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Clinical Significance of Post-Procedural TIMI Flow in Patients With Cardiogenic Shock Undergoing Primary Percutaneous Coronary Intervention

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Objectives We sought to evaluate the impact of post-primary percutaneous coronary intervention (PCI) Thrombolysis In Myocardial Infarction (TIMI) flow grades in the infarct-related artery (IRA) in patients with ST-segment elevation myocardial infarction (STEMI) and cardiogenic shock.

Background The clinical implications and correlates of post-procedural TIMI flow grades in patients with STEMI and cardiogenic shock treated with primary PCI have not been elucidated.

Methods We evaluated 4,731 STEMI patients with cardiogenic shock undergoing primary PCI at 567 hospitals participating in the American College of Cardiology–National Cardiovascular Database CathPCI Registry to determine the association of post-procedural TIMI flow grades 0 to 2 with in-hospital outcomes.

Results Post-PCI TIMI flow grades 0 to 2 in the IRA were present in 14.7% of patients. Compared with patients with TIMI flow grade 3, those with TIMI flow grades 0 to 2 were more likely to undergo coronary artery bypass graft surgery after PCI (20% vs. 5.4%), and develop renal failure (10.1% vs. 5.1%), cardiac tamponade (1.0% vs. 0.5%), and bleeding requiring blood transfusion (35.2% vs. 21.6%). Unadjusted mortality was more than 2-fold higher with TIMI flow grades 0 to 2 versus TIMI flow grade 3 (63% vs. 27%). There was a graded inverse relationship with TIMI flow in the IRA and the adjusted mortality (odds ratio [OR] for TIMI flow grades 0/1: 5.47 [95% confidence interval (CI): 4.13 to 7.24] and for TIMI flow grade 2: 2.63 [95% CI: 2.02 to 3.42] compared with TIMI flow grade 3). Our study also identified factors associated with post-PCI TIMI flow grades 0 to 2.

Conclusions Lack of procedural success (post-PCI TIMI flow grades 0 to 2 in the IRA) after primary PCI for STEMI among patients with cardiogenic shock is associated with a much higher risk of mortality compared with the risk for patients with normal post-PCI TIMI flow grade 3. (J Am Coll Cardiol Intv 2009;2:56–64) © 2009 by the American College of Cardiology Foundation

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Thrombolysis In Myocardial Infarction (TIMI) flow grades have been shown to have significant prognostic implication among patients undergoing reperfusion therapy for ST-segment elevation myocardial infarction (STEMI) (1–3). Both short- and intermediate-term outcomes have been shown to be significantly higher among patients with TIMI flow grades 0 to 2 following reperfusion than in those with TIMI flow grade 3 (1,2,4–6). Because of its significant relevance to the overall outcomes among patients receiving reperfusion therapy for STEMI, multiple investigations have focused on describing risk factors and strategies to minimize TIMI flow grades 0 to 2 following reperfusion (7–13).

Some studies have reported higher incidence of TIMI flow grades 0 to 2 in STEMI patients with cardiogenic shock (14) compared with that reported by others in STEMI patients without cardiogenic shock (2,7–9). However, these studies were generally small and/or involved selected patient populations and the true incidence of TIMI flow grades 0 to 2 in STEMI patients with cardiogenic shock is currently not known. Furthermore, the clinical correlates and implications of TIMI flow grades in patients with STEMI complicated by cardiogenic shock are less well studied.

Accordingly, the goal of the current investigation was to describe the incidence, clinical features, and outcomes of patients with STEMI and presenting with cardiogenic shock undergoing primary percutaneous coronary interventions (PCI) who have post-procedural TIMI flow grades 0 to 2 compared with the incidence, clinical features, and outcomes of patients with normal TIMI flow grade 3 in the infarct-related artery (IRA).

Methods

Study population. Data from 708,481 consecutive patients undergoing PCI at 638 hospitals in the U.S. were entered into the American College of Cardiology–National Cardiovascular Database Registry (ACC-NCDR) between January 1, 2004, and March 30, 2007. Details of this registry have been previously published (15). Participation in ACC-NCDR was subject to the approval of the institutional review board of each hospital. As patient information was collected anonymously without unique patient identifiers, individual informed consent was not required.

We included patients with STEMI and cardiogenic shock (n = 7,070). From this cohort, we excluded those treated with fibrinolysis (n = 396), those transferred in from another facility for primary PCI (n = 1,928), and those with missing information on post-PCI TIMI flow grades (n = 15). The final study population consisted of 4,731 patients treated at 567 hospitals. We did not exclude the small proportion of patients arriving >24 h from symptom onset as ACC/American Heart Association guidelines for STEMI recommends invasive strategy as class I indication up to 36 h from symptom onset in patients with STEMI and cardiogenic shock (16).

Data definitions. Hospital characteristics and patient-level data, including demographic, clinical, angiographic, and procedural variables, were collected retrospectively via a standardized set of data elements and definitions that are available on the ACC-NCDR website (15). Data on periprocedural medications were collected before or during procedure (combined) and at discharge. Cardiogenic shock was defined as systolic blood pressure ≤80 mm Hg and/or cardiac index <1.8 l/min/m^2 despite maximal treatment or intravenous inotropes and/or intra-aortic balloon pump necessary to maintain systolic blood pressure >80 mm Hg and/or cardiac index ≥1.8 l/min/m^2. Infarct-related artery was defined as the first artery treated during primary PCI for these patients. The TIMI flow grades in the IRA were determined both before and after PCI by the treating physicians and ascertained for the present study from that entered in the data collection form by participating sites. The use of medications in the periprocedural period as well as interventional strategies were not outlined specifically in ACC-NCDR and left to the discretion of the operator, but expected to be in accordance with the ACC/American Heart Association guidelines (16).

Statistical analyses. Continuous variables are presented as medians with 25th and 75th percentiles. Categorical variables are expressed as frequencies with percentages. Comparisons between the 2 groups (patients with and without TIMI flow grade 3 after the procedure) were made using Mann-Whitney *U* and Wilcoxon rank sum tests for continuous variables and Pearson chi-square test for categorical variables. Mortality—overall and during and after cardiac catheterization in various TIMI flow grades—was examined. Several sensitivity analyses were also performed. Thus, we examined the relationship of TIMI flow grade with this outcome: 1) excluding patients who died in cardiac catheterization laboratory (in whom early death may have precluded completion of the diagnostic and/or the PCI procedure); 2) restricting our population to only those who received coronary stents (to account for the complexity of the coronary anatomy in patients with shock that would have posed significant difficulty in deploying stents in the IRA); 3) restricting our population to those undergoing single vessel PCI to eliminate the error of misclassification of the IRA as defined in the current study; and 4) in patients whose ages were ≤75 and >75 years.

Abbreviations and Acronyms

ACC-NCDR = American College of Cardiology–National Cardiovascular Database Registry

CABG = coronary artery bypass graft surgery

IRA = infarct-related artery

PCI = percutaneous coronary interventions

STEMI = ST-segment elevation myocardial infarction

TIMI = Thrombolysis In Myocardial Infarction

A multivariable logistic regression model was used to adjust for the influence of baseline confounders on mortality. The generalized estimating equation method with exchangeable working correlation structure was used to account for within-hospital clustering, because patients at the same hospital are more likely to have similar responses relative to patients in other hospitals (i.e., within-center correlation for response) (17). The exchangeable structure assumes that any 2 distinct patients from the same hospital have the same correlation coefficient. The method produces estimates similar to those from ordinary logistic regression, but the estimated variances of the estimates are adjusted for the correlation of outcomes within each hospital. Variables adjusted in the model were age, sex, race, family history of coronary artery disease, body mass index, hypertension, diabetes mellitus, dyslipidemia, peripheral vascular disease, cerebrovascular disease, prior myocardial infarction, prior PCI, prior coronary artery bypass grafting (CABG), renal insufficiency or creatinine >2 mg/dl at baseline, smoking status, time of symptom onset to arrival, signs of congestive heart failure at the time of admission, New York Heart Association functional class, and time from symptom onset to arrival. Additionally, angioplasty variables adjusted in the model included door-to-balloon time, multivessel disease, multivessel PCI, lesion location, lesion in graft, and pre-procedure TIMI flow grade. Adjusted mortality was also examined in various TIMI flow rates after restricting our patient population to those <12 h from symptom onset to hospital arrival.

For the determination of factors associated with TIMI flow grades 0 to 2, baseline variables and angioplasty variables were entered into a multivariable model. In addition, generalized estimating equation models were again used to adjust for correlations within hospital correlations. Wald chi-square statistic was used to determine the relative significance of the factors associated with TIMI flow grades 0 to 2. The C statistic was calculated to assess model discrimination. Finally, factors associated with TIMI flow grades 0 to 2 were also examined after restricting the patients to those arriving at the hospital within 12 h of their symptom onset.

A p value <0.05 was considered significant for all tests. All statistical analyses were performed using SAS software, version 9.0 (SAS Institute, Cary, North Carolina).

Results

TIMI flow grades: incidence and clinical and angiographic characteristics. Of 4,731 patients with cardiogenic shock who underwent primary PCI, post-procedure TIMI flow grades 0, 1, 2, and 3 occurred in 229 (4.8%), 125 (2.6%), 342 (7.2%), and 4,035 (85.3%) patients, respectively. Excluding death in cardiac catheterization laboratory, these rates were observed in 169 (3.7%), 97 (2.1%), 307 (6.8%), and 3,952 (87.3%) of patients, respectively. Compared with patients who had TIMI flow grade 3, those with TIMI flow grades 0 to 2 were older with no significant difference in other demographic features including gender, race, and body mass index (Table 1). These patients were also more likely to have a history of hypertension, diabetes, cerebrovascular disease, and prior CABG and have signs of congestive heart failure at the time of presentation. Patients with TIMI flow grades 0 to 2 were also likely to present later after their symptom onset and have a higher serum creatinine before their procedure. In contrast, these patients were significantly less likely to be current smokers or have a history of chronic lung disease.

Median door-to-balloon time was longer and fewer patients with TIMI flow grades 0 to 2 received primary PCI within 90 min of their hospital arrival (Table 2). Pre-procedural TIMI flow grade 0 and multivessel coronary disease were significantly more frequent among patients with TIMI flow grades 0 to 2 than in those who had TIMI flow grade 3. The location of the IRA was more commonly the left main or left anterior descending arteries or saphenous vein graft in patients with TIMI flow grades 0 to 2. These patients also had a lower median left ventricular ejection fraction and had more dissection of coronary arteries after the procedure. The median fluoroscopy time was also longer in the patients with TIMI flow grades <3.

Medical treatments and in-hospital events. The use of aspirin, clopidogrel, and glycoprotein IIb/IIIa was significantly lower in patients with TIMI flow grades 0 to 2, whereas the use of most other treatments was not significantly different between the 2 groups. In contrast, intra-aortic balloon pump use was 1.3-fold higher, and CABG was 4-fold higher among patients with TIMI flow grades 0 to 2 (Table 3).

Many in-hospital adverse events were significantly higher among patients with TIMI flow grades 0 to 2. Thus, renal failure and cardiac tamponade was 2-fold higher and need for blood transfusion was 1.6-fold higher in patients with than in those without TIMI flow grades 0 to 2. In particular, in-hospital mortality was 2.3-fold higher with one-third of deaths occurring early, that is, in the cardiac catheterization laboratory, in patients with TIMI flow grades 0 to 2. Median time to death was 1 day earlier in these patients than in those with TIMI flow grade 3. Even after exclusion of patients who died in the cardiac catheterization laboratory, in-hospital mortality was higher among those with TIMI flow grades 0 to 2 (53.6% vs. 25.3%, $p < 0.0001$). Similarly, when we excluded patients with inadequate IRA PCI results (dissection, percentage of stenosis >50, or immediate need for CABG), the relationship between post-procedural TIMI flow and outcomes did not change (58.3% and 26.5% in patients with post-procedural TIMI flow grades <3 vs. 3). Mortality was also higher among stented patients with TIMI flow grades 0 to 2 compared with mortality in those with TIMI flow grade 3 (51.2% vs. 24.6%, $p < 0.0001$).

Table 1. Baseline Clinical Characteristics

Variables	Overall	TIMI Flow Grade 0–2	TIMI Flow Grade 3	p Value
n, %	4,731 (100)	696 (14.7)	4,035 (85.3)	
Demographics				
Age, median (IQR), yrs	64 (55–74)	67 (57–78)	63 (54–74)	<0.0001
Age ≥75 yrs, %	24.7	31.6	23.5	<0.0001
Weight, median (IQR), kg	80 (69–93)	80 (68–93)	81 (69–93)	0.7228
Height, median (IQR), cm	173 (163–178)	173 (163–178)	173 (163–178)	0.4027
Body mass index, median (IQR), kg/m^2	27 (24–31)	27 (24–31)	27 (24–31)	0.6554
Females, %	35.4	35.8	35.3	0.8049
Caucasians, %	84.6	82.0	85.0	0.0783
Medical history				
Prior myocardial infarction, %	21.6	23.0	21.3	0.3285
Smoker—current, %	40.6	31.2	42.3	<0.0001
Hypertension, %	60.6	64.8	59.8	0.0132
Hyperlipidemia, %	50.9	45.8	51.7	0.0041
Diabetes mellitus, %	25.5	28.9	24.9	0.0264
Peripheral vascular disease, %	10.3	10.6	10.3	0.7811
Cerebrovascular disease, %	10.3	12.5	9.9	0.0381
Prior coronary artery bypass surgery, %	7.0	9.6	6.5	0.0027
Prior percutaneous coronary intervention, %	18.4	17.8	18.5	0.6725
Prior congestive heart failure, %	9.5	8.8	9.6	0.4791
Chronic lung disease, %	17.8	13.2	18.6	0.0006
Renal failure or dialysis, %	6.9	8.1	6.7	0.1846
Last serum creatinine, median (IQR), mg/dl	1.2 (1.0–1.5)	1.3 (1.0–1.6)	1.2 (1.0–1.5)	<0.0001
Symptoms of heart failure at presentation, %	30.0	35.9	29.0	0.0002
Time from symptom onset to hospital arrival, %				<0.0001
0 to ≤6 h	82.7	76.0	83.9	
>6 to ≤12 h	7.7	8.5	7.5	
>12 to ≤24 h	3.8	5.5	3.5	
>24 h to ≤7 days	5.3	8.9	4.7	

IQR = interquartile range; TIMI = Thrombolysis In Myocardial Infarction.

In-hospital mortality was inversely related to TIMI flow rates, decreasing significantly from TIMI flow grades 0/1 to 2, and was lowest among those with TIMI flow grade 3 after the procedure (Fig. 1). This relationship persisted even after exclusion of patients who died in the cardiac catheterization laboratory (in-hospital death: 54.7%, 65.0%, 49.6%, and 25.3% with TIMI flow grades 0, 1, 2, and 3, respectively) and in patients with single-vessel (in-hospital death: 66.3%, 70.9%, 53.2%, and 25.3% with TIMI flow grades 0, 1, 2, and 3, respectively) or multivessel (in-hospital death: 81.5%, 86.4%, 67.4%, and 42.6% with TIMI flow grades 0, 1, 2, and 3, respectively) PCI. Albeit, mortality was higher for each post-procedural TIMI flow in the multivessel PCI cohort than in those only undergoing infarct-artery PCI. Additionally, a similar inverse relationship was observed among patients with TIMI flow grades 2 or 3 before PCI with mortality of 54.4% and 29.3% in those with post-procedural TIMI flow grades <3 and 3, respectively. TIMI flow grades 0 to 2 remained an independent correlate of in-hospital mortality after adjustments for baseline confounding (odds ratio [OR]: 3.72, 95% confidence interval [CI]: 3.07 to 4.51, $p < 0.001$ vs. TIMI flow grade 3). A graded inverse relationship was observed in patients between TIMI flow grades 0/1 (OR: 5.47, 95% CI: 4.13 to 7.24) and 2 (OR: 2.63, 95% CI: 2.02 to 3.42) and adjusted mortality when compared with patients with TIMI flow grade 3. Even when we restricted our population to those patients with symptom onset to hospital arrival time <12 h, the inverse relationship between TIMI flow grade and in-hospital mortality persisted (TIMI flow grades 0/1 OR: 6.25, 95% CI: 4.61 to 8.47 and TIMI flow grade 2 OR: 2.63, 95% CI: 1.99 to 3.48 [referent TIMI flow grade 3]). Furthermore, this inverse relationship between TIMI flow grade and in-hospital mortality was present in patients <75 years as well as ≥75 years of age, with higher mortality for each flow grade in the older cohort (Fig. 2).

Clinical correlates of post-primary PCI TIMI flow grades 0 to 2. Independent factors associated with post-procedural TIMI flow are shown in Table 4 (model C statistic: 0.67).

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Table 2. Angiographic Variables

Variable	Overall	TIMI Flow Grade 0–2	TIMI Flow Grade 3	p Value
n, %	4,731 (100)	696 (14.7)	4,035 (85.3)	
Door-to-balloon time, median (IQR), min	88 (64–121)	93 (66–131)	88 (63–120)	0.0145
Door-to-balloon time ≥90 min, %	48.7	52.7	48.0	0.0020
Angiographic factors				
No. of narrowed coronary arteries (>50% stenosis)				<0.0001
1	36.0	28.5	37.3	
2	33.9	35.9	33.5	
3	29.5	35.2	28.5	
Infarct-related artery				<0.0001
Left main	2.4	5.5	1.8	
Left anterior descending	40.6	45.8	39.7	
Left circumflex	12.9	13.4	12.9	
Right	43.8	35.2	45.3	
SVG	3.2	5.8	2.8	<0.0001
Multivessel PCI (>1 vessel), %	10.9	15.5	10.1	<0.0001
Pre-PCI TIMI flow of the infarct-related artery				<0.0001
0	70.5	80.0	68.9	
1	11.6	11.1	11.7	
2	9.3	5.3	9.9	
3	8.2	3.6	9.0	
Ejection fraction, median (IQR), %	40 (28–50)	35 (20–45)	40 (30–50)	<0.0001
Post-PCI TIMI flow of the infarct-related artery				
0	4.8	32.9	0	
1	2.6	18.0	0	
2	7.2	49.1	0	
3	85.3	0	100	
Final infarct artery stenosis, median (IQR), %	0 (0–0)	20 (0–100)	0 (0–0)	<0.0001
Stent implantation, %	85.7	54.0	91.2	<0.0001
Stent implantation excluding patients who died in the cardiac catheterization laboratory, %	87.4	59.0	91.5	<0.0001
Dissection of infarct artery, %	2.4	4.5	2.0	<0.0001
Fluoroscopy time, median (IQR), min	14 (9–21)	16 (10–25)	13 (9–21)	<0.0001

PCI = percutaneous coronary intervention; SVG = saphenous vein graft; other abbreviations as in Table 1.

Even when we restricted our analysis to patients presenting to the hospital within 12 h of their symptom onset, the clinical correlates of TIMI flow grades 0 to 2 remained the same (data not shown).

Discussion

Our study findings. Our findings suggest that suboptimal coronary flow (TIMI flow grades 0 to 2) occurs in up to 1 in 7 patients with cardiogenic shock undergoing primary PCI and has a significant impact on the prognosis of these patients. Those with TIMI flow grades 0 to 2 have up to 2-fold higher risk for in-hospital complications including cardiac tamponade, renal failure, and blood transfusion. Strikingly, the in-hospital mortality occurred in two-thirds of patients with TIMI flow grades 0 to 2 and was 2.3-fold higher than in patients with TIMI flow grade 3 and remained independently related to mortality even after accounting for baseline confounders. Although approximately one-third of the deaths in these patients occurred in the catheterization laboratory, the majority occurred after the procedure. Furthermore, an inverse relationship was seen between in-hospital mortality and TIMI flow grades with mortality decreasing significantly as flow rates increased from TIMI flow grades 0 and 1 to 3. Even when we excluded deaths in the cardiac catheterization laboratory that may not have permitted sufficient time for the use of stents or therapeutic agents (antithrombotics and microvascular vasodilators such as adenosine) to improve coronary flow, or when we restricted our patients to those presenting <12 h from their symptom onset, or to those who received stents, the inverse relationship between post-

Table 3. Medical Treatments and In-Hospital Events

Variable	Overall (n = 4,731, 100%)	TIMI Flow Grade 0–2 (n = 696, 14.7%)	TIMI Flow Grade 3 (n = 4,035, 85.3%)	p Value
Treatment before admission or in periprocedural period				
Aspirin, %	82.5	79.2	83.1	0.0152
Beta-blockers, %	56.7	50.6	57.8	0.0008
Clopidogrel or ticlopidine, %	52.1	33.2	55.4	<0.0001
Unfractionated heparin or low-molecular weight heparin, %	88.2	86.3	88.5	0.0882
Thrombin inhibitors, %	11.7	11.0	11.8	0.5426
Glycoprotein IIb/IIIa antagonists, %	77.7	67.1	79.5	<0.0001
Statins, %	29.2	26.6	29.7	0.0985
Intra-aortic balloon pump	52.3	64.4	50.3	<0.0001
Coronary artery bypass surgery*	7.1	20.0	5.4	<0.0001
In-hospital events				
Stroke/transient ischemic attacks	1.6	1.8	1.6	0.7174
Cardiac tamponade	0.6	1.0	0.5	0.2046
Renal failure	5.7	10.1	5.1	<0.0001
Bleeding complications				
Any	11.1	13.3	10.8	0.0925
Retroperitoneal	0.9	1.2	0.9	0.4898
Transfusion—post-procedure	23.2	35.2	21.6	<0.0001
Death, %	32.3	63.0	27.0	<0.0001
Death in cardiac catheterization laboratory, %	5.0	20.3	2.3	<0.0001
Death beyond cardiac catheterization laboratory, %	27.3	42.7	24.7	<0.0001
Time from hospital arrival to death, median (IQR), days	3.0 (1.0–7.0)	2.0 (1.0–6.0)	4.0 (1.0–8.0)	0.0028
Post-procedure length of stay, median (IQR), days	6.0 (3.0–10.0)	4.0 (1.0–10.0)	6.0 (4.0–10.0)	<0.0001

*Related to complications of the procedure or multivessel coronary disease requiring revascularization.
Abbreviations as in Table 1.

procedural TIMI flow grades and mortality persisted. Finally, our data also provide insight into the clinical, angiographic, and treatment factors independently associated with TIMI flow grades 0 to 2 in STEMI patients with cardiogenic shock undergoing primary PCI.

Comparisons with prior studies. Similar to our findings, the few studies that have reported TIMI flow grades after primary PCI in patients with cardiogenic shock have suggested higher TIMI flow grades 0 to 2 in these patients compared with that seen in patients without cardiogenic shock undergoing primary PCI (18,19). Only 1 prior study has reported the relationship between TIMI flow grade after primary PCI and in-hospital mortality in these patients. Zeymer et al. (19) evaluated predictors of in-hospital mortality in 1,333 patients with acute myocardial infarction complicated by cardiogenic shock treated with primary PCI between 1994 and 2001. They showed that mortality decreased as TIMI flow grades increased (78%, 66%, and 37% in patients with TIMI flow grades 0/1, 2, and 3, respectively), a finding similar to that seen in our study. Additionally, they demonstrated that on multivariate analysis, TIMI flow grades 0 to 2 were independently associated with increased mortality (OR: 3.4, 95% CI: 2.4 to 4.8). This

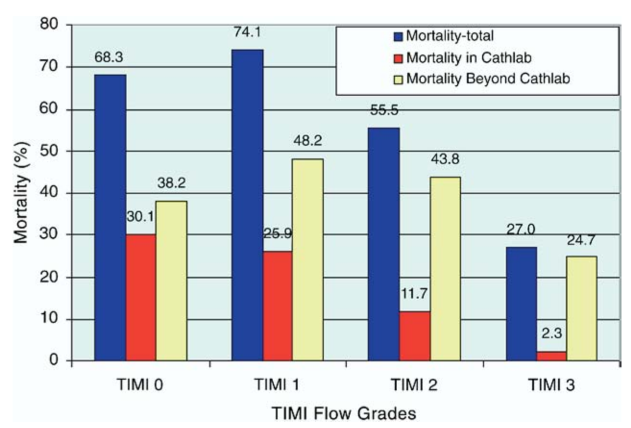

Figure 1. TIMI Flow Grade and Mortality

Post-procedural TIMI flow grades in patients with cardiogenic shock undergoing primary percutaneous coronary interventions and in-hospital death. Cathlab = cardiac catheterization laboratory; TIMI = Thrombolysis In Myocardial Infarction.

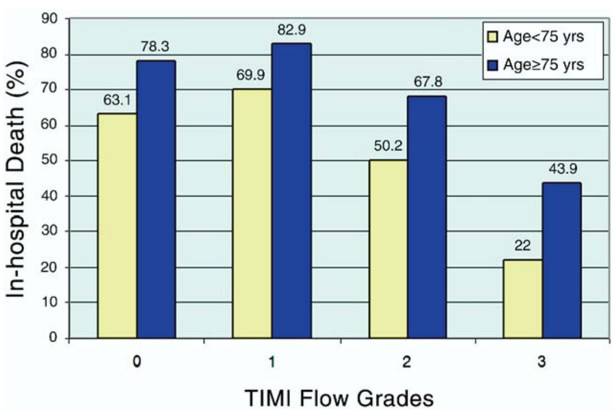

Figure 2. Age, TIMI Flow Grade, and Mortality

Post-procedural TIMI flow grades in patients age ≥75 years versus <75 years and in-hospital death with cardiogenic shock undergoing primary percutaneous coronary interventions. Abbreviation as in Figure 1.

study and our investigation not only clearly suggest extremely grave prognosis with TIMI flow grades 0 to 2 for patients with cardiogenic shock, but also provide quantitative insights into this association in patients with cardiogenic shock.

The rate of TIMI flow grades 0 to 2 observed in our study among patients with cardiogenic shock undergoing primary PCI is twice as high as that reported after primary PCI in patients with STEMI without cardiogenic shock (2,7–9,20). In addition, these studies and our findings also suggest that although TIMI flow grades 0 to 2 are adversely related to mortality in STEMI patients undergoing primary PCI with or without underlying cardiogenic shock, the magnitude of this relationship is much greater for patients with cardiogenic shock underlying the importance of TIMI flow grades 0 to 2 in the prognosis of these patients.

Clinical implications. The reservation in giving glycoprotein IIb/IIIa and clopidogrel before diagnostic angiography in cardiogenic shock patients in general is understandable in view of higher proportion of these patients that would need CABG, either because of multivessel disease or mechanical complications. However, the opportunity to use these agents was missed even during the procedure once it was decided to proceed with primary PCI (all patients with cardiogenic shock in this study). Perhaps more frequent use of glycoprotein IIb/IIIa agents (and clopidogrel) may have the potential for improving outcomes for these patients (21–23). The importance of decreasing the time from symptom onset to hospital arrival as well as of improving door-to-balloon time in reducing adverse events cannot be overemphasized and remains a primary focus of many national collaborative initiatives (24). Similarly, greater use of intra-aortic balloon pumps or other circulatory assist devices may have the potential for improving coronary flow and/or outcomes, especially because intracoronary nitroglycerine, nitroprusside, verapamil, and nicardipine all have the potential of worsening the hypotension. While intracoronary adenosine may be potentially useful in these patients and should be used liberally, the role of administration of the other agents mentioned in distal coronary bed in improving TIMI flow grade and outcomes in shock patients without exacerbating hypotension needs future evaluation. Despite early promise for improving microcirculation, agents such as l-n-monomethyl-arginine (a nonselective

Table 4. Independent Correlate of Post-Procedural TIMI Flow Grades 0 to 2 in Patients With Cardiogenic Shock Undergoing Primary PCI

Variable	Chi-Square	Odds Ratio	95% Confidence Interval	p Value
Pre-procedural TIMI flow grade 0 (vs. other)	35.35	2.04	1.61–2.57	<0.001
Infarct artery segment (vs. other)	27.00			<0.001
Left main		3.15	1.94–5.13	
LAD		1.53	1.27–1.86	
Symptom onset to hospital arrival (vs. ≤6 h)	18.10			<0.001
>6 to ≤12 h		1.20	0.90–1.59	
>12 to ≤24 h		1.58	1.04–2.39	
>24 h or silent MI		2.03	1.51–2.72	
Dyslipidemia	13.74	0.72	0.60–0.86	<0.001
Age (per 10-yr increase)	11.80	1.14	1.06–1.23	<0.001
Number of diseased vessels	7.20			0.003
2-vessel coronary artery disease		1.22	1.00–1.49	
3-vessel coronary artery disease		1.31	1.07–1.61	
Bypass vein graft	6.93	2.10	1.21–3.66	0.008
Current smoker	3.64	0.83	0.68–1.01	0.056
Overall model chi-square	4,750.40			
Model C statistic				0.668

LAD = left anterior descending; MI = myocardial infarction; other abbreviations as in Tables 1 and 2.

nitric oxide synthase inhibitor) (25) and a novel anti-inflammatory agent pexelizumab (a humanized monoclonal antibody that binds the C5 component of complement) (26) have failed to show any benefits in large phase III clinical trials, precluding any recommendations for their use. Similarly, thrombectomy and distal protection devices have failed to demonstrate unequivocal benefits, and their use should at best be individualized at this time (27,28).

Finally, although observational studies have supported merits of CABG over primary PCI among these patients (29,30), it is unsettled currently if CABG is associated with better post-procedural TIMI flow grade in IRA than primary PCI for this cohort. The use of CABG in patients with multivessel coronary disease and cardiogenic shock has some theoretical advantage. Primary PCI has a potential for distal embolization and slow flow. Additionally, PCI of a noninfarct artery during the initial procedure may also cause distal embolization and/or side branch closure, compromising collateral circulation to infarct and noninfarct zones. These problems are less likely with CABG. Future studies are needed to determine the best reperfusion strategy in patients with multivessel coronary disease and cardiogenic shock.

Study limitations. This is a retrospective analysis and caution needs to be exerted while inferring causation. We are unable to account for the influence of unmeasured confounders on TIMI flow grade and outcomes. We do not have information of ST-segment resolution or myocardial blush score that may have additional prognostic implications. Additionally, we only have information on in-hospital outcomes and are unable to provide any insight into the relationship of TIMI flow grades and long-term outcomes.

Conclusions

Our study shows that TIMI flow grades 0 to 2 occur frequently in patients with cardiogenic shock undergoing primary PCI and are associated with worse in-hospital outcomes and higher in-hospital mortality. Our data also provide insights into the risk factors for suboptimal coronary flow and suggest potential strategies for reducing this event. We believe that physicians will find this information useful in the risk assessment, treatment, and triaging of patients with cardiogenic shock undergoing primary PCI with a potential for improving their outcomes.

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Key Words: acute myocardial infarction ■ cardiogenic shock ■ percutaneous coronary interventions ■ Thrombolysis In Myocardial Infarction flow.