

# 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

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**Background**—Whereas survival after lytic therapy for myocardial infarction is strongly dependent on early administration, it is unknown whether the otherwise excellent outcomes in patients undergoing primary PTCA for acute myocardial infarction, in whom TIMI-3 flow rates of >90% may be achieved, can be further improved by early reperfusion.

**Methods and Results**—Among 2507 patients enrolled in 4 PAMI trials undergoing primary PTCA, spontaneous reperfusion (TIMI-3 flow) was present in 16% at initial angiography. Compared with patients without TIMI-3 flow, those with TIMI-3 flow before PTCA had greater left ventricular ejection fraction ( $57 \pm 10\%$  versus  $53 \pm 11\%$ ,  $P=0.003$ ) and were less likely to present in heart failure (7.0% versus 11.6%,  $P=0.009$ ). Patients with initial TIMI-3 flow had significantly lower in-hospital rates of mortality, new-onset heart failure, and hypotension and had a shorter hospital stay. Cumulative 6-month mortality was 0.5% in patients with initial TIMI-3 flow, 2.8% with TIMI-2 flow, and 4.4% with initial TIMI-0/1 flow ( $P=0.009$ ). By multivariate analysis, TIMI-3 flow before PTCA was an independent determinant of survival (odds ratio 2.1,  $P=0.04$ ), even when corrected for by postprocedural TIMI-3 flow.

**Conclusions**—Patients undergoing primary PTCA in whom TIMI-3 flow is present before angioplasty present with greater clinical and angiographic evidence of myocardial salvage, are less likely to develop complications related to left ventricular failure, and have improved early and late survival. These data warrant prospective randomized trials of pharmacological strategies to promote early reperfusion before definitive mechanical intervention in acute myocardial infarction. (*Circulation*. 2001;104:636-641.)

**Key Words:** angioplasty ■ survival ■ myocardial infarction ■ reperfusion

By restoring high rates of normal antegrade epicardial (Thrombolysis In Myocardial Infarction grade 3 [TIMI-3]) flow and avoids intracranial bleeding, primary PTCA has been shown to improve survival in patients with acute myocardial infarction (AMI) compared with thrombolytic therapy.<sup>1</sup> Nonetheless, the inherent delay from hospital arrival to angioplasty, which averages  $\approx 2$  hours in the United States,<sup>2-10</sup> is considered a major drawback of primary PTCA and may adversely affect survival.<sup>3,11</sup> It has therefore been suggested that early pharmacological reperfusion before angiography and definitive mechanical intervention when appropriate (so-called facilitated primary angioplasty<sup>12,13</sup>) may further improve outcomes in AMI. If this theory is true, the outcomes of patients presenting to the cardiac catheterization laboratory with spontaneous TIMI-3 flow before primary PTCA should be improved compared with those in whom angioplasty is required to establish patency. This has not been demonstrated conclusively.

### See p 624

To determine the impact of TIMI-3 flow before angioplasty on early and late outcomes of a mechanical reperfusion strategy in patients with AMI, we examined the pooled database of 2507 consecutive acute infarct procedures from the 4 major Primary Angioplasty in Myocardial Infarction (PAMI) trials.

### Methods

Data from the 4 major PAMI trials (PAMI-1,<sup>4,5</sup>  $n=195$ ; PAMI-2,<sup>6,7</sup>  $n=1100$ ; PAMI Stent Pilot,<sup>8,9</sup>  $n=312$ ; and the PAMI Stent Randomized Trial,<sup>10</sup>  $n=900$ ) were pooled in a computerized database. The major entry criteria of these trials were similar and deliberately nonrestrictive<sup>4-10</sup>; patients of any age were enrolled with evidence of AMI of <12 hours' duration. ECG criteria for entry included  $\geq 1$  mm of ST-segment elevation or left bundle branch block in PAMI-1; any ECG patterns consistent with the clinical syndrome of AMI were permitted in the other 3 trials, provided that acute

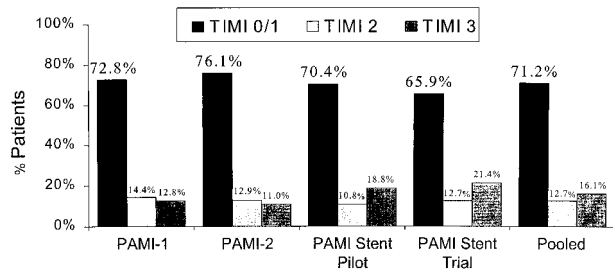
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**Figure 1.** TIMI flow grades present at initial angiography in each of 4 major PAMI trials and pooled.

catheterization documented an occluded vessel with associated wall-motion abnormality. Major exclusion criteria consisted of cardiogenic shock, absolute contraindications to aspirin or heparin (and ticlopidine in the stent trials), prior use of thrombolytic therapy during the same hospitalization, and refusal or inability to provide written, informed consent. After arteriography and left ventriculography, PTCA was performed if appropriate with standard equipment and techniques.<sup>2,4–10,14</sup> However, per protocol, PTCA was deferred in selected patients for either medical therapy or bypass surgery on the basis of anatomic and clinical considerations.<sup>2,4–10,14</sup>

### Definitions

Reinfarction was defined as recurrent clinical symptoms in association with any increase in creatine kinase-MB above its previous nadir. Recurrent ischemia was defined as clinical symptoms associated with either new ECG ST-segment or T-wave changes, hypotension, new murmur, creatine kinase-MB elevation, or necessity for urgent repeat PTCA or CABG. Target-vessel revascularization was defined as the performance of CABG or repeat percutaneous intervention of the infarct vessel after the index procedure.

### Data Collection and Statistical Analysis

Clinical data were collected prospectively by research nurses and verified at each site by study monitors. Follow-up was performed by physician office visits and study nurse interview. All adverse events were adjudicated by an independent data coordinating center after review of original source documentation. Antegrade blood flow in the infarct vessel was evaluated with the TIMI scale<sup>15</sup> at independent core angiographic laboratories in each study<sup>5–10</sup> (William Beaumont Hospital, Royal Oak, Mich, in PAMI-1 and PAMI-2; The Washington, DC, Hospital Center in the PAMI Stent Pilot trial; and Cardialysis in Rotterdam, the Netherlands, and the Washington, DC, Hospital Center in the PAMI Stent Randomized trial). Identical methodology was used to grade TIMI flow at the 3 laboratories; specifically, TIMI-3 flow was uniformly defined as complete filling of the distal vessel by the third cardiac cycle.

Categorical variables were compared by  $\chi^2$  analysis or Fisher's exact test. Continuous variables are presented as mean  $\pm$  SD and were compared by Student's *t* test or Mann-Whitney *U* test. All probability values are two-tailed. Follow-up clinical events were analyzed with actuarial methods, and Kaplan-Meier curves were constructed. The influence of baseline demographic and angiographic variables on mortality during the follow-up period was evaluated with the log rank test. Cox proportional hazard regression was then used to determine the independent predictors of late adverse events.

## Results

### Coronary Blood Flow in the Infarct Vessel Before Mechanical Intervention

Of 2507 index procedures, 2327 films (93%) were technically adequate for core laboratory TIMI flow determination. As seen in Figure 1, angiographic TIMI flow rates before PTCA were similar among the 4 studies; TIMI-3 flow was present before PTCA in 15.7% of infarct vessels, TIMI-2 flow was

**TABLE 1. Baseline Characteristics in Patients With TIMI 0–2 Flow vs TIMI-3 Flow Before Intervention**

	TIMI 0–2 (n=1952)	TIMI 3 (n=375)	P
<b>Clinical features</b>			
Age, y	60.3 $\pm$ 12.0	59.7 $\pm$ 12.6	NS
Female sex, %	24.8	31.5	0.007
Hypertension, %	44.5	47.8	NS
Diabetes, %	14.8	18.2	NS
Hyperlipidemia, %	38.5	42.6	NS
Current cigarette use, %	40.8	43.3	NS
Prior bypass surgery, %	3.7	2.7	NS
Prior myocardial infarction, %	14.3	15.2	NS
Killip class 2–3, %	11.6	7.0	0.009
SBP, mm Hg	112 $\pm$ 23	113 $\pm$ 24	NS
Heart rate, bpm	85 $\pm$ 20	86 $\pm$ 21	NS
Chest pain to hospital, min	160 $\pm$ 150	151 $\pm$ 182	NS
Chest pain to angiography, min	261 $\pm$ 175	264 $\pm$ 200	NS
<b>Angiographic characteristics</b>			
Infarct vessel=LAD, %	38.7	39.4	NS
Infarct vessel=SVG, %	1.7	1.6	NS
Baseline diameter stenosis, %	96 $\pm$ 10	70 $\pm$ 14	<0.0001
Three-vessel disease, %	17.4	15.7	NS
LVEF, %	53 $\pm$ 11	57 $\pm$ 10	0.003

SBP indicates systolic blood pressure; LAD, left anterior descending artery; and SVG, saphenous vein graft.

found in 12.6% of vessels, and the remainder of infarct arteries were occluded. Compared with patients without TIMI-3 flow at baseline, patients with TIMI-3 flow before PTCA were more likely to be women and had less evidence of heart failure and left ventricular dysfunction at presentation (Table 1).

### Impact of Baseline TIMI-3 Flow on Procedural and In-Hospital Outcomes

Compared with patients with TIMI-0 to -2 flow before intervention, patients with TIMI-3 flow at baseline were less likely to undergo intervention but more likely to leave the catheterization laboratory with TIMI-3 flow (Table 2). Stent use was also more frequent in patients with TIMI-3 flow before intervention, although the final core laboratory–determined diameter stenosis was similar in both groups.

In-hospital mortality was significantly lower in patients with higher grades of TIMI flow before intervention (2.6% mortality with baseline TIMI-0/1 flow, 1.5% with TIMI-2 flow, and 0.5% with TIMI-3 flow,  $\chi^2$  *P* for trend=0.027). As seen in Table 2, patients with baseline TIMI-3 flow were also less likely to develop heart failure or hypotension or to require intubation and had a shorter hospital stay than patients with TIMI-0 to -2 flow before intervention.

### Effect of Baseline TIMI Flow on Long-Term Mortality

Similar to in-hospital mortality, 6-month mortality was lowest in patients with TIMI-3 flow at baseline, intermediate in

**TABLE 2. Impact of Baseline TIMI Flow on In-Hospital Outcomes**

	TIMI 0–2 (n=1952)	TIMI 3 (n=375)	P
<b>Procedural outcomes</b>			
PTCA performed, %	98.3	95.2	0.002
Stent implantation (PTCA patients), %	30.8	40.6	0.0006
IIb/IIIa inhibitor used (PTCA patients), %	2.8	3.9	NS
Final TIMI-3 flow (all patients), %	91.4	98.1	<0.0001
Final diameter stenosis (all patients), %	24±14	23±13	NS
<b>In-hospital outcomes</b>			
Death, %	2.4	0.5	0.02
Reinfarction, %	2.6	1.3	NS
Stroke, %	0.5	0.8	NS
New-onset congestive heart failure,* %	11.2	6.7	0.002
New-onset sustained hypotension,* %	5.2	1.6	0.002
Intubation, %	2.0	0.3	0.02
Major arrhythmia,† %	8.1	5.4	NS
Target-vessel revascularization, %	9.5	10.1	NS
Hospital days	6.2±4.7	4.6±3.2	<0.0001

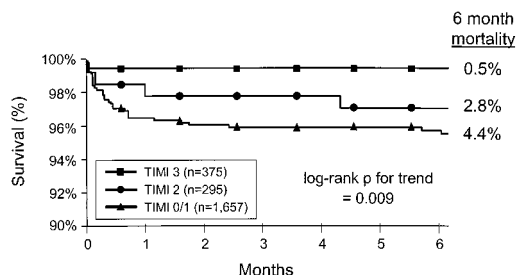
\*New onset in patients not presenting with these conditions before angiography.

†Sustained ventricular tachycardia, ventricular fibrillation, or bradycardia/conduction block requiring pacemaker insertion.

patients with initial TIMI-2 flow, and highest in patients with baseline TIMI-0/1 flow (Figure 2). By Cox proportional hazards regression, independent baseline determinants of late mortality were advanced age, female sex, anterior myocardial infarction location, triple-vessel disease, and preintervention TIMI flow <3 (Table 3). When baseline left ventricular ejection fraction (LVEF) was entered into this model as a continuous variable (available by core laboratory measurement in 63% of patients), reduced LVEF was an independent determinant of mortality (risk ratio=1.12,  $P=0.02$ ), and baseline TIMI flow <3 was of borderline significance (risk ratio=1.7,  $P=0.09$ ).

### Interaction of TIMI-3 Antegrade Flow Before and After Intervention on Mortality

Restoration of TIMI-3 flow after the procedure was also a powerful predictor of survival; 6-month mortality was 22.2% with final TIMI 0/1 flow, 6.1% with TIMI-2 flow, and 2.6% with final TIMI-3 flow ( $P<0.0001$ ). As seen in Figure 3,



**Figure 2.** Cumulative (in-hospital plus late) survival after primary PTCA in AMI stratified by initial TIMI flow grades. Mortality strongly correlated with TIMI flow before intervention.

**TABLE 3. Multivariate Baseline Predictors of Cumulative Mortality**

	Risk Ratio (95% CI)	P
Age (continuous)	1.06 (1.02, 1.10)	<0.0001
Anterior MI location	4.6 (2.1, 10.0)	<0.0001
Female sex	3.3 (1.6, 6.7)	0.0008
Triple-vessel disease	2.5 (1.2, 5.6)	0.01
Preintervention TIMI 0–2 flow	2.1 (1.2, 36.8)	0.04

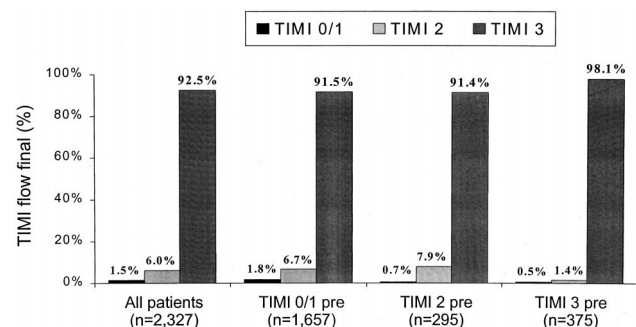
MI indicates myocardial infarction.

Unrelated to mortality in this model were diabetes, hypertension, hyperlipidemia, cigarette smoking, prior MI, time from symptom onset to emergency department arrival, admission Killip class, and admission hypotension or tachycardia.

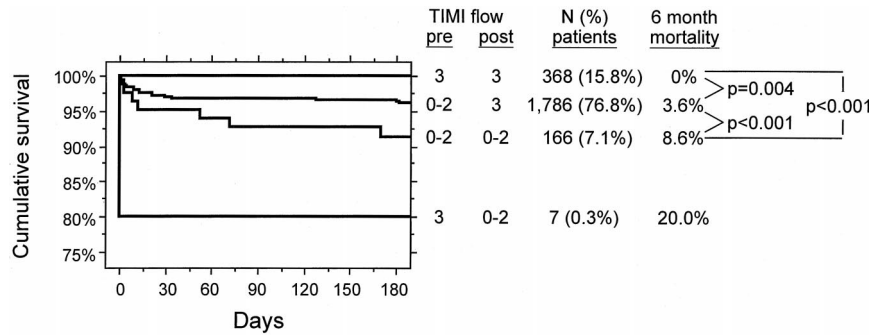
normal antegrade TIMI-3 flow was more likely to be present at the end of the interventional procedure if TIMI-3 flow was also present before the angioplasty (98.1% with TIMI-3 flow before versus 91.5% with TIMI-0 to -2 before,  $P<0.0001$ ). Early and late survival were significantly affected by the normalcy of epicardial coronary blood flow present both before and after the procedure (Figure 4). Of note, among patients leaving the catheterization laboratory with TIMI-3 flow, 6-month mortality was 0% in patients presenting with TIMI-3 flow versus 3.6% in patients with lesser initial degrees of epicardial flow ( $P=0.004$ ). When the postprocedural TIMI flow grade was entered into the multivariate analysis of cumulative mortality, the presence of TIMI-3 flow before intervention was a more powerful predictor of survival than TIMI-3 flow after intervention (Table 4).

### Discussion

The alliance of pharmacological and mechanical approaches for AMI reperfusion, as embodied in the facilitated primary PTCA strategy, is currently an area of intense interest.<sup>12,13</sup> Facilitated primary PTCA, that is, early pharmacological reperfusion to rapidly restore TIMI-3 flow in as many patients as possible (typically 50% to 60% with fibrin-specific agents), followed by immediate PTCA to achieve ultimate TIMI-3 flow rates in >90% of patients, offers the potential to overcome both the delay to reperfusion inherent in primary PTCA and the patency plateau after pharmacologic



**Figure 3.** Impact of initial TIMI flow grade (x-axis) on final TIMI flow grade (y-axis). Postprocedural TIMI-3 flow was significantly more likely to be restored in patients who presented with TIMI-3 flow on initial angiography (see text).



**Figure 4.** Interaction of initial and final procedural TIMI flow on cumulative survival. Mortality was lowest in patients with TIMI-3 flow both at baseline and after PTCA, intermediate in patients in whom TIMI-3 flow was not present at baseline but was restored after angioplasty, and greatest in patients in whom TIMI-3 flow could not be restored, regardless of preprocedural antegrade flow.

ical reperfusion therapy. Early pharmacological administration may also encourage ambulance transfer strategies so that the maximum number of patients may realize the patency and plaque-stabilizing benefits of mechanical reperfusion. Although studies of the immediate PTCA strategy after thrombolysis more than a decade ago were less than encouraging,<sup>16-19</sup> many investigators now believe that the advent and widespread use of stents, ADP antagonists, and glycoprotein IIb/IIIa receptor inhibitors (in concert with reduced-dose lytic agents) will provide a vascular milieu conducive to an integrated pharmacological and mechanical reperfusion approach.

Does earlier reperfusion improve outcomes in patients undergoing primary PTCA? Inherent in the facilitated primary PTCA approach is the assumption that earlier reperfusion will improve outcomes in patients undergoing a mechanical reperfusion strategy. Whereas an extensive literature has documented the powerful impact of time to thrombolytic drug administration on survival,<sup>20-22</sup> this relationship has been more difficult to demonstrate with primary PTCA, for which survival in patients without cardiogenic shock is typically excellent at all treatment intervals. No association was found between time from symptom onset to angioplasty and mortality after primary PTCA in a previous analysis from the PAMI trials; rather, the establishment of TIMI-3 flow was the predominant determinant of survival,<sup>23</sup> emphasizing the primacy of the open-artery hypothesis.<sup>24,25</sup> Brodie et al<sup>26</sup> found that patients reperfused within 2 hours of symptom onset had lower mortality and greater myocardial salvage after primary PTCA than those who presented later; however, this applied to only 12% of a large patient population. More recently, in

the GUSTO-IIb (Global Use of Strategies To Open occluded coronary arteries in acute coronary syndromes) and NRMI-2 (National Registry of Myocardial Infarction-2) studies, survival was found to be adversely affected by delays to primary PTCA that occurred after hospital arrival, although in both studies, the total time from symptom onset to PTCA (reperfusion time) was similar in patients who died and those who survived.<sup>3,11</sup>

An alternative method to examine the importance of early reperfusion in patients undergoing primary PTCA is to analyze outcomes in those patients who spontaneously achieve TIMI-3 flow. In prior studies of primary PTCA, TIMI-3 flow has been found in  $\approx 10\%$  to  $20\%$  of patients at the time of initial angiography, possibly owing to endogenous fibrinolysis or pretreatment with aspirin, ADP antagonists, and heparin.<sup>2-10</sup> Spontaneous (or pharmacologically mediated) reperfusion before definitive angioplasty would be expected to improve outcomes by enhancing myocardial salvage.<sup>27,28</sup> Patients achieving TIMI-3 flow before PTCA thus would be expected to present with less heart failure and demonstrate greater preservation of regional and global LVEF. Theoretically, the procedural success rate of PTCA may also be improved by lytic-mediated thrombus-burden reduction (resulting in less distal microembolization<sup>29</sup>) and a patent infarct vessel before angioplasty, facilitating roadmap-guided and proper device selection. The effect of spontaneous reperfusion on outcomes of patients undergoing primary PTCA has not been examined in detail previously.

### Results of the Present Study

In the present analysis of the 2507 patients from the 4 major PAMI trials, TIMI-3 flow was present at initial angiography (spontaneous reperfusion) in 16% of patients. No baseline demographic characteristics clearly predicted spontaneous reperfusion, although it is of note that initial TIMI-3 rates were higher in the PAMI Stent Pilot and Randomized trials, in which patients received ticlopidine in addition to aspirin and heparin in the emergency department before angiography, than in PAMI-1 or PAMI-2, in which patients were given only aspirin and heparin (20.7% versus 11.3%,  $P<0.0001$ ). Despite the similar baseline features of patients with and without spontaneous reperfusion, patients with TIMI-3 flow before PTCA did indeed present in more stable condition, with less congestive heart failure and a higher LVEF, presumably owing to enhanced myocardial salvage from earlier patency.<sup>27,28</sup>

**TABLE 4. Multivariate Predictors of Cumulative Mortality (Including Postprocedural Flow)**

	Risk Ratio (95% CI)	P
Age (continuous)	1.04 (1.02, 1.07)	0.005
Female sex	3.1 (1.5, 6.2)	0.006
Anterior MI location	3.0 (1.4, 5.6)	0.008
Triple-vessel disease	2.9 (1.3, 6.1)	0.01
Preintervention TIMI 0-2 flow	1.9 (1.1, 38.5)	0.045
Postintervention TIMI 0-2 flow	1.6 (0.8, 4.2)	0.11

MI indicates myocardial infarction.

When LVEF was entered into the model as a continuous variable, a trend toward significance was present for preintervention TIMI 0-2 flow (risk ratio=1.6,  $P=0.11$ ).



The major finding of the present study is that early reperfusion with initial TIMI-3 flow before PTCA was a powerful and independent predictor of in-hospital and late survival in patients undergoing a mechanical reperfusion strategy. Although the mechanisms of this benefit cannot be determined with certainty by the present study, patients with initial TIMI-3 flow had lower in-hospital rates of new-onset heart failure and hypotension and were less likely to require intubation for respiratory failure, all surrogates of improved myocardial function. The presence of TIMI-3 flow at baseline was associated with better initial left ventricular function. The observation that baseline LVEF, when entered into the multivariate model, was a stronger independent correlate of survival than baseline TIMI-3 flow supports the contention that early TIMI-3 flow improves survival by enhancing myocardial recovery. In contrast, rates of recurrent ischemia, reinfarction, and major arrhythmias were similar in patients with and without spontaneous reperfusion.

Improved procedural success is a second mechanistic explanation for the benefits seen with spontaneous reperfusion. Patients with TIMI-3 flow at initial angiography were more likely to have TIMI-3 flow at the end of the procedure, despite both requiring angioplasty less often because of more lesions with a low-grade residual stenosis<sup>30</sup> and having more frequent stent implantation (which was associated with lower TIMI-3 flow rates in the randomized Stent PAMI Trial<sup>10</sup>). Although speculative, the higher final TIMI-3 flow rates in patients with initial TIMI-3 flow may be due to lower residual thrombus burden, less distal microvascular obstruction, or improved technical success from the advantages of initial lesion delineation and roadmapping. The notion that baseline TIMI-3 flow may improve outcomes independently of its effect on myocardial salvage is supported by the observation that a multivariate trend was still present for baseline TIMI-3 flow to correlate with improved survival even after LVEF was added to the model.

Of critical importance, the independent effect of initial TIMI-3 flow on survival persisted even when corrected for postprocedural TIMI-3 flow. This observation suggests that early pre-PTCA reperfusion has salutary benefits independent of promoting ultimate restoration of TIMI-3 flow. The fact that among patients leaving the catheterization laboratory with TIMI-3 flow, the 6-month mortality rate was 0% in patients presenting with TIMI-3 flow versus 3.6% in patients with lesser initial degrees of epicardial flow ( $P=0.004$ ) suggests that the excellent prognosis generally present after successful primary PTCA may be further enhanced if TIMI-3 flow is restored before angioplasty.

### Potential Study Limitations

Given the generally excellent results of primary angioplasty, pooling of the data from 4 studies was required for adequate power to examine the potential benefits of restored flow before intervention. Nonetheless, the outcomes were significant by multivariate analysis and clinically relevant (absolute 3.6% mortality reduction in patients achieving TIMI-3 flow after the procedure in whom preprocedural TIMI-3 flow was present versus absent). Second, although different core laboratories were used in the 4 studies and interlaboratory

variability has not been examined, the similarity of baseline and final TIMI flows across the studies, in concert with the identical methodology used to determine TIMI flow grades, suggests uniformity and reproducibility. Third, ECG core laboratories were not routinely used, and thus the effects of baseline ECG patterns and extent of injury on TIMI flows and survival were not examined. Finally, baseline differences were present in patients with TIMI-3 versus TIMI  $\leq 2$  flow before reperfusion, including better initial left ventricular function. Although pathophysiologically, it appears more likely that earlier reperfusion was responsible for the apparent myocardial preservation, the possibility that better left ventricular function contributes to early patency cannot be ruled out. Also, although baseline demographic differences were most likely adjusted for by the multivariate analysis, the effect of unknown confounders cannot be excluded. Given these limitations, the present study, while strongly supporting efforts to evaluate the role of early reperfusion before definitive angioplasty, must be considered hypothesis generating, as discussed below.

### Implications for Clinical Care and Future Studies

Studies evaluating pharmacologically mediated reperfusion before intervention have begun. In the Plasminogen-activator Angioplasty Compatibility Trial (PACT), 606 patients with AMI were randomized to low-dose tissue plasminogen activator versus placebo before catheterization and angioplasty when appropriate.<sup>12</sup> That study demonstrated that patients who achieved early TIMI-3 flow (whether spontaneous or pharmacologically mediated) had improved myocardial salvage compared with patients in whom TIMI-3 flow was restored only by PTCA. The present analysis extends the findings from PACT by suggesting that in addition to promoting myocardial recovery, early reperfusion before PTCA has the potential to improve survival.

Unfortunately, by intention-to-treat analysis, PACT was underpowered to show improved clinical outcomes or even improved myocardial function with early pharmacological reperfusion, because TIMI-3 flow was restored in only 33% of low-dose tissue plasminogen activator-treated patients compared with 15% of patients who received placebo before PTCA.<sup>12</sup> Greater patency rates before intervention will be required to justify the additional costs and possible hemorrhagic risks of combination therapy. Rather than using higher doses of thrombolytic agents to achieve greater rates of TIMI-3 flow before PTCA, current interest has shifted to the combination of glycoprotein IIb/IIIa receptor inhibitors plus reduced-dose lytics, which in dose-ranging studies has been found to promote earlier and more complete reperfusion than full-dose lytics alone.<sup>13,31</sup> It must be emphasized, however, that although the present study supports the concept of early reperfusion before PTCA in AMI, differences may exist between pharmacologically mediated and spontaneous reperfusion. Specifically, the routine safety of these regimens has not yet been established, and a careful risk-benefit analysis will be necessary to determine whether the benefits realized by early reperfusion outweigh the potential risks of intracranial hemorrhage and access-site bleeding (as well as the additional costs). Well-designed, large-scale randomized tri-

als are thus required to evaluate the facilitated primary percutaneous coronary intervention approach before its use can be recommended routinely.

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