Journal of the American College of Cardiology
© 2004 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 44, No. 6, 2004
ISSN 0735-1097/04/$30.00
doi:10.1016/j.jacc.2004.06.053

Prognostic Utility of Comparative Methods for Assessment of ST-Segment Resolution After Primary Angioplasty for Acute Myocardial Infarction

The Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) Trial

Michael G. McLaughlin, MD,* Gregg W. Stone, MD, FACC,† Eve Aymong, MD, MS,† Graham Gardner, MD,* Roxana Mehran, MD, FACC,† Alexandra J. Lansky, MD, FACC,† Cindy L. Grines, MD, FACC,‡ James E. Tcheng, MD, FACC,§ David A. Cox, MD, FACC,‖ Thomas Stuckey, MD, FACC,¶ Eulogio Garcia, MD,# Giulio Guagliumi, MD,** Mark Turco, MD, FACC,†† Mark E. Josephson, MD, FACC,* Peter Zimetbaum, MD, FACC*

Boston, Massachusetts; New York, New York; Royal Oak, Michigan; Charlotte, Durham, and Greensboro, North Carolina; Madrid, Spain; Bergamo, Italy; and Doylestown, Pennsylvania

OBJECTIVE This study was done to assess and compare the prognostic significance of multiple methods for measuring ST-segment elevation resolution (STR) following primary percutaneous coronary intervention (PCI).

BACKGROUND Resolution of ST-segment elevation (STE) is a powerful predictor of both infarct-related artery patency and mortality in acute myocardial infarction (AMI). Recent thrombolytic studies have suggested that simple measures of STR may be as powerful as more complex algorithms. The optimal method of assessing STR following primary PCI has not been studied.

METHODS We analyzed 700 patients with technically adequate baseline and post-PCI electrocardiograms from the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) trial. Five methods were used to assess STR: 1) summed %STR across multiple leads (ΣSTR); 2) %STR in the single lead with maximum baseline STE (MaxSTR); 3) absolute maximum STE before the procedure; 4) absolute maximum STE after intervention (MaxSTPost); and 5) a categorical variable based upon MaxSTPost (High Risk).

RESULTS At 30 days, ΣSTR, MaxSTR, and MaxSTPost all correlated strongly with mortality ($p = 0.004$, $p = 0.005$, and $p < 0.0001$, respectively) and the combined end point of mortality or reinfarction ($p = 0.001$, $p = 0.001$, and $p < 0.0001$). At one year, ΣSTR and MaxSTPost correlated with mortality ($p = 0.04$, $p = 0.0001$), reinfarction ($p = 0.02$, $p = 0.0015$), and the combined end point ($p = 0.02$, $p < 0.0001$). By multivariate analysis, only the simpler measures of MaxSTPost and High Risk categorization independently predicted all outcomes at both time points.

CONCLUSIONS The STR following primary PCI in AMI correlates strongly with mortality and reinfarction, independent of target vessel patency. The simple measure of the maximal residual degree of STE after primary PCI is a strong independent predictor of both survival and freedom from reinfarction at 30 days and 1 year. (J Am Coll Cardiol 2004;44:1215–23) © 2004 by the American College of Cardiology Foundation

Assessment of ST-segment elevation resolution (STR) after thrombolytic therapy has established utility for predicting both target vessel patency and prognosis in acute myocardial infarction (AMI) (1–14). A number of methods for measuring STR have been studied, mostly involving percent resolution of ST-segment deviation. Some use a single electrocardiogram (ECG) lead (2,9,11,15), whereas others use sum deviation across multiple leads (6–8,10,12,13,16,17); some include ST-segment elevation (STE) alone (2,7,8,17) and others include reciprocal depression (6,12,13). Few studies have directly compared the various methods (11,18,19). The patterns and significance of STR after primary percutaneous coronary intervention (PCI) have been less extensively studied (9,10,16,20,21) than those after thrombolysis. Furthermore, the relative prognostic value of different measures of STR has not been evaluated after mechanical reperfusion therapy. Since ST-segment changes correlate with epicardial vessel flow rates (2,4,5,

From the *Beth Israel Deaconess Medical Center, Boston, Massachusetts; †Cardiovascular Research Foundation and Lenox Hill Heart and Vascular Institute, New York, New York; ‡William Beaumont Hospital, Royal Oak, Michigan; §Duke Clinical Research Institute, Durham, North Carolina; ‖Mid Carolina Cardiology, Charlotte, North Carolina; ¶Moses Cone Memorial Hospital, Greensboro, North Carolina; #Hospital Gregorio Maranon, Madrid, Spain; **Ospedali Riuniti di Bergamo, Bergamo, Italy; and ††Doylestown Hospital, Doylestown, Pennsylvania.

Manuscript received April 22, 2004; revised manuscript received June 9, 2004, accepted June 14, 2004.

Abbreviations and Acronyms

AMI	= acute myocardial infarction
CADILLAC	= Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications
ECG	= electrocardiogram
LBBB	= left-bundle branch block
MI	= myocardial infarction
MSTD	= minimal ST-segment deviation
PCI	= percutaneous coronary intervention
STE	= ST-segment elevation
STR	= ST-segment elevation resolution
TIMI	= Thrombolysis In Myocardial Infarction

8,12), which are more commonly normalized after primary PCI than after thrombolysis, ST-segment evolution may be more homogeneous and, therefore, less predictive after primary PCI. Additionally, the extent and pattern of myocardial reperfusion, which has also been shown to correlate with both STR and outcomes (21,22), may differ after mechanical and pharmacological reperfusion. Therefore, we examined the predictive accuracy and clinical utility of several different scoring methodologies of STR from a large prospective, controlled study of patients with AMI undergoing primary PCI.

METHODS

Patient population and study protocol. The Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) trial protocol has been previously described (23). In brief, non-shock patients with AMI with symptom duration of <12 h and STE in two or more contiguous leads or left-bundle branch block (LBBB) were consented. Patients with other ECG patterns were also enrolled if angiography showed a high-grade coronary stenosis with an associated left ventricular wall motion abnormality. Following angiography, patients with coronary anatomy suitable for stenting were randomized in a 2×2 factorial design to balloon angioplasty versus stenting, each ±abciximab. A total of 2,082 patients were randomized at 76 international centers.

Inclusion in the formal STR substudy required the following: 1) paired ECGs at baseline and within 4 h after PCI; 2) ≥1 mm STE in two contiguous leads in the infarct territory on the baseline ECG; and 3) absence of conditions on both ECGs that would confound interpretation, including LBBB, pacing, pre-excitation, ectopy, missing leads, artifact, and multiple ECG AMI territories. Anterior myocardial infarction (MI) was defined as occurring when STE was present in leads V_1 to V_6, I, and aVL. Inferior MI was defined when STE was confined to leads II, III, aVF, and V_5 to V_6.

ECG analysis. All ECG assessments were made at an independent ECG core laboratory at the Beth Israel Deaconess Medical Center. Measurements were made by two readers blinded to clinical and angiographic results. The absolute level of STE was measured with digital calipers to the nearest 0.01 mV, 20 ms after the end of the QRS interval, using the TP-segment as the isoelectric baseline. On the basis of previously validated algorithms (6,7), summed STE was calculated as follows: for anterior MI, the sum of STE in V_1 to V_6, I; and aVL; for inferior MI, the sum of STE in leads II, III, aVF, V_5, and V_6.

The following five electrocardiographic scoring systems were studied: 1) summed STR (ΣSTR), the percent reduction in the summed score between the pre- and post-procedure ECG; 2) maximum STR (MaxSTR), the percent reduction in the absolute STE in the single lead in the infarct territory with maximum STE on the baseline ECG; 3) MaxSTPre, the absolute maximum STE in a single lead in the infarct territory on the baseline ECG; 4) MaxSTPost, the absolute maximum STE in a single lead in the infarct territory on the post-procedure ECG; and 5) High Risk (for multivariate analysis only), for inferior MI, MaxSTPost >1 mm, and for anterior MI, MaxSTPost >2 mm. For statistical analysis, summed STR parameters were categorized as none (<30%), partial (30% to 70%), and complete (>70%) (6,7). MaxSTPre was categorized as <2, 2 to 3, 3 to 4, and <4 mm, and MaxSTPost was categorized as <1, 1 to 2, and >2 mm.

Angiography. Independent core angiographic laboratory analysis was performed as previously described by technicians who had no knowledge of clinical outcomes (23).

Statistical analysis. Categorical variables were summarized as percentages and compared with the Fisher exact test for two groups and chi-squared tests for three or more groups. Continuous variables are presented as medians with interquartile ranges and were compared using the Kruskal-Wallis nonparametric test or the Wilcoxon two-sample test. All 30-day and 1-year outcomes are summarized as Kaplan-Meier estimates and compared between groups using log-rank tests. The influence of baseline variables, time to reperfusion, and (separately) each of the STR measures on mortality were evaluated with Cox proportional hazards regression, and the results were expressed as hazard ratios with 95% confidence intervals for the STR measures. The other variables included in the multivariate analysis were age, female gender, diabetes, current smoker, hypercholesterolemia, prior MI, prior PCI, prior bypass surgery, Killip class, anterior MI location, three-vessel disease, randomization to stent, randomization to abciximab, pre-procedure Thrombolysis In Myocardial Infarction (TIMI) flow grade 3, post-procedure TIMI flow grade 3, and left anterior descending infarct vessel. To confirm the relative prognostic value of the different ST-segment parameters, we used the -2 log L statistic (minus twice the logarithm of the maximum likelihood) model fit statistic, which represents the summary measure of agreement between the

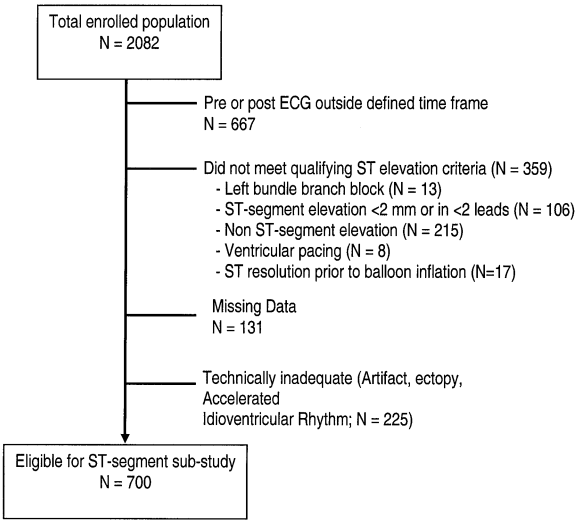

Figure 1. Reasons for exclusion from the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) ST-segment substudy. ECG = electrocardiogram.

model and the data (similar to the likelihood ratio, but independent of the number of the covariates chosen by the model). Smaller values indicate a more predictive model.

RESULTS

Baseline characteristics. Of 2,082 enrolled patients, 700 met criteria for inclusion in the STR substudy (Fig. 1). The baseline characteristics of the patients included in the STR substudy were similar to those excluded, except that those in the STR substudy were more likely to have an anterior MI and had slightly worse baseline left ventricular function, reduced infarct artery flow at presentation (but not after PCI), and shorter times to hospital arrival and first balloon inflation (Table 1). Patients specifically excluded for technical reasons or artifacts were older (62 vs. 59 years; p = 0.002) and more commonly had left circumflex artery infarction confounding ECG interpretation (18.7% vs. 12.0%; p = 0.01); otherwise, they were similar in all procedural variables and outcomes to the substudy patients. The time from final balloon inflation to the post-procedure ECG was 1.77 ± 0.83 h.

ST-segment parameters: frequency and relationship with TIMI flow. The baseline incidences of each MaxSTPre category and of each category of the three measures of STR are shown in Figure 2. Of the 700 patients in the study, 146 qualified for High Risk categorization.

Table 1. Baseline Characteristics and Procedural Data of Patients Included and Excluded From the ST-Segment Substudy

	ST-Segment Substudy (n = 700)	Excluded (n = 1,382)	p Value
Age (yrs)	59 (50, 68)	60 (51, 69)	0.34
Female gender (%)	26.4	27.3	0.68
Anterior infarct by electrocardiogram (%)	45.0	32.3	<0.0001
Inferior infarct by electrocardiogram (%)	55.0	56.6	0.49
Infarct vessel			
Left anterior descending (%)	42.9	33.6	<0.0001
Left circumflex (%)	12.1	20.4	<0.0001
Right (%)	45.0	45.9	0.70
Left ventricular ejection fraction	48 (40, 55)	50 (40, 58)	0.002
Diabetes mellitus (%)	16.9	16.5	0.84
Current smoker (%)	45.0	42.2	0.22
Hypercholesterolemia (%)	36.4	38.6	0.33
Hypertension (%)	47.1	48.6	0.54
Prior myocardial infarction (%)	11.9	14.6	0.08
Killip class ≥2 (%)	9.1	11.8	0.06
Chest pain to hospital arrival (h)	1.58 (1.00, 2.87)	2.00 (1.00, 3.86)	<0.0001
Hospital arrival to balloon inflation (h)	1.82 (1.42, 2.33)	2.12 (1.55, 2.97)	<0.0001
Number of diseased vessels			
One (%)	53.7	49.9	0.10
Two (%)	32.3	33.7	0.51
Three (%)	14.0	16.4	0.16
Stent(s) implanted (%)	56.6	56.9	0.90
Abciximab used (%)	50.7	54.3	0.12
TIMI flow grade			
Before			
Zero/one (%)	72.3	65.7	0.002
Two (%)	11.0	9.5	0.30
Three (%)	16.7	24.8	<0.0001
After			
Zero/one (%)	1.3	1.4	0.86
Two (%)	2.7	3.2	0.54
Three (%)	96.0	95.4	0.53

TIMI = Thrombolysis In Myocardial Infarction.

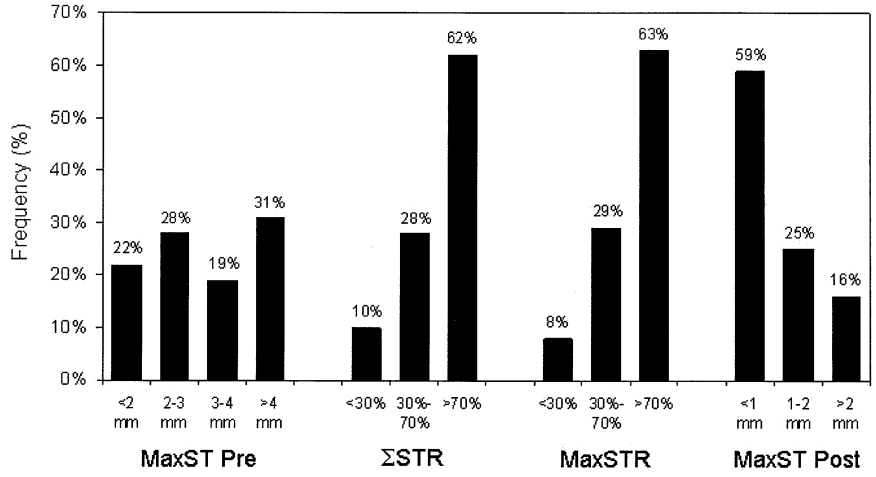

Figure 2. Distribution of ST-segment elevation and ST-segment elevation resolution (STR) measurements.

A TIMI flow grade 3 was achieved in 96% of all patients. Relationships between the various measures of STR and post-procedure TIMI flow are shown in Figure 3. Only MaxSTPost significantly correlated with post-PCI TIMI flow grade 3.

Impact of ST-segment evolution on death and reinfarction. Mortality in the STR substudy was 2.7% at 30 days and 5.1% at 1 year. These rates are not significantly higher than in the entire CADILLAC population (2.1% and 4.2%, respectively; $p = 0.09$ and $p = 0.17$, respectively).

As seen in Table 2, ΣSTR, MaxSTR, and MaxSTPost all correlated strongly with mortality, reinfarction, and the combined end point of mortality or reinfarction at 30 days. At one year, ΣSTR and MaxSTPost again correlated with mortality, reinfarction, and the combined end point. When only the 96% of patients with final TIMI flow grade 3 were analyzed, the results were nearly identical to those for the entire population (Table 3).

MaxSTPre correlated with mortality, reinfarction, and the combined end point at 1 year, but did not correlate with any outcome at 30 days.

Multivariate analyses: death and reinfarction. 30-DAY EVENTS. As shown in Figure 4, ΣSTR >70%, MaxSTR >70%, and MaxSTPost >1 mm were statistically significant independent predictors of mortality, reinfarction, and the combined end point at 30 days. When MaxSTPre was forced into the multivariate model with MaxSTPost, MaxSTPost remained independently correlated with all outcomes at similar p values and hazard ratios. High Risk categorization also correlated with mortality, reinfarction, and the combined end point.

1-YEAR EVENTS. Only MaxSTPost and High Risk categorization were independently predictive of one-year mortality (Fig. 5). The ΣSTR and MaxSTR inversely correlated with reinfarction and the combined end point, but not with one-year mortality. Of all clinical, angiographic, and ECG

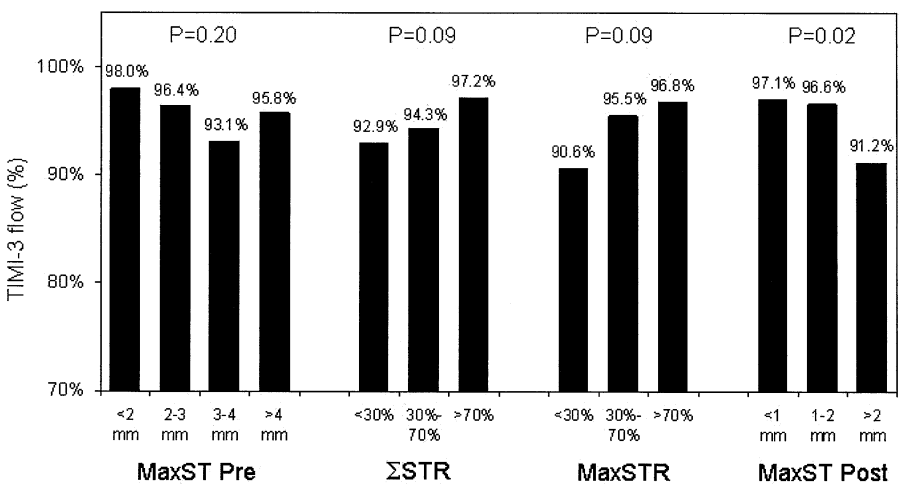

Figure 3. Percentage of patients in each ST-segment elevation and ST-segment elevation resolution (STR) category with Thrombolysis In Myocardial Infarction (TIMI) flow grade 3.

Table 2. Impact of ST-Segment Parameters on Death and Reinfarction: All Patients

	Relative Extent of ST-Segment Elevation Resolution			
	<30%	**30%–70%**	**>70%**	**p Value**
ΣSTR	(n = 71)	(n = 193)	(n = 436)	
30-day				
Death (%)	8.5	3.1	1.6	0.004
Reinfarction (%)	1.5	2.1	0.2	0.06
Death/reinfarction (%)	9.9	5.2	1.8	0.001
1-yr				
Death (%)	9.9	5.2	4.2	0.04
Reinfarction (%)	1.5	3.8	0.7	0.02
Death/reinfarction (%)	11.3	8.3	4.9	0.02
MaxSTR	(n = 53)	(n = 204)	(n = 443)	
30-day				
Death (%)	9.4	2.9	1.8	0.005
Reinfarction (%)	2.1	2.0	0.2	0.06
Death/reinfarction (%)	11.3	4.9	2.0	0.001
1-yr				
Death (%)	9.4	5.9	4.1	0.15
Reinfarction (%)	4.1	3.0	0.7	0.04
Death/reinfarction (%)	13.2	8.4	4.8	0.02
	Absolute Extent of ST-Segment Deviation			
	<1 mm	**1–<2 mm**	**>2 mm**	
MaxSTPost	(n = 445)	(n = 152)	(n = 103)	
30-day				
Death (%)	0.9	3.3	9.7	<0.0001
Reinfarction (%)	0.2	0.7	4.2	0.0008
Death/reinfarction (%)	1.1	3.9	13.6	<0.0001
1-yr				
Death (%)	3.2	4.6	13.6	<0.0001
Reinfarction (%)	0.5	2.7	5.2	0.0015
Death/reinfarction (%)	3.7	7.3	17.5	<0.0001
	<2 mm	**2–<3 mm**	**3–<4 mm**	**>4 mm**	
MaxSTPre	(n = 182)	(n = 188)	(n = 131)	(n = 199)	
30-day					
Death (%)	1.1	2.1	3.8	4.0	0.18
Reinfarction (%)	0	1.1	0.0	2.1	0.11
Death/reinfarction (%)	1.1	3.2	3.8	6.1	0.08
1-yr					
Death (%)	2.8	2.7	7.7	7.6	0.02
Reinfarction (%)	1.1	1.1	0.0	3.7	0.05
Death/reinfarction (%)	4.0	3.7	7.7	10.6	0.01

STR = ST-segment elevation resolution.

parameters included in the multivariate analysis, only MaxSTPost and High Risk categorization correlated with all outcomes at one year. MaxSTPre did not independently correlate with any of the outcomes at either of the time points in the multivariate analysis. As in the 30-day analysis, controlling for pre-procedure STE by forcing MaxSTPre into the multivariate analysis did not change the predictive power of MaxSTPost.

Model fit statistics. The ΣSTR, MaxSTR, MaxSTPost, and High Risk categorization were all statistically significant components of the multivariate models for the occurrence of death, reinfarction, and the combined endpoint, at both 30 days and 1 year. For five of the six outcomes, the model fit statistic for MaxSTPost and High Risk categorization were superior to those for the other measures (Table 4). For the sixth (reinfarction at 30 days), MaxSTPost was similar to the other two and High Risk categorization was superior.

DISCUSSION

Our analysis, the largest study to date of the significance of STR after mechanical reperfusion therapy in AMI, demonstrates that resolution of STE is a powerful predictor of short- and long-term mortality and reinfarction after primary PCI, despite the achievement of very high rates of TIMI flow grade 3. Measures of absolute as well as relative STR strongly correlated with survival and freedom from reinfarction. Notably, the simplest measures of STR—assessment of absolute STE in a single lead on a single

Table 3. Impact of ST-Segment Parameters on Death and Reinfarction: Patients With TIMI Flow Grade 3 After Procedure

	Relative Extent of ST-Segment Elevation Resolution			
	<30%	**30%–70%**	**>70%**	**p Value**
ΣSTR	(n = 65)	(n = 181)	(n = 419)	
30-day				
Death (%)	7.7	2.8	1.7	0.02
Reinfarction (%)	1.7	2.3	0.2	0.05
Death/reinfarction (%)	9.2	5.0	1.9	0.004
1-yr				
Death (%)	9.2	5.0	4.4	0.08
Reinfarction (%)	1.6	4.0	0.7	0.02
Death/reinfarction (%)	10.8	8.3	5.1	0.045
MaxSTR	(n = 48)	(n = 192)	(n = 425)	
30-day				
Death (%)	8.3	2.6	1.9	0.03
Reinfarction (%)	2.3	2.1	0.2	0.05
Death/reinfarction (%)	10.4	4.7	2.1	0.006
1-yr				
Death (%)	8.3	5.8	4.3	0.32
Reinfarction (%)	4.4	3.2	0.7	0.03
Death/reinfarction (%)	12.5	8.4	5.0	0.04
	Absolute Extent of ST-Segment Deviation			
	<1 mm	**1–<2 mm**	**>2 mm**	
MaxSTPost	(n = 428)	(n = 144)	(n = 93)	
30-day				
Death (%)	0.9	3.5	8.6	<0.0001
Reinfarction (%)	0.2	0.7	4.6	0.0005
Death/reinfarction (%)	1.2	4.2	12.9	<0.0001
1-yr				
Death (%)	3.3	4.9	12.9	0.0005
Reinfarction (%)	0.5	2.9	5.7	0.001
Death/reinfarction (%)	3.8	7.7	17.2	<0.0001
	<2 mm	**2–<3 mm**	**3–<4 mm**	**>4 mm**	
MaxSTPre	(n = 176)	(n = 177)	(n = 122)	(n = 190)	
30-day					
Death (%)	1.1	1.7	4.1	3.7	0.18
Reinfarction (%)	0.0	1.1	0.0	2.2	0.11
Death/reinfarction (%)	1.1	2.8	4.1	5.8	0.10
1-yr					
Death (%)	2.9	2.3	8.3	7.4	0.01
Reinfarction (%)	1.2	1.1	0.0	3.9	0.05
Death/reinfarction (%)	4.1	3.4	8.3	10.6	0.01

Abbreviations as in Tables 1 and 2.

post-intervention ECG—were at least prognostically equivalent to more complex algorithms. Moreover, these simple measures (MaxSTPost and High Risk categorization) were the only STR parameters to correlate with one-year mortality in multivariate analysis, and the only parameters (even including all clinical and angiographic variables) to correlate with all three outcomes (death, reinfarction, and the combined end point) at one year.

Our findings are consistent with and extend the results from recently published thrombolytic therapy trials showing that uncomplicated measures of absolute maximum STE after reperfusion are at least as powerful as more complex algorithms requiring relative percent STR calculations over multiple summed leads (18, 19). The ΣSTR parameter we utilized is based upon one of the most widely studied STR algorithms, which sums STE across leads in the infarct territory and then categorizes percent resolution as complete, partial, or none (6,7). In several large thrombolysis trials, this measure has correlated with TIMI flow, left ventricular function, and mortality. Although powerful, this method is cumbersome in research settings and difficult for the clinician to apply. Schroder et al. (18), the originator of the summed STR algorithm, more recently described a simpler parameter, MaxSTE, that categorizes patients as low- or high-risk based upon maximum ST-segment deviation after thrombolysis. In a large thrombolysis population, MaxSTE predicted short- and medium-term mortality more accurately than the ΣSTR algorithm (19). Although substantially easier to use than %STR algorithms, this method requires stratification by MI location and the extent

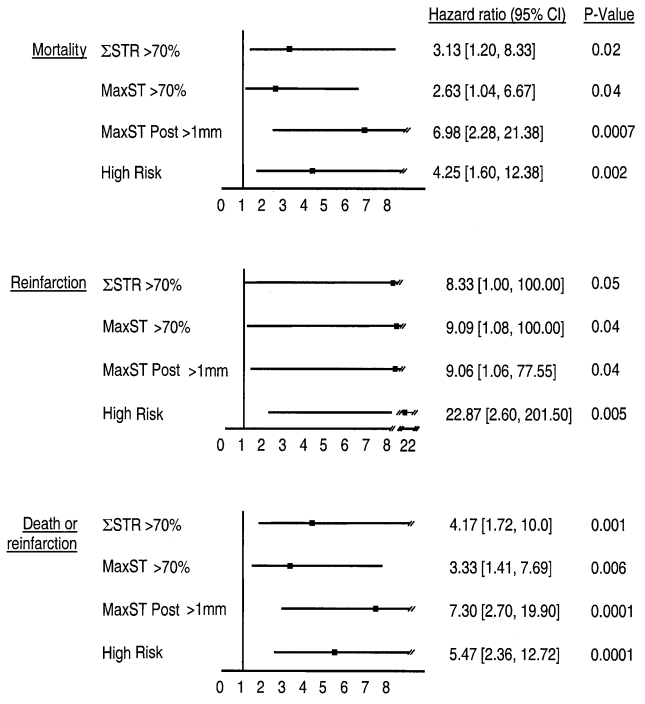

Figure 4. Multivariate ST-segment elevation resolution predictors of 30-day outcomes for mortality **(top)**, reinfarction **(middle)**, and the combined end point **(bottom)**. CI = confidence interval; STR = ST-segment elevation resolution.

of pre-procedure STE. More recently, Cooper et al. (19) described a simpler parameter, minimal ST-segment deviation (MSTD), also based upon maximum STE after thrombolysis. This measure predicted target vessel patency,

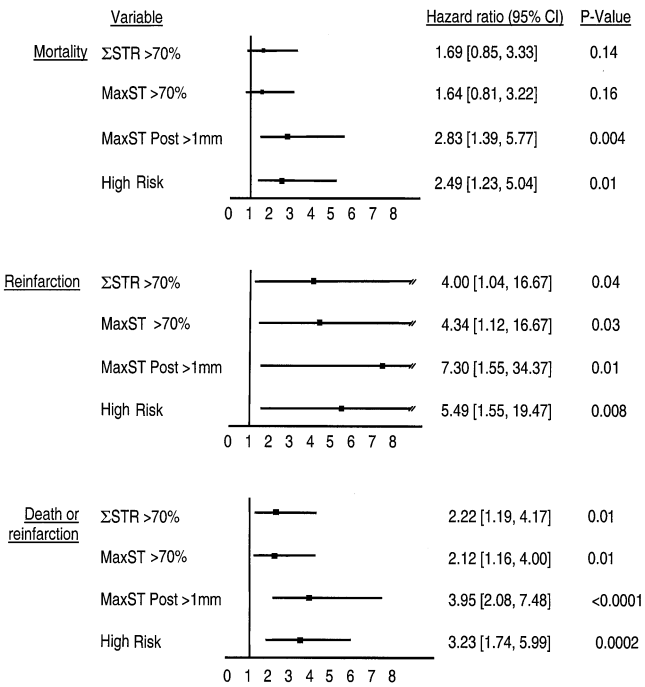

Figure 5. Multivariate ST-segment elevation resolution predictors of one-year outcomes for mortality **(top)**, reinfarction **(middle)**, and the combined end point **(bottom)**. Abbreviations as in Figure 4.

Table 4. Model Fit Statistics for the Multivariate Analyses of Outcomes, Examining the Relative Prognostic Value of Different ST-Segment Parameters*

Event	ST Parameter	−2 Log L
1-yr death or reinfarction	Summed STR >70%	503.39
	MaxST >70%	503.90
	MaxSTPost >1 mm	494.59
	High risk	495.89
1-yr death	Summed STR >70%	386.53
	MaxST >70%	386.81
	MaxSTPost >1 mm	380.23
	High risk	380.50
1-yr reinfarction	Summed STR >70%	123.91
	MaxST >70%	123.40
	MaxSTPost >1 mm	120.15
	High risk	121.56
30-day death or reinfarction	Summed STR >70%	264.45
	MaxST >70%	269.15
	MaxSTPost >1 mm	257.60
	High risk	261.31
30-day death	Summed STR >70%	205.24
	MaxST >70%	206.67
	MaxSTPost >1 mm	196.28
	High risk	198.54
30-day reinfarction	Summed STR >70%	71.76
	MaxST >70%	71.33
	MaxSTPost >1 mm	71.45
	High risk	66.87

*The lower the number; the greater the relative prognostic value.
STR = ST-segment elevation resolution.

but not mortality, with similar accuracy to ΣSTR. Our High Risk categorization is similar to MSTD categorization, but even less complex. The MSTD requires identifying the lead with maximum STE at baseline and then assessing that lead after thrombolysis. Our High Risk categorization (as well as MaxSTPost) requires only the post-procedure ECG. The ability to derive prognostic utility from a single lead on a single ECG has obvious advantages over serial assessments and complex calculations, in both the clinical and research settings. The High Risk variable thus extends the benefits of the Schroder et al. (18) MaxSTE, the Cooper et al. (19) MSTD, and our MaxSTPost in that it is a simple categorical variable based upon a single lead after treatment, accounting for infarct location to improve predictive accuracy.

To exclude the possibility that post-procedure STE may simply be a reflection of pre-procedure STE (and therefore the magnitude of the MI rather than the efficacy of therapy), we also assessed baseline STE with MaxSTPre. This parameter correlated weakly with outcomes in univariate analysis and not at all in multivariate analyses. Moreover, when MaxSTPre was forced into the multivariate analysis of MaxSTPost, MaxSTPost remained a potent, independent predictor of outcomes, whereas MaxSTPre lost prognostic utility. In combination, these data support the premise that absolute STE after procedure is not just a surrogate for the magnitude of myocardium at risk at presentation, but rather a valid index of STR and reperfusion success.

Notably, most previously published data on STR in AMI are from thrombolysis trials, in which TIMI flow grade 3 is

restored in 50% to 60% of patients. In this setting, STR has been studied as a means for predicting target vessel patency and thereby stratifying patients for rescue angioplasty. In contrast, TIMI flow grade 3 is restored in most patients after primary PCI, and their prognosis is favorable. Several smaller, single-center retrospective trials have found a relationship between the relative degree of STR after primary PCI and mortality (16,24,25). The present study is the first to demonstrate the independent value of STR from a large, multicenter primary PCI trial. Moreover, the novel demonstration that simple measures such as MaxSTPost and High Risk categorization are at least as prognostically useful as more complex traditional algorithms has immediate applications for further risk stratification and identification of patients who may benefit from additional therapies, such as interventions to enhance microvascular perfusion.

An additional important finding from the present investigation is that the absolute and relative degree of STR is an important independent predictor of reinfarction during the follow-up period. The mechanism underlying the higher rates of reinfarction with incomplete STR is unknown, although it may involve decreased microcirculatory patency (16,25) or the presence of a prothrombotic state in patients with extensive reperfusion injury (26).

Study limitations. As with most prior trials investigating STR, the current report describes a post-hoc analysis and thus should be validated in future prospective studies. Quantitative ST-segment evaluation was not part of the original study protocol, explaining the relatively high rate of exclusion. Thus, strict inclusion criteria were specified for this study with regard to ECG quality, ECG timing, and degree of baseline STE to maintain a homogeneous and high-quality population. Almost one-third of patients were excluded because ECGs were outside our specified time frame. The pre-specified window of up to 4 h after PCI is wider than that used in some prior trials. However, the average time from balloon inflation to post-procedure ECG (1.77 h) was similar to previous studies (6,7,18–20,24). Moreover, the optimal time interval to measure STR after primary PCI has not been determined, and it is unknown whether earlier STR determination carries more prognostic weight. Regardless, the present study demonstrates that STR utilizing the current time window is prognostically meaningful, independent of epicardial vessel patency.

The most significant difference between the substudy cohort and excluded patients was the greater percentage of anterior MIs in the substudy. This is likely due to the fact that infarcts associated with right coronary and left circumflex coronary artery lesions were less likely to achieve our pre-specified level of STE in multiple leads and were more likely to have been assessed as an indeterminate location. Moreover, in the final stage of exclusion, 225 patients (11%) were excluded because of technically inadequate ECGs. The majority of these patients had baseline artifacts in one or more ECG leads that precluded precise assessment of STE throughout the infarct territory. This rate of exclusion, which is common in our core laboratory experience with static ECG tracings, highlights a limitation of traditional complex STR algorithms, which can be confounded by even modest technical inadequacies. Additional final-stage exclusions were also due to transient arrhythmias, ectopy, pacing, or indeterminate infarct location (reflecting the greater number of left circumflex lesions excluded at this stage). Nonetheless, the otherwise similar baseline characteristics and event-free survival rates between patients excluded and included suggest that the bias created was minimal.

Future directions. This study has established that the simple measure of the maximal residual degree of STE on a single post-procedure ECG is a strong independent predictor of both survival and freedom from reinfarction after primary PCI. Notably, however, despite restoration of TIMI flow grade 3 in 96% of patients, MaxSTPost <1 mm was present in only 59% of patients after PCI. By this measure, reperfusion is suboptimal in 41% of patients after contemporary percutaneous interventional approaches. Future studies evaluating reperfusion strategies should emphasize nontraditional measures of reperfusion success, including STR and myocardial perfusion (16,20,24,27), rather than epicardial flow rates.

Reprint requests and correspondence: Dr. Peter Zimetbaum, Beth Israel Deaconess Medical Center, One Deaconess Road, Baker 4, Boston, Massachusetts 02215. E-mail: pzimetba@bidmc.harvard.edu.

REFERENCES

1. von Essen R, Schmidt W, Uebis R, et al. Myocardial infarction and thrombolysis. Electrocardiographic short term and long term results using precordial mapping. Br Heart J 1985;54:6–10.
2. Saran RK, Been M, Furniss SS, Hawkins T, Reid DS. Reduction in ST-segment elevation after thrombolysis predicts either coronary reperfusion or preservation of left ventricular function. Br Heart J 1990;64:113–7.
3. Bren GB, Wasserman AG, Ross AM. The electrocardiogram in patients undergoing thrombolysis for myocardial infarction. Circulation 1987;76:II18–24.
4. Blanke H, Scherff F, Karsch KR, et al. Electrocardiographic changes after streptokinase-induced recanalization in patients with acute left anterior descending artery obstruction. Circulation 1983;68:406–12.
5. Krucoff MW, Green CE, Satler LF, et al. Noninvasive detection of coronary artery patency using continuous ST-segment monitoring. Am J Cardiol 1986;57:916–22.
6. Schroder R, Dissmann R, Bruggemann T, et al. Extent of early ST-segment elevation resolution: a simple but strong predictor of outcome in patients with acute myocardial infarction. J Am Coll Cardiol 1994;24:384–91.
7. Schroder R, Wegscheider K, Schroder K, Dissmann R, Meyer-Sabellek W. Extent of early ST-segment elevation resolution: a strong predictor of outcome in patients with acute myocardial infarction and a sensitive measure to compare thrombolytic regimens. J Am Coll Cardiol 1995;26:1657–64.
8. Buszman P, Szafranek A, Kalarus Z, Gasior M. Use of changes in ST-segment elevation for prediction of infarct artery recanalization in acute myocardial infarction. Eur Heart J 1995;16:1207–14.
9. Santoro GM, Antoniucci D, Valenti R, et al. Rapid reduction of ST-segment elevation after successful direct angioplasty in acute myocardial infarction. Am J Cardiol 1997;80:685–9.
10. Matetzky S, Novikov M, Gruberg L, et al. The significance of persistent ST elevation versus early resolution of ST-segment elevation after primary PTCA. J Am Coll Cardiol 1999;34:1932–8.

11. Shah A, Wagner GS, Granger CB, et al. Prognostic implications of TIMI flow grade in the infarct related artery compared with continuous 12-lead ST-segment resolution analysis. J Am Coll Cardiol 2000;35:666–72.
12. Doevendans PA, Gorgels AP, van der Zee R, et al. Electrocardiographic diagnosis of reperfusion during thrombolytic therapy in acute myocardial infarction. Am J Cardiol 1995;75:1206–10.
13. de Lemos JA, Antman EM, Giugliano RP, et al. ST-segment resolution and infarct-related artery patency and flow after thrombolytic therapy. Am J Cardiol 2000;85:299–304.
14. de Lemos JA, Morrow DA, Gibson CM, et al. Early noninvasive detection of failed epicardial reperfusion after fibrinolytic therapy. Am J Cardiol 2001;88:353–8.
15. Timmis GC, Gangadharan V, Hauser AM, et al. Intracoronary streptokinase in clinical practice. Am Heart J 1982;104:925–38.
16. Poli A, Fetiveau R, Vandoni P, et al. Integrated analysis of myocardial blush and ST-segment elevation recovery after successful primary angioplasty: real-time grading of microvascular reperfusion and prediction of early and late recovery of left ventricular function. Circulation 2002;106:313–8.
17. Mauri F, Maggioni AP, Franzosi MG, et al. A simple electrocardiographic predictor of the outcome of patients with acute myocardial infarction treated with a thrombolytic agent. J Am Coll Cardiol 1994;24:600–7.
18. Schroder K, Wegscheider K, Zeymer U, Tebbe U, Schroder R. Extent of ST-segment deviation in a single electrocardiogram lead 90 min after thrombolysis as a predictor of medium-term mortality in acute myocardial infarction. Lancet 2001;358:1479–86.
19. Cooper HA, de Lemos JA, Morrow DA, et al. Minimal ST-segment deviation: a simple, noninvasive method for identifying patients with a patent infarction-related artery after fibrinolytic administration. Am Heart J 2002;144:790–5.
20. van't Hof AW, Liem A, Suryapranata H, et al. Angiographic assessment of myocardial reperfusion in patients treated with primary angioplasty for acute myocardial infarction: myocardial blush grade. Circulation 1998;97:2302–6.
21. Santoro GM, Valenti R, Buonamici P, et al. Relation between ST-segment changes and myocardial perfusion evaluated by myocardial contrast echocardiography in patients with acute myocardial infarction treated with direct angioplasty. Am J Cardiol 1998;82:932–7.
22. Watanabe J, Nakamura S, Sugiura T, et al. Early identification of impaired myocardial reperfusion with serial assessment of ST segments after percutaneous transluminal coronary angioplasty during acute myocardial infarction. Am J Cardiol 2001;88:956–9.
23. Stone GW, Grines CL, Cox DA, et al. Comparison of angioplasty with stenting, with or without abciximab, in acute myocardial infarction. N Engl J Med 2002;346:957–66.
24. van't Hof AW, Liem A, de Boer MJ, Zijlstra F. Clinical value of the 12-lead electrocardiogram after successful reperfusion therapy for acute myocardial infarction. Lancet 1997;350:615–9.
25. Claeys MJ, Bosmans J, Veenstra L, et al. Determinants and prognostic implications of persistent ST-segment elevation after primary angioplasty for acute myocardial infarction. Circulation 1999;99:1972–7.
26. Okada H, Woodcock-Mitchell J, Mitchell J, et al. Induction of plasminogen activator inhibitor type 1 and type 1 collagen expression in rat cardiac microvascular endothelial cells by interleukin-1 and its dependence on oxygen-centered free radicals. Circulation 1998;97:2175–82.
27. Stone GW, Peterson M, Lansky AJ, et al. Impact of normalized myocardial perfusion after successful angioplasty in AMI. J Am Coll Cardiol 2002;39:591–7.