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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

JACC Vol. 47, No. 11, 2006
June 6, 2006:2180–6

**Table 1.** Patient Characteristics, Door-to-Balloon Time, and In-Hospital Mortality

| Description | Prevalence n (%) | Door-to-Balloon Time Median, min (Quartile Range) | Door-to-Balloon Time p | Mortality n (%) | Mortality p |
|---|---|---|---|---|---|
| All | 29,222 (100.00) | 102 (54) | | 1,329 (4.55) | |
| Demographics | | | | | |
| Age | | | <0.0001 | | <0.0001 |
| <65 yrs | 17,314 (59.25) | 99 (52) | | 356 (2.06) | |
| 65–80 yrs | 9,425 (32.25) | 106 (56) | | 623 (6.61) | |
| >80 yrs | 2,483 (8.50) | 115 (59) | | 350 (14.10) | |
| Gender | | | | | |
| Male | 20,712 (70.88) | 100 (52) | <0.0001 | 739 (3.57) | <0.0001 |
| Female | 8,510 (29.12) | 108 (57) | | 590 (6.93) | |
| Race | | | <0.0001 | | 0.7847 |
| White | 25,082 (85.83) | 101 (53) | | 1,147 (4.57) | |
| Black | 1,428 (4.89) | 118 (63) | | 58 (4.06) | |
| Hispanic | 971 (3.32) | 114 (61) | | 47 (4.84) | |
| Other | 1,741 (5.96) | 102 (52) | | 77 (4.42) | |
| Health insurance | | | <0.0001 | | <0.0001 |
| Medicare only | 5,218 (17.86) | 107 (58) | | 397 (7.61) | |
| Medicare and (commercial or other) | 5,037 (17.24) | 107 (57) | | 381 (7.56) | |
| Medicare and Medicaid | 473 (1.62) | 113 (62) | | 51 (10.78) | |
| Commercial | 13,483 (46.14) | 100 (52) | | 313 (2.32) | |
| Medicaid only | 751 (2.57) | 104 (56) | | 37 (4.93) | |
| Veterans Administration | 156 (0.53) | 95 (55) | | 6 (3.85) | |
| Other | 1,302 (4.46) | 98 (53) | | 49 (3.76) | |
| Self | 2,502 (8.56) | 97 (50) | | 80 (3.20) | |
| Unknown | 300 (1.03) | 105 (61) | | 15 (5.00) | |
| Medical history | | | | | |
| Current smoker | 11,320 (38.74) | 99 (52) | <0.0001 | 282 (2.49) | <0.0001 |
| Chronic renal insufficiency | 698 (2.39) | 117 (65) | <0.0001 | 109 (15.62) | <0.0001 |
| Diabetes mellitus | 5,440 (18.62) | 110 (59) | <0.0001 | 380 (6.99) | <0.0001 |
| Previous myocardial infarction | 4,800 (16.43) | 106 (59) | <0.0001 | 237 (4.94) | 0.1565 |
| Hypertension | 14,218 (48.66) | 105 (55) | <0.0001 | 749 (5.27) | <0.0001 |
| Hypercholesterolemia | 11,065 (37.87) | 101 (54) | 0.0124 | 327 (2.96) | <0.0001 |
| Family history of coronary artery disease | 8,490 (29.05) | 101 (53) | 0.0005 | 230 (2.71) | <0.0001 |
| Congestive heart failure | 913 (3.12) | 118 (65) | <0.0001 | 126 (13.80) | <0.0001 |
| Percutaneous coronary intervention | 4,259 (14.57) | 104 (57) | 0.0032 | 150 (3.52) | 0.0005 |
| Coronary artery bypass | 1,698 (5.81) | 120 (65) | <0.0001 | 109 (6.42) | 0.0001 |
| Chronic obstructive pulmonary disease | 2,319 (7.94) | 107 (58) | <0.0001 | 152 (6.55) | <0.0001 |
| Stroke | 1,357 (4.64) | 114 (65) | <0.0001 | 149 (10.98) | <0.0001 |
| Angina | 2,312 (7.91) | 105 (58) | 0.0288 | 123 (5.32) | 0.0633 |
| Presentation | | | | | |
| Prehospital 12-lead ECG | 2,915 (9.98) | 83 (50) | <0.0001 | 103 (3.53) | 0.0056 |
| Chest pain at presentation | | | | | <0.0001 |
| No | 1,527 (5.23) | 123 (73) | <0.0001 | 336 (22.00) | |
| Yes | 27,375 (93.68) | 101 (52) | <0.0001 | 937 (3.42) | |
| Unknown | 320 (1.10) | 111 (61) | <0.0001 | 56 (17.50) | |
| Systolic blood pressure | | | <0.0001 | | <0.0001 |
| <100 mm Hg | 2,963 (10.14) | 96 (51) | | 452 (15.25) | |
| 100–180 mm Hg | 23,433 (80.19) | 102 (54) | | 786 (3.35) | |
| >180 mm Hg | 2,724 (9.32) | 112 (57) | | 53 (1.95) | |
| Unknown | 102 (0.35) | 117 (69) | | 38 (37.25) | |
| Heart rate | | | <0.0001 | | <0.0001 |
| <50 beats/min | 1,766 (6.04) | 95 (48) | | 143 (8.10) | |
| 50–100 beats/min | 23,969 (82.02) | 102 (53) | | 793 (3.31) | |
| >100 beats/min | 3,376 (11.55) | 113 (64) | | 355 (10.52) | |
| Unknown | 111 (0.38) | 118 (65) | | 38 (34.23) | |
| First assessment of heart failure | | | <0.0001 | | <0.0001 |
| No congestive heart failure | 25,908 (88.66) | 101 (53) | | 722 (2.79) | |
| Rales/jugular venous distension | 1,895 (6.48) | 110 (60) | | 195 (10.29) | |
| Pulmonary edema | 536 (1.83) | 124 (76) | | 105 (19.59) | |
| Cardiogenic shock | 883 (3.02) | 105 (56) | | 307 (34.77) | |

*Continued on next page*

**Table 1** Continued

| Description | Prevalence n (%) | Door-to-Balloon Time Median, min (Quartile Range) | Door-to-Balloon Time p | Mortality n (%) | Mortality p |
|---|---|---|---|---|---|
| First 12-lead ECG | | | | | |
| Anterior/septal location | 10,631 (36.38) | 104 (55) | <0.0001 | 656 (6.17) | <0.0001 |
| No. of leads with ST-segment elevation | | | <0.0001 | | <0.0001 |
| Left bundle branch block | 580 (1.98) | 132 (84) | | 85 (14.66) | |
| 2 | 3,174 (10.86) | 118 (67) | | 129 (4.06) | |
| 3 and 4 | 19,609 (67.10) | 101 (52) | | 728 (3.71) | |
| 5 and more | 5,565 (19.04) | 97 (48) | | 367 (6.59) | |
| Unknown | 294 (1.01) | 109 (62) | | 20 (6.80) | |
| First 12-lead ECG: ST-segment depression | 13,758 (47.08) | 99 (50) | <0.0001 | 584 (4.24) | 0.0190 |
| Nonspecific ST or T-wave deltas | 856 (2.93) | 114 (71) | <0.0001 | 31 (3.62) | 0.1867 |
| Q-wave (acute infarct zone) | 3,565 (12.20) | 106 (57) | <0.0001 | 196 (5.50) | 0.0037 |
| Times | | | | | |
| Symptom onset-to-door | | | <0.0001 | | 0.0073 |
| ≤1 h | 9,487 (32.47) | 96 (50) | | 462 (4.87) | |
| >1–2 h | 8,557 (29.28) | 99 (50) | | 339 (3.96) | |
| >2 h | 11,178 (38.25) | 110 (61) | | 528 (4.72) | |
| Time/weekday of the admission day | | | <0.0001 | | 0.3824 |
| Weekday 8:00AM–3:59PM | 10,916 (37.36) | 90 (52) | | 492 (4.51) | |
| Weekday 4:00PM–11:59PM | 5,690 (19.47) | 105 (51) | | 280 (4.92) | |
| Weekday 12:00AM–7:59AM | 4,827 (16.52) | 109 (56) | | 198 (4.10) | |
| Weekend 8:00AM–3:59PM | 3,639 (12.45) | 110 (55) | | 160 (4.40) | |
| Weekend 4:00PM–11:59PM | 2,412 (8.25) | 109 (49) | | 120 (4.98) | |
| Weekend 12:00AM–7:59AM | 1,738 (5.95) | 119 (54) | | 79 (4.55) | |
| Calendar time | | | <0.0001 | | 0.0531 |
| First year | 7,978 (27.30) | 105 (57) | | 394 (4.94) | |
| Second year | 7,238 (24.77) | 102 (54) | | 344 (4.75) | |
| Third year | 7,791 (26.66) | 100 (53) | | 339 (4.35) | |
| Fourth year | 6,215 (21.27) | 102 (52) | | 252 (4.05) | |

ECG = electrocardiogram.

transferred out and assumed they survived to discharge. To evaluate the potential effect of decreasing length of stay on our results, we also performed secondary analyses that evaluated mortality within 72 h. The results of both of these secondary analyses were not substantially different from the original.

Statistical analyses were performed using SAS version 9.1 (SAS Institute Inc., Cary, North Carolina), HLM 5.04 for Windows (SSI, Lincolnwood, Illinois), and Stata version 8.0 (Stata Corp., College Station, Texas). The investigators had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

## RESULTS

**Sample characteristics.** The cohort was predominantly male (71%) and white (86%), with a mean age of 61.6 years (Table 1). A substantial proportion of patients had a prior diagnosis of coronary artery disease and/or traditional cardiac risk factors. Almost 10% received a prehospital ECG, 94% had chest pain, 11% were in overt heart failure, and 2% had left bundle branch block. A total of 62% presented within 2 h of symptom onset. There were 58% of the patients who had an ACC/AHA high-risk feature (36% with anterior/septal location, 19% with diabetes mellitus, 12% with heart rate ≥100 beats/min, and 10% with systolic blood pressure <100 mm Hg).

**Association with in-hospital mortality.** In unadjusted analysis, many patient characteristics were significantly associated with both door-to-balloon time and in-hospital mortality (Table 1). Notable exceptions were race/ethnicity and time/day of presentation. In hierarchical multivariable analysis, many patient characteristics continued to be significantly associated with mortality (Table 2). In particular, all four ACC/AHA high-risk factors were associated with increased mortality. In contrast, symptom onset-to-door time was not significantly associated with mortality.

**Door-to-balloon time and mortality.** In-hospital mortality increased significantly with increasing door-to-balloon times (Fig. 1). This relationship was seen in patients regardless of symptom onset-to-door time (Fig. 2). The association between shorter door-to-balloon times and lower mortality was seen both for patients with ACC/AHA high-risk factors and for those without these risk factors (Fig. 3). In hierarchical multivariable analysis, the odds of in-hospital mortality increased with increasing door-to-balloon time for all subgroups, whether by symptom onset-to-door time (Fig. 4A) or presence or absence of risk factors (Fig. 4B).

JACC Vol. 47, No. 11, 2006
June 6, 2006:2180–6

**Table 2.** Factors Independently Associated With In-Hospital Mortality in Multivariate Hierarchical Logistic Regression Model ($p < 0.01$)

| Description | Odds Ratio (95% Confidence Interval) | p |
|---|---|---|
| Demographics | | |
| Age | | |
| <65 yrs | 0.41 (0.36–0.47) | <0.0001 |
| >80 yrs | 1.98 (1.72–2.27) | <0.0001 |
| Female | 1.27 (1.14–1.42) | <0.0001 |
| Medical history | | |
| Current smoker | 0.74 (0.64–0.84) | <0.0001 |
| Chronic renal insufficiency | 1.70 (1.36–2.13) | <0.0001 |
| Diabetes | 1.38 (1.22–1.57) | <0.0001 |
| Hypercholesterolemia | 0.63 (0.56–0.72) | <0.0001 |
| Family history of coronary artery disease | 0.82 (0.71–0.94) | 0.0056 |
| Percutaneous coronary intervention | 0.74 (0.63–0.88) | 0.0005 |
| Coronary artery bypass | 1.40 (1.14–1.72) | 0.0014 |
| Stroke | 1.44 (1.20–1.74) | 0.0001 |
| Presentation | | |
| Chest pain at presentation | | |
| No | 3.63 (3.13–4.20) | <0.0001 |
| Unknown | 3.76 (2.76–5.12) | <0.0001 |
| Systolic blood pressure | | |
| <100 mm Hg | 3.75 (3.27–4.30) | <0.0001 |
| >180 mm Hg | 0.43 (0.33–0.55) | <0.0001 |
| Unknown | 4.59 (2.23–9.46) | <0.0001 |
| Heart rate | | |
| <50 beats/min | 0.84 (0.69–1.03) | 0.0992 |
| >100 beats/min | 2.31 (2.02–2.64) | <0.0001 |
| Unknown | 2.27 (1.08–4.75) | 0.0299 |
| First assessment of heart failure | | |
| Rales/jugular venous distension | 2.19 (1.87–2.56) | <0.0001 |
| Pulmonary edema | 3.30 (2.63–4.14) | <0.0001 |
| Cardiogenic shock | 7.25 (6.13–8.58) | <0.0001 |
| First 12-lead electrocardiogram | | |
| Anterior/septal location | 1.81 (1.61–2.03) | <0.0001 |
| No. of leads with ST-segment elevation | | |
| Left bundle branch block | 2.20 (1.63–2.98) | <0.0001 |
| 3 and 4 | 0.98 (0.81–1.18) | 0.8147 |
| 5 and more | 1.44 (1.18–1.77) | 0.0005 |
| Unknown | 1.43 (0.86–2.38) | 0.1659 |
| Q-wave (acute infarct zone) | 1.24 (1.06–1.45) | 0.0065 |
| Times | | |
| Door-to-balloon time per 30 min | 1.08 (1.05–1.11) | <0.0001 |

## DISCUSSION

In this large observational study of patients with STEMI undergoing primary PCI, we found clear evidence of increased mortality with longer door-to-balloon times. This association was seen for patients regardless of symptom onset-to-door time and for patients with and without high-risk factors. These findings support the current guideline-based recommendations for rapid PCI and provide evidence that this recommendation is valid for all patients with STEMI and presentation within 6 h of the onset of symptoms.

**Time from symptom onset to reperfusion.** Shorter time from symptom onset to the administration of fibrinolytic therapy has been consistently shown to be associated with lower mortality for patients with STEMI (1–3,17,18). However, a meta-analysis of randomized trials found time from symptom onset to reperfusion related to mortality for fibrinolytic therapy in all patients, but for PCI only in those treated within 2 h (10). Large single-center observational studies have found similar results (4,6). In contrast, analysis of previous patients in NRMI-1 and -2 found no significant relationship between symptom onset-to-balloon time and mortality (7). Similarly, our study of NRMI-3 and -4 did not find improved survival for patients with decreased symptom onset-to-door time after adjusting for patient characteristics. In support of our findings, myocardial salvage has been found to be related to time from symptom onset to fibrinolytic therapy but independent of time from symptom onset to balloon (19). In addition to biological explanations, methodological issues may account for the poor relationship. First, the accuracy of the time of symptom onset is limited because of patient reporting error. Patients frequently are unsure of the exact time of symptom onset and usually give an estimate. Second, patients with less certainty of time of symptom onset may be more likely to get PCI than fibrinolytic therapy because of the increased risk of bleeding for fibrinolytic therapy. Finally, some of the deaths from STEMI may occur before hospital presentation. These patients would not be entered into the registry,

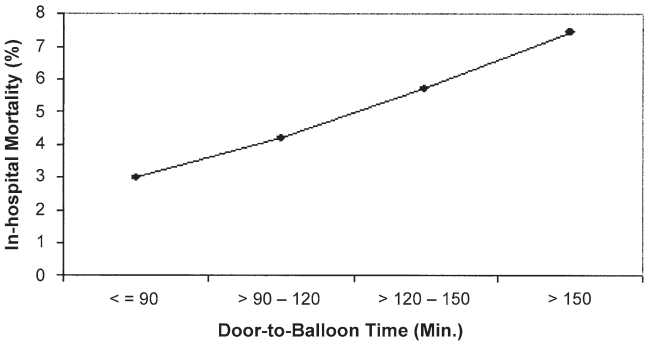


**Figure 1.** In-hospital mortality and door-to-balloon time; p for trend < 0.001.

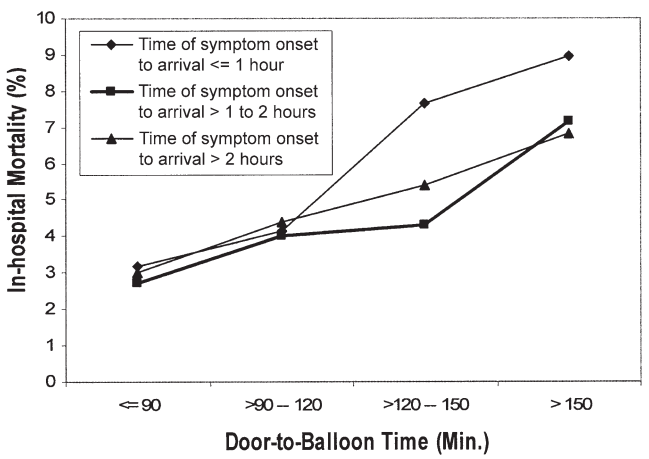


**Figure 2.** In-hospital mortality and door-to-balloon time in patients stratified by symptom onset-to-door time; p for trend < 0.001 for each line.

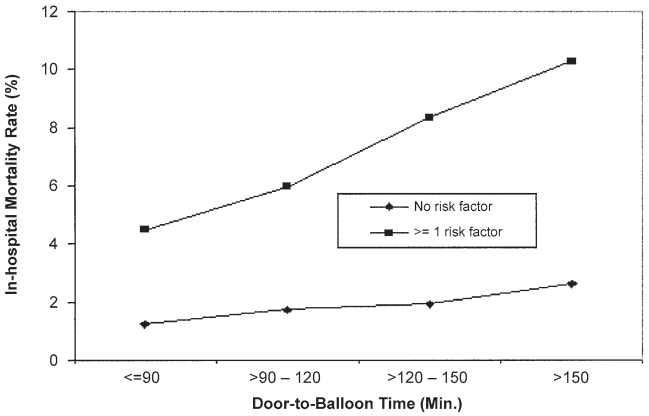


**Figure 3.** In-hospital mortality and door-to-balloon time in patients stratified by risk factor status; p for trend < 0.001 for each line. Risk factors include anterior/septal location, diabetes mellitus, heart rate >100 beats/min, systolic blood pressure <100 mm Hg.

and their absence likely dilutes the relationship between symptom onset-to-door time and mortality.

**Door-to-balloon time.** We evaluated a subset of the symptom onset-to-balloon time, the door-to-balloon time. In addition to improving the accuracy of estimate, door-to-balloon time is easier to influence because it is more under the control of individual hospitals and physicians than symptom onset-to-door time (20). As with symptom onset-to-balloon time, prior studies evaluating the association between door-to-balloon time and mortality have had mixed results. In the Global Use of Strategies to Open Occluded Arteries in Acute Coronary Syndromes (GUSTO) IIb trial, 30-day mortality rates increased progressively with time from randomization to balloon inflation, a close surrogate for door-to-balloon time (8). Analysis of patients in a prior cohort of NRMI also found increasing mortality with door-to-balloon times (7). Our study confirms this association in patients with more recent data as well as in various subgroups of patients.

In contrast, a recent study finding that symptom onset-to-balloon time was an independent predictor of mortality failed to find a similar relationship between door-to-balloon time and mortality (4). The discrepancy between these findings and those of our study may be explained by the fact that only 11% of patients in this single-center study had door-to-balloon times >90 min. In contrast, a majority of patients in the NRMI registry had door-to-balloon times in excess of 90 min. A low number of patients with times >90 min may decrease sensitivity of finding a relationship. In

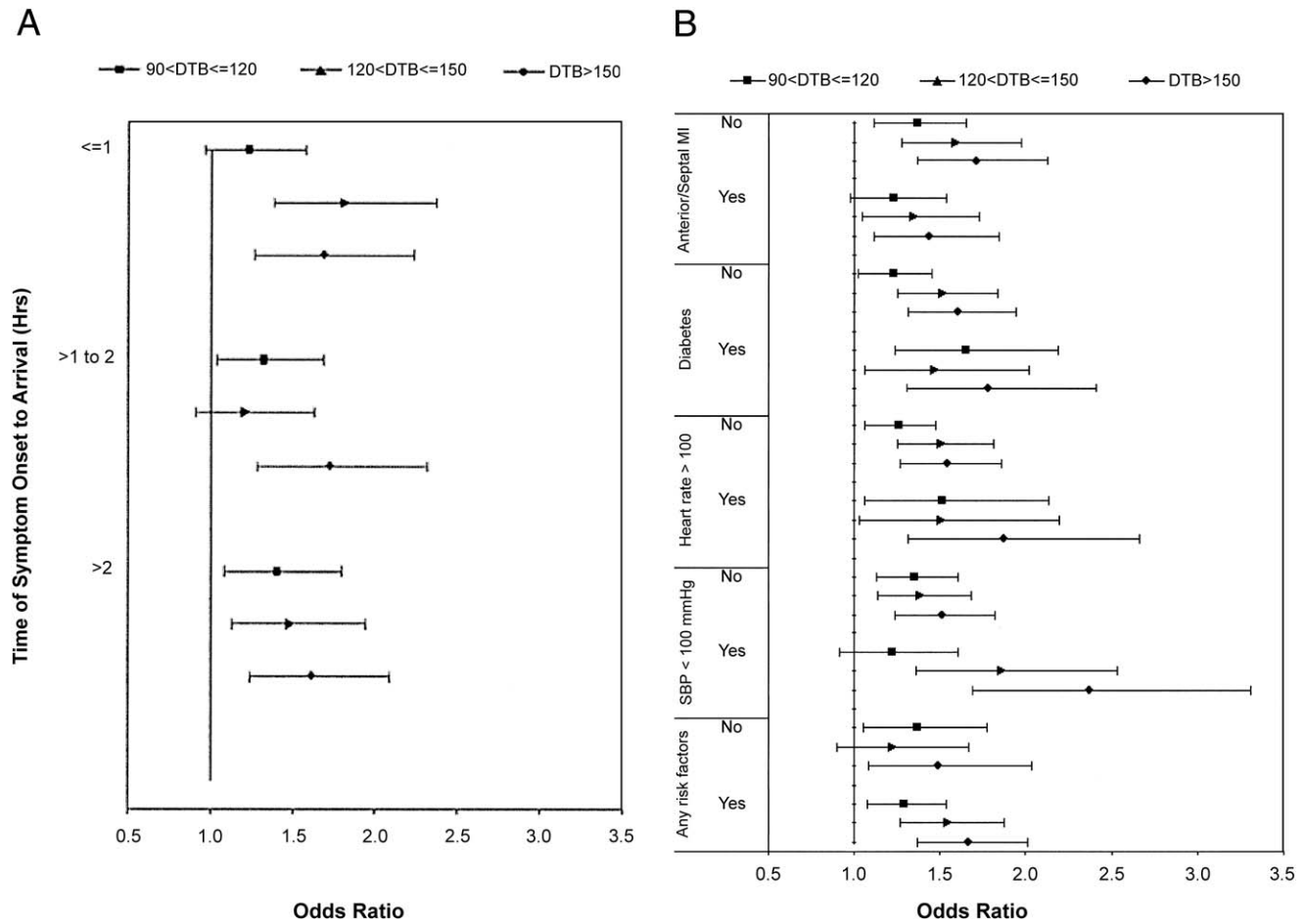


**Figure 4.** Independent effect of door-to-balloon time on in-hospital mortality in subgroups by **(A)** symptom onset-to-door time and **(B)** risk factor status. Reference group: door-to-balloon time <90 min. DTB = door-to-balloon; MI = myocardial infarction; SBP = systolic blood pressure.

one study, time to reperfusion was found to be important only in those at high risk (5). Our study found increasing door-to-balloon time to be related to increasing mortality for all risk groups. The magnitude of the mortality depended on the baseline risk, but the relationship with time did not differ.

**Study limitations.** Although this database is large and has been found to be reasonably generalizable (16), there are limitations. First, as mentioned previously, the time from symptom onset is obtained from the patient and may not be accurate. However, a more accurate time from symptom onset likely would not affect the main conclusions regarding door-to-balloon time. Second, there may be other risk factors that we did not examine that could identify a subgroup of patients in which door-to-balloon time is not important. Third, most of the patients were treated with door-to-balloon times greater than guideline recommendations. The importance of further reductions beyond 90 min has not been clarified. Fourth, these results cannot be extended to patients transferred from one hospital to another. Finally, door-to-balloon time may be a proxy for general quality of care, with the relationship with mortality reflecting unobserved quality measures.

**Study implications.** Efforts should continue to decrease the door-to-balloon time for all patients with STEMI undergoing primary PCI. Degree of urgency should not depend on time of symptom onset or baseline risk factors.

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