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Effect of Door-to-Balloon Time on Mortality in Patients With ST-Segment Elevation Myocardial Infarction

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OBJECTIVES We sought to determine the effect of door-to-balloon time on mortality for patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI).

BACKGROUND Studies have found conflicting results regarding this relationship.

METHODS We conducted a cohort study of 29,222 STEMI patients treated with PCI within 6 h of presentation at 395 hospitals that participated in the National Registry of Myocardial Infarction (NRMI)-3 and -4 from 1999 to 2002. We used hierarchical models to evaluate the effect of door-to-balloon time on in-hospital mortality adjusted for patient characteristics in the entire cohort and in different subgroups of patients based on symptom onset-to-door time and baseline risk status.

RESULTS Longer door-to-balloon time was associated with increased in-hospital mortality (mortality rate of 3.0%, 4.2%, 5.7%, and 7.4% for door-to-balloon times of ≤90 min, 91 to 120 min, 121 to 150 min, and >150 min, respectively; p for trend <0.01). Adjusted for patient characteristics, patients with door-to-balloon time >90 min had increased mortality (odds ratio 1.42; 95% confidence interval [CI] 1.24 to 1.62) compared with those who had door-to-balloon time ≤90 min. In subgroup analyses, increasing mortality with increasing door-to-balloon time was seen regardless of symptom onset-to-door time (≤1 h, >1 to 2 h, >2 h) and regardless of the presence or absence of high-risk factors.

CONCLUSIONS Time to primary PCI is strongly associated with mortality risk and is important regardless of time from symptom onset to presentation and regardless of baseline risk of mortality. Efforts to shorten door-to-balloon time should apply to all patients. (J Am Coll Cardiol 2006;47: 2180–6) © 2006 by the American College of Cardiology Foundation

Time to reperfusion for patients with ST-segment elevation myocardial infarction (STEMI) consistently predicts mortality for fibrinolytic therapy (1–3). In contrast, studies have found conflicting results regarding the relationship between mortality and time to reperfusion with primary percutaneous coronary intervention (PCI). Some investigators have found lower mortality for shorter symptom onset-to-reperfusion time for all patients (4) or just certain subgroups such as high-risk patients (5) or those presenting within 2 h of symptom onset (6). Other studies found no lower mortality for shorter symptom onset-to-balloon time but did find lower mortality for shorter door-to-balloon time (7,8). Finally, some studies failed to find an association between either symptom onset-to-balloon time or door-to-balloon time and mortality (9,10).

Although the American College of Cardiology/American Heart Association (ACC/AHA) guidelines for management of patients with STEMI recommend door-to-balloon times of 90 min or less (11,12), a minority of patients are currently treated within this time period, and this pattern has not changed recently (13). The perception that time to reperfusion is less important in PCI (9,10) may contribute to the current inertia in performance. To evaluate the effect of door-to-balloon time on mortality in these patient groups, we used detailed patient-level and hospital-level longitudinal data from a national sample of patients with STEMI admitted from 1999 to 2002 from the National Registry of Myocardial Infarction (NRMI)-3 and -4 (14).

METHODS

Study design and sample. We used NRMI, a voluntary acute myocardial infarction (AMI) registry sponsored by

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Abbreviations and Acronyms

ACC = American College of Cardiology
AHA = American Heart Association
AMI = acute myocardial infarction
CI = confidence interval
ECG = electrocardiogram
NRMI = National Registry of Myocardial Infarction
PCI = percutaneous coronary intervention
STEMI = ST-segment elevation myocardial infarction

Genentech Inc. (South San Francisco, California), to define a cohort of patients with STEMI who received acute reperfusion therapy with primary PCI. The NRMI criteria (15,16) include a diagnosis of AMI according to the *International Classification of Diseases, Ninth Revision, Clinical Modification* (code 410.X1) and any one of the following criteria: total creatine kinase or creatine kinase-MB that was two or more times the upper limit of the normal range or elevations in alternative cardiac markers; electrocardiographic evidence of AMI or nuclear medicine testing, echocardiography, or autopsy evidence of AMI. During our study period of January 1, 1999, to December 31, 2002, there were 830,473 AMI admissions in NRMI. The following patients were excluded sequentially: patients transferred to or from another acute care institution (n = 341,730); with neither ST-segment elevation (2+ leads) nor left bundle branch block on the first electrocardiogram (ECG) (n = 334,013); with AMI symptom onset after the admission date and time (n = 4,305); with a nondiagnostic first ECG (e.g., the first ECG did not show ST-segment elevation or left bundle branch block; n = 14,314); with diagnostic ECG that preceded hospital presentation by more than 1 h (prehospital ECG), or with time from door-to-diagnostic ECG that was more than 6 h or missing (n = 6,467); who did not receive primary PCI (n = 92,772); with door-to-balloon times that were negative, more than 6 h, or missing (n = 925); and with unknown time of symptom onset (n = 4,804). In addition, to avoid including hospitals that performed primary PCI uncommonly, patients treated in hospitals reporting fewer than 20 PCI patients over the four-year time period (n = 1,921) were excluded. The final cohort included 29,222 patients from 395 hospitals. Mortality status at the time of discharge was known for all patients.

Data collection and measures. Our outcome was in-hospital mortality, and the principal independent variable was door-to-balloon time, which is the time from hospital arrival to balloon inflation, derived from the corresponding date/time noted in the medical record and recorded in the NRMI case report form. Patients were stratified based on their time from symptom onset-to-door time (≤1 h, >1 to 2 h, >2 h) and whether they had ACC/AHA high-risk factors (anterior/septal location, diabetes mellitus, heart rate >100 beats/min, systolic blood pressure <100 mm Hg) (11).

Other patient-level variables included age (<65 years, 65 to 79 years, ≥80 years), gender, race/ethnicity (white, black, Hispanic, other), insurance status, and clinical characteristics. Clinical characteristics consisted of medical history (current smoker, chronic renal insufficiency, previous AMI, hypertension, family history of coronary artery disease, hypercholesterolemia, congestive heart failure, previous percutaneous transluminal coronary angioplasty, previous coronary artery bypass graft surgery, chronic obstructive pulmonary disease, stroke, angina, diabetes); presentation characteristics (time from symptom onset-to-presentation, whether a prehospital ECG was performed, the admission time of day [day, evening, or night], admission day of week [weekday or weekend], chest pain at presentation, systolic blood pressure, heart rate, heart failure); and the results of the diagnostic ECG (number of leads with ST-segment elevation, AMI location, ST-segment depression, nonspecific ST/T-wave changes, Q-wave). Calendar time, measured as the number of days between January 1, 1999, and the hospital admission date, was included as an independent variable to account for any secular trends as well as for differing reporting periods by hospitals.

Statistical analysis. We first examined the bivariate association between patient characteristics and in-hospital mortality, using chi-square tests to assess for the association between categorical variables and in-hospital mortality and *t* tests or F tests to assess for the association between continuous variables and in-hospital mortality.

We then examined the bivariate association between door-to-balloon time and in-hospital mortality with door-to-balloon time as a categorical variable. We did this for the whole cohort and stratified by symptom onset-to-door time (≤1 h, >1 to 2 h, >2 h) and presence or absence of anterior/septal location, diabetes mellitus, heart rate >100 beats/min, systolic blood pressure <100 mm Hg, and any of these baseline risk factors.

For the independent effect of door-to-balloon time on in-hospital mortality, we used a multivariable logistic regression model using in-hospital death as the dependent variable. Because NRMI enrolls hospitals that then report patients, we could not assume that measurements were independent of hospital; assessment of intraclass correlations indicated that variation in both time to treatment (p = 0.1099, 95% CI 0.0916 to 0.1282) and mortality (p = 0.0084, 95% CI 0.0052 to 0.0434) was partly explained by hospital. Thus, we used hierarchical models to account for clustering of patients within hospitals. Random effects were specified for the main intercept and the coefficients of calendar time in the model. We replicated the model in all the strata of symptom onset-to-door time and baseline risk factors, as defined above; the stratification variable was not included in the corresponding subgroup model. We also estimated a final set of models using the whole cohort, each of which included the interaction between door-to-balloon time and one of these stratification variables. We performed secondary analyses that included the 2.0% of patients