.5±0.4 2.5±0.3 2.4±0.3 2.6±0.4 0.12

P values are for trend. CABG indicates coronary artery bypass grafting.

Failure to account for clustering at the hospital level may overestimate the magnitude of statistical significance of an association14; this modeling strategy also allowed adjustment for clustering both within hospitals and within reporting study periods. In addition to the overall relationship described above, these models were used to examine the relationship between DB-DN time delay and the mortality difference in patient subgroups stratified by age (<65 versus ≥65 years), infarct location (anterior versus other), and time from symptom onset to hospital presentation (<120 or >120 minutes).

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

TABLE 1. Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>&lt;60</th>
<th>60–89</th>
<th>90–120</th>
<th>&gt;120</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients (%)</td>
<td>35 902 (18.6)</td>
<td>116 756 (60.6)</td>
<td>34 189 (17.8)</td>
<td>5662 (2.9)</td>
<td>...</td>
</tr>
<tr>
<td><strong>Patient characteristics</strong></td>
<td></td>
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</tr>
<tr>
<td>Age (mean±SD), y</td>
<td>61.9±13.0</td>
<td>61.3±12.7</td>
<td>60.9±12.6</td>
<td>61.6±13.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female, %</td>
<td>28.8</td>
<td>29.0</td>
<td>29.0</td>
<td>30.6</td>
<td>0.10</td>
</tr>
<tr>
<td>White, %</td>
<td>87.8</td>
<td>86.2</td>
<td>86.5</td>
<td>82.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>17.4</td>
<td>18.1</td>
<td>18.7</td>
<td>18.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>39.3</td>
<td>41.4</td>
<td>41.5</td>
<td>40.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior MI, %</td>
<td>16.7</td>
<td>16.9</td>
<td>17.2</td>
<td>17.0</td>
<td>0.12</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>45.2</td>
<td>46.0</td>
<td>47.1</td>
<td>49.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypercholesterolemia, %</td>
<td>36.9</td>
<td>34.9</td>
<td>31.4</td>
<td>33.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prehospital delay (mean±SD), h</td>
<td>2.2±2.1</td>
<td>2.2±2.1</td>
<td>2.2±2.1</td>
<td>2.2±2.1</td>
<td>0.86</td>
</tr>
<tr>
<td>Anterior infarction, %</td>
<td>35.9</td>
<td>35.8</td>
<td>36.7</td>
<td>37.6</td>
<td>0.002</td>
</tr>
<tr>
<td>Prior congestive heart failure, %</td>
<td>3.4</td>
<td>3.2</td>
<td>3.3</td>
<td>3.7</td>
<td>0.76</td>
</tr>
<tr>
<td>Prior PTCA, %</td>
<td>11.1</td>
<td>11.3</td>
<td>10.3</td>
<td>10.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior CABG, %</td>
<td>6.0</td>
<td>6.5</td>
<td>6.4</td>
<td>6.7</td>
<td>0.007</td>
</tr>
<tr>
<td>Systolic blood pressure (mean±SD), mm Hg</td>
<td>139.0±31.2</td>
<td>138.7±31.0</td>
<td>138.5±31.1</td>
<td>139.6±31.4</td>
<td>0.27</td>
</tr>
<tr>
<td>Pulse (mean±SD), bpm</td>
<td>76.7±20.0</td>
<td>77.1±19.9</td>
<td>77.3±19.8</td>
<td>77.7±20.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Hospital characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DB time (mean of median±SD), min</td>
<td>91±11.7</td>
<td>114±11.1</td>
<td>138±11.1</td>
<td>179±20.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DN time (mean of median±SD), min</td>
<td>41.9±8.6</td>
<td>38.7±8.0</td>
<td>37.2±7.7</td>
<td>37.8±8.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PCI-related delay (DB-DN; mean of median±SD), min</td>
<td>49.1±10.3</td>
<td>75.2±8.1</td>
<td>100.4±8.0</td>
<td>140.7±19.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Proportion transferred in, %</td>
<td>24.1</td>
<td>29.3</td>
<td>33.9</td>
<td>36.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Proportion anterior MI, %</td>
<td>36.2</td>
<td>36.4</td>
<td>37.1</td>
<td>39.6</td>
<td>0.004</td>
</tr>
<tr>
<td>PPCI volume per year (n=SD)</td>
<td>23.8±17.9</td>
<td>21.6±14.9</td>
<td>15.7±12.7</td>
<td>10.6±9.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Proportion of STEMI patients treated with PPCI, %</td>
<td>46.2</td>
<td>37.9</td>
<td>27.6</td>
<td>22.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>STEMI volume per year (n=SD)</td>
<td>118±74</td>
<td>140±80</td>
<td>140±83</td>
<td>127±82</td>
<td>0.12</td>
</tr>
<tr>
<td>TIMI risk score of STEMI patients (mean±SD)</td>
<td>2.5±0.4</td>
<td>2.5±0.3</td>
<td>2.4±0.3</td>
<td>2.6±0.4</td>
<td>0.12</td>
</tr>
</tbody>
</table>
The mortality rate increased as the DB-DN time increased ($P<0.001$ for trend; Figure 2). For every 30-minute increase in DB-DN time, there was an $\approx 10\%$ increase in the relative risk of in-hospital death (odds ratio 1.095, 95% confidence interval 1.065 to 1.126, $P<0.001$). In the overall cohort of 192 509 patients, the multivariate adjusted odds of death were identical with either PCI or fibrinolytic therapy when the PCI-related delay was 114 minutes (95% confidence interval 96 to 132 minutes, $P<0.001$; Figure 3). In this adjusted analysis, the association of increasing PCI-related delay (increasing DB-DN) with increasing mortality remained significant ($P<0.001$), and the interaction of treatment with fibrinolytic therapy and DB-DN time was also significant ($P<0.001$), which confirms that the benefit of 1 treatment strategy over another varied on the basis of increasing DB-DN.

In stratified analyses based on patient age, duration of symptoms, and infarct location, a wide range of PCI implementation delays for which survival with PPCI no longer exceeded that with fibrinolytic therapy were observed (Table 2). For example, the survival advantage associated with PCI was lost after 71 minutes of delay among patients aged $<65$ years compared with 155 minutes in those $\geq 65$ years. In those with anterior MI, the point of equivalence occurred at 115 minutes compared with 112 minutes for nonanterior MI. In those presenting $\leq 120$ minutes after symptom onset, the survival advantage associated with PCI was lost after 94 minutes compared with 190 minutes in patients presenting $>120$ minutes after symptom onset. Because age, infarct location, and duration of symptoms can be colinear and associated with each other, the results are also presented with all 3 strata taken into account at the same time. Figure 4 displays results stratified on the basis of the simultaneous assessment of 3 patient factors: age, prehospital delay, and infarct location.

**Discussion**

The present analysis demonstrates that longer DB-DN times are associated with increased mortality, and as DB-DN times increase, the survival advantage of PPCI over fibrinolysis decreases; however, the DB-DN time after which the survival benefit of PPCI was lost was quite variable depending on patient characteristics. These observations reinforce the ACC/AHA STEMI guidelines, which recommend that the selection of the optimal reperfusion strategy should be based not only on the anticipated DB-DN time but also on patient characteristics. As emphasized in the AHA/ACC STEMI guidelines, some patients, such as those with cardiogenic shock, should be selected for invasive therapy, whereas others may not realize the benefit if delays to treatment are extensive.

Depending on whether randomized, controlled trials or registry data and patient-level data are used to evaluate the DB-DN time at which PPCI loses its mortality advantage, different answers emerge. Whereas randomized, controlled trials suggest that PPCI is preferred over fibrinolysis when DB times are rapid at high-volume hospitals, this “real-world” registry analysis differs in that it includes a much larger proportion of patients with prolonged DB-DN times. Several analyses have been performed that were based on randomized trial data. Boersma observed that PPCI was superior to fibrinolytic therapy across a range of DB-DN times. The odds reduction in mortality with PPCI decreased from 67% when DB-DN times were $\leq 35$ minutes to only 28% when the DB-DN times were longer. The Boersma analysis and the present analysis differ, however, in several important respects. In the Boersma analysis, streptokinase administration was more frequent than in the present analysis, in which fibrin-specific agents predominated. Furthermore, insofar as the data were drawn from randomized, controlled trials in which DB and DN times were relatively rapid, compared with the present analysis, the highest quintile of DB-DN in the Boersma analysis was only 80 to 120 minutes, much shorter than the present analysis of real-world data drawn from a broad range of clinical practice. Stated simply, the Boersma analysis focuses on the upper left-hand side of Figure 3, in which DB-DN times are relatively rapid and PPCI is superior to fibrinolysis. Although quite large...
and patient-level data involving longer treatment delays and demonstrates a 0.15% reduction in the PPCI survival advantage for every 10-minute delay in the overall cohort. One major finding of the present study, however, is that the rate of loss of survival advantage varies depending on patient characteristics.

Although there is tremendous appeal in identifying a sole DB-DN time as the optimal goal of STEMI reperfusion care (eg, 60 minutes or 114 minutes), the present analysis demonstrates that the significant variability in patient characteristics and clinical outcomes that exists within the STEMI population may modify the selection of an optimal reperfusion strategy. Indeed, patient factors including age, duration of symptoms, and infarct location significantly modulated how rapidly the survival advantage of PPCI was lost (Table 2). It is the complex interplay between the risks and benefits of the 2 reperfusion strategies, which in turn is modified by the patient’s risk profile, that likely accounts for the variability in the DB-DN at which a survival advantage with PPCI is present.

For example, the survival advantage of PPCI was lost sooner among patients who presented earlier (Table 2). This is consistent with a potential survival advantage of fibrinolytic therapy among patients who present with symptoms within 2 hours that has been observed in randomized studies. In contrast, PPCI maintained its survival advantage with longer DB-DN times among patients who presented late.

<table>
<thead>
<tr>
<th>Symptom Duration</th>
<th>Symptom Duration</th>
<th>Age</th>
<th>Age</th>
<th>Anterior Infarction</th>
<th>Nonanterior Infarction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time, min (No. of patients)*</td>
<td>94 (n=125 737)</td>
<td>71 (n=115 293)</td>
<td>115 (n=69 331)</td>
<td>112 (n=123 178)</td>
<td></td>
</tr>
<tr>
<td>≥120 min</td>
<td>&gt;120 min</td>
<td>&lt;65 y</td>
<td>≥65 y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P†</td>
<td>&lt;0.001</td>
<td>0.01</td>
<td>0.001</td>
<td>&lt;0.001</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*Times represent PCI-related delay (DB-DN time) at which mortality with PCI and fibrinolysis were equal, stratified by symptom duration, age, or location of infarct. To ensure a stable estimate of the mortality difference when primary PCI and fibrinolysis were compared in these subgroups, hospitals were excluded if fewer than 10 STEMI patients were treated with either PCI or fibrinolysis in each category.
†P values for the interaction of patient-level confounders, the mortality advantage of PPCI was lost at a DB-DN time of only 85 minutes.

Estimates of the loss in survival advantage for every 10 minutes of DB-DN time vary as well depending on the proportion of patients with prolonged DB-DN times and whether one adjusts for patient-level confounders. In analyses from randomized, controlled trials that do not use patient-level data and include very rapid treatment times, every 10-minute increase in DB-DN time was associated with a 1% reduction in the PCI mortality advantage. The incorporation of patient-level data modifies the rate that the PCI survival advantage is lost to 0.24% for every 10 minutes of delay. This larger, “real-world” analysis utilizes hospital-
perhaps because of the emergence of thromboresistance among patients with more mature clots.\textsuperscript{19} The risk of intracranial hemorrhage associated with fibrinolytic administration increases as patient age increases.\textsuperscript{20} This may explain the finding that the survival advantage of PPCI was maintained with longer DB-DN times among patients over the age of 65 years (Table 2).

Because age, infarct location, and duration of symptoms can be collinear and associated with one another, the results are also presented with all 3 strata taken into account at the same time. Figure 4 displays results stratified on the basis of the simultaneous assessment of 3 patient factors: age, prehospital delay, and infarct location. The survival advantage of PPCI persisted with DB-DN times to 179 minutes in patients \( \geq 65 \) years presenting \( >2 \) hours from symptom onset and with a nonanterior infarction. Such a patient, presenting late, may have a greater tendency toward thromboresistance (reduced fibrinolytic efficacy), as well as an increased risk of intracranial hemorrhage due to age (reduced fibrinolytic safety). In this patient with an inferior MI, rapid restoration of flow with a fibrinolytic may not yield the same preservation of left ventricular function as those with an anterior MI.

In contrast, a patient who is \( <65 \) years old who presents with an anterior MI within 2 hours of symptom onset only gains a mortality advantage from PPCI if the DB-DN time is \( \leq 40 \) minutes. It could be speculated that this finding is due to the fact that thromboresistance has less likely emerged (better fibrinolytic efficacy), the risk of intracranial hemorrhage is low (improved fibrinolytic safety), and there are advantages of more rapid restoration of flow (an advantage of fibrinolytic therapy) to preserve left ventricular function. Figure 4 suggests that in some subgroups, PPCI could likely be implemented within a time frame associated with benefit (eg, the patient \( >65 \) years of age with symptoms for \( >2 \) hours who presents with an inferior MI). Nevertheless, with the recognition that median DB times exceed 180 minutes if a transfer is involved,\textsuperscript{7} it may be impractical to implement PPCI before the benefit is lost in some subgroups.

Therefore, when a reperfusion strategy for STEMI is selected, the benefits and limitations of the reperfusion strategy, patient characteristics, and system delays (eg, location, weather, and traffic) should be considered. All hospitals should attempt to minimize delays to both PPCI and fibrinolysis using strategies that encompass environmental, operational, and cultural modifications.\textsuperscript{21} Registry data from Europe show that rapid DB times can be achieved in routine practice.\textsuperscript{22,23} Use of prehospital ECGs, collaborative, interdisciplinary teams, and routine data review have been shown to improve the care of STEMI patients outside the clinical trial setting and should be considered.\textsuperscript{21,24}

**Study Limitations**
This analysis is a nonrandomized analysis from registry data in the United States, and as such, it is possible that both identified and unidentified confounders may have influenced the outcomes. DB-DN times may be a surrogate of a hospital’s quality of care. It is possible that outcomes among hospitals that administer fibrinolytic therapy infrequently but perform PPCI frequently may be overrepresented among hospitals with very short DB-DN times. Likewise, long DB-DN times may be a surrogate for poor-quality PPCI among hospitals that perform PPCI infrequently and fibrinolysis frequently. Improved clinical outcomes at hospitals that perform a large volume of PPCIs may be due in part to both institutional and operator expertise, and the present analysis did adjust for STEMI and PPCI volume. Some patients, such as those with cardiogenic shock, should be selected for invasive therapy, but Figure 4 and Table 2 offer general guidelines for those for whom the decision may be difficult. Although the precision of individual DB-DN times shown in Figure 4 and Table 2 is not clear, the large variability in DB-DN times underscores the observation that the association between the PCI-related delay and mortality varies substantially depending on patient characteristics. The question of whether PPCI is superior to fibrinolytic therapy has been well studied in randomized comparisons that offer valuable insight, but only for the relatively select number of patients who satisfy the inclusion and exclusion criteria of the trial and for healthcare systems capable of performing PPCI quickly.

**Conclusions**
As DB-DN times increase, the mortality advantage of PPCI over fibrinolysis declines, and this advantage varies considerably depending on patient characteristics. As indicated in the ACC/AHA guidelines, both the hospital-based PCI-related delay (DB-DN time) and patient characteristics should be considered when a reperfusion strategy is selected.

**Sources of Funding**
This study was supported by a grant from Genentech, Inc, South San Francisco, Calif.

**Disclosures**
P.D. Frederick and D.P. Miller are employed by Ovation Research Group, a company that receives research funding from Genentech, Inc, South San Francisco, Calif. Drs Pinto and Gibson have pending research grant support from Genentech, Inc, South San Francisco, Calif; Dr Pinto has served on the speakers’ bureau of Genentech, Inc, and Dr Gibson has received honoraria from Genentech, Inc. The remaining authors report no conflicts.

**References**


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**CLINICAL PERSPECTIVE**

Randomized, controlled trials provide valuable insight when one compares primary percutaneous coronary intervention (PPCI) and fibrinolytic therapy for ST-segment myocardial infarction (STEMI). Analyses from these studies show that PPCI, compared with fibrinolysis, has lower rates of death, recurrent infarction, and stroke. It is unknown, however, whether the results of these studies can be generalized to STEMI populations for whom treatment times are not as rapid and for whom transfer for PPCI is more common. This analysis, drawn from 192 509 patients enrolled in the National Registry of Myocardial Infarction, demonstrates that longer delays to implementing PPCI are associated with increased mortality, and as PPCI-related delays increase, the survival advantage of PPCI over fibrinolysis decreases. Importantly, the PPCI-related delay at which the mortality benefit of PPCI was lost was quite variable depending on patient risk characteristics. Given these data, the practicing clinician should recognize that long reperfusion times reduce the magnitude of benefit from any reperfusion therapy for STEMI, and efforts should continue to be made to shorten reperfusion times. When selecting the optimal reperfusion strategy for STEMI patients, the clinician should consider the anticipated PPCI-related delay. This analysis supports the American College of Cardiology/American Heart Association consensus guidelines that suggest that hospital-based factors, such as PPCI-related delay, and patient risk factors should be considered when the optimal reperfusion strategy is selected for management of patients with STEMI.

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Circulation. 2006;114:2019-2025; originally published online October 30, 2006;
doi: 10.1161/CIRCULATIONAHA.106.638353
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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