estimate resting LVEF if pharmacologic stress has been used and the time interval between stress and SPECT collection is above 1 hr. As for the influence of LVEDD, problems may have arisen if enlarged ventricles with normal function had to be considered, as would have been the care in patients with aortic valve disease. Since there were no patients with significant left ventricular enlargement but normal LVEF in our patient population, no conclusions can be drawn about these subjects.

## CONCLUSION

This study demonstrates that the $^{99m}$Tc-sestamibi C/M ratio can be used for an approximate assessment of left ventricular function. The accuracy of this parameter in resting $^{99m}$Tc-sestamibi SPECT scans appears similar to that reported for $^{201}$Tl.

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# PET Perfusion and Vasodilator Function After Angioplasty for Acute Myocardial Infarction


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The aims of this study were to validate invasive coronary Doppler flows against noninvasive PET assessments of myocardial perfusion and to examine the timing and degree of regional coronary vasodilator reserve recovery in patients who are successfully reperfused with primary angioplasty (PTCA) for acute myocardial infarction. **Methods:** PTCA was performed in 21 consecutive patients with acute myocardial infarction; the final diameter stenosis was 25% ± 7%. After restoration of TIMI Grade 3 flow, all patients underwent quantitative coronary angiography and distal Doppler coronary blood flow studies (basal and after adenosine-induced hyperemia) in the infarct and noninfarct vessels. Regional myocardial perfusion and vasodilator function were quantitated after intravenous adenosine infusion PET in all patients at 26 ± 9 hr after acute PTCA. These were repeated in 17 patients 9 ± 3 days later. **Results:** Post-PTCA resting coronary flow was 35 ± 15 ml/min in the infarct-related vessels and 50 ± 24 ml/min during peak hyperemia ($p < 0.05$). Coronary flow reserve (CFR) was 1.48 ± 0.34 and 2.08 ± 0.62 in the infarct and noninfarct vessels, respectively ($p < 0.001$). Early (<36 hr) PET myocardial perfusion reserves (MPR) in the infarct and noninfarct regions were 1.59 ± 0.33 and 2.03 ± 0.62 ($p < 0.01$). Doppler CFR and PET MPR were correlated in the infarct ($r = 0.61$, $p < 0.01$) and noninfarct ($r = 0.77$, $p < 0.0001$) regions. Follow-up PET studies demonstrated improved MPR in both infarct and noninfarct regions (1.93 ± 0.52 versus 2.54 ± 0.97, $p < 0.01$). The improvement in coronary vasodilator function from the time of acute PTCA to follow-up PET in the infarct region was significant ($p = 0.005$). **Conclusion:** After successful mechanical revascularization by PTCA after acute myocardial infarction, intracoronary Doppler blood flows and noninvasive PET regional myocardial perfusion are correlated within the wide range of reperfusion blood flows observed in patients with contrast angiographic TIMI Grade 3 flow. Serial PET studies demonstrated a trend towards continued improvement in the vasodilator response in infarct-related myocardial regions after the restoration of blood flow by PTCA. PET offers the potential for accurate noninvasive serial assessment of reperfusion blood flow after primary angioplasty for acute myocardial infarction.



**Key Words:** myocardial infarction; coronary flow; angioplasty; PET

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The immediate treatment goals for acute myocardial infarction are to re-establish blood flow, salvage myocardium and limit

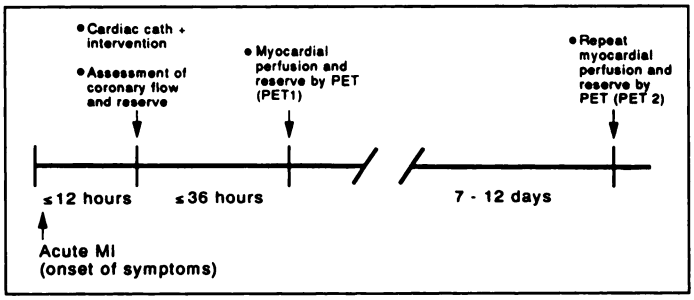


**FIGURE 1.** Schematic diagram of study protocol.

myocardial injury (*1,2*). The long-term goals are to sustain blood flow and enhance recovery of ventricular function in the infarct zone. Despite angiographic evidence of acute reperfusion after thrombolysis and the re-establishment of epicardial coronary blood flow, recovery of coronary vasodilator reserve may be variably attenuated (*3,4*). The regional vasodilator response after acute myocardial infarction has been studied using PET, and reduced myocardial vasodilator reserve has been demonstrated in both the infarct and noninfarct regions after successful thrombolytic therapy (*5*). In addition to the presence of residual stenosis after spontaneous or pharmacologic thrombolysis, impaired coronary vasodilator reserve may contribute to persistent or recurrent ischemia, and infarct expansion (*5,6*). Residual coronary obstruction is less severe after primary coronary angioplasty, but coronary vasomotor dysfunction may persist.

The purpose of this study was to directly assess and quantify coronary blood flow and myocardial vasodilator reserve in the infarct and noninfarct arterial beds of the same patients after the re-establishment of TIMI Grade 3 blood flow by primary angioplasty (PTCA). These findings were correlated and compared with early (<36 hr) and delayed (10 days) assessment of regional tissue perfusion and perfusion reserve by PET to fully characterize the early postinfarct time course of vasodilator function recovery.

## MATERIALS AND METHODS

### Patients

The study population consisted of 21 patients (age 54 ± 13 yr, 76% men) with acute Q-wave myocardial infarction confirmed by standard institutional enzyme and ECG criteria, representing 10% of patients treated with primary PTCA for acute myocardial infarction from July 1994 to April 1995. All patients were enrolled within 12 hr of symptom onset.

Twenty patients were treated for primary PTCA, and one patient received salvage PTCA for ischemia after intravenous tissue plasminogen activator. Patients were excluded from the study for systolic blood pressure <90 mmHg, evidence for prior myocardial infarction in the region subtended by the infarct artery and angiographic evidence of collaterals to the infarct artery. Two patients had prior myocardial infarction in a remote vascular region, and one patient had previous coronary bypass surgery. All patients provided written informed consent according to a protocol approved by the Human Investigations Committee of William Beaumont Hospital.

### Study Protocol

All 21 patients underwent quantitative coronary angiography before and after PTCA. Figure 1 outlines the study protocol. Doppler flow velocity studies were performed in the cardiac catheterization laboratory immediately after PTCA. Initial (early) PET studies were performed at rest and after pharmacologically-induced hyperemia in all patients (26 ± 9 hr after PTCA) and delayed PET studies were obtained in 17 patients (9 ± 3 days after PTCA). Four patients refused a follow-up PET study.

### Coronary Flow Velocity Measurements

Coronary blood flow velocity was measured with a 0.014- or 0.018-in diameter Doppler flowire as previously described (*7–9*). The Doppler wire was advanced to a location ≥2 cm distal to the target lesion, and placement into side branches or poststenotic velocity jets was carefully avoided. Basal and hyperemic Doppler flow velocity spectra were recorded at least 5 min after successful PTCA. Maximal hyperemia was induced by intracoronary adenosine (10 μg in the RCA, 20 μg in the LCA, as established by dose response curve) (*7*), and coronary flow reserve (CFR) was calculated as the ratio of hyperemic/basal average peak velocity (APV). Normal CFR was defined as ≥2.0 (*8*). Blood pressure, heart rate and Doppler wire position were recorded during each measurement.

The Doppler wire was then repositioned in a reference coronary artery (angiographically normal or <50% stenosis) supplying myocardium with preserved contractility; basal and hyperemic flow velocity measurements were repeated.

### Quantitative Coronary Angiography

All patients underwent selective coronary angiography with ioxaglute sodium or diatrizoate meglumine, before and after intracoronary nitroglycerin (100–200 μg). Quantitative angiography was performed using computerized edge detection by experienced operators blinded to the Doppler and PET data (*10*). Coronary artery dimensions were measured 2 cm distal to the flowire tip. Volumetric coronary flow was calculated according to the method of Doucette et al. (*11*).

### PET Imaging

Patients were studied in a fasting state. After positioning the patient in the whole-body tomograph, a transmission scan was acquired for 20 min. After an intravenous bolus administration of $^{13}$N-ammonia (20–25 mCi), serial emission myocardial images were acquired for 21 min (12 frames × 10 sec, 2 frames × 120 sec, 1 frame × 900 sec). Forty-five minutes later, after the physical decay of $^{13}$N activity, intravenous adenosine was infused at 0.14 mg · kg$^{-1}$ · min$^{-1}$ over 6 min, producing sustained coronary hyperemia similar to that produced by intracoronary adenosine (*12*). Heart rate and blood pressure were monitored during and after adenosine infusion. Patient movement was minimized by using a velcro strap across the thorax.

### PET Myocardial Image Analysis

The serially acquired 31-plane transaxial images were reconstructed using a Hanning filter with a cutoff frequency of 0.35 cycles/cm, yielding a spatial resolution of approximately 6.0 mm FWHM. Contiguous transaxial images were then reoriented on a Macintosh IIfx workstation (Apple Computer Inc., Cupertino, CA) into left ventricular short-axis slices as described previously (*13,14*). Operator-defined ROIs were placed over infarct and noninfarct myocardium on the short-axis cross-sections. ROIs were assigned based on polar map analysis of regional myocardial activity (>2 s.d. below normal in-plane activity or the lowest $^{13}$N activity on visual inspection was considered abnormal) (*15–17*). All sectorial ROIs encompassed between 40° and 60° of the myocardial circumference on a given short-axis cross-section to minimize statistical noise, were of similar dimensions in all regions, and were exactly reproduced on the follow-up (late) studies. Regional time-activity curves were generated by copying these sectional ROIs to all dynamic frames. The time-activity curves for $^{13}$N activity concentrations in arterial blood were derived from small (area = 50 mm$^2$) elliptical ROIs assigned to the left ventricular blood pool on dynamic images (*18*).

### Regional Myocardial Perfusion

Myocardial perfusion was quantified from the arterial input function of $^{13}$N-ammonia and the myocardial tissue time-activity curves using a previously validated two-compartment tracer kinetic model (*13*) and commercially available software (SIMPLE™, UCLA/Crump Institute for Biological Imaging, Los Angeles, CA). All time-activity curves were corrected for spillover of activity from the blood pool and physical radiotracer decay. Errors caused by patient motion and $^{13}$N-metabolites were reduced by fitting the first 3 min of tissue and arterial blood time-activity data acquired (*18,19*). The effects of partial volume were corrected with a constant recovery coefficient of 0.80, assuming a uniform myocardial activity thickness of 1 cm (*19*). Arterial blood and tissue time-activity curves were averaged from three contiguous ventricular planes (avoiding the apex and base of the heart) to minimize noise artifacts (*20*). Regional myocardial perfusion was expressed in terms of ml · g$^{-1}$ · min$^{-1}$. Myocardial perfusion reserve (MPR) was calculated as the ratio of basal-to-hyperemic regional myocardial perfusion.

### Short-Term Clinical Follow-up

Clinical follow-up was performed on 17 patients who had both early and delayed PET studies by phone interview and medical record review. Adverse clinical events recorded were death, reinfarction and recurrent angina.

### Statistical Analysis

Continuous data are reported as mean ± s.d. Linear regression was used to evaluate the relationships between the Doppler and PET-derived measurements of coronary blood flow and myocardial perfusion. Relationships are expressed as the Pearson correlation coefficient (r) and the coefficient of determination ($R^2$). Analysis-of-variance (ANOVA) for repeated measures was used to compare early and delayed PET parameters, and contingency table analysis (Fisher's exact test) was used to compare categorical variables. Multiple logistic regression was used to evaluate the effect of potential confounding variables (infarct location, infarct size, diabetes, previous infarction, time to reperfusion, heart rate and mean arterial blood pressure) on vasodilator reserve. A p value of $<0.05$ was considered statistically significant.

## RESULTS

### Clinical and Hemodynamic Status

The location of myocardial infarction was anterior in 10, inferior in 6 and lateral in 5. Creatine kinase was 1,808 ± 1,538 U/liter (range 680–7,556 U/liter). Mean arterial blood pressure was 96 ± 11 mmHg during PTCA, 84 ± 10 mmHg during early PET, and 83 ± 11 mmHg during delayed PET ($p < 0.01$ versus PTCA, p = ns between PET studies). Mean heart rate was 76 ± 12 bpm, 81 ± 13 bpm and 76 ± 14 bpm, respectively (p = ns). There was no significant change in clinical status (recurrent angina, reinfarction or arrhythmia) in any patient during hospitalization and the duration of the study protocol. Cardiac medications (beta-blockers, ACE inhibitors, nitrates) were unchanged between initial and late PET in 15 patients (88%); two patients had oral nitrates added during this interval.

### Coronary Angiography and Angioplasty

The extent of coronary artery disease was single-vessel disease in 14 patients, two-vessel disease in six patients and three-vessel disease in one patient. The infarct-related artery was the left anterior descending in nine, a diagonal artery in one, the right coronary artery in six and the left circumflex artery in five patients. In one patient with previous bypass surgery, the infarct-related artery was an ungrafted native vessel. The left ventricular ejection fraction was >40% in all patients at the time of PTCA.

PTCA was successful in all patients (defined as TIMI 3 flow and final diameter stenosis <50%). The average time from symptom onset to restoration of TIMI 3 flow was 5.1 ± 3 hr. The percent diameter stenosis decreased from 96% ± 7% (including 13 patients with baseline total occlusion and TIMI 0 flow) to 25% ± 7% after PTCA ($p < 0.0001$). All patients had TIMI 3 flow after PTCA, and there were no angiographic or clinical complications (Table 1).

### Basal and Hyperemic Coronary Flow Data (Doppler)

Basal Doppler APV in the infarct-related and noninfarct vessels were 17 ± 7 cm/sec and 21 ± 8 cm/sec, respectively, corresponding to basal volumetric flow of 35 ± 15 ml/min (range 14–67 ml/min) and 69 ± 51 ml/min (range 17–194 ml/min) ($p < 0.001$). After intracoronary adenosine, hyperemic APV was 23 ± 9 cm/sec in the infarct vessel, and 39 ± 16 cm/sec in the noninfarct vessel ($p < 0.01$); corresponding volumetric flow was 50 ± 24 ml/min (range 21–110 ml/min, $p < 0.05$ versus baseline) and 132 ± 87 ml/min (range 34–336 ml/min, $p < 0.01$ versus baseline), respectively.

### Basal and Hyperemic Myocardial Perfusion (PET)

The initial assessment of regional tissue perfusion by PET (Fig. 2) was obtained 26 ± 9 hr after PTCA. Resting (basal) myocardial perfusion was 0.54 ± 0.14 ml · g$^{-1}$ · min$^{-1}$ in the infarct regions and 0.82 ± 0.26 ml · g$^{-1}$ · min$^{-1}$ in the noninfarct regions ($p < 0.0001$); at peak hyperemia, regional perfusion increased to 0.89 ± 0.30 ml · g$^{-1}$ · min$^{-1}$ and 1.59 ± 0.44 ml · g$^{-1}$ · min$^{-1}$, respectively ($p < 0.0001$ versus infarct regions). The hyperemic response in both the infarct and noninfarct regions was statistically significant ($p < 0.001$).

Myocardial PET perfusion studies were repeated 9.4 ± 3 days after the initial study (approximately 10 days after infarction) in 17 patients. Basal perfusion in the infarct regions (0.55 ± 0.24 ml · g$^{-1}$ · min$^{-1}$) and the noninfarct regions (0.73 ± 0.26 ml · g$^{-1}$ · min$^{-1}$) were similar to early PET. However, peak hyperemic perfusion increased significantly in both the infarct and noninfarct regions (1.05 ± 0.59 and 1.79 ± 0.76 ml · g$^{-1}$ · min$^{-1}$ respectively, $p < 0.001$ versus basal perfusion, Fig. 3).

### Correlation of Doppler Coronary Flow and PET Myocardial Perfusion

Basal ($r = 0.58$, $R^2 = 0.34$, $p < 0.01$) and hyperemic ($r = 0.48$, $R^2 = 0.24$, $p < 0.05$) Doppler volumetric flow in the infarct artery weakly correlated with early regional PET perfusion. A similar correlation was identified during the basal state ($r = 0.58$, $R^2 = 0.33$, $p < 0.01$) and peak hyperemia, ($r = 0.65$, $R^2 = 0.42$, $p < 0.01$) in the noninfarct regions.

### Vasodilator Reserve

After PTCA, Doppler CFR was 1.48 ± 0.34 in the infarct arteries, and 2.08 ± 0.62 in the noninfarct arteries ($p < 0.001$). Early (<36 hr) PET myocardial perfusion reserve (MPR) in the infarct and noninfarct regions was 1.59 ± 0.33 and 2.03 ± 0.62, respectively ($p < 0.01$).

There was a significant correlation between CFR and MPR in the infarct ($r = 0.61$, $R^2 = 0.37$, $p < 0.01$, Fig. 4A), and noninfarct regions ($r = 0.77$, $R^2 = 0.60$, $p < 0.0001$, Fig. 5). On delayed PET images, MPR increased to 1.93 ± 0.52 in the infarct ($p = 0.07$ versus early PET) and 2.54 ± 0.97 in the noninfarct regions ($p = 0.16$ versus early PET, $p < 0.01$ between regions). Having established a correlation between Doppler CFR and early PET MPR, an overall assessment of vasodilator reserve (CFR and MPR) was performed over three

**TABLE 1**
Patient Data

| Patient no. | Infarct artery | Reference artery | Diameter stenosis-pre | Diameter stenosis-post | Basal flow IA (ml/min) | Hyperemic flow IA (ml/min) |
|---|---|---|---|---|---|---|
| 1 | RCA | LCX | 92 | 12 | 21.7 | 31.8 |
| 2 | LAD | LCX | 87 | 13 | 35.5 | 52.3 |
| 3 | LAD | LCX | 100 | 27 | 45.8 | 74.1 |
| 4 | LCX | LAD | 100 | 28 | 22.8 | 28.6 |
| 5 | RCA | LAD | 96 | 25 | 66.8 | 80.2 |
| 6 | LAD | LCX | 88 | 28 | 54.0 | 60.2 |
| 7 | LCX | LCX[§] | 91 | 21 | 60.0 | 62.0 |
| 8 | LAD | LCX | 100 | 29 | 44.3 | 67.8 |
| 9 | LAD | LCX | 100 | 19 | 31.0 | 52.6 |
| 10 | LCX | LAD | 100 | 23 | 23.4 | 30.9 |
| 11 | LAD | LCX | 100 | 21 | 23.8 | 23.8 |
| 12 | LAD | LCX | 100 | 34 | 13.8 | 21.6 |
| 13 | RCA | LCX | 100 | 18 | 56.4 | 109.9 |
| 14 | RCA | LAD | 100 | 29 | 31.8 | 53.1 |
| 15 | RCA | LAD | 100 | 33 | 20.7 | 35.6 |
| 16 | RCA | LCX | 96 | 38 | 31.8 | 42.0 |
| 17 | LAD | LCX | 100 | 22 | 29.2 | 30.0 |
| 18 | LAD | LCX | 100 | 26 | 14.6 | 21.3 |
| 19 | LAD | LCX | 82 | 38 | 40.7 | 58.8 |
| 20 | LCX | LAD | 78 | 17 | 48.7 | 88.7 |
| 21 | LCX | RCA | 100 | 27 | 20.6 | 27.4 |
| Mean ± s.d. | | | 97 ± 7[‡] | 25 ± 7[‡] | 35 ± 15[*] | 50 ± 24[*] |

| Patient no. | Basal flow RA (ml/min) | Hyperemic flow RA (ml/min) | PET 1 BAS-IA $(ml \cdot g^{-1} \cdot min^{-1})$ | PET 1 HYP-IA $(ml \cdot g^{-1} \cdot min^{-1})$ | PET 1 BAS-RA $(ml \cdot g^{-1} \cdot min^{-1})$ | PET 1 HYP-RA $(ml \cdot g^{-1} \cdot min^{-1})$ | PET 2 BAS-IA $(ml \cdot g^{-1} \cdot min^{-1})$ | PET 2 HYP-IA $(ml \cdot g^{-1} \cdot min^{-1})$ | PET 2 BAS-RA $(ml \cdot g^{-1} \cdot min^{-1})$ | PET 2 HYP-RA $(ml \cdot g^{-1} \cdot min^{-1})$ |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 84.9 | 143.3 | 0.43 | 0.63 | 0.76 | 1.36 | 0.48 | 0.97 | 0.83 | 1.82 |
| 2 | 31.3 | 62.3 | 0.51 | 0.65 | 0.62 | 1.52 | — | — | — | — |
| 3 | 36.3 | 122.2 | 0.71 | 1.07 | 0.63 | 1.48 | 0.45 | 0.74 | 0.84 | 1.25 |
| 4 | 72.1 | 93.7 | 0.52 | 0.71 | 0.73 | 1.03 | — | — | — | — |
| 5 | 147.4 | 163.8 | 0.74 | 1.00 | 1.60 | 1.58 | — | — | — | — |
| 6 | 23.7 | 47.8 | 0.63 | 0.67 | 0.92 | 1.59 | 0.47 | 1.28 | 0.64 | 2.59 |
| 7 | 152.0 | 152.6 | 0.61 | 0.80 | 1.47 | 1.62 | — | — | — | — |
| 8 | 127.0 | 335.0 | 0.46 | 0.77 | 0.77 | 1.77 | 0.40 | 0.86 | 0.51 | 1.31 |
| 9 | 81.5 | 246.0 | 0.74 | 1.67 | 0.80 | 2.81 | 0.50 | 1.11 | 0.64 | 1.25 |
| 10 | 38.9 | 94.7 | 0.43 | 0.95 | 0.94 | 1.79 | 0.30 | 0.51 | 0.68 | 0.99 |
| 11 | 69.2 | 132.0 | 0.33 | 0.55 | 0.65 | 1.50 | 0.44 | 0.50 | 1.21 | 1.30 |
| 12 | 36.3 | 75.9 | 0.50 | 0.72 | 0.59 | 1.14 | 0.42 | 0.50 | 0.48 | 0.61 |
| 13 | 193.7 | 293.7 | 0.66 | 1.38 | 0.82 | 1.96 | 0.41 | 1.11 | 0.49 | 2.06 |
| 14 | 43.0 | 168.3 | 0.65 | 0.99 | 0.74 | 2.27 | 0.35 | 0.72 | 0.43 | 1.65 |
| 15 | 32.9 | 76.0 | 0.37 | 1.38 | 0.63 | 1.46 | 0.75 | 1.18 | 1.00 | 1.95 |
| 16 | 127.2 | 268.3 | 0.70 | 0.94 | 0.94 | 2.03 | 0.85 | 1.33 | 0.93 | 2.36 |
| 17 | 37.3 | 67.5 | 0.41 | 0.63 | 0.81 | 0.97 | 0.67 | 0.88 | 0.87 | 1.70 |
| 18 | 22.0 | 34.2 | 0.33 | 0.60 | 0.83 | 1.21 | 0.50 | 0.93 | 0.75 | 2.03 |
| 19 | 17.0 | 38.1 | 0.37 | 0.68 | 0.62 | 1.44 | 0.67 | 1.29 | 0.56 | 2.14 |
| 20 | 26.7 | 37.7 | 0.68 | 1.21 | 0.80 | 1.39 | 1.18 | 3.02 | 1.30 | 3.82 |
| 21 | 47.8 | 114.1 | 0.56 | 0.83 | 0.57 | 1.32 | 0.48 | 1.26 | 0.42 | 1.23 |
| Mean ± s.d. | 69 ± 51[†] | 132 ± 87[†] | 0.54 ± 0.14 | 0.89 ± 0.30 | 0.82 ± 0.30 | 1.59 ± 0.44 | 0.55 ± 0.24 | 1.05 ± 0.59 | 0.73 ± 0.26 | 1.79 ± 0.76 |

[*]$p < 0.05$.
[†]$p < 0.01$.
[‡]$p < 0.0001$.
[§]proximal obtuse marginal artery.
IA = infarct artery region; RA = reference artery region; PET 1 = initial PET study; PET2 = follow-up PET study; PRE = pre-angioplasty; POST = post-angioplasty; LAD = left anterior descending artery (including diagonals); RCA = right coronary atery (including posterior descending); LCX = circumflex artery (including obtuse marginals).

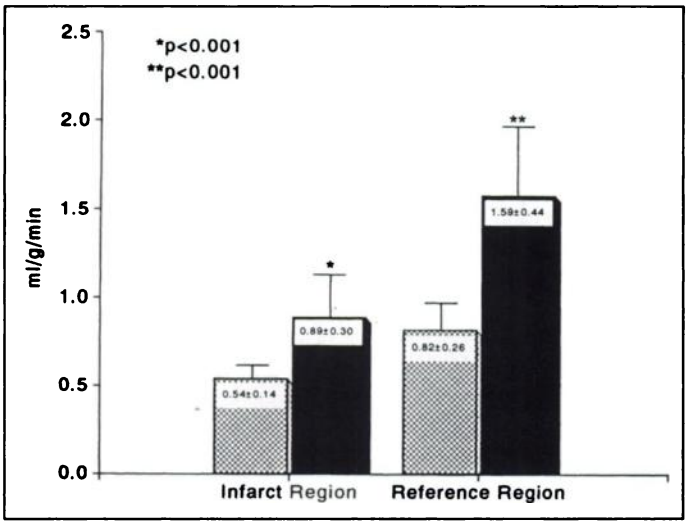


**FIGURE 2.** Regional myocardial perfusion (basal and hyperemic) in the infarct and reference (noninfarct) regions as assessed by early PET (n = 21). Cross-hatched bars represent basal state, solid bars represent peak hyperemia (*p < 0.001, basal versus peak hyperemia; **p < 0.001, basal versus peak hyperemia).

time points (Doppler, PET 1, PET 2). There was significant improvement in overall vasodilator reserve in the infarct regions (p = 0.005) but not in the noninfarct regions (p = 0.09). The percent of patients with vasodilator reserve >2.0 in the infarct regions increased from 5% immediately after angioplasty (by Doppler) to 47% at 10 days (by PET, p = 0.005, Fig. 6). Improvement in vasodilator function was not associated with infarct location or size, diabetes, history of previous infarction, time to reperfusion, heart rate or mean arterial pressure.

### Clinical Follow-up

The mean time of follow-up was 8 ± 2 mo after hospitalization for acute infarction. Five patients (29%) were hospitalized for recurrent angina or reinfarction; the other 12 patients remained asymptomatic. Although there was no difference in MPR early after PTCA (1.52 ± 0.45 versus 1.66 ± 0.31, p = ns), patients with adverse cardiac events demonstrated a lower MPR in the infarct regions on delayed (10 days) PET studies (1.54 ± 0.34 versus 2.07 ± 0.52, p = 0.058).

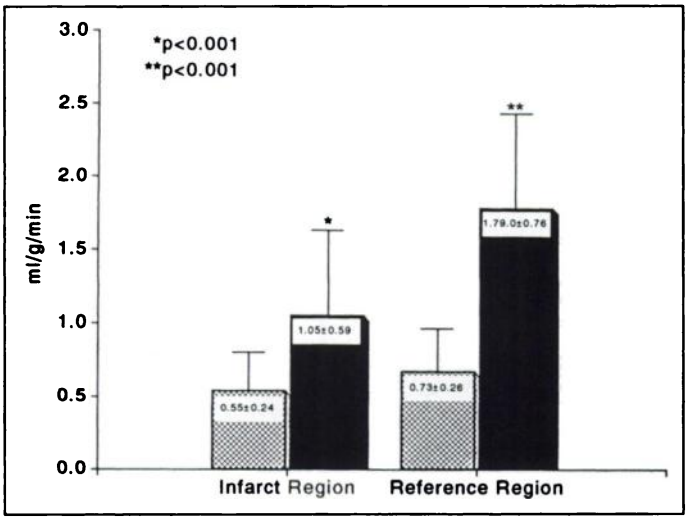


**FIGURE 3.** Delayed PET (n = 17) showing regional basal and hyperemic perfusion, with persistent basal hypoperfusion in both the infarct and noninfarct regions. *p < 0.001; ** p < 0.001.

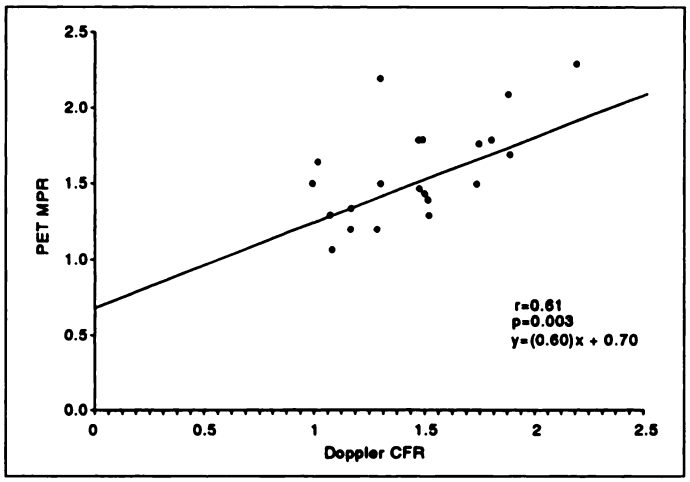


**FIGURE 4.** Plot of the linear relationship between Doppler-derived CFR and PET-derived MPR in the infarct regions. These indices of vasodilator reserve significantly correlated, with r = 0.61 (p < 0.01).

## DISCUSSION

Primary coronary angioplasty is an established therapeutic alternative to thrombolytic therapy for reperfusion of acute myocardial infarction (*21,23*). The current study demonstrates a significant early impairment of basal and hyperemic Doppler coronary blood flow and PET perfusion in the infarct-related arterial bed, despite angiographically successful PTCA with insignificant residual coronary stenosis. This post-PTCA study confirms recent findings of abnormal tissue perfusion after successful thrombolytic therapy and restoration of TIMI 3 flow (*24*), and extends the current understanding of coronary flow-myocardial perfusion correlation in both the infarct and noninfarct regions, suggesting that either technique can be used to assess the early impact of successful acute PTCA. The incomplete improvement in PET MPR at approximately 10 days after successful PTCA indicates that coronary vasodilator function is slow to improve, despite initial angiographic stenosis reduction and restoration of TIMI 3 flow in the infarct artery. The wide range of Doppler and PET coronary flow and perfusion reserve within this TIMI 3 flow group suggests that a physiologic assessment is more sensitive than angiography for estimating the degree of reperfusion after successful PTCA.

### Previous Assessments of Reperfusion After Acute Myocardial Infarction

Attenuated coronary flow reserve and myocardial perfusion has been observed in proximal segments of coronary arteries

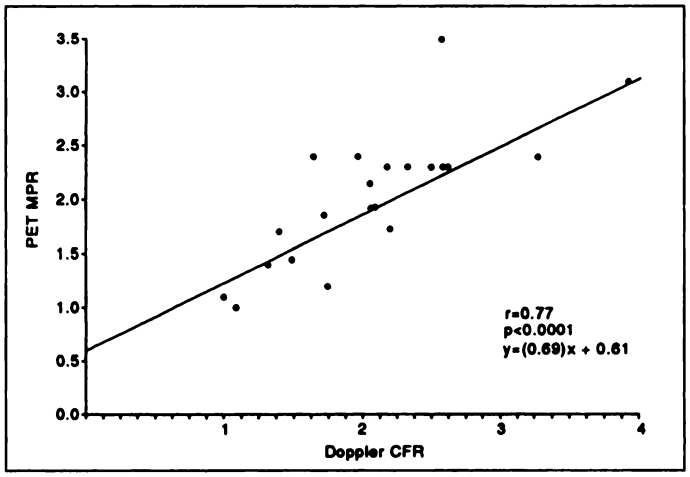


**FIGURE 5.** Correlation of vasodilator reserve in the noninfarct regions, showing a significant relationship (r = 0.77, p < 0.0001).

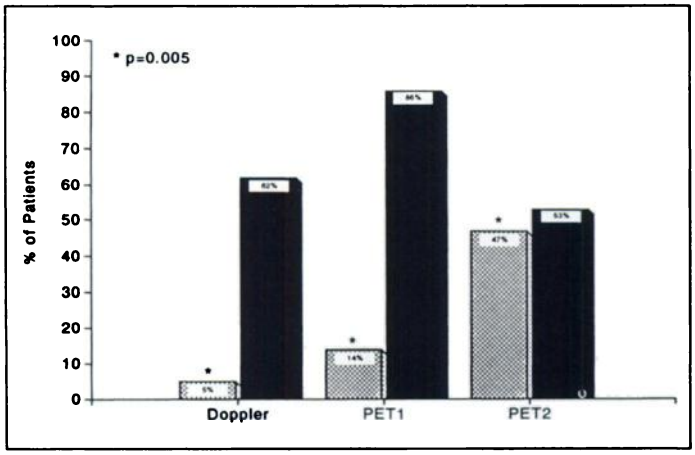


**FIGURE 6.** Percent of patients with vasodilator reserve >2.0 on serial assessment. Crosshatched bars represent infarct regions and solid bars correspond to noninfarct regions. PET 1 = early study, PET 2 = delayed study. Overall improvement in vasodilator reserve was significant in the infarct regions (*p = 0.005).

after successful angioplasty (*4*) or thrombolysis (*3,4,24,25*) for acute myocardial infarction. This vasodilator impairment has been attributed to dysfunction of arterial resistance vessels or microvascular spasm (*3,26*). This study demonstrates a wide range of vasodilator function in the infarct regions after successful primary PTCA which may be the result of a no-reflow phenomenon in some vascular beds. Studies performed during the early phases of acute myocardial infarction have reported discrepancies between angiographic measurements of flow and stenosis severity, and physiologic assessment of coronary blood flow using contrast echocardiographic myocardial perfusion (*23,25*) and intracoronary Doppler flow measurements (*3,4*).

Proximal Doppler coronary flow reserve was severely impaired immediately after successful PTCA for acute myocardial infarction, but improved to near baseline at 16 days after PTCA (*4*). Similar findings were observed in this study at 10 days after PTCA using quantitative PET imaging.

### Physiologic Assessment of Stable Coronary Stenosis

Successful elective PTCA for stable coronary artery disease does not immediately improve proximal CFR (*27*), suggesting that abnormal vasodilator function can persist beyond the time of successful revascularization. Previous studies demonstrated that distal Doppler coronary flow reserve was highly correlated with semiquantitative measurements of myocardial perfusion in patients with stable coronary artery disease (*28,29*). While improvements in PET myocardial perfusion (*30*) and distal intracoronary Doppler blood flow velocity (*9*) have been demonstrated in separate studies of patients undergoing PTCA, the current study correlates these two physiologic parameters in patients undergoing primary PTCA for acute myocardial infarction.

### Acute Physiologic versus Angiographic Assessment of Coronary Reperfusion

TIMI flow has become the clinical standard for the early postreperfusion evaluation of coronary flow (*31*). Both TIMI Grade 2 and 3 angiographic flow have been considered indicative of successful reperfusion, with associated improvement in left ventricular function and reduced cardiac event rates after thrombolysis or primary PTCA (*32*). Recent studies have identified a disparity in clinical outcomes when patients are stratified into TIMI flow ≤2 and TIMI flow = 3 (*33*). The outcome of TIMI flow = 2 is similar to that of TIMI flow ≤1.

Preliminary coronary flowire studies in patients undergoing primary PTCA within 6 hr of an acute myocardial infarction demonstrate a severe distal impairment of coronary vasodilatory reserve, which gradually improved over 2 wk but remained attenuated for up to 6 mo after PTCA (*34*). In another study, poststenotic coronary flow velocity did not differ between TIMI 0, 1 and 2, while patients with TIMI 3 flow had widely variable but significantly higher coronary flow velocities (*35*).

A similar phenomenon was recorded in the current study in infarct-related vessels using both Doppler techniques and noninvasive PET myocardial perfusion imaging after successful PTCA. The range of coronary flow velocities recorded within this angiographic flow subset (i.e., TIMI Grade 3) may reflect differences in vasodilator functional recovery, and could potentially contribute to differences in functional recovery and cardiac event rates after successful revascularization for acute myocardial infarction. Preliminary data (*36*) suggests that Doppler blood flow parameters can predict improvement in regional ventricular wall motion after mechanical revascularization for acute infarction. Improvement in myocardial perfusion similar to that documented in the current study would be expected to enhance postinfarction ventricular functional recovery.

### Physiologic Covariables of Reperfusion

Coronary vasodilator physiology is but one of the factors that may influence functional recovery after myocardial infarction. Carlson et al. (*37*) reported that tissue edema can affect myocardial perfusion, infarct size and ventricular function in a canine model of coronary occlusion and reperfusion. Using proton nuclear magnetic relaxation (NMR) spectroscopy, these investigators demonstrated that mechanisms other than local tissue edema contribute to persistent perfusion abnormalities (i.e., no-reflow phenomenon) and contractile dysfunction after coronary reperfusion. Previous studies have demonstrated that the infusion of mannitol diminishes tissue edema, reduces NMR relaxation parameters, and attenuates ultrastructural myocyte injury in ischemic-reperfused canine myocardium (*38*).

Serial measurements early after reperfusion in experimental myocardial infarction (*39*) and in humans have demonstrated persistent depression of regional vasodilator reserve in noninfarct territories 6 mo after myocardial infarction (*5*). In the current study, myocardial perfusion reserve had not increased significantly in the noninfarct myocardial regions after PTCA (from 2.0 ± 0.6 acutely to 2.5 ± 1.0 at 10 days). Although this finding could be attributed in seven patients to multivessel disease, PET myocardial perfusion measurements in the current and previous (*5*) studies have demonstrated a persistent abnormality of vasodilator reserve in noninfarcted myocardium that may negatively affect global ventricular functional recovery after successful reperfusion. In this study, Doppler and PET measurements were obtained in myocardial regions subtended by vessels with <50% diameter stenosis.

### Clinical Implications

This study demonstrates the comparable clinical utility of a noninvasive (PET) and intracoronary Doppler techniques for the assessment of vasodilator function in patients after acute myocardial infarction. Our findings also extend prior studies of thrombolytic reperfusion by studying patients treated with primary PTCA, and by the observation of a wide range of reperfusion blood flows within the TIMI 3 grade. In addition, basal and hyperemic perfusion remained impaired up to 10 days in the infarct myocardial regions, although there was a trend towards improvement after primary PTCA that has not been reported after thrombolytic therapy. This may be the result of less microvascular injury after mechanical revascularization.

Although not the main purpose of this study, a trend was also noted towards increased future cardiac events in patients with impaired regional MPR on the delayed (10-day) PET studies. The implications of these data for determining the likelihood of recurrent ischemic events after primary PTCA remain to be confirmed. Quantitative PET may prove useful in evaluating patients prognostically in this postinfarction setting.

### Study Limitations

Hyperemic blood flow during Doppler assessment was achieved with intracoronary adenosine, but an intravenous infusion was used for PET studies. Both techniques have been shown to create reproducible levels of hyperemia (*7*). Reference coronary flow velocities were obtained in vessels supplying noninfarcted myocardium adjacent to the infarct zone. It is conceivable that abnormal flow in these regions may have influenced vasodilator reserve measurements in the reference regions. Doppler measurements in reference regions were recorded in vessels that subtended myocardium with preserved contractility.

While initial PET studies were obtained 26 ± 9 hr after Doppler assessment, there were minimal differences in the hemodynamic status, and no difference in the clinical status of any patient during these two time periods. Finally, there are potential technical limitations to the quantification of myocardial perfusion by $^{13}$N-ammonia PET, including patient motion, position and the assumption of a homogeneous ventricular wall thickness. Patient motion was minimized as described previously, and the position of the patient on initial PET was recorded and reproduced exactly during the delayed study.

## CONCLUSION

The current study validates the direct invasive measurements of Doppler coronary flow and flow reserve using noninvasive PET myocardial perfusion and perfusion reserve in patients treated with primary PTCA for acute myocardial infarction. The correlation between these techniques over a range of basal and hyperemic flows, and the comparability of the invasive and noninvasive indices of vasodilator function suggest that either technique could be applied in this setting to evaluate coronary physiology. The relative imprecision of angiographic TIMI 3 flow for reperfusion assessment is illustrated by the wide range of measured intracoronary blood flow and myocardial perfusion values in the same vascular beds. The variable degree of improvement in infarct zone myocardial perfusion reserve after successful PTCA suggests that precise quantification of regional vasodilator function may be a better predictor of ventricular functional recovery and clinical outcomes than currently used angiographic assessments of reperfusion flow.

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# Severe Right Ventricular Contraction Asynchronism Revealing a Large Pericardial Effusion

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A gated blood-pool equilibrium radionuclide angiography was performed in a patient to determine the ejection fraction for doxorubicin cardiotoxicity evaluation. The phase image of the first harmonic of the Fourier analysis revealed a severe delay of the right ventricular contraction compared with that of the left ventricle. This right ventricular contraction asynchronism was due to a large pericardial effusion, confirmed by the presence of the halo sign on the summed gated images and by echocardiography. The phase delay moves towards normalization after pericardiocentesis. Although radionuclide angiocardiography is not the best method for identification of pericardial effusion, this diagnosis should be evoked when a severe homogenous delay of the right ventricular contraction is observed.

**Key Words**: pericardial effusion; Fourier phase analysis; radionuclide angiography

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In most nuclear medicine departments, routine interpretation of gated blood-pool equilibrium scintigraphy includes the study of the first harmonic of the Fourier analysis (*1*). The parametric phase image has demonstrated a pattern of delayed right ventricular contraction in many heart diseases involving the right ventricle, such as right bundle branch block (*2*), right ventricular myocardial infarction (*3*) and arrhythmogenic right ventricular dysplasia (*4*).

In this article, we report a severely delayed right ventricular contraction demonstrated by the phase image revealing a large pericardial effusion.

## CASE REPORT

A 47-yr-old woman, a smoker, without previous history of cardiac disease was admitted to the hospital after the discovery of bilateral nodular opacities and a left pleural effusion on chest radiograph. Bronchoscopy guided biopsies showed a lung adenocarcinoma and the pleural aspiration revealed a metastatic pleural dissemination (mammography, CT scan of the abdomen, gastroscopy and barium enema were negative). The patient underwent a treatment based on cancer chemotherapy and was referred to the nuclear medicine department for left ventricular ejection fraction determination after a cumulated dose of doxorubicin of 200 mg/m$^2$. At the time of this examination the patient did not complain of dyspnea or chest pain. The cardiac examination showed a tachycardia of about 95 bpm without other clinical abnormalities. The electrocardiogram was normal except for tachycardia (Fig. 1). The blood pool was labeled with 555 MBq of $^{99m}$Tc. Imaging was performed using a small field of view Philips gamma-camera equipped with a general-purpose, parallel-hole collimator. Data were acquired in the left anterior oblique view adjusted to obtain the best separation between right and left ventricles. Thirty two 64 × 64 frames were recorded with a total of 6 million counts. The image of the first harmonic of the Fourier analysis showed that the right ventricular contraction was delayed by 79° compared with the left ventricle (Fig. 2A,B). This delay corresponded to 139 msec. On the phase image, the contraction of the right atrium appears also paradoxical. The left ventricular ejection fraction was 47% and the right ventricular ejection fraction was 32% (Table 1).

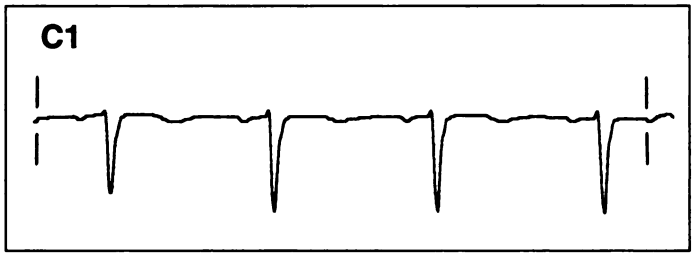


**FIGURE 1.** Electrocardiogram (before pericardiocentesis) shows the lack of right ventricular electrical conduction delay.

The examination of the left and right ventricular volume curves confirmed the delayed right ventricular minimum of counts with a shortened right ventricular filling (Fig. 3A). The late right ventricular filling was mainly due to the atrial contraction. The examination of the added 32 frames showed the "halo sign" surrounding the heart (Fig. 4). A two-dimensional echocardiography was performed and confirmed the presence of a large circumferential pericardial effusion with a 24 mm anterior echo-free space, a diastolic collapse of the right ventricle and a collapse of the right atrium suggestive of cardiac tamponade (Fig. 5). The pericardiocentesis aspirated 500 cc of cloudy fluid. A cytologic study of the pericardial fluid confirmed the metastatic effusion of an adenocarcinoma.

Further evaluation using two-dimensional echocardiography showed an important reduction of the effusion and normal right heart chambers. Another radionuclide angiography was performed 2 mo later to estimate anthracycline cardiotoxicity. The right

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