Door-to-Balloon Time and Mortality among Patients Undergoing Primary PCI

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ABSTRACT

BACKGROUND

Current guidelines for the treatment of ST-segment elevation myocardial infarction recommend a door-to-balloon time of 90 minutes or less for patients undergoing primary percutaneous coronary intervention (PCI). Door-to-balloon time has become a performance measure and is the focus of regional and national quality-improvement initiatives. However, it is not known whether national improvements in door-to-balloon times have been accompanied by a decline in mortality.

METHODS

We analyzed annual trends in door-to-balloon times and in-hospital mortality using data from 96,738 admissions for patients undergoing primary PCI for ST-segment elevation myocardial infarction from July 2005 through June 2009 at 515 hospitals participating in the CathPCI Registry. In a subgroup analysis using a linked Medicare data set, we assessed 30-day mortality.

RESULTS

Median door-to-balloon times declined significantly, from 83 minutes in the 12 months from July 2005 through June 2006 to 67 minutes in the 12 months from July 2008 through June 2009 (P<0.001). Similarly, the percentage of patients for whom the door-to-balloon time was 90 minutes or less increased from 59.7% in the first year to 83.1% in the last year (P<0.001). Despite improvements in door-to-balloon times, there was no significant overall change in unadjusted in-hospital mortality (4.8% in 2005–2006 and 4.7% in 2008–2009, P=0.43 for trend) or in risk-adjusted in-hospital mortality (5.0% in 2005–2006 and 4.7% in 2008–2009, P=0.34), nor was a significant difference observed in unadjusted 30-day mortality (P=0.64).

CONCLUSIONS

Although national door-to-balloon times have improved significantly for patients undergoing primary PCI for ST-segment elevation myocardial infarction, in-hospital mortality has remained virtually unchanged. These data suggest that additional strategies are needed to reduce in-hospital mortality in this population. (Funded by the National Cardiovascular Data Registry of the American College of Cardiology Foundation.)

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PRIMARY PERCUTANEOUS INtervention (PCI) is currently the preferred treatment for acute ST-segment elevation myocardial infarction. Previous observational studies have shown a strong association between prompt performance of primary PCI, as assessed in terms of the door-to-balloon time (the interval from the patient's arrival at the hospital to inflation of the balloon to restore flow), and reduced mortality.[1-3] On the basis of these data, current joint clinical practice guidelines of the American College of Cardiology and the American Heart Association (ACC–AHA) endorse a door-to-balloon time of 90 minutes or less as the goal, giving it a Class I (highest level) recommendation.[4] Because of this recommendation, door-to-balloon time has become the focus of local, regional, and national quality-improvement initiatives and is currently tracked by a number of clinical registries.[5,6] Consequently, door-to-balloon times are now publicly reported, and the percentage of patients for whom the door-to-balloon time is 90 minutes or less has evolved into a key quality metric. Institutional door-to-balloon times also have financial implications, since they are now tied to reimbursement from the Centers for Medicare and Medicaid Services (CMS).[7]

Although these efforts have been remarkably successful in reducing national door-to-balloon times, it is not known whether these improvements are associated with an overall reduction in mortality.[8] A recent study from a large regional cardiovascular collaborative did not show that annual mortality decreased among patients undergoing primary PCI, despite large reductions in door-to-balloon times.[9] However, that study was limited to regional results and may have lacked sufficient power to detect a survival benefit related to the improved treatment times. Therefore, we used national data to evaluate annual trends in door-to-balloon times to assess whether shorter times are associated with a change in in-hospital mortality among patients undergoing primary PCI for ST-segment elevation myocardial infarction.

METHODS

STUDY POPULATION

The study population consisted of all patients undergoing primary PCI at hospitals participating in the CathPCI Registry of the National Cardiovascular Data Registry (NCDR) from July 2005 through June 2009, a period that coincided with the national effort aimed at reducing door-to-balloon times. The CathPCI Registry, which is the largest national clinical registry of patients undergoing either elective or emergency PCI, currently gathers data from more than 1400 hospitals across the United States. It is a joint initiative of the ACC and the Society for Cardiovascular Angiography and Interventions. Details of this registry, including the data quality program, have been published previously.[10,11] The registry collects data on a standardized set of clinical, demographic, and procedural variables, along with in-hospital outcomes, for consecutive patients treated at participating institutions.[12] Version 3 of the NCDR data set was used for this analysis.

We excluded patients who had been transferred from another facility for primary PCI and those who were undergoing nonemergency PCI. We also excluded patients for whom the door-to-balloon times were longer than 3 hours, in an effort to include the patients who had the most to gain with respect to myocardial salvage. To maintain data consistency for the examination of trend, we excluded hospitals that did not report any data for the entire study period.

STUDY DESIGN AND OVERSIGHT

The study was designed by the first and last authors and approved by the NCDR. The CathPCI research and publication subcommittee reviewed and approved the proposal; the NCDR provided the necessary funding. The data were analyzed at the Center for Outcomes Research and Evaluation of Yale–New Haven Hospital. The Yale human investigation committee waived the requirement for informed consent and approved analyses of the limited data set provided by the NCDR. The authors vouch for the accuracy and completeness of the data and the analyses.

STATISTICAL ANALYSIS

The data were analyzed with the use of SAS software, version 9.2. Baseline characteristics and outcomes were compared across the 4 years with the use of the chi-square test for categorical variables and the analysis-of-variance F-test for continuous variables. Discrete variables are expressed

as percentages, and continuous variables as means and standard deviations. P values of less than 0.05 were considered to indicate statistical significance. We examined temporal trends in annual median door-to-balloon times and in the percentage of patients for whom door-to-balloon times were 90 minutes or less.

The primary outcomes of the study were in-hospital mortality (defined as the rate of death from any cause) and door-to-balloon time. Multivariable model analyses were performed with in-hospital mortality as the dependent variable in a logistic-regression model and door-to-balloon time as the dependent variable in a linear-regression model. The independent variables that were considered in the models were those for patients with ST-segment elevation myocardial infarction in the NCDR model for in-hospital mortality.[13] The analyses were repeated in high-risk subgroups of patients: those older than 75 years of age, those presenting with cardiogenic shock, and those with an anterior myocardial infarction.

To assess our ability to characterize the trend in mortality during this period, we developed a hierarchical model using the NCDR model and, for each patient record, the median door-to-balloon time in the year the patient was treated to produce an estimate of the odds ratio for death per 10-minute change in median door-to-balloon time. Finally, we used probabilistic matching to link the records for patients 65 years of age or older in the CathPCI registry with the CMS national claims database, using a combination of indirect identifiers as previously described,[14] and assessed the association between changes in door-to-balloon times from 2005 to 2009 and 30-day mortality.

RESULTS

PATIENTS

A total of 95,007 patients accounted for 96,738 admissions for primary PCI for the treatment of ST-segment elevation myocardial infarction at the 515 participating sites from July 2005 through June 2009. Table 1 shows the baseline demographic, clinical, and procedural characteristics overall and for each year. The mean age of the study population was 60.8 years; 28.0% of the patients were women. A total of 61.0% of the pa-

tients had hypertension, 59.2% had dyslipidemia, 43.3% were current smokers, and 18.8% had diabetes. The prevalence of diabetes, hypertension, and dyslipidemia increased in each year of the study. Similarly, the proportion of patients with a prior myocardial infarction and of patients with previous PCI increased slightly each year. The mean ejection fraction was 46.8% and was essentially unchanged from year to year. Patients presenting with cardiogenic shock accounted for 9.9% of all patients, a proportion that remained relatively constant.

Thrombectomy was performed in 20.5% of the patients, and the percentage of patients who underwent that procedure doubled over the course of the study period, from 13.4% in the first year to 27.8% in the last year (P<0.001). Stents were implanted in 89.3% of all patients. The use of drug-eluting stents tended to decline over the study period, from a peak rate of 76.8% in 2005–2006 to a nadir of 37.4% in 2007–2008. The percentage of patients receiving glycoprotein IIb/IIIa inhibitors declined steadily, whereas the percentage of patients receiving direct thrombin inhibitors increased from 10.8% to 21.9%. The overwhelming majority of PCI procedures were performed through femoral access, which remained the access site of choice each year, accounting for 98.0% of all cases in 2005–2006 and 98.5% of all cases in 2008–2009.

DOOR-TO-BALLOON TIME AND MORTALITY

The median door-to-balloon time decreased significantly each year, from 83 minutes in 2005–2006 to 67 minutes in 2008–2009 (P<0.001) (Fig. 1A). In comparison, the overall unadjusted in-hospital mortality was 4.8% the first year and remained virtually unchanged during the study period, with a rate in the last year of 4.7% (P=0.43) (Fig. 1A). The percentage of patients for whom the door-to-balloon time was 90 minutes or less increased from 59.7% to 83.1% over the course of the study (P<0.001), and the unadjusted mortality for these patients remained constant over the study period at 3.7% (P=0.40 for trend) (Fig. 2A). The percentage of patients with a door-to-balloon time of more than 90 minutes decreased from 40.3% to 16.9% over the course of the study (P<0.001), and an increase in unadjusted mortality was observed within this group, from 6.5% in the first year to 8.9% in the last (P<0.001)

Table 1. Baseline Demographic, Clinical, and Procedural Characteristics.*

Characteristic	Total (N = 96,738)	2005–2006 (N = 19,664)	2006–2007 (N = 24,101)	2007–2008 (N = 25,728)	2008–2009 (N = 27,245)	P Value
Demographic characteristics						
Age (yr)	60.8±13.1	60.5±13.0	60.7±13.0	60.7±13.2	61.0±13.1	<0.001
Female sex (% of patients)	28.0	27.8	28.1	28.3	27.9	0.64
Clinical history						
Hypertension (% of patients)	61.0	58.4	60.5	61.1	63.1	<0.001
Diabetes mellitus (% of patients)	18.8	17.8	18.5	19.1	19.5	<0.001
Dyslipidemia (% of patients)	59.2	57.0	58.5	59.7	60.9	<0.001
Current smoker (% of patients)	43.3	43.5	43.8	42.8	43.0	0.13
Congestive heart failure (% of patients)	4.0	3.8	4.0	3.8	4.2	0.03
Renal failure necessitating dialysis (% of patients)	0.8	0.6	0.8	0.8	0.9	0.01
Peripheral vascular disease (% of patients)	6.1	6.2	6.0	6.1	6.1	0.92
Chronic lung disease (% of patients)	11.4	11.2	11.4	11.4	11.6	0.68
Prior myocardial infarction (% of patients)	18.5	17.9	18.3	18.5	18.9	0.03
Previous PCI (% of patients)	20.5	18.6	19.9	21.3	21.7	<0.001
Previous CABG (% of patients)	5.6	5.2	5.7	5.7	5.8	0.05
Ejection fraction (%)	46.8±12.6	46.7±12.6	46.7±12.6	46.8±12.6	47.0±12.6	0.10
Cardiogenic shock (% of patients)	9.9	9.7	9.7	10.2	9.7	0.13
Length of stay in hospital (days)	4.3±6.1	4.3±7.0	4.3±7.7	4.3±4.8	4.2±5.0	0.02
Procedural variables (% of patients)						
Thrombectomy	20.5	13.4	17.2	21.4	27.8	<0.001
Use of stent	89.3	91.0	89.4	88.3	88.8	<0.001
Bare metal	36.7	14.1	34.0	50.8	42.0	—
Drug-eluting	52.6	76.8	55.5	37.4	46.8	—
Use of glycoprotein IIb/IIIa inhibitors	68.7	73.1	71.5	68.5	63.3	—
Use of direct thrombin inhibitors	15.7	10.8	12.4	16.1	21.9	—
Femoral approach	98.5	98.0	98.6	98.6	98.5	—
Radial approach	0.8	0.7	0.7	0.7	1.0	—
Target coronary artery for PCI (% of patients)						
Left main	3.0	2.8	2.9	3.1	3.2	0.03
Left anterior descending	55.4	54.8	55.8	55.4	55.6	0.18
Left circumflex	33.0	33.3	32.9	33.0	32.8	0.74
Right coronary	59.7	60.6	59.5	59.6	59.4	0.04
Door-to-balloon time						
Median (min)	73	83	76	70	67	<0.001
<90 min (% of patients)	73.8	59.7	69.6	78.7	83.1	<0.001

* Plus–minus values are means ±SD. CABG denotes coronary-artery bypass grafting, and PCI percutaneous coronary intervention.

(Fig. 2B). Throughout the study, the unadjusted mortality was lower among patients with a door-to-balloon time of 90 minutes or less than among those with a door-to-balloon time longer than 90 minutes (3.7% vs. 7.3%, P<0.001).
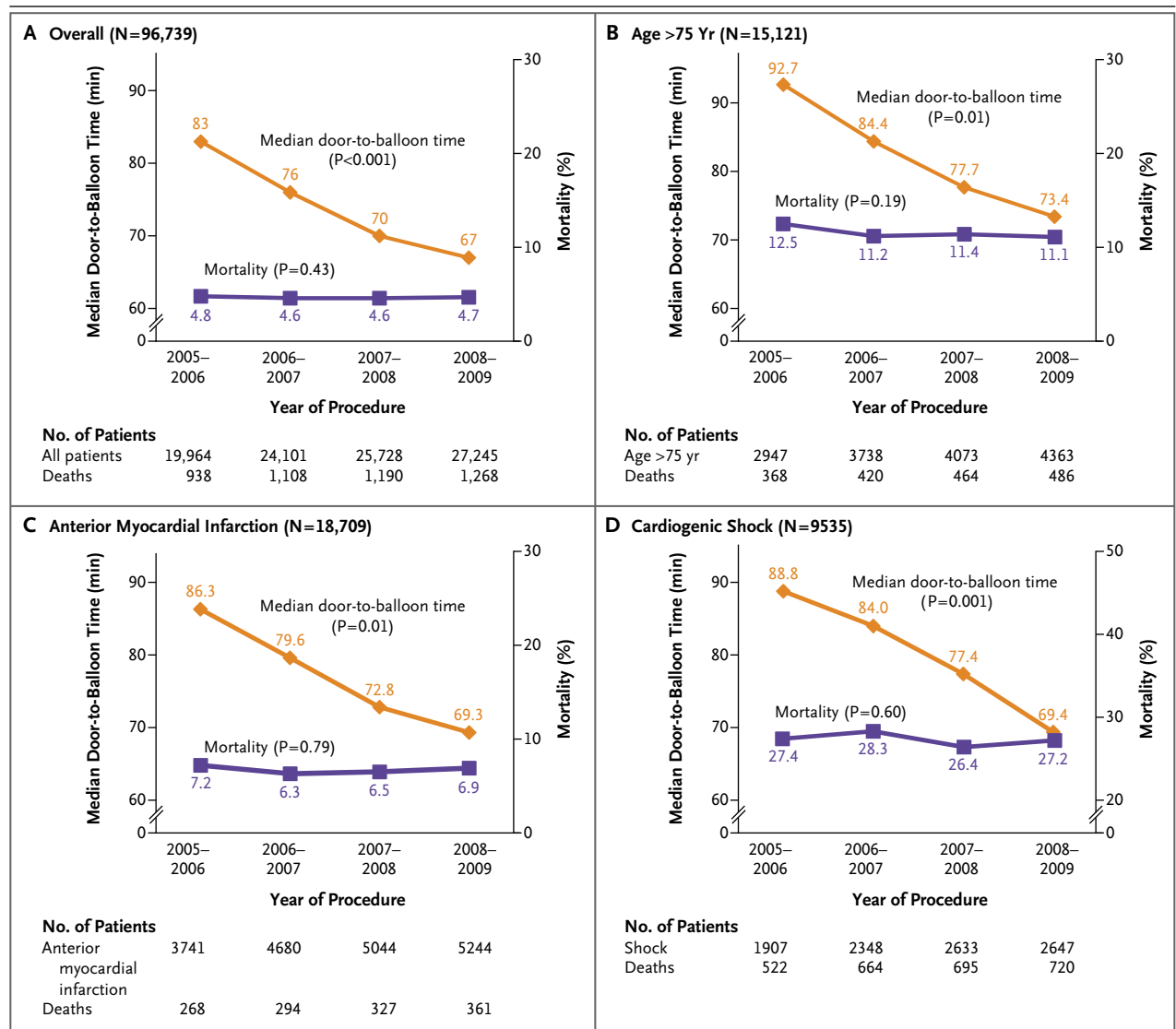
In a risk-adjusted analysis, no significant

Figure 1. Door-to-Balloon Times and Mortality in the Overall Population and High-Risk Subgroups, 2005 to 2009.

Shown are the median door-to-balloon times and unadjusted in-hospital mortality among patients with ST-segment elevation myocardial infarction who underwent primary PCI between July 2005 and June 2009. Results are shown in the overall population (Panel A) and in selected high-risk subgroups: patients older than 75 years of age (Panel B), those with anterior myocardial infarction (Panel C), and those in cardiogenic shock (Panel D). The P values are for the comparison between findings in 2005–2006 and those in 2008–2009.

change in in-hospital mortality was noted during the course of the study period (5.0% in 2005–2006 and 4.7% in 2008–2009, P=0.34) (Fig. 3). Similarly, no significant change in mortality was observed in any of the prespecified high-risk subgroups, including patients older than 75 years of age (P=0.19), those with anterior myocardial infarction (P=0.79), and those presenting in cardiogenic shock (P=0.60), despite consistently improved door-to-balloon times in each of these groups over the course of the study period (Fig. 1B, 1C, and 1D). After adjusting for variables in the NCDR model, we identified no significant association between the annual reduction in door-to-balloon time and mortality (odds ratio for a 10-minute reduction in door-to-balloon time, 1.04; 95% confidence interval, 0.99 to 1.09; P=0.17). In post hoc
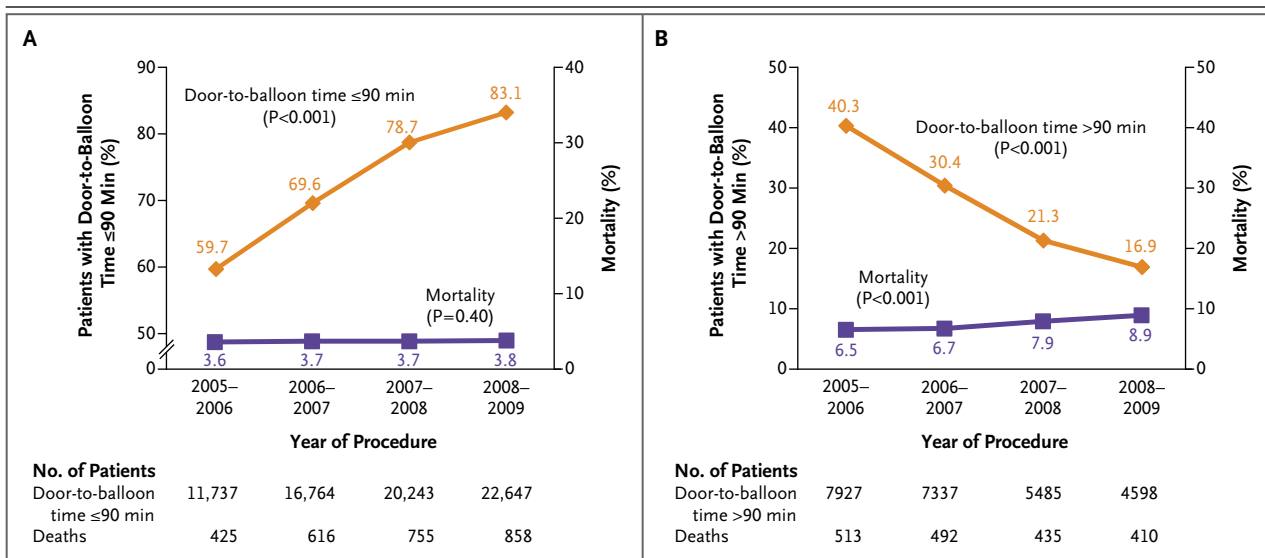
Figure 2. Mortality According to Door-to-Balloon Time, 2005 to 2009.

Shown are the percentages of patients for whom the door-to-balloon time was 90 minutes or less (Panel A) and those for whom the door-to-balloon time was longer than 90 minutes (Panel B), as well as the unadjusted in-hospital mortality for both subgroups, for the period from July 2005 through June 2009. The P values are for the comparison between findings in 2005–2006 and those in 2008–2009.

analyses, when the study population was limited to patients undergoing primary PCI for the first presentation with ST-segment elevation myocardial infarction (95,007 patients) or when patients with door-to-balloon times exceeding 3 hours were included (101,121 patients), a similar decline in door-to-balloon time was seen without any change in mortality.

Using the linked Medicare data set, we identified a total of 26,202 patients with follow-up data. Among these patients, door-to-balloon times declined significantly over time, from a median of 88 minutes in 2005 to 68 minutes in 2009 (P<0.001). We observed almost no change in unadjusted 30-day mortality associated with the annual decline in door-to-balloon times (9.7% in 2005 and 9.8% in 2009, P=0.64) (Fig. 4).

DISCUSSION

Over the past decade, the door-to-balloon time has been a major focus in both quality assessment and quality improvement for patients undergoing primary PCI for ST-segment elevation myocardial infarction. This study reflects the effect of these efforts, showing significant reductions in door-to-balloon times across the United
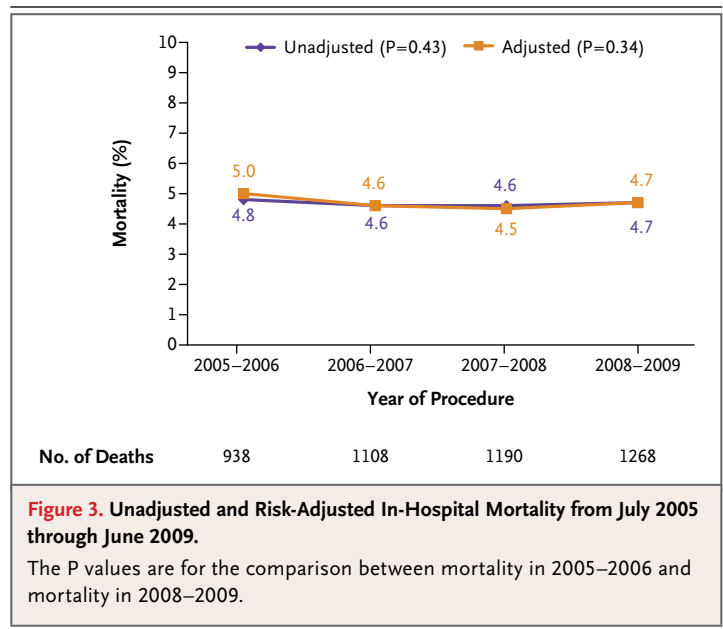
States between June 2005 and July 2009. Similarly, by 2009, more than 80% of patients undergoing primary PCI for ST-segment elevation myocardial infarction met the goal specified in the ACC–AHA clinical practice guidelines of a door-to-balloon time of 90 minutes or less — a marked improvement in just 4 years. Despite these improvements and despite the fact that mortality among patients with shorter door-to-balloon times was lower than mortality among those with longer times, overall unadjusted and risk-adjusted in-hospital mortality remained virtually unchanged. These results were consistent in multiple high-risk subgroups, including patients older than 75 years of age, those presenting in cardiogenic shock, and those with anterior myocardial infarction. Our findings raise questions about the role of door-to-balloon time as a principal focus for performance measurement and public reporting.

The current emphasis on achieving a door-to-balloon time of 90 minutes or less has been driven, in part, by the concept that a shorter interval between ischemia and reperfusion results in improved myocardial salvage and, thus, presumably better clinical outcomes. This idea, along with observational data associating shorter

door-to-balloon times with lower mortality, has spurred the national focus on door-to-balloon time as a quality metric, leading the CMS to begin publicly reporting these data in 2005 and linking them to financial reimbursement. In addition, both the ACC and the AHA launched national campaigns promoting strategies to improve door-to-balloon times through the creation of the D2B Alliance and Mission: Lifeline, respectively.[5,6]
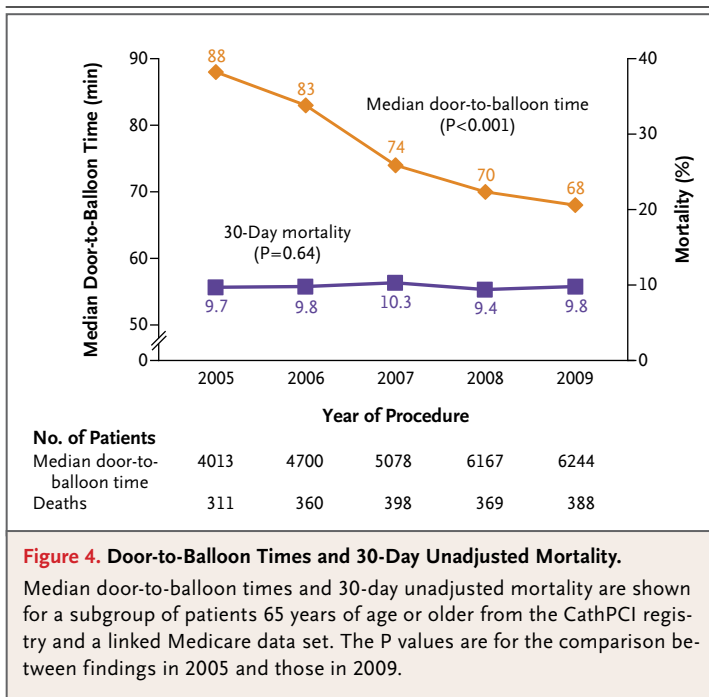
In fact, however, data regarding the relationship between door-to-balloon time and mortality are inconsistent. Berger et al. observed lower 30-day mortality among patients with a door-to-balloon time of less than 60 minutes and an increase in mortality with increasing door-to-balloon times in data from the Global Use of Strategies to Open Occluded Arteries in Acute Coronary Syndromes (GUSTO-IIb) trial.[2] McNamara et al., in a study of data from the National Registry of Myocardial Infarction, reported an odds ratio for increased mortality of 1.42 among patients for whom the door-to-balloon time was longer than 90 minutes, as compared with those for whom the door-to-balloon time was shorter.[1] In contrast, Brodie et al. found that improved door-to-balloon times were not associated with a mortality benefit at 1 month or 6 months,[15] and an analysis of pooled data from randomized trials, performed by Zijlstra et al., showed a linear association of mortality with longer time to treatment among patients receiving thrombolytic therapy but not among those undergoing primary angioplasty.[16]

The discordant findings to date may be the result of multiple confounding factors. Animal models have shown a time-dependent "wavefront" of ischemic cell death associated with arterial occlusion, showing that the degree of myocardial salvage is greatly diminished after prolonged periods of ischemia.[17,18] Thus, total ischemic time may be a more important clinical variable than door-to-balloon time. Results from some previous studies suggest a correlation between symptom-to-balloon times and mortality; yet these data, too, have been inconsistent.[19,20] Furthermore, it has been suggested that the association between door-to-balloon time and mortality may be affected by an "immigration bias" (i.e., bias whereby patients at lower baseline risk either self-select or are selected to be treated dif-

Figure 3. Unadjusted and Risk-Adjusted In-Hospital Mortality from July 2005 through June 2009.

The P values are for the comparison between mortality in 2005–2006 and mortality in 2008–2009.

ferently from patients at greater risk),[9] since healthier patients are likely to have shorter door-to-balloon times than are sicker patients with more complex conditions, for whom treatment may be delayed because of the time needed for medical stabilization.[20] In addition, institutions with high patient volumes are often better equipped than those with lower volumes to reduce door-to-balloon times along with other improved performance measures.[21-23] Thus, improved clinical outcomes may be, in part, a reflection of institutional or operator experience and expertise.

Although multiple studies have evaluated the relationship between door-to-balloon time and clinical end points, data evaluating the effect of a reduction in door-to-balloon time on patient outcomes are more limited. In 2008, Gibson et al., in an analysis of data from the National Registry of Myocardial Infarction, reported a significant reduction in mortality, from 8.6% to 3.1%, associated with a decline in door-to-balloon times from 111 minutes in 1994 to 79 minutes in 2006.[24] In 2010, Flynn et al., in a study involving patients included in a quality-improvement database in Michigan, found no change in short-term mortality between 2003 and 2008 despite a decrease in door-to-balloon time from 113 minutes to 76 minutes.[9] These data, together with our own, show that remark-

Figure 4. Door-to-Balloon Times and 30-Day Unadjusted Mortality.

Median door-to-balloon times and 30-day unadjusted mortality are shown for a subgroup of patients 65 years of age or older from the CathPCI registry and a linked Medicare data set. The P values are for the comparison between findings in 2005 and those in 2009.

able results are achievable through multidisciplinary collaboration aimed at improving an important process of care yet leave open the question of why overall mortality has not declined in the two more recent studies.

Our data suggest that further efforts to reduce door-to-balloon time may not reduce mortality. We therefore conclude that additional factors will probably need to be targeted to accomplish this goal. Door-to-balloon time is one component of total ischemic time; as door-to-balloon time is reduced, it becomes a smaller fraction of total ischemic time, making the time before arrival at a hospital a more important factor. Therefore, efforts with potential to improve outcomes may include increasing patients' awareness of symptoms, reducing the interval from the time of symptom onset to treatment, and shortening the transfer time between medical facilities. In addition, improving both in-hospital care and postdischarge care remain key targets for enhancing long-term outcomes after ST-segment elevation myocardial infarction.

There were some limitations to this study. First, it was an observational study. There were demographic, clinical, and procedural differences among the patients over the course of the study. In addition, it is possible that there were unmeasured changes in the characteristics of

the patient population such that an increase in risk during the study period could have prevented a decrease in overall mortality despite improvements in door-to-balloon times. However, the effect of differences in door-to-balloon time cannot be tested in randomized trials; therefore, larger observational studies such as this trial are likely to be the best way to evaluate the effect of current practice. Second, this study may have been underpowered to detect very small differences in mortality. Third, although current door-to-balloon times may have reached the point at which further reductions are unlikely to improve in-hospital mortality, it remains possible that the benefits of shorter door-to-balloon times will be seen in long-term reductions in mortality, improvements in left ventricular function, or reductions in the number of admissions for heart failure. Fourth, the 30-day data should be interpreted cautiously, since the cohort in this linked data set represents only approximately a quarter of the total study population. Finally, this study included patients who were undergoing primary PCI, and therefore the results cannot be generalized to all patients with ST-segment elevation myocardial infarction.

In conclusion, this study shows that between 2005 and 2009, there was a significant decline in national door-to-balloon times along with a steadily increasing percentage of patients meeting the guideline recommendation of a door-to-balloon time of 90 minutes or less for those presenting with an ST-segment elevation myocardial infarction. Despite these improvements, in-hospital and short-term mortality remained virtually unaffected. The lack of significant change in mortality was observed in both the risk-adjusted cohort and high-risk subgroups.

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