

Angiographic perfusion score: An angiographic variable that integrates both epicardial and tissue level perfusion before and after facilitated percutaneous coronary intervention in acute myocardial infarction

C. Michael Gibson, MS, MD,^a Sabina A. Murphy, MPH,^a David A. Morrow, MD,^a Julian M. Aroesty, MD,^a Raymond J. Gibbons, MD,^b Steven G. Gourlay, MBBS, PhD,^c Hal V. Barron, MD,^c Robert P. Giugliano, MD, SM,^a Elliott M. Antman, MD,^a and Eugene Braunwald, MD^a *Boston, Mass, Rochester, Minn, and San Francisco, Calif*

Background Both epicardial and myocardial perfusion have been associated with clinical outcomes in the setting of ST elevation myocardial infarction (STEMI), and the performance of adjunctive/rescue percutaneous coronary intervention (PCI) may further improve clinical outcomes after fibrinolytic administration.

Methods The goal was to develop a simple, broadly applicable angiographic metric that takes into account indices of epicardial and myocardial perfusion both before and after PCI to arrive at a single perfusion grade in patients undergoing cardiac catheterization after fibrinolysis. The angiographic perfusion score (APS) is the sum of the Thrombolysis in Myocardial Infarction (TIMI) flow grade (TFG; 0–3) added to the TIMI myocardial perfusion grade (TMPG; 0–3) before and after PCI (total possible grade, 0–12). Failed perfusion was defined as an APS of 0 to 3, partial perfusion was defined as an APS of 4 to 9, and full perfusion was defined as an APS of 10 to 12. The APS was evaluated in patients from the Double-blind, Placebo-controlled, Multicenter Angiographic Trial of Rhumab CD18 in Acute Myocardial Infarction (LIMIT-AMI; $n = 394$) and Enoxaparin as Adjunctive Anti-thrombin Therapy for ST-Elevation Myocardial Infarction-Thrombolysis In Myocardial Infarction (ENTIRE-TIMI) 23 trials ($n = 483$), and infarct size (120–216 hours after AMI SPECT Technetium-99m Sestamibi data) was assessed in the LIMIT-AMI trial.

Results The APS was associated with the incidence of death or myocardial infarction (failed, 16.7% [$n = 18$]; partial, 2.5% [$n = 155$]; full, 2.4% [$n = 82$]; $P = .039$ for trend) and larger SPECT infarct sizes (failed, median 39% [$n = 10$]; partial, 12% [$n = 79$]; and full, 8% [$n = 35$]; $P = .002$). No patient with full APS died, whereas the mortality rate was 11.1% in patients with a failed APS ($P = .03$).

Conclusions The APS combines grades of epicardial and tissue level perfusion before and after PCI or at the end of diagnostic cardiac catheterization to arrive at a single angiographic variable that is associated with infarct size and the rates of 30-day death or MI. Partial or full angiographic perfusion scores are associated with a halving of infarct size, and no patients with full angiographic perfusion died. (*Am Heart J* 2004;148:336–40.)

The goal of myocardial reperfusion therapy is to restore both epicardial Thrombolysis in Myocardial

Infarction (TIMI) grade 3 flow^{1–6} and normal tissue level perfusion (TIMI Myocardial Perfusion Grade [TMPG] 3 flow).⁷ There are also data to suggest that adjunctive/rescue percutaneous coronary intervention (PCI) may further improve clinical outcomes after thrombolytic administration.^{8–14} Thus, both the epicardial flow before and after adjunctive/rescue PCI and myocardial perfusion both before and after PCI are associated with clinical outcomes. No single angiographic score currently exists, however, that takes into account both epicardial and myocardial flow grades both before and after PCI to gauge reperfusion success.

From the ^aTIMI Study Group, the Department of Medicine, Brigham & Women's Hospital, Boston, Mass, ^bCardiovascular Division, Mayo Clinic, Rochester, Minn, and ^cCardiovascular Division, University of California San Francisco, San Francisco, Calif. Supported in part by a grant from Genentech, South San Francisco, Calif (LIMIT-AMI) and Aventis Pharma, Antony, France (ENTIRE/TIMI 23). Drs Gourlay and Barron are employees of Genentech.

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Reprint requests: C. Michael Gibson, MS, MD, director, TIMI Data Coordinating Center, 350 Longwood Ave, 1st Floor, Boston MA 02115.

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Table I. Baseline characteristics by Angiographic Perfusion Score*

	Failed APS (n = 73)	Partial APS (n = 305)	Full APS (n = 301)	P
Age (y)	57.4 ± 11.8	59.1 ± 11.1	56.9 ± 10.5	.036
Sex (% male)	64.4%, 47/73	57.4%, 175/305	66.8%, 201/301	.054
Prior MI	11.0%, 8/73	11.8%, 36/305	13.0%, 39/301	.856
Smoker	50.7%, 37/73	44.1%, 134/304	59.8%, 180/301	.001
Diabetes	19.2%, 14/73	14.4%, 44/305	12.3%, 37/301	.301
Hypertension	38.4%, 28/73	33.8%, 103/305	29.2%, 88/301	.244
Hypercholesterolemia	27.4%, 20/73	35.1 %, 107/305	30.2%, 91/301	.291
Prior PCI	4.1%, 3/73	7.9%, 24/305	7.3%, 22/301	.535
LAD infarct-related artery	30.6%, 22/72	32.5%, 99/305	40.1%, 120/299	.091
Pulse (beats/min)	71.7 ± 16.1	73.8 ± 17.1	73.8 ± 15.5	.569
SBP	138.3 ± 21.3	134.2 ± 22.1	135.6 ± 22.3	.327
Sx onset to treatment (h) (median, IQ range)	3 (2.4, 4)	2.9 (2, 3.8)	2.8 (2, 4.2)	.339

*For patients who did not undergo PCI, final TIMI Flow Grade and the final TIMI Myocardial Perfusion Grade on diagnostic arteriography instead of the post-PCI values.

The goal of this analysis was to develop such a simple, broadly applicable metric that takes into account epicardial and myocardial flow grades both before and after PCI. We hypothesized that an improved angiographic perfusion score (APS) would be associated with smaller infarct sizes and improved clinical outcomes. We evaluated this hypothesis in the Enoxaparin as Adjunctive Antithrombin Therapy for ST-Elevation Myocardial Infarction-Thrombolysis In Myocardial Infarction (ENTIRE-TIMI) 23 and Double-blind, Placebo-controlled, Multicenter Angiographic Trial of Rhumab CD18 in Acute Myocardial Infarction (LIMIT-AMI) trials.^{15,16}

Methods

Data were drawn from the ENTIRE-TIMI 23 (n = 483) and LIMIT-AMI (n = 394) trials. The ENTIRE-TIMI 23 trial randomized patients with ST elevation myocardial infarction (STEMI) to receive a combination of abciximab and reduced-dose tenecteplase (TNK) or full-dose TNK, and enoxaparin versus unfractionated heparin.¹⁵ The LIMIT-AMI trial was a randomized, double-blind, placebo-controlled study of rhuMab CD-18, a novel neutrophil inhibitor in patients with STEMI.¹⁶ One of 2 doses of rhuMab CD-18 (0.5 or 2.0 mg/kg) or placebo was administered before tissue plasminogen activator (tPA) or as soon as possible thereafter. There was no difference in TIMI flow grade (TFG) and TMPG in the efficacy of the various pharmacologic arms in ENTIRE-TIMI 23 or of antibody and placebo in the LIMIT-AMI trial. Accordingly, the multiple treatment arms were analyzed together in this study. The use of PCI was at the discretion of the treating physician in both trials.

Angiographic analysis methods

The TFG was assessed as previously defined at the TIMI Angiographic Core Laboratory.¹⁷ The TMPG was used to assess tissue-level perfusion and has been previously defined as⁷: grade 0, no or minimal angiographic blush; grade 1, stain

or prolonged persistence of dye on next contrast injection; grade 2, dye bright at the end of injection, gone by next injection; and grade 3, normal ground glass appearance of blush. All flow data were assessed by a single observer (C.M.G.) who was blinded to the clinical and nuclear imaging outcomes of the patients. In the LIMIT-AMI trial, infarct size was assessed with a 120- to 216-hour post-AMI SPECT technetium-99m sestamibi data. Infarct size was measured as the percentage of the left ventricle with no sestamibi uptake on SPECT imaging.¹⁸ Personnel in the nuclear core laboratory were blinded to treatment assignment and angiographic and clinical outcomes.

The APS is the sum of the TFG (0-3) added to the TMPG (0-3) before and after PCI (total possible score, 0-12). The score was further broken down into categories of full perfusion (APS total score, 10-12), partial perfusion (APS total score, 4-9), and failed perfusion (APS total score, 0-3). In a second analysis, data from patients who did not undergo PCI were incorporated by using the final TFG and the final TMPG on diagnostic arteriography instead of the post PCI values.

Statistical analysis

All analyses were performed with Stata software version 7.0.¹⁹ All continuous variable values are reported as the mean plus or minus SD or the median and interquartile range. The Student *t* test was used for the analysis of continuous variables. The non-parametric Wilcoxon rank sum test or Kruskal-Wallis test was used when the data were not normally distributed. When appropriate, the χ^2 test or Fisher exact test was used for the analysis of categorical variables.

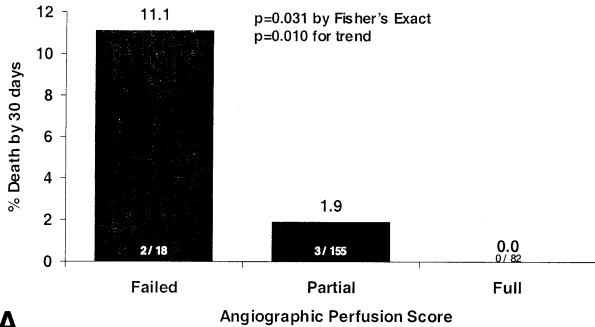
Results

Baseline characteristics

Patients with failed APS were less likely to be current smokers and tended to more frequently have a history of diabetes mellitus and hypertension (Table I). There was no difference for prior MI, prior PCI, history of hypercholesterolemia, time from symptom-on-

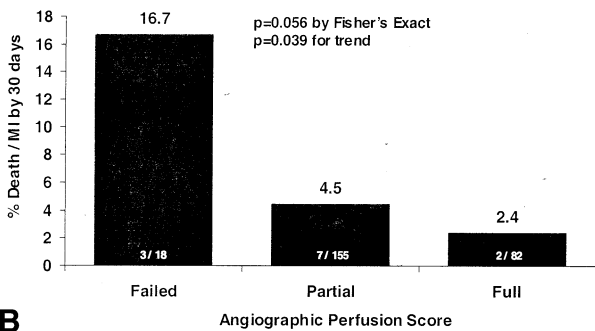
Figure 1

Relationship of Angiographic Perfusion Score to 30 Day Mortality



A

Relationship of Angiographic Perfusion Score to 30 Day Death / MI



B

Patients with a poorer APS were associated with a higher frequency of mortality by 30 days ($P = .010$ for trend). Likewise, patients with a poorer APS were associated with an increased rate of death or MI by 30 days ($P = .039$ for trend).

set to treatment, and pulse or systolic blood pressure on admission.

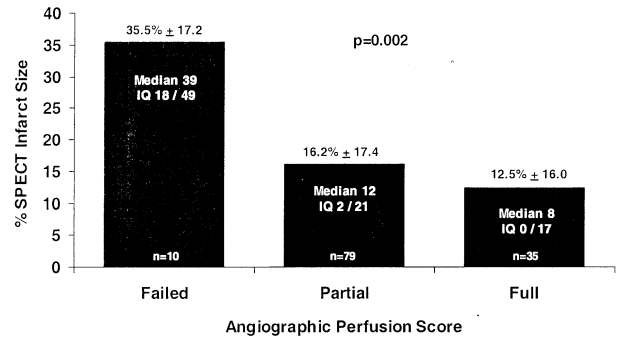
Clinical outcomes

The mortality rate by 30 days increased with worsening APS ($P = .010$ for trend, Figure 1, A). Likewise, the number of patients who were at risk of death or MI by 30 days increased with worsening APS ($P = .039$ for trend Figure 1, B). Lower APS was associated with larger SPECT infarct sizes ($P = .004$): failed, 39%, 18%–49% ($n = 10$); partial: 12%, 2%–21% ($n = 79$); full: 8%, 0%–17% ($n = 35$; Figure 2).

In a second analysis, data from patients who did not undergo PCI were incorporated by using the final TFG

Figure 2

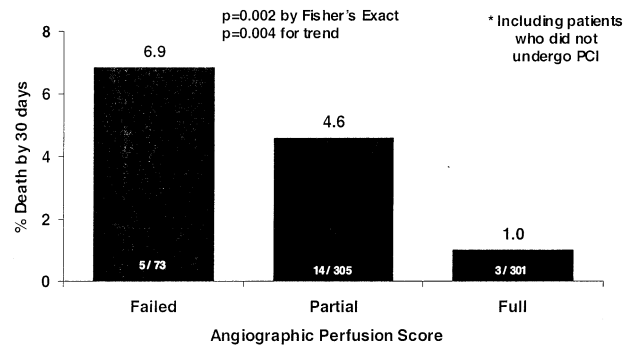
Relationship of Angiographic Perfusion Score to SPECT Infarct Size



Larger SPECT infarct sizes were observed in patients with a poorer APS ($P = .002$).

Figure 3

Relationship of Angiographic Perfusion Score to Mortality*



For patients who did not undergo PCI, final TFG and the final TMPG diagnostic arteriography instead of the post-PCI values. Patients with a poorer APS were associated with a higher frequency of death by 30 days ($P = .004$ for trend).

and the final TMPG on diagnostic arteriography instead of the post-PCI values, and similar results were seen; a lower APS was associated with a higher mortality rate ($P = .004$ for trend, Figure 3). SPECT infarct sizes were larger for failed APS (34.5%; 18%–45%; $n = 14$) versus partial APS (12%; 3%–23%; $n = 111$) or full APS (5%; 0%–16%; $n = 86$; $P = .0001$).

There were non-significant trends for either the pre-PCI grade (sum of pre-PCI TFG and TMPG) or the post-PCI grade (sum of post-PCI TFG and TMPG) to be associated with death or MI on their own (Figure 4).

Discussion

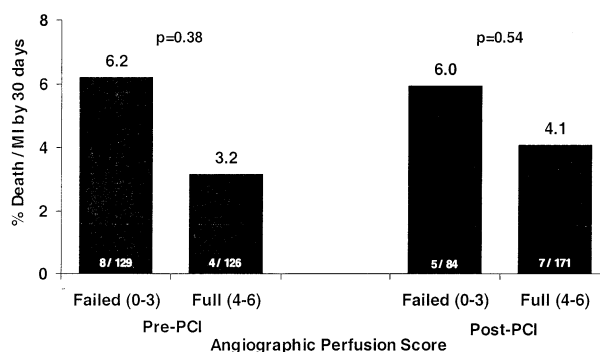
Several indices of epicardial and microvascular perfusion in the setting of STEMI have been associated with clinical outcomes.¹⁻¹¹ This study combines 2 of these measures, the TFG and the TMPG, at 2 points in the revascularization pathway (before and after PCI) to arrive at a single angiographic perfusion score that is associated with infarct size and the 30-day risk of death or MI. The reliance of the APS on ordinary visual inspection of the angiogram without the use of sophisticated equipment allows the method to be conveniently and broadly applied. Partial or full APSs were associated with a halving of infarct size as compared with failed perfusion, and no patients with full angiographic perfusion died.

Until recently, the goal of reperfusion therapy was simply to restore TIMI grade 3 flow in the epicardial artery. However, the TFG alone provides valuable, although limited, information whether determined before⁷ or after PCI.^{8,12} Patients with TIMI grade 3 flow with absent or near absent myocardial perfusion (TMPG 0/1) after fibrinolytic administration have a mortality rate of 5.0%, which is as high as that in patients with unsuccessful restoration of optimal epicardial artery patency (TIMI 0-2) but preservation of myocardial perfusion (TMPG 3; 4.7%).⁷ Conversely, restoration of both TIMI grade 3 epicardial and myocardial flow was associated with a 7-fold reduction in mortality rate, to 0.7%. Despite most patients with STEMI achieving TIMI grade 3 epicardial flow after either rescue or primary PCI, improved post-PCI myocardial blush grades are independently associated with improved outcomes,²⁰⁻²³ possibly mediated by improvements in myocardial salvage.²¹

There is no angiographic measure that incorporates both restoration of epicardial patency and microvascular perfusion in patients treated with fibrinolytic therapy, PCI, or both. The APS we describe combines epicardial and myocardial perfusion data both before and after PCI and is a more powerful discriminator of clinical outcomes than a grading system that combined epicardial and myocardial data either before or after PCI. In the APS system, equal weighting was assigned to both the pre-PCI TFG and TMPG because of their similar association with mortality in the previously published TIMI 10B trial (Cox hazard ratio [HR] for 2-year mortality 0.41 for TFG 2/3 and HR = 0.51 for TMPG 2/3).⁸ The increased risk for post-PCI TMPG 3 was slightly more powerful (odds ratio = 0.31 for 30-day death or MI). However, doubling the weight of the post-PCI TMPG added no further discriminatory value. Few patients left the laboratory without TFG 3 rendering an accurate evaluation of the odds ratio in these patients less reliable.

Figure 4

Relationship of pre-PCI and post-PCI Angiographic Perfusion Score Individually to Clinical Outcomes



There was a non-significant trend for a failed APS pre-PCI grade (sum of pre-PCI TFG and TMPG) to be associated with death or MI and likewise for a failed APS post-PCI grade (sum of post-PCI TFG and TMPG). These associations, however, were not as powerful as the 12-point scale that combines pre- and post-PCI data.

Limitations

This was a retrospective substudy analysis and may be confounded by both known and unidentified variables. These findings require further prospective validation. All TFG and TMPG data were assessed by a single observer. Although the TFG has been shown to be reproducible, studies using TMPG assessment are ongoing.

Conclusions

This simple, broadly applicable APS allows risk stratification of patients with STEMI who are undergoing coronary angiography. The APS combines indexes of epicardial and tissue level perfusion before and after PCI or at the end of diagnostic cardiac catheterization to arrive at a single grade that is associated with the 30-day death rate, MI rate, or both and infarct size.

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