Time Delay to Treatment and Mortality in Primary Angioplasty for Acute Myocardial Infarction
Every Minute of Delay Counts

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**Background**—Although the relationship between mortality and time delay to treatment has been demonstrated in patients with acute ST-segment elevation myocardial infarction (STEMI) treated by thrombolysis, the impact of time delay on prognosis in patients undergoing primary angioplasty has yet to be clarified. The aim of this report was to address the relationship between time to treatment and mortality as a continuous function and to estimate the risk of mortality for each 30-minute delay.

**Methods and Results**—The study population consisted of 1791 patients with STEMI treated by primary angioplasty. The relationship between ischemic time and 1-year mortality was assessed as a continuous function and plotted with a quadratic regression model. The Cox proportional hazards regression model was used to calculate relative risks (for each 30 minutes of delay), adjusted for baseline characteristics related to ischemic time. Variables related to time to treatment were age (>70 years (P<0.0001), female gender (P=0.004), presence of diabetes mellitus (P=0.002), and previous revascularization (P=0.035). Patients with successful reperfusion had a significantly shorter ischemic time (P=0.006). A total of 103 patients (5.8%) had died at 1-year follow-up. After adjustment for age, gender, diabetes, and previous revascularization, each 30 minutes of delay was associated with a relative risk for 1-year mortality of 1.075 (95% CI 1.008 to 1.15; P=0.041).

**Conclusions**—These results suggest that every minute of delay in primary angioplasty for STEMI affects 1-year mortality, even after adjustment for baseline characteristics. Therefore, all efforts should be made to shorten the total ischemic time, not only for thrombolytic therapy but also for primary angioplasty. *(Circulation. 2004;109:1223-1225.)*

**Key Words:** myocardial infarction ■ prognosis ■ mortality ■ angioplasty

Although the relationship between mortality and time delay to treatment has been demonstrated in patients with acute ST-segment elevation myocardial infarction (STEMI) treated by thrombolysis,1–3 the impact of time delay on prognosis in patients undergoing primary angioplasty has yet to be clarified.4–6 In a recent study,7 we have shown that time from symptom onset to balloon inflation, but not door-to-balloon time, is strongly related to 1-year mortality in patients treated by primary angioplasty. The aim of this report was to address the relationship between time to treatment and mortality as a continuous function and to estimate the risk of mortality for each 30-minute delay in treatment.

**Methods**

From 1994 to 2001, a total of 1791 patients with STEMI underwent primary angioplasty.7 Informed consent was obtained from each patient (or from their relatives in case of patient’s inability) before the angiogram. All patients presenting within 6 hours from symptom onset or between 6 and 24 hours if they had continuous symptoms and signs of ischemia (persistent or recurrent chest pain and/or persistent elevation or reelevation of ST segment) were included.7 All patients received aspirin (500 mg) and heparin (10 000 IU) intravenously before the procedure. Therapy after stenting changed during the study period. All patients were taking aspirin and were treated with an additional 3 months of warfarin (before 1996) or 1 month of ticlopidine or clopidogrel (since January 1996). Time to treatment was calculated from symptom onset to first balloon inflation (true ischemic time).

**Angiographic Data Analysis**

All angiograms were analyzed by an independent core laboratory (Diagram, Zwolle, The Netherlands) blinded to all data apart from the coronary angiogram. TIMI (Thrombolysis In Myocardial Infarction) flow and myocardial blush grade were assessed after the angioplasty procedure, as described previously.8 Residual stenosis was assessed visually. Successful reperfusion was defined as postprocedural TIMI 3 flow, residual stenosis <50%, and myocardial blush grade 2 to 3.

**Ejection Fraction**

Left ventricular ejection fraction was measured by radionuclide ventriculography at discharge, as described previously.8
Relationship between time to treatment and 1-year mortality, as continuous function, was assessed with quadratic regression model. Dotted lines represent 95% CIs of predicted mortality.

A major explanation for our findings is that as demonstrated in animal models, infarct size is significantly affected by the duration of coronary occlusion. Therefore,
late reperfusion is expected to result in less myocardial salvage and a higher mortality rate than found with early reperfusion, even when optimal mechanical reperfusion is applied. In support of these data, Stone et al.\(^\text{12}\) found preprocedural TIMI-3 flow to be an independent predictor of mortality. Furthermore, a delay in reperfusion may be associated with an older, organized intracoronary thrombus compared with an early reperfusion. This may result in a higher incidence of distal embolization with lower postprocedural TIMI-3 flow and poor myocardial perfusion.\(^\text{8}\) In fact, we found that patients with successful reperfusion (postprocedural TIMI-3 flow with residual stenosis $<$50% and optimal myocardial perfusion [myocardial blush grade 2 to 3]) had a significantly shorter ischemic time.

Because of the time dependence of thrombolytic therapy in obtaining optimal restoration of epicardial flow, time delay to treatment would be expected to increase the relative risk of mortality more remarkably when thrombolysis is administered than when mechanical reperfusion is used. Although primary angioplasty, in comparison with thrombolysis, may guarantee a higher rate of reperfusion in patients presenting late, it cannot prevent myocardial necrosis, which is related to the duration of occlusion, particularly in higher-risk patients.\(^\text{5–7}\)

**Conclusions**

The results of this study strongly support the prognostic implication of time delay in patients with STEMI undergoing primary angioplasty. Therefore, all efforts should be made to shorten total ischemic time, not only for thrombolytic therapy but also for primary angioplasty.

**References**

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_Circulation_. 2004;109:1223-1225; originally published online March 8, 2004;
doi: 10.1161/01.CIR.0000121424.76486.20

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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