Threshold Values for Preserved Viability With a Noninvasive Measurement of Collateral Blood Flow During Acute Myocardial Infarction Treated by Direct Coronary Angioplasty

Timothy F. Christian, MD; Peter B. Berger, MD; Michael K. O’Connor, PhD; David O. Hodge, MD; Raymond J. Gibbons, MD

Background—Quantitative measures of myocardial perfusion defect severity from acute $^{99m}$Tc-sestamibi tomographic images (nadir) have correlated closely with collateral and residual antegrade blood flow during acute myocardial infarction. The purpose of this study was to determine whether a viability threshold could be identified from this measure in patients with acute myocardial infarction treated in a homogeneous manner with successful reperfusion therapy.

Methods and Results—The study group consisted of 61 patients with acute myocardial infarction with a risk area of >6% LV treated with primary angioplasty between 120 and 240 minutes after symptom onset. All patients were injected with 20 to 30 mCi of $^{99m}$Tc-sestamibi before primary angioplasty and imaged after the procedure. Acute myocardium at risk (MAR) and subsequent infarct size (IS) were quantified by a threshold program. Severity (nadir) from the acute image was the lowest ratio of minimal/maximum counts from 5 short-axis slices. Infarct location was anterior in 22 and inferior in 39 patients. MAR was 33±15% LV and IS was 13±15% LV; 23 patients had no infarction despite MAR similar to those with infarction. Receiver-operator characteristic curve analysis identified a nadir value of 0.26 as providing the best separation of patients with and without infarction (sensitivity, 74%; specificity, 74%). This nadir threshold varied by infarct location: anterior defect, 0.21; inferior defect, 0.31. The sensitivity and specificity for absent infarction for these values were anterior, 69% and 67%, and inferior, 88% and 84%, respectively.

Conclusions—In a time frame in which the presence of residual blood flow is important, the severity of the acute $^{99m}$Tc-sestamibi defect can be used to predict whether infarction will develop despite successful reperfusion.

(Circulation. 1999;100:2392-2395.)

Key Words: myocardial infarction ■ blood flow ■ angioplasty ■ tomography

Collateral blood flow during coronary occlusion is an independent determinant of infarct size in animal and clinical studies.1–3 Preserved degrees of antegrade flow are also prognostically important during an acute ischemic event.4 These factors have greater impact with increasing duration of occlusion.2 We previously reported a method to quantify the degree of residual blood flow to the risk zone by use of noninvasive radionuclide imaging with $^{99m}$Tc-based perfusion tracers.3,5 Because residual blood flow can extend the time window of benefit for reperfusion therapy,2 a potential application of this methodology is to apply measures of residual flow to patients presenting late in the course of infarction, in whom the benefit of reperfusion therapy is uncertain. The purpose of this study was to determine optimal threshold values for residual blood flow to identify patients with potentially viable myocardium by this technique.

Methods

Study Group

The study group consisted of patients treated with direct coronary angioplasty for acute myocardial infarction between 120 and 240 minutes after symptom onset. Previous reports have shown that very early reperfusion (<120 minutes) during acute infarction invariably produces small or absent infarction, irrespective of collateral or antegrade blood flow.6 Patients were injected with $^{99m}$Tc-sestamibi before first balloon inflation as part of 1 of 2 randomized trials of reperfusion therapy during acute myocardial infarction7,8 and had an acute perfusion defect >6% of the left ventricle (LV) (representing 2 SD of the reproducibility of the measurement). Eighty patients met these criteria. Patients were excluded for the following reasons: TIMI flow after PTCA <3 (n=4), no follow-up scan (n=4), or previous myocardial infarction (n=11). Antegrade flow by angiography before and after the procedure was evaluated subjectively by a blinded observer (P.B.B.) using the Thrombolysis in Myocardial Infarction (TIMI) criteria. No stents were used.
Single Photon Emission CT Imaging
Before direct coronary angioplasty, 20 to 30 mCi of 99mTc-sestamibi was injected intravenously. Imaging acquisition occurred 1 to 6 hours after the angioplasty procedure. This methodology has been presented in previous publications. A follow-up image was obtained between 5 and 10 days after the acute scan and was processed in an identical fashion. Risk area and infarct size were quantified with a threshold of 60% of maximal counts as previously described. Myocardial salvage was quantified from the change in defect size adjusted for the risk area: (risk area - infarct size)/risk area.

Collateral (Residual) Flow Measurement
Defect severity was calculated from the acute tomographic image by previously described methods. Briefly, 5 short-axis slices were selected and displayed as circumferential count profiles by sampling for maximal activity at 6° radii from the center of the left ventricular cavity. Activity was then plotted against circumferential angle. The lowest ratio of minimal/maximal counts from these 5 slices was chosen as the nadir value for the left ventricle. A broader sample of values was taken by analyzing the nadir at 5 contiguous pixel thick slices in the central portion of the defect and averaging these values. Finally, the integral of the area falling below a 60% threshold of maximal counts was analyzed as a ratio of the maximal potential space that such a defect of a given extent could occupy calculated over 5 short-axis slices as previously described (severity index).

Statistical Analysis
The study group was prospectively divided into 2 groups: patients with a final infarct size of ≤3% of LV (group 1) and those with an infarct size >3% of LV (group 2). This value represents the lower limit of reliable detection of infarction. Receiver-operator characteristic curves were generated to define the optimum dichotomization of the radionuclide residual flow measure (nadir value) for separation of patients with absent versus measurable myocardial necrosis. Because previous data have indicated that the nadir measurement is significantly influenced by infarct location, separate analyses were performed for anterior and nonanterior infarct locations. Unpaired t tests were performed to compare risk area between groups.

Results
The mean age of the 61 patients was 59±11 years; 48 were men and 13 were women. The location of the injury was anterior in 22 patients and inferior or lateral in 39 patients. There were 23 patients in group 1 (final infarct size ≤3% LV) and 38 patients in group 2 (final infarct size >3% LV). The risk area for the 2 groups did not differ significantly (group 1, 31±20% LV; group 2, 32±17% LV; P=NS), nor did the percentage of patients with anterior infarction (group 1, 39%; group 2, 34%). The nadir measurement of residual flow was significantly different by group, with those patients who developed measurable necrosis having more severe acute perfusion defects: group 1 nadir, 0.32±0.14 versus group 2 nadir, 0.20±0.11, P=0.0003. Infarct size, by definition, was significantly different by group: group 1, 0.5±0.8% LV versus group 2, 19±14% LV; P<0.0001. Infarct size as a function of residual blood flow (nadir) is shown in Figure 1.

Sensitivity and specificity curves as a function of the nadir value for patients with anterior infarction were analyzed separately. Sensitivity and specificity of 69% and 67% for absent infarction, respectively, for patients with anterior infarction. The optimal value for patients with inferior infarction was 0.31, with a sensitivity of 88% and a specificity of 84% (see Figure 1). Myocardial salvage of the risk area was significantly greater for patients with nadir values above the 0.26 threshold (79% of risk area versus 48% of risk area salvaged, P=0.002). The difference remained significant when location-specific nadir values were used. Examples of patients with and without significant infarction are shown in Figure 3.

The severity index, which examines a broader portion of the hypoperfused zone, did not perform as well. A severity index of 0.31 provided a sensitivity of 63% and specificity of 65% for identifying patients with absent infarction. The broader sampling of nadir values (average of 5 thin slices within the defect) provided an optimal cutoff of 0.30, with a sensitivity of 68% and specificity of 70%.
Despite its simplicity, the nadir of the acute perfusion defect, generated before reperfusion therapy, is predictive of subsequent myocardial viability. Patients with no significant infarction could be separated from those with measurable necrosis on the basis of this measure of residual blood flow with a fair degree of confidence, although both false-positive and negative predictions occurred when any dichotomization was used. Analyzing a larger portion of the hypoperfused zone (rather than just the most severe area within the myocardium) did not improve the results. This finding is consistent with earlier studies examining these methods of quantification.3

We chose a homogeneous patient cohort to test this measure to control for variables known to affect infarct size. By separate analysis by infarct location, some of the variability in risk area can be eliminated.10 The narrow time frame for successful reperfusion was necessary to minimize the impact of time to treatment. The requirement of TIMI 3 flow after PTCA controlled for variability in reperfusion success.

The purpose of this study was simply to develop specific values that could be tested prospectively for preserved viability on the basis of residual flow. We used absent infarction because it leaves no room for ambiguity as to the benefit of reperfusion. However, prediction of a specific infarct size based solely on this measure is not possible. In carefully controlled animal studies in which all determinants of infarct size can be measured, only 80% of the variability in subsequent infarct size after reperfusion can be accounted for.1 Clinically, by measurement of risk area by 99mTc-sestamibi, collateral flow, and an estimate of the duration of coronary occlusion, ≈70% of the variability in infarct size can be accounted for.3 Figure 1 would demonstrate tighter confidence intervals if all these factors were included to predict infarct size.

A common reason that patients do not receive reperfusion therapy for myocardial infarction is late presentation. Yet, it is known that the presence of significant residual blood flow into the risk zone can extend the time window of benefit for reperfusion therapy.2 This noninvasive measure of residual blood flow could be applied to patients who present late in the course of myocardial infarction as a marker for potential myocardial salvage, because the benefit of reperfusion in this group is uncertain. However, we acknowledge that there may be benefits of restoring arterial patency independent of myocardial salvage. The measures described in this study could help to identify those patients most likely to benefit from late perfusion, but with some (30 to 60 minutes) delay for image acquisition. Given the uncertain benefit for late therapy, the delay is probably reasonable. Prospective studies are needed to test this approach.
Scatter from adjacent nonischemic myocardium (which contains high activity) tends to spill into the nadir of an inferior defect more than an anterior defect because of differences in risk area. This has been demonstrated clinically and in phantom experiments.3,11 For this reason, we recommend use of the separate dichotomization nadir values by infarct location.

References
Threshold Values for Preserved Viability With a Noninvasive Measurement of Collateral Blood Flow During Acute Myocardial Infarction Treated by Direct Coronary Angioplasty

Timothy F. Christian, Peter B. Berger, Michael K. O'Connor, David O. Hodge and Raymond J. Gibbons

Circulation. 1999;100:2392-2395
doi: 10.1161/01.CIR.100.24.2392

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1999 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/100/24/2392

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/