achieved on wards with an adequate number of single-patient rooms.

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RESEARCH LETTER

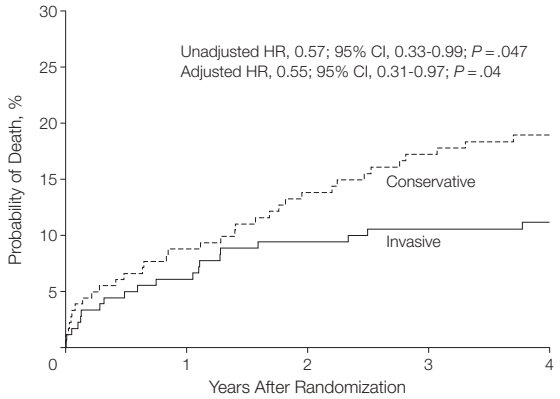
Mechanical Reperfusion and Long-term Mortality in Patients With Acute Myocardial Infarction Presenting 12 to 48 Hours From Onset of Symptoms

To the Editor: Nearly one-third of patients with acute ST-segment elevation myocardial infarction (STEMI) do not receive early reperfusion therapy, mostly due to late presentation after symptom onset.[1] Current guidelines do not recommend primary percutaneous coronary intervention (PCI) in patients with STEMI who present later than 12 hours from symptom onset.[2] The Beyond 12 hours Reperfusion Alternative Evaluation (BRAVE-2) Trial[3,4] demonstrated that an invasive treatment is associated with substantial myocardial salvage and reduction in infarct size in patients with STEMI presenting from 12 to 48 hours after symptom onset. No studies to date have investigated the long-term prognosis after PCI in these patients. In this study, we present the results of the 4-year follow-up of the patients enrolled in the BRAVE-2 trial.[3]

Methods. The BRAVE-2 trial was an international, multicenter, open-label, randomized controlled study conducted from May 2001 to December 2004; it included 365 patients with STEMI who were assessed between 12 and 48 hours from symptom onset. Details of the primary study have been previously reported.[3] The patients were assigned to either an invasive PCI strategy (n=182) or a conservative treatment strategy (n=183). The primary end point was final infarct size measured by single-photon emission computed tomography with technetium 99m sestamibi 5 to 10 days after randomization. The present study focused on the prespecified analysis of 4-year outcomes with mortality as the primary outcome.

All analyses were performed as intention-to-treat. Percentage data are presented as Kaplan-Meier estimates. Cox proportional hazards models were used to assess differences in 4-year outcomes, adjusted for sex, age, diabetes, arterial hypertension, smoking, hypercholesterolemia, previous myocardial infarction, previous coronary artery bypass surgery, Killip class, and pain-to-randomization interval; proportional hazards assumptions were met. S-PLUS version 4.5 (Insightful Corp, Seattle, Washington) was used for all statistical analyses. A 2-tailed $P<.05$ was considered to indicate statistical significance.

Figure. Kaplan-Meier Mortality Curves in the Invasive and Conservative Therapy Groups



No. at risk					
Conservative	183	166	153	146	125
Invasive	182	170	162	159	142

Hazard ratios (HRs) with their 95% confidence intervals (CIs) as well as *P* values were calculated from unadjusted and adjusted Cox proportional hazards models relating treatment group with mortality. Adjustment was performed for sex, age, diabetes, arterial hypertension, smoking, hypercholesterolemia, previous myocardial infarction, previous coronary artery bypass surgery, Killip class, and pain-to-randomization interval.

Results. Four-year follow-up was complete in all but 44 of 365 patients (20 patients in the invasive group and 24 patients in the conservative group). Among the patients who did not complete the 4-year follow-up, median duration of follow-up was 44 months (interquartile range [IQR], 39-46 months) in the invasive group vs 44 months (IQR, 38-46 months) in the conservative group ($P=.36$). Death occurred in 20 patients (11.1%; 95% confidence interval [CI], 7.3%-16.7%) in the invasive group and 34 patients (18.9%; 95% CI, 13.9%-25.4%) in the conservative group (unadjusted hazard ratio [HR], 0.57; 95% CI, 0.33-0.99; $P=.047$; adjusted HR, 0.55; 95% CI, 0.31-0.97; $P=.04$) (FIGURE).

Myocardial reinfarction occurred in 12 patients (6.8%; 95% CI, 3.9%-11.7%) in the invasive group and 10 patients (5.6%; 95% CI, 3.0%-10.1%) in the conservative group (unadjusted HR, 1.20; 95% CI, 0.52-2.78; $P=.66$). Stroke occurred in 3 patients (1.6%) in the invasive group and 2 patients (1.1%) in the conservative group ($P=.65$). Subsequent revascularization of the infarct-related artery was performed in 45 patients in the invasive group and 125 patients in the conservative group (25.8% vs 69.1%; $P<.001$).

Comment. To our knowledge, this is the first study to address the prognostic effect of PCI in patients with STEMI who present between 12 and 48 hours from symptom onset, showing that PCI may reduce 4-year mortality in these patients. The divergence in mortality curves suggests that

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the clinical benefit from PCI needs time to become evident. These findings, in addition to those demonstrating reduction of infarct size,[3] may support the use of invasive PCI treatment in this subset of patients.

However, the major limitation of this study is that the trial was underpowered to demonstrate a mortality advantage of PCI (the power of the study to show statistical significance for the observed difference in mortality was 57%). Given the wide CIs and the risk of inflation of type I error by comparisons of multiple outcomes in the BRAVE 2 trial, these results should be seen as hypothesis generating. Larger trials are required to confirm this effect and clarify its magnitude.

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