Spontaneous reperfusion in ST-elevation myocardial infarction: Comparison of angiographic and electrocardiographic assessments

Kevin R. Bainey, MD,[a] Yuling Fu, MD,[a] Galen S. Wagner, MD,[b] Shaun G. Goodman, MD,[c] Allan Ross[d] Christopher B. Granger, MD,[b] Frans Van de Werf, MD,[e] and Paul W. Armstrong, MD[a] for the ASSENT 4 PCI Investigators ***Edmonton, Alberta and Toronto, Ontario, Canada; Durham; NC; Washington, DC and Leuven, Belgium***

Introduction Spontaneous reperfusion (SR) in ST-elevation myocardial infarction has traditionally been assessed by coronary angiography. The frequency of SR varies widely in prior studies, and the clinical implications in the modern reperfusion era are unclear. Accordingly, using data from the ASSENT 4 PCI (ASsessment of the Safety and Efficacy of a New Treatment Strategy with Percutaneous Coronary Intervention) study, we undertook a systematic assessment of SR using both electrocardiographic (ECG) and angiographic techniques.

Methods and Results Five hundred eighty-five patients randomized to the primary percutaneous coronary intervention (PCI) arm of ASSENT 4 PCI were studied: all had ECG and thrombolysis in myocardial infarction flow data available approximately 60 minutes after randomization and before PCI. Electrocardiographic SR (≥70% ST-segment resolution) occurred in 14.9% (87/585) and angiographic SR (thrombolysis in myocardial infarction grade 3) in 14.7% (86/585) of patients. Thirty-day clinical outcomes of patients with ECG SR versus no ECG SR tended to have lower mortality (0% vs 3.4%, $P = .091$), a lower composite of death/shock/congestive heart failure (6.9% vs 12.2%, $P = .148$), and significant reductions in death/reinfarction (0% vs 5.6%, $P = .014$). By contrast, no such differences were evident in patients with angiographic SR versus no SR for death (2.3% vs 3.0%, $P = 1.00$), death/shock/congestive heart failure (9.3% vs 11.8%, $P = .498$), or death/reinfarction (2.3% vs 5.2%, $P = .409$).

Conclusions Whereas the frequency of SR was comparable using either ECG or angiographic criteria, clinical outcomes were best aligned with ECG SR. These data support the role of the ECG in assessing reperfusion and likely reflect the overall impact of myocardial perfusion versus infarct-related artery epicardial patency alone. (Am Heart J 2008;156:248-55.)

The mainstay of therapy for patients with an ST-elevation acute myocardial infarction (STEMI) is early reperfusion by either pharmacologic or mechanical intervention to restore epicardial coronary blood flow to the infarct-related artery (IRA). Yet, it is appreciated that some patients undergo early spontaneous reperfusion (SR) before receiving reperfusion therapy. More than a quarter century ago, De Wood et al[1] reported that 12.7% of patients presenting with a STEMI had a patent IRA on angiography 4 hours after the onset of chest pain. Subsequent studies have reported SR incidence rates ranging from 4% to 57%.[2-8] In part, the discrepancy likely relates to both the timing of assessments and/or diverse definitions of SR. Coronary angiography is the traditional criterion standard for assessment of SR and is supported by the improved prognosis of patients with enhanced thrombolysis in myocardial infarction (TIMI) flow grade of the epicardial IRA after fibrinolytic therapy.[9] More recently, the electrocardiogram (ECG) has been used to determine SR as the occurrence of spontaneous ST-segment resolution before any intervention has also been associated with improved clinical outcomes.[2,8] Yet, there has been no direct comparison of SR using these 2 diagnostic modalities. Accordingly, in a unique data set derived from STEMI patients randomized to receive primary percutaneous coronary intervention (PCI) in the ASSENT 4 PCI (Assessment of the Safety and Efficacy of a New Thrombolytic) study, we evaluated the frequency and prognostic implications of SR using systematic and independently analyzed ECG and angiographic assessments.

Methods

The ASSENT 4 PCI trial has previously been described.[10] Briefly, 1,667 patients with ST-segment elevation acute

From the [a]University of Alberta, Edmonton, Alberta, Canada, [b]Duke Clinical Research Institute, Durham, NC, [c]University of Toronto and the Canadian Heart Research Centre, Toronto, Ontario, Canada, [d]Washington, DC, and [e]University Hospital Gasthuisberg, Leuven, Belgium.

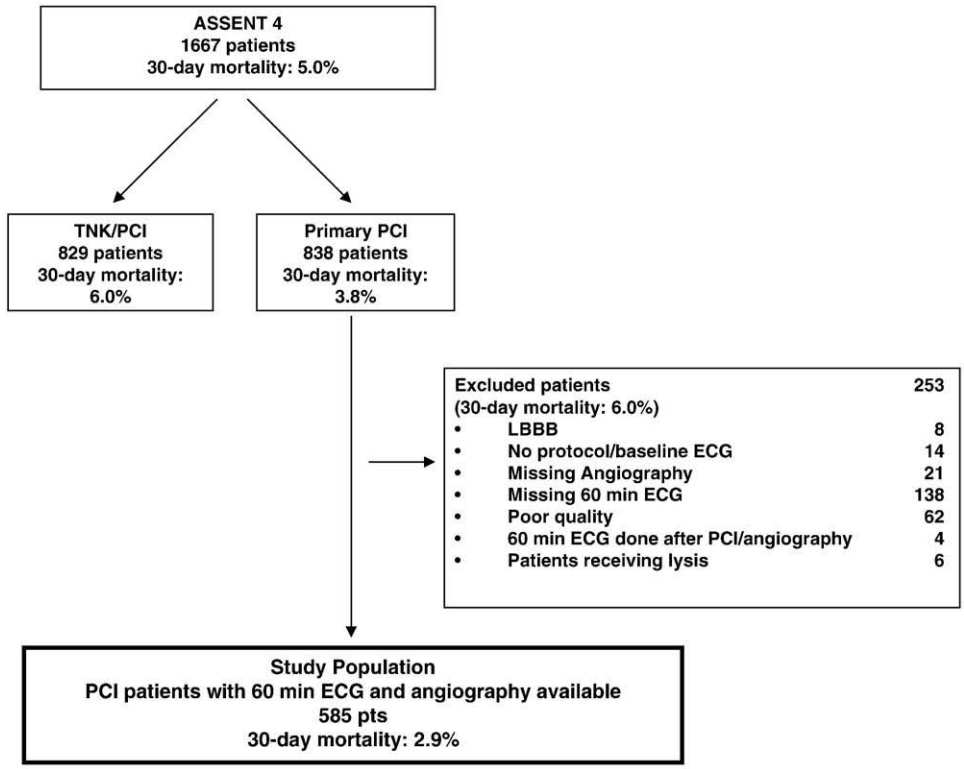
Submitted January 21, 2008; accepted March 12, 2008.

Reprint requests: Paul W. Armstrong, MD, Division of Cardiology, University of Alberta, 251 Medical Sciences Building Edmonton, Alberta Canada T6G 2H7.
E-mail: paul.armstrong@ualberta.ca

0002-8703/$ - see front matter

doi:10.1016/j.ahj.2008.03.018

Figure 1



Disposition of patients and their 30-day mortality.

myocardial infarction of less than 6 hours, scheduled to undergo primary PCI, were randomized to a standard PCI procedure or one preceded by full-dose tenecteplase administration (facilitated PCI). The primary end point was a combination of death, shock, or congestive heart failure (CHF) within 90 days. Congestive heart failure and shock were centrally adjudicated by a clinical event committee unaware of the allocated treatment and defined as is described in the original manuscript.[10] Other end points included reinfarction, which was not adjudicated but defined as per previous ASSENT trials.[11,12] All patients received 150 to 325 mg of aspirin and a single intravenous bolus of unfractionated heparin (70 U/kg without a maximum dose in primary PCI). If required, additional intravenous heparin was given according to the activated clotting time at the time of angiography. The use of a glycoprotein IIb/IIIa antagonist was left to the discretion of the investigator at the time of primary PCI. If a stent was deployed, a loading dose of clopidogrel was used, followed by a maintenance dose of 75 mg daily. Electrocardiographic criteria for admission were ST-segment elevation ≥0.6 mV across multiple leads or, for inferior infarction, a total of ≥0.6 mV ST-segment deviation, provided ≥0.4 mV ST-segment elevation was present in leads II, III, and aVF.

The current study is restricted to the 585 patients randomized to the primary PCI arm of ASSENT 4 PCI, with a 12-lead ECG recorded at baseline and 60 minutes thereafter, who then underwent immediate coronary angiography. The ST-segment measurements were evaluated centrally without knowledge of treatment assignment or clinical outcome at the ECG core laboratories (Canadian VIGOUR Centre, University of Alberta, Edmonton, Alberta, Canada; Canadian Heart Research Center, Toronto, Ontario, Canada; and Duke Clinical Research Institute, Durham, NC). Thrombolysis in myocardial infarction (TIMI) flow grade from the preinterventional angiogram was assessed by the site principal investigators. In Figure 1, the derivation of the patient population and the basis for any exclusions are provided.

Electrocardiographic analysis

The amount of ST-segment elevation was measured at the J point with magnified calipers from leads I, aVL, and V_1 to V_6 for anterior myocardial infarction, and leads II, III, aVF, V_5, and V_6 for inferior myocardial infarction (MI). For the total ST-segment deviation, the sum of the ST-segment depression in leads II, III, and aVF for anterior and that in V_1 to V_4 for inferior myocardial infarction was added. The resolution of ST-segment elevation (or total deviation if present) at 60 minutes was classified according to the Schroder's method[13]: complete (ie, resolution of the initial sum of ST-segment elevation ≥70%), partial (ie, ST-segment resolution <70% to 30%), and none (ie, ST-segment resolution <30%). Electrocardiographic SR was defined as those patients who achieved complete (≥70%) ST-segment resolution.

Table I. Baseline characteristics according to each reperfusion method

	ECG		Angiography	
	SR (≥70% STR)	**No-SR (<70% STR)**	**SR (TIMI = 3)**	**No-SR (TIMI <3)**
n	87 (14.9%)	498 (85.1%)	86 (14.7%)	499 (85.3%)
Age (y)	58 (49, 68)	59 (50, 68)	60 (51, 69)	59 (50, 68)
Female (%)	26.4	22.1	32.6*	21.0
Weight (kg)	74 (63, 85)	77 (70, 86)	73 (65, 83)*	77 (70, 86)
Hypertension (%)	40.2	46.2	44.2	45.5
Diabetes (%)	10.3	16.9	25.6*	14.2
Previous myocardial infarction (%)	11.6	10.6	12.8	10.4
Prior coronary artery bypass graft (%)	1.2	1.4	2.3	1.2
Prior PCI (%)	8.1	8.7	5.8	9.1
Current smoker (%)	58.5	47.8	47.0	49.8
Chronic treatment with ASA (%)	14.0	18.5	29.1*	15.9
Killip class I (%)	94.3	93.8	98.8*	93.0
Systolic blood pressure (mm Hg)	135 (120, 150)	134 (120, 150)	130 (120, 150)	135 (120, 150)
Heart rate (beats/min)	77 (66, 88)	75 (64, 86)	80 (66, 90)	75 (64, 86)
∑ST baseline (mm)	12 (9, 20)	13 (9, 19)	13 (8, 16)	13 (9, 19)
Infarct location by ECG				
Noninferior (%)	39.0	49.0	52.3	46.7
Infarct location by angiography				
LAD (%)	35.6	45.0	44.2	43.5
LCx (%)	12.6	11.4	7.0	12.4
RCA (%)	51.7	41.8	41.9	43.5
Other (%)	0.0	1.8	7.0	0.6
Time from symptom onset—60-min ECG (min)	220 (157, 305)	215 (155, 294)	204 (147, 310)	215 (158, 293)
Time from symptom onset—angiography (min)	242 (190, 327)	245 (185, 325)	247 (184, 337)	245 (190, 323)

*$P \leq .03$; for comparison of SR versus no SR within each reperfusion method. Data are medians with interquartile ranges. *STR*, ST resolution.

Thrombolysis in myocardial infarction flow grade analysis

All patients in the current study received a preinterventional angiogram immediately after the 60-minute ECG. Thrombolysis in myocardial infarction flow grade of the IRA before PCI (first contrast injection) was recorded according to protocol. Patients were divided into 3 angiographic groups: (1) TIMI flow grade 0 to 1, (2) TIMI flow grade 2, and (3) TIMI flow grade 3. Angiographic SR was defined as achievement of TIMI 3 flow and assessed by the site investigators.

Statistical analysis

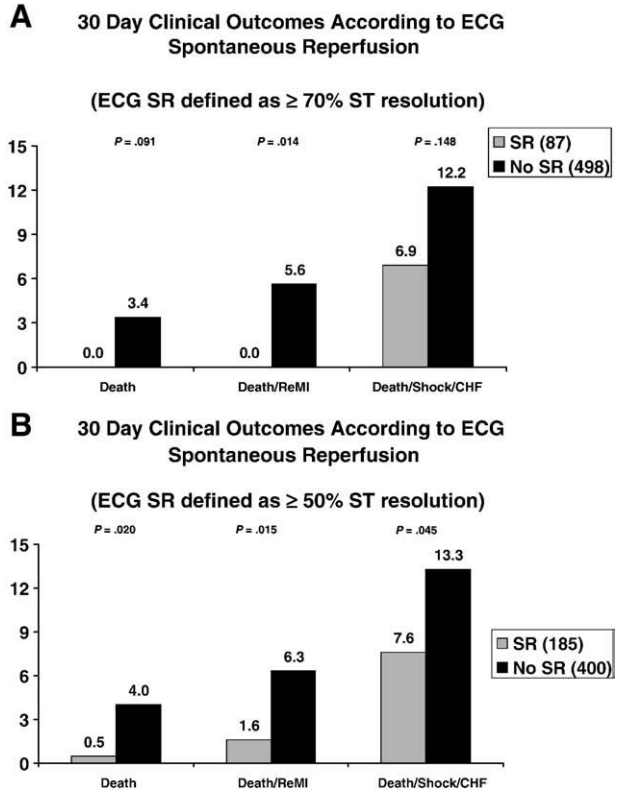
Descriptive statistics were summarized as medians with 25th and 75th percentiles for continuous variables, and the Mann-Whitney *U* test was used for group comparisons. For categorical variables, the data were summarized in percentages and χ^2 testing used to assess group differences. Multivariable logistic regression, using backward stepwise variable selection procedures, was used to assess the independent prognostic value of SR for 30-day composite end point of death, shock, or CHF adjusted for clinical key risk factors, which included age, sex, presence of hypertension or diabetes, current smoking, previous MI, systolic blood pressure, heart rate, location of infarction, Killip class, time from symptom onset to treatment, prior PCI, prior coronary artery bypass graft, chronic treatment with aspirin, and total ST- segment deviation at baseline. Congestive heart failure and shock were centrally adjudicated by a clinical event committee unaware of the allocated treatment. All tests were 2 sided, with a 5% level of significance. All analyses were performed using SPSS (Version 14; SPSS, Chicago, IL).

Results

Among the 585 patients, 14.9% had ECG SR and 14.7% had angiographic SR. In Table I, baseline demographic and clinical characteristics are shown according to each reperfusion method. Patient characteristics were generally similar irrespective of whether or not SR occurred and comparable between ECG and angiographic groups. However, patients with angiographic SR weighed less, were more likely to have prior diabetes and acetylsalicylic acid use, and be in Killip class I. In addition, female patients were more likely to have angiographic SR than male patients.

The median time intervals (25th and 75th percentiles) from symptom onset to the acquisition of the 60-minute ECG were 220 minutes (157,305) in patients with ECG SR and 215 minutes (155,294) for those without ECG SR ($P = .48$). The median time intervals (25th and 75th percentiles) from symptom onset to angiography was 247 minutes (184,337) in patients with angiographic SR

Figure 2



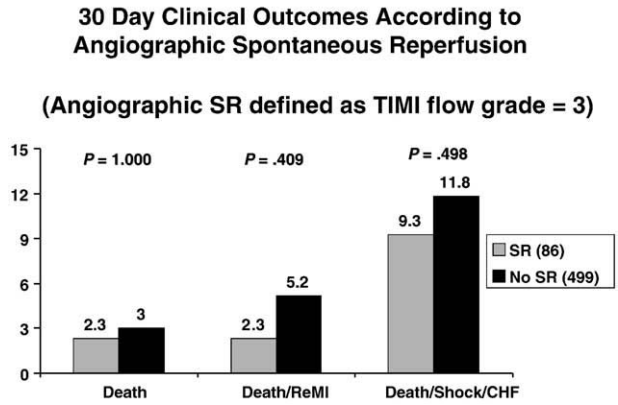
Thirty-day clinical outcomes of ECG SR. **A**, ECG SR defined as ≥70% ST-segment resolution. **B**, ECG SR defined as ≥50% ST-segment resolution.

Table II. Multivariate predictors of 30-day composite death/shock/CHF

	Odds ratio (95% CI)	*P*
Age (y)	1.06 (1.03-1.09)	<.001
Previous MI	2.76 (1.31-5.83)	.008
Noninferior MI	1.98 (1.11-3.55)	.021
Systolic BP (mm Hg)	0.99 (0.97-1.00)	.018
Time to treatment (h)	1.09 (0.99-1.20)	.084
∑ST at baseline (mm)	1.07 (1.04-1.10)	<.001
ECG SR (≥70% STR)	0.51 (0.20-1.27)	.147

BP, blood pressure.

Figure 3



Thirty-day clinical outcomes of angiographic SR defined as TIMI 3 flow.

versus 245 minutes (190,323) for those without angiographic SR (*P* = .91). The median time interval (25th and 75th percentile) between acquisition of the 60-minute ECG and initiation of the angiogram was 25 minutes (15, 42).

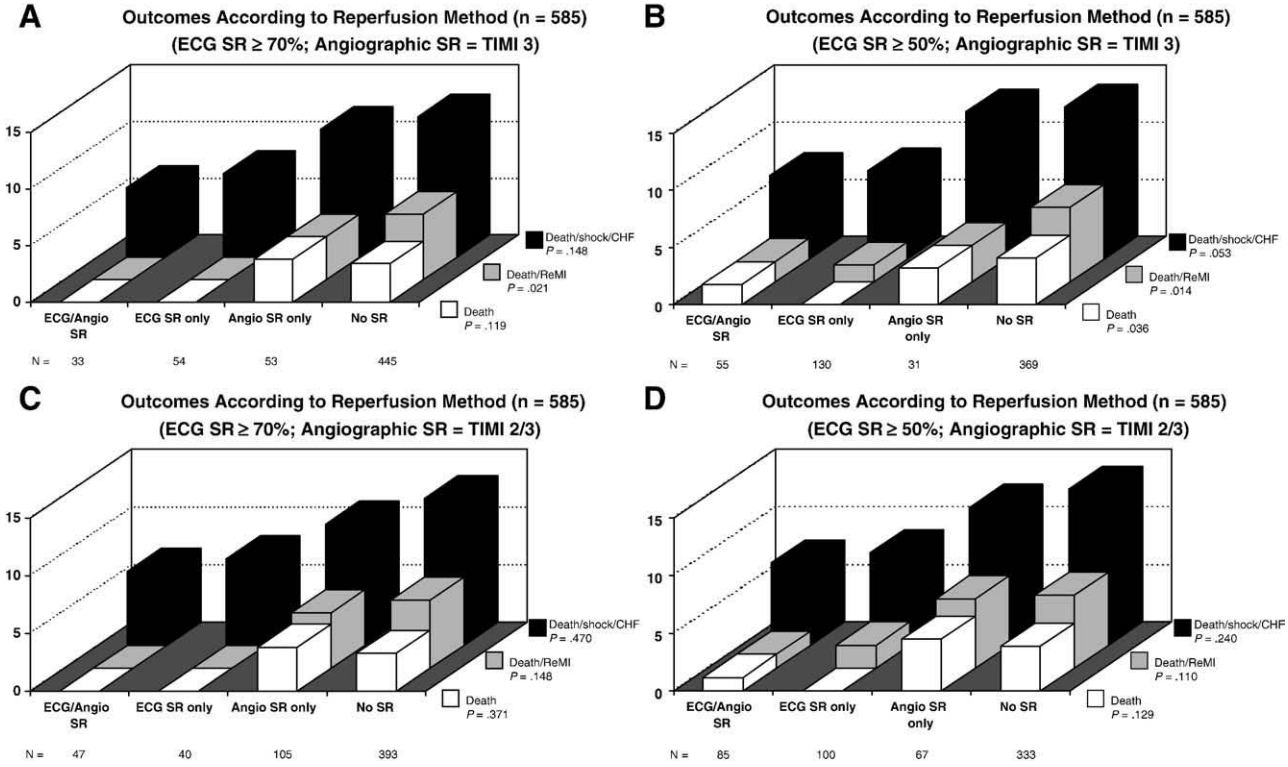
In Figure 2, *A*, 30-day clinical outcomes are shown for patients classified according to ECG SR (defined as ≥70% ST-segment resolution). Those with versus without ECG SR tended to have a lower mortality (0% vs 3.4%, *P* = .091) and a lower composite outcome of death/shock/CHF (6.9% vs 12.2%, *P* = .148). Patients with ECG SR also had a significantly lower rate of death/reinfarction (0% vs 5.6%, *P* = .014) compared with those without ECG SR. After adjustment for baseline key risk factors, the 30-day composite outcome of death/shock/CHF continued to show a trend toward significant reduction for patients with ECG SR (*P* = .147) (Table II).

As outlined in Figure 2, *B*, if ECG SR was defined as ≥50% ST-segment resolution[14] rather than ≥70%, similar findings were seen: ie, lower mortality (0.5% vs 4%, *P* = .020), death/reinfarction (1.6% vs 6.3%, *P* = .015), and death/shock/CHF (7.6% vs 13.3%, *P* = .045) with ECG SR. After baseline adjustment, the 30-day death and death/reinfarction were significantly lower in patients with ECG SR (*P* = .042, *P* = .021, respectively). As well, there was a strong trend toward significant reduction of death/shock/CHF in patients with ECG SR (*P* = .055).

In Figure 3, 30-day clinical outcomes are shown for patients classified according to angiographic SR (defined as TIMI 3 flow). There were no differences in death (2.3% vs 3.0%, *P* = 1.00), death/reinfarction (2.3% vs 5.2%, *P* = .409), or death/shock/CHF (9.3% vs 11.8%, *P* = .498) according to SR defined by angiography. When 30-day outcomes were evaluated using angiographic SR defined as TIMI 2 or 3 flow, similar results were seen, that is, no difference in death (2.6% vs 3.0%, *P* = 1.00), death/reinfarction (3.3 vs 5.3%, *P* = .383), or death/shock/CHF (9.2 vs 12.2%, *P* = .375).

Because there was diversity among patients relating to alignment with ECG and angiographic criteria for SR, 30-day clinical outcomes are depicted in Figure 4, *A* according to those who achieved SR by both study methods (ECG SR ≥ 70% ST-segment resolution; angiographic SR = TIMI 3 flow) (n = 33), ECG criteria alone

Figure 4



Thirty-day clinical outcomes according to reperfusion method. Note that the median time intervals between acquisition of the 60-minute ECG and initiation of the angiogram was 25 minutes for patients with both ECG and angiographic SR, 25 minutes for those with ECG SR only, 26.5 minutes for those with angiographic SR only, and 26 minutes for patients without SR. **A**, ECG SR defined as ≥70% ST-segment resolution; angiographic SR defined as TIMI 3 flow. **B**, ECG SR defined as ≥50% ST-segment resolution; angiographic SR defined as TIMI 3 flow. **C**, ECG SR defined as ≥70% ST-segment resolution; angiographic SR defined as TIMI 2 or 3 flow. **D**, ECG SR defined as ≥50% ST-segment resolution; angiographic SR defined as TIMI 2 or 3 flow.

(n = 54), angiographic criteria alone (n = 53), or neither criteria for SR (n = 445). Lower mortality was seen in patients whom either met both criteria for SR (0%) or ECG criteria alone (0%) compared with patients who met angiographic criteria alone (3.8%) or no criteria for SR (3.4%, $P = .119$). Similarly, no death/reinfarction was evident in patients with both criteria (0%) or ECG criteria alone (0%) as compared with those who achieved either angiographic SR (3.8%) or no SR (5.8%, $P = .021$). Lastly, reduced rates of death/shock/CHF were seen in patients whom either met both criteria for SR (6.1%) or ECG criteria alone (7.4%) compared with patients with just angiographic SR (11.3%) or no SR (12.4%, $P = .148$). Notably, only 37.9% of ECG SR patients also had angiographic SR, whereas 38.4% of angiographic SR patients had ECG SR.

If ECG SR is defined as ≥50% ST-segment resolution with angiographic SR represented as TIMI 3 flow, similar results were seen in patients with both criteria (n = 55) or ECG criteria alone (n = 130) versus angiographic criteria alone (n = 31) or no criteria for SR (n = 369) (Figure 4, *B*), that is, lower mortality (1.8%, 0% vs 3.2%, 4.1%, $P = .036$), reduced death/reinfarction (1.8%, 1.5% vs 3.2%, 6.5%, $P = .014$), and lower death/shock/CHF (7.3%, 7.7% vs 12.9%, 13.3%, $P = .053$).

If angiographic SR is defined as TIMI 2 or 3 flow with ECG SR measured as ≥70% ST-segment resolution, analogous findings were also seen in patients with both criteria (n = 47) or ECG criteria alone (n = 40) versus angiographic criteria alone (n = 105) or no criteria for SR (n = 393) (Figure 4, *C*), that is, reduced mortality (0%, 0%, vs 3.8%, 3.3%, $P = .371$), lower death/reinfarction (0%, 0%, vs 4.8%, 5.9%, $P = .148$), and reduced death/shock/CHF (6.4%, 7.5% vs 10.5%, 12.7%, $P = .470$).

Finally, if angiographic SR is defined as TIMI 2 or 3 flow with ECG SR measured as ≥50% ST-segment resolution, similar outcomes were still seen in patients with both criteria (n = 85) or ECG criteria alone (n = 100) versus angiographic criteria alone (n = 67) or no criteria for SR (n = 333) (Figure 4, *D*), that is, reduced mortality (1.2%,

Table III. Reported rates of SR

	SR definition	SR rate (%)	Timing of assessment (h)	n
De Wood et al[1]	Angiographic (any flow)	12.7	4.0	126
Steg et al[3]	Angiographic (TIMI = 3)	13.3	3.6	325
Christian et al[4]	Angiographic (TIMI 1-3)	57.0	18	21
Ross et al[5]	Angiographic (TIMI = 3)	15.0	2.2	304
Lee et al[6]	Angiographic (TIMI ≥2)	22.4	3.8	196
Stone et al[7]	Angiographic (TIMI = 3)	16.0	4.4	2507
Rimar et al[2]	ECG (>50% STR)	4.0	approximately 2.3	98
Terkelsen et al[8]	ECG (≥70% STR)	23.9	–	92
Bainey et al (current study)	Angiographic (TIMI = 3)	14.7	4.1	585
	ECG (≥70% STR)	14.9	4.2	

Timing of assessment, time from symptom onset to acquisition of the reperfusion (ECG/angiogram) assessment. *STR,* ST resolution.

0%, vs 4.5% 3.9%, $P = .129$), lower death/reinfarction (1.2%, 2.0% vs 6.0%, 6.3%, $P = .0110$), and reduced death/shock/CHF (7.1%, 8.0% vs 11.9%, 13.5%, $P = .240$).

Discussion

The results of our study, derived from a systematic analysis of ST-segment resolution and TIMI flow grade in 585 patients with STEMI randomized to primary PCI in the ASSENT 4 PCI study, provide new insight into the frequency and clinical implications of SR. Interestingly, although the rates of SR assessed by ECG and angiography were remarkably similar (15%), the clinical outcomes differed. Specifically, clinical outcomes best tracked SR defined by ECG criteria. Thus, the ECG, a simple, widely used, and readily applicable tool, not only offers early recognition of SR but also provides further risk stratification before the time of primary PCI.

Previous studies documenting the rates of SR before PCI have varied widely (Table III): this diversity likely relates to the timing of ascertainment, prior duration of symptoms, as well as differing definitions of SR. An advantage of the current study is the use of systematically applied SR definitions in a well-defined population, early proximal assessments in time, and close temporal relationships between ECG and angiographic methods revealing virtually identical SR rates of 15%.

The mechanism whereby SR occurs remains unclear and is likely multifactorial. In part, this may be due to an intrinsic pharmacologic response in patients who are able to achieve SR while on early aspirin and heparin therapy.[8,15] Experimental studies have suggested that adenosine may play a role in mediating vasomotor activity resulting in early perfused myocardium.[16] Preinfarct angina has been linked to enhanced SR,[2,6] possibly resulting from release of endogenous adenosine from ischemic/reperfused myocardium.[2,16] Because prior angina was not documented in ASSENT 4 PCI, we are unable to comment on this point. Other factors may include endogenous fibrinolytic activity affecting fibrinogen, tissue plasminogen activator and its inhibitor 1,[17] the size of the culprit thrombus, and the presence of recruitable collaterals.

Although the frequency of SR between the 2 different methods of assessing reperfusion were similar, the key finding of the present study is that early SR defined by the ECG best tracked 30-day clinical outcomes. Hence, ST-segment resolution provides additional prognostic insight over that already known to be established through angiographic patency.[18] This finding likely reflects the fact that ST-segment recovery in STEMI patients signals both epicardial vessel recanalization as well as microvascular flow at the cellular level.[19,20] Previously, ST-segment resolution has proven to be a powerful clinical predictor of 35-day, 6-month, 1-year, and long-term mortality.[18,20-22]

Of note in our study was that patients with anterior myocardial infarcts were less likely to achieve ECG SR. Similar findings have been observed in patients receiving pharmacologic reperfusion, that is, a 36% rate of complete ST-segment resolution in anterior infarcts using reteplase fibrinolytic therapy compared with a 65% success rate in those with inferior infarcts.[13] Prior results from the Global Utilization of Streptokinase and Tissue Plasminogen Activation for Occluded Coronary Arteries (GUSTO-I) angiographic study also found more patients with a patent IRA postfibrinolysis involving the right coronary artery (RCA) or left circumflex artery (LCx) (62%) as compared with the left anterior descending coronary artery (LAD) (32%).[23] This is in keeping with our study with ECG SR, that is, the culprit IRA most commonly was the RCA/LCx (64.3%) compared with the LAD (35.6%) artery. However, in those with angiographic SR, there was a more balanced distribution of IRA TIMI 3 flow between LAD (44.2%) and RCA/LCx (48.9%). Thus, spontaneous angiographic epicardial patency is just as likely to occur in the LAD or RCA/LCx distribution; yet, successful myocardial perfusion as defined by ST-segment resolution is less likely if the culprit artery is the LAD. The basis for this finding is unclear but could relate to a more extensive epicardial/myocardial jeopardized territory and larger potential for microvascular injury. Our finding that females were more likely to achieve angiographic SR is

consistent with that of Stone et al.[7] The basis for this is unclear but could represent pathophysiologic differences modulated by thrombotic burden or coronary tone and is deserving of further study.

It is noteworthy that angiographic SR was present in only 37.9% of patients with ECG SR providing further support to alternate mechanisms of myocardial perfusion such as the recruitment of coronary collaterals to the infarct zone. Alternatively, reocclusion of the IRA may have occurred in the interval between the 60-minute ECG and the angiogram—albeit, less likely, given angiography was performed in a timely fashion. Thus, in cases of discordance (ie, ECG SR without angiographic SR), the electrocardiogram appears to be a more reliable measure of improved clinical outcomes. Also, note that ECG SR was present in only 38.4% of patients with angiographic SR supporting the notion that a patent IRA does not always lead toward improved microvascular perfusion. Alternatively, this discrepancy could relate in part to angiographic SR occurring after the 60-minute ECG, although the interval between these was brief, that is, 25 minutes.

Our study has some limitations. We excluded 253 patients with incomplete electrocardiographic and TIMI flow grade data whose mortality was higher (Figure 1). This likely relates to a higher risk group with early morbidity precluding acquisition of complete study data, and it is feasible that they were less likely to experience SR. It is conceivable that the rates of SR we observed might have been greater with the use of clopidogrel loading and heparin infusions coupled with the initial bolus. Although TIMI flow grades were determined by site investigators, our angiographic data correspond well with core angiographic SR data from other studies[3,5,7] that report similar angiographic SR rates. Provision of other angiographic measures to assess microvascular/myocardial tissue perfusion such as myocardial blush grade or TIMI frame count might have altered our results; yet, our intent was to use a simple noninvasive tool (ie, the ECG) to predict clinical outcomes. The presence of coronary collateral circulation was not recorded in our study. Although every attempt was made to perform angiography immediately after the 60-minute ECG, there was a median time delay of 25 minutes between assessments. Lastly, although clinical outcomes were best aligned with the occurrence of ECG SR, our study was a subgroup analysis not adequately powered to definitively prove this point and, thus, deserves confirmation.

In an era where much emphasis is placed upon the success of reperfusion (pharmacologic vs mechanical) in STEMI, it is key to appreciate the proportion of patients who will achieve SR. Incorporating this understanding into future management strategies and the interpretation of clinical trials will provide better estimates of the efficacy of planned interventions.

References

1. De Wood MA, Spores J, Notske R, et al. Prevalence of total coronary occlusion during the early hours of transmural myocardial infarction. N Engl J Med 1980;303:897-902.
2. Rimar D, Crystal E, Battler A, et al. Improved prognosis of patients presenting with clinical markers of spontaneous reperfusion during acute myocardial infarction. Heart 2002;88:352-6.
3. Steg PG, Himbert D, Benamer H, et al. Conservative management of patients with acute myocardial infarction and spontaneous acute patency of the infarct-related artery. Am Heart J 1997;134: 248-52.
4. Christian TF, Milavetz JJ, Miller TD, et al. Prevalence of spontaneous reperfusion and associated myocardial salvage in patients with acute myocardial infarction. Am Heart J 1998;135: 421-7.
5. Ross AM, Coyne KS, Reiner JS, et al. A randomized trial comparing primary angioplasty with a strategy of short-acting thrombolysis and immediate planned rescue angioplasty in acute myocardial infarction: the PACT trial. J Am Coll Cardiol 1999;34: 1954-62.
6. Lee CW, Hong MK, Lee JH, et-al. Determinants and prognostic significance of spontaneous coronary recanalization in acute myocardial infarction. Am J Cardiol 2001;87:951-4, A953.
7. Stone GW, Cox D, Garcia E, et al. Normal flow (TIMI-3) before mechanical reperfusion therapy is an independent determinant of survival in acute myocardial infarction: analysis from the primary angioplasty in myocardial infarction trials. Circulation 2001;104: 636-41.
8. Terkelsen CJ, Norgaard BL, Lassen JF, et al. Potential significance of spontaneous and interventional ST-changes in patients transferred for primary percutaneous coronary intervention: observations from the ST-MONitoring in Acute Myocardial Infarction study (The MONAMI study). Eur Heart J 2006;27: 267-75.
9. Simes RJ, Topol EJ, Holmes Jr DR, et al. Link between the angiographic substudy and mortality outcomes in a large randomized trial of myocardial reperfusion. Importance of early and complete infarct artery reperfusion. GUSTO-I Investigators. Circulation 1995;91:1923-8.
10. Assessment of the Safety and Efficacy of a New Treatment Strategy with Percutaneous Coronary Intervention (ASSENT-4 PCI) Investigators. Primary versus tenecteplase-facilitated percutaneous coronary intervention in patients with St-segment elevation acute myocardial infarction (ASSENT-4 PCI): randomized trial. Lancet 2006;367:569-78.
11. Assessment of the Safety and Efficacy of a New Thrombolytic Regimen (ASSENT-3) Investigators. Efficacy and safety of tenecteplase in combination with enoxaparin, abciximab, or unfractionated heparin: the ASSENT-3 randomised trial in acute myocardial infarction. Lancet 2001;358: 605-13.
12. Assessment of the Safety and Efficacy of a New Thrombolytic Investigators. Single-bolus tenecteplase compared with front-loaded alteplase in acute myocardial infarction: the ASSENT-2 double-blind randomized trial. Lancet 1999;354:716-22.
13. Schroder R, Wegscheider K, Schroder K, et al, for the INJECT trial group. 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.

14. Purcell IF, Newall N, Farrer M. Change in ST segment elevation 60 minutes after thrombolytic initiation predicts clinical outcome as accurately as later electrocardiographic changes. Heart 1997;78: 465-71.
15. Zijlstra F, Ernst N, de Boer MJ, et al. Influence of prehospital administration of aspirin and heparin on initial patency of the infarct-related artery in patients with acute ST elevation myocardial infarction. J Am Coll Cardiol 2002;39:1733-7.
16. Hata K, Whittaker P, Kloner RA, et al. Brief antecedent ischemia attenuates platelet-mediated thrombosis in damaged and stenotic canine coronary arteries: role of adenosine. Circulation 1998;97: 692-702.
17. Margaglione M, Grandone E, Di Minno G. Plasma predictors of ischemic complications of atherosclerosis: open issues. Biomed Pharmacother 1993;47:445-9.
18. Andrews J, Straznicky IT, French JK, et al. ST-segment recovery adds to the assessment of TIMI 2 and 3 flow in predicting infarct wall motion after thrombolytic therapy. Circulation 2000;101: 2138-43.
19. Roe MT, Ohman EM, Maas AC, et al. Shifting the open-artery hypothesis downstream: the quest for optimal reperfusion. J Am Coll Cardiol 2001;37:9-18.
20. de Lemos JA, Braunwald E. ST segment resolution as a tool for assessing the efficacy of reperfusion therapy. J Am Coll Cardiol 2001; 38:1283-94.
21. Schroder K, Wegscheider K, Zeymer U, et al. 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.
22. van't Hof AW, Liem A, de Boer M, et al. Clinical value of 12-lead electrocardiogram after successful reperfusion therapy for acute myocardial infarction. Lancet 1997;350:615-9.
23. Lundergan CF, Reiner JS, McCarthy WF, et al. Clinical predictors of early infarct-related artery patency following thrombolytic therapy: importance of body weight, smoking history, infarct-related artery and choice of thrombolytic regimen: the GUSTO-I experience. J Am Coll Cardiol 1998;32: 641-7.

Correction

In the article "Effects of pioglitazone on major adverse cardiovascular events in high-risk patients with type 2 diabetes: Results from PROspective pioglitAzone Clinical Trial In macro Vascular Events (PROactive 10)," by Wilcox et al in the April 2008 issue of *American Heart Journal* (*Am Heart J* 2008;712-717), there is an error in the Methods section. The fourth bulleted item on page 713 currently reads "Peripheral arterial obstructive disease of the leg (previous leg amputation above the ankle, or intermittent claudication with an ankle or toe brachial pressure index >0.9." "The value at the end of the sentence should actually be <0.9 and thus the sentence should correctly read as follows: "Peripheral arterial obstructive disease of the leg (previous leg amputation above the ankle, or intermittent claudication with an ankle or toe brachial pressure index <0.9."