and do not necessarily represent the official views of the Centers for Disease Control and Prevention, the National Institutes of Health, or the Arkansas Biosciences Institute.

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Relationship Between Patient's Risk Profile and Benefits in Mortality From Adjunctive Abciximab to Mechanical Revascularization for ST-Segment Elevation Myocardial Infarction: A Meta-Regression Analysis of Randomized Trials

To the Editor: Adjunctive abciximab has been shown to reduce mortality in patients undergoing mechanical revascularization for ST-segment elevation myocardial infarction (STEMI) (1). The goal of this study was to investigate, by the use of a meta-regression analysis of randomized trials, whether the benefits in long-term mortality from abciximab administration correlated with the patient's risk profile.

The literature was scanned by formal searches of electronic databases (MEDLINE, PubMed) and the scientific session abstracts in *Circulation*, the *Journal of American College of Cardiology*, and the *European Heart Journal* from January 1990 to December 2004. The following key words were used: randomized trial, myocardial infarction, reperfusion, primary angioplasty, facilitated angioplasty, stenting, glycoprotein IIb/IIIa inhibitors, abciximab. All data were extracted by two investigators. Data were managed according to the intention-to-treat principle.

The end point was mortality at 6 to 12 months of follow-up. Statistical analysis was performed using the Review Manager 4.27 freeware package (Cochrane Collaboration, Oxford, United Kingdom), the SPSS 11.5 statistical package (SPSS Inc., Chicago, Illinois), and SAS version 8.2 (SAS Institute Inc., Cary, North Carolina). Odds ratio (OR) and 95% confidence intervals (CIs) were used as summary statistics (1).

A fixed-effect meta-regression analysis for the log-odds ratio on mortality (expressed as odds) of the control group was carried out by resorting to the Proc MIXED procedure of SAS version 8.2 (SAS Institute Inc.) according to the approach proposed by van Houwelingen et al. (2). Results are reported as regression coefficients with associated 95% CI and two-sided p values. The estimated meta-regression line was plotted in graph together with the observed log-odds ratios.

A total of seven randomized trials with available follow-up data were analyzed (Table 1), involving 3,918 patients (1,999 in the abciximab group and 1,919 in the placebo group). In almost all trials, abciximab was started after initial angiography. Abciximab was associated with a significant reduction in 6- to 12-month mortality (4.4% vs. 6.2%, OR [95% CI] = 0.69 [0.52 to 0.92], p = 0.01, p heterogeneity = 0.15). Figure 1 shows the relationship between the patient's risk profile and the benefits from abciximab administration in terms of 6- to 12-month mortality (b = −9.9 [−20.1 to 0.21], p = 0.053).

The main finding of this meta-analysis is that the mortality benefits of adjunctive abciximab therapy to mechanical revascularization for ST-segment elevation myocardial infarction are related to the patient's risk profile.

The benefits in mortality may be the effects of abciximab in reducing distal embolization and improving myocardial perfusion, factors known to be determinants of long-term survival (3).

It should be remarked that highly selected non-high-risk patients are commonly enrolled in randomized trials, whereas benefits in mortality have been shown mostly in trials enrolling high-risk patients. In fact, by using a meta-regression analysis, a direct correlation was found between the patient's risk profile and the benefits from abciximab administration in terms of long-term

Table 1. Characteristics of Randomized Trials Included in the Meta-Analysis

	Study Period	n	Study-Drug Design (Number of Patients)	Long-Term Mortality (%)		p Value
				Abciximab	Control	
RAPPORT (1)	1995–1997	483	Abciximab* (n = 241) vs. placebo (n = 242)	4.1	4.5	0.83
ADMIRAL (2)	1997–1998	300	Stenting + abciximab* (n = 151) vs. placebo (n = 149)	3.4	7.3	0.13
CADILLAC (3)	1997–1999	2,082	Abciximab* + stent (n = 524) or balloon (n = 528), control + stent (n = 512) or balloon (n = 518)	4.2	4.4	0.83
ISAR-2 (4)	1997–1998	401	Stenting (n = 200) vs. abciximab* + stenting (n = 201)	6.0	8.5	0.33
Petronio et al. (5)	1998–2000	89	Abciximab* (n = 44) vs. placebo (n = 45)	4.5	13.3	0.15
Zorman et al. (6)	1998–2001	163	Early (n = 56) vs. late (postangiography; n = 56) Abciximab* vs. placebo (n = 51)	4.5	13.7	0.036
ACE (7)	2001–2002	400	Stenting (n = 200) vs. abciximab* + stenting (n = 200)	5.0	10.5	0.04

*0.25 mg/kg + 12-h infusion 0.125 μg/kg/min. From (1) Circulation 1998;98:734–41. (2) N Engl J Med 2001;344:1895–903. (3) N Engl J Med 2002;346:957–66. (4) J Am Coll Cardiol 2000;35:915–21. (5) Am Heart J 2002;143:334–41. (6) Am J Cardiol 2002;90:533–6. (7) Circulation 2004;109:1704–6.

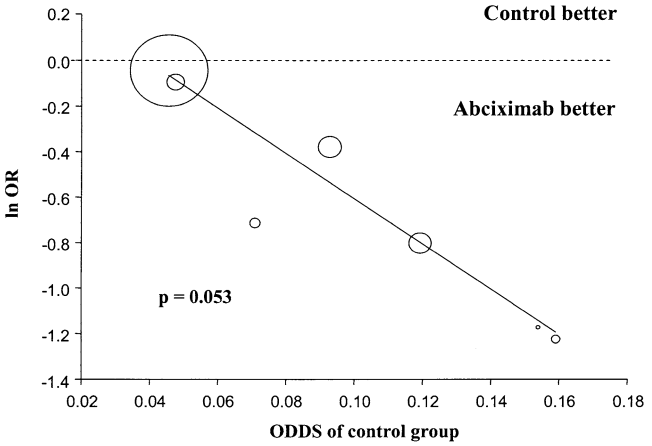

Figure 1. Fixed-effect meta-regression analyses for the log-odds ratio (ln OR) on mortality (expressed as odds) of the control group at 6- to 12-month follow-up. Negative values of the ln OR (y axis) mean more benefits in mortality associated with abciximab administration, whereas the mortality rate of the control group (x axis) represents the risk profile of the patient population included in each trial. The size of the circle corresponds to the inverse variance of the log-odds ratio, and thus is related to the statistical weight of the study.

mortality. Furthermore, several non-randomized studies have shown significantly better survival in patients with cardiogenic shock treated with primary angioplasty and abciximab (4).

Recent investigations have shown that time to treatment is a relevant issue in primary angioplasty and has a significant impact on mortality (5). Therefore, early administration of pharmacologic therapy may improve earlier reperfusion with subsequent smaller infarct size and better clinical outcome, particularly in high-risk patients and when long-distance transportation is required. In the majority of the trials, abciximab was given just before the angioplasty procedure. Only a few and small randomized trials have been conducted so far to investigate the role of early abciximab administration during transportation. Data from large ongoing randomized trials hopefully will clarify this relevant issue, particularly in high-risk patients.

This meta-analysis shows a direct correlation between the patient's risk profile and the benefits in mortality from abciximab administration as an adjunctive therapy to mechanical revascularization for STEMI. Thus, adjunctive abciximab should be considered in primary angioplasty, particularly in high-risk patients, that may be identified by the use of validated risk scores for STEMI (6).

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Integrated Backscatter in Becker Muscular Dystrophy Patients With Functionally Normal Heart: Myocardial Ultrasound Tissue Characterization Study

To the Editor: Becker muscular dystrophy (BMD) is an allelic X-linked recessive disorder characterized by an in frame deletion encompassing one or more exons of the dystrophin gene, with a large phenotypic spectrum, ranging between severe childhood-onset muscular disease to asymptomatic cases. Cardiac involvement (leading to cardiomyopathy and heart failure) is frequent, age-dependent, and unpredictable (1). Since there is no direct relationship between severity of skeletal and cardiac involvement, cardiomyopathy frequently develops in patients with normal skeletal muscle function (2).

Recently, we showed that ultrasound tissue characterization (UTC) of myocardium is able to detect widespread signs of cardiac involvement even in Duchenne muscular dystrophy (DMD) children with normal electrocardiographs (ECGs) and left ventricular systolic function (3). This surprising observation lead to the hypothesis that UTC may be a useful tool in assessing early myocardial involvement in patients with other genetic diseases causing structural changes of myocardium (4). To further explore this hypothesis, we performed UTC analysis in a group of 34 BMD patients with no cardiac symptoms (ages 4 to 33 years, mean 17 $\pm$ 10 years), all with normal ECGs, left ventricular diastolic and systolic function, and segmental wall motion at baseline two-dimensional echocardiography, and in 34 healthy age-matched control subjects. The diagnosis of BMD was confirmed by muscular biopsy in all cases. None of the patients was under pharmacological treatment.