*Clinical Investigation*

# Left Ventricular Remodeling after Late Revascularization

## Correlates with Baseline Viability

**Pravin K. Goel, DM, FACC**
**Tanuj Bhatia, MD, DM**
**Aditya Kapoor, DM, FACC**
**Sanjay Gambhir, MD**
**Prasanta K. Pradhan, MD**
**Sukanta Barai, MD**
**Satyendra Tewari, DM, FACC**
**Naveen Garg, DM, FACC**
**Sudeep Kumar, DM, FACC**
**Suruchi Jain, MD**
**Ponnusamy Madhusudan, MD**
**Siddegowda Murthy, MBBS**

*The ideal management of stable patients who present late after acute ST-elevation myocardial infarction (STEMI) is still a matter of conjecture. We hypothesized that the extent of improvement in left ventricular function after successful revascularization in this subset was related to the magnitude of viability in the infarct-related artery territory. However, few studies correlate the improvement of left ventricular function with the magnitude of residual viability in patients who undergo percutaneous coronary intervention in this setting.*

*In 68 patients who presented later than 24 hours after a confirmed first STEMI, we performed resting, nitroglycerin-enhanced, technetium-99m sestamibi single-photon emission computed tomography–myocardial perfusion imaging (SPECT–MPI) before percutaneous coronary intervention, and again 6 months afterwards. Patients whose baseline viable myocardium in the infarct-related artery territory was more than 50%, 20% to 50%, and less than 20% were divided into Groups 1, 2, and 3 (mildly, moderately, and severely reduced viability, respectively). At follow-up, there was significant improvement in end-diastolic volume, end-systolic volume, and left ventricular ejection fraction in Groups 1 and 2, but not in Group 3.*

*We conclude that even late revascularization of the infarct-related artery yields significant improvement in left ventricular remodeling. In patients with more than 20% viable myocardium in the infarct-related artery territory, the extent of improvement in left ventricular function depends upon the amount of viable myocardium present. The SPECT–MPI can be used as a guide for choosing patients for revascularization.* ***(Tex Heart Inst J 2014;41(4):381-8)***

***Key words:*** *Comparative study; infarct-related artery territory; left ventricular remodeling; myocardial infarction, acute ST-elevation/therapy; myocardial reperfusion; percutaneous coronary intervention; prospective studies; residual viability; time factors; technetium Tc 99m sestamibi/diagnostic use; tissue survival; tomography, emission-computed, single-photon; ventricular function, left*

***From:*** *Departments of Cardiology (Drs. Bhatia, Garg, Goel, Kapoor, Kumar, and Tewari) and Nuclear Medicine (Drs. Barai, Gambhir, Jain, Madhusudan, Murthy, and Pradhan), Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow 226014, India*

***Address for reprints:*** *Tanuj Bhatia, MD, DM, Department of Cardiology, SGPGIMS, Lucknow 226014, India*

***E-mail:*** *tanujbhatia21@rediffmail.com*



Late presentation of acute ST-elevation myocardial infarction (STEMI) is not uncommon on the Indian subcontinent, or indeed in much of the rest of the world. Late presenters contribute an important portion of acute myocardial infarction (MI) patients in the day-to-day practice of a great many physicians.[1-3] Yet studies of late revascularization and its effects on myocardial salvage and clinical outcomes have yielded conflicting results.[4,5]

The largest study of the efficacy of late revascularization, the Occluded Artery Trial (OAT)[6]—together with a few small studies[7,8]—concluded that late intervention in acute-STEMI patients affords no clinical benefit. This, however, defies the basic concept of the "open-artery" hypothesis[9] and all the reported secondary benefits[10,11] of revascularization—even when performed late. Indeed, several smaller studies[12-14] have shown the recovery of left ventricular (LV) function after late revascularization.

At the outset of this prospective single-center study, our hypothesis was that recovery of LV function after revascularization would relate to the magnitude of myocardial viability within the territory of the infarct-related artery (IRA). The Occluded Artery Trial–Viability Ancillary Study (OAT–NUC)[15] attempted to study this aspect by classifying viability into 2 broad categories on the basis of an arbitrary cutoff point of 40%: an average infarct zone uptake of less than 40% indicated severely reduced viability. Viability, however, lies on a continuum[16,17] that includes grades not categorized on an all-or-none basis. In the setting of late presentation of STEMI, we critically examined the magnitude of baseline infarct-zone viability and attempted to relate that to the extent of LV remodeling and to the recovery of LV function at 6 months after successful revascularization.

## Patients and Methods

Table I shows the baseline clinical characteristics of the study patients. Patients enrolled in the study were from 30 to 76 years of age (mean age, 57.04 ± 10.38 yr). These were patients with confirmed first-index STEMI (that is, ischemic symptoms, elevated cardiac markers, and typical MI electrocardiographic changes) more than 24 hours after the onset of pain (3rd calendar day and up to 28 d), in the absence of signs of continued or recurrent ischemia. None of the patients had any prior history of infarction. All patients entering the paired analysis showed either occlusion of the IRA or significant stenosis in the patent IRA, regardless of the baseline preprocedural Thrombolysis in Myocardial Infarction (TIMI) flow grade on coronary angiography.

From June 2011 through June 2012, 92 patients were initially enrolled in the study. All 92 patients underwent single-photon emission computed tomography–myocardial perfusion imaging (SPECT–MPI) before angiography. All patients were administered 0.4 mg of sublingual nitroglycerin followed 5 to 10 minutes later by 15 to 20 mCi of technetium-99m sestamibi; one hour later, they underwent imaging at rest, by use of standard algorithms optimized for each Infinia™ Hawkeye™ 4 camera and computer system (GE Healthcare; Wausheka, Wis).

Eight patients were excluded after angiography showed that they had recanalized IRAs due to thrombolysis, either spontaneous or pharmacologic. Follow-up scans could not be performed in 12 patients, 2 for reason of death during the follow-up period and 10 for various other reasons. In 4 patients, either baseline or follow-up data were unusable for analysis. The exclusion criteria were substantial persistent or recurrent ischemia, cardiogenic shock, New York Heart Association functional class III or IV heart failure, serum creatinine level >2.5 mg/dL, and angiographically significant left main or 3-vessel coronary artery disease. A detailed history was taken of each patient's risk factor profile, index event, time to presentation, TIMI score, Killip score, and record of receiving thrombolytic therapy. After the elimination of these 24 patients, paired analysis was performed for the remaining 68 patients (Fig. 1).

The characteristics of the precipitating MI are described in Table II. Myocardial infarction was localized to the anterior wall in 70.6% of the study patients. The time to presentation varied from 3 to 28 days, with a mean presentation delay of 11.59 ± 8.5 days and a median delay of 9 days. Fifty percent of the patients

**TABLE I.** Baseline Clinical Characteristics

| Variable | **Overall** (N=68) | **Group 1** (n=37) | **Group 2** (n=19) | **Group 3** (n=12) | ***P* Value** |
|---|---|---|---|---|---|
| **Demographics** | | | | | |
| Age (yr) | 57.04 ± 10.38 | 58.76 ± 9.92 | 54.68 ± 11 | 55.5 ± 10.7 | 0.329 |
| Male sex | 54 (79.4) | 28 (75.7) | 16 (84.2) | 10 (83.3) | 0.706 |
| **Clinical history** | | | | | |
| Diabetes mellitus | 17 (25) | 11 (29.7) | 4 (21.1) | 2 (16.7) | 0.593 |
| Hypertension | 22 (32.4) | 12 (32.4) | 4 (21.1) | 5 (41.6) | 0.245 |
| Family history of CAD | 6 (8.8) | 4 (10.8) | 2 (10.5) | 0 | 0.494 |
| Tobacco use | 21 (30.9) | 7 (18.9) | 7 (36.8) | 7 (58.3) | 0.03 |
| Height (cm) | 163.68 ± 6.4 | 163.46 ± 6.64 | 164.84 ± 6.33 | 162.67 ± 6.01 | 0.615 |
| Weight (kg) | 68.66 ± 10.55 | 67.35 ± 9.72 | 68.47 ± 11.61 | 73 ± 11.03 | 0.275 |
| Body mass index (kg/m$^2$) | 25.74 ± 4.46 | 25.35 ± 4.39 | 25.25 ± 4.27 | 27.73 ± 4.8 | 0.237 |
| **Laboratory findings** (mg/dL) | | | | | |
| Fasting blood sugar | 117.41 ± 63.65 | 119.84 ± 70 | 115.95 ± 54.73 | 112.25 ± 60.78 | 0.933 |
| Triglycerides | 129.15 ± 58.06 | 123.03 ± 54.68 | 135.53 ± 61.6 | 137.92 ± 65.23 | 0.64 |
| Total cholesterol | 131.74 ± 42.94 | 121.35 ± 42.25 | 143.11 ± 41.52 | 145.75 ± 42.04 | 0.09 |
| LDL cholesterol | 75.54 ± 31.64 | 67.16 ± 29.87 | 83.89 ± 33.07 | 88.17 ± 29.29 | 0.052 |
| HDL cholesterol | 30.68 ± 8.41 | 29.73 ± 8.09 | 32.79 ± 9.95 | 30.25 ± 6.64 | 0.434 |
| VLDL cholesterol | 25.22 ± 11.31 | 23.95 ± 10.69 | 26.16 ± 11.68 | 27.67 ± 12.99 | 0.507 |

CAD = coronary artery disease; HDL = high-density-lipoprotein; LDL = low-density-lipoprotein; VLDL = very-low-density-lipoprotein

Data are presented as mean ± SD or as number and percentage. $P < 0.05$ was considered statistically significant.

had received thrombolysis. The risk-factor profile was relatively high, with a mean TIMI risk score of 6.07 ± 2.72. However, the patients were relatively stable, with a mean Killip score of 1.62 ± 0.65.

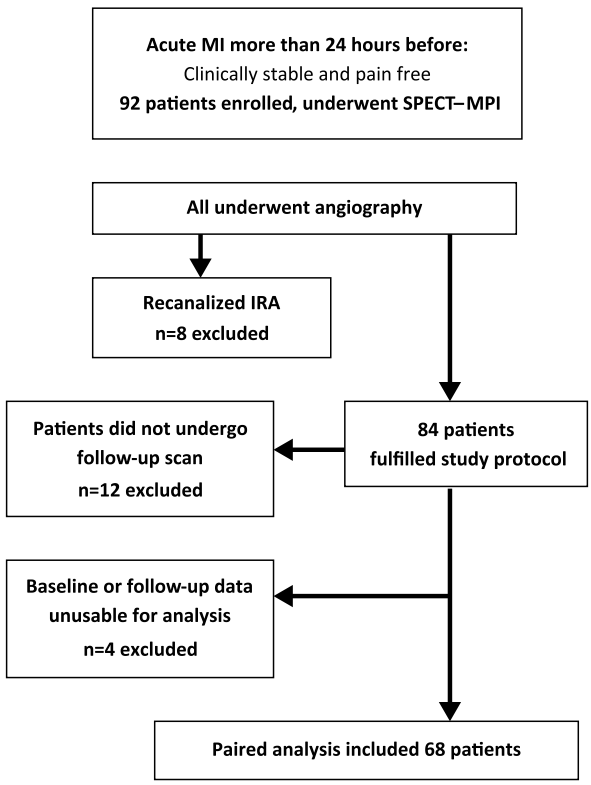


***Fig. 1*** *Study enrollment and patient flow*

*IRA = infarct-related artery; MI = myocardial infarction; SPECT–MPI = single-photon emission computed tomography–myocardial perfusion imaging*

The qualifying angiogram was reviewed critically for preprocedural and postprocedural angiographic status and for TIMI flow. That baseline angiographic picture is summarized in Table III. The culprit IRA was most frequently the left anterior descending coronary artery.

In regard to SPECT–MPI, the polar plot method of quantification was used to estimate the area of nonviable myocardium, because it is precisely quantitative and easily reproducible and provides better insight into other vascular territories. In preparing the polar maps, we used a 50% peak-uptake value as the cutoff standard for viability.[18] The estimated area of nonviable myocardium was recorded as a percentage of the IRA zone, as a percentage of the total LV, and as the estimated mass of nonviable myocardium. The Emory Cardiac Toolbox 3.1™ (Koninklijke Philips N.V.; Best, The Netherlands) was used to process the images, and validated commercially available software was used to perform quantitative analysis. The percentage of viable myocardium in the IRA territory was noted. The IRA territory was defined in advance on the basis of the standard anatomic territory supplied by each of the 3 coronary arteries, and we noted the percentage of viable myocardium remaining in those IRA territories. On the basis of this percentage of remaining viable myocardium, we divided patients into 3 groups: Group 1 (mildly reduced viability), in whom the amount of viable myocardium in the IRA territory was more than 50%; Group 2 (moderately reduced viability), in whom the amount of viable myocardium in the IRA territory ranged from 20% through 50%; and Group 3 (severely reduced viability), in whom the amount of viable myocardium in the IRA territory was less than 20%. The baseline characteristics of patients in these 3 groups were similar with respect to age, sex distribution, and prevalence of traditional cardiovascular risk factors—except for the prevalence of tobacco use, which was most common in

**TABLE II.** Baseline Characteristics of Index Myocardial Infarction

| Variable | **Overall** (N=68) | **Group 1** (n=37) | **Group 2** (n=19) | **Group 3** (n=12) | ***P* Value** |
|---|---|---|---|---|---|
| **Infarction location** | | | | | 0.299 |
| Anterior wall | 47 (69.2) | 29 (78.4) | 11 (57.9) | 7 (58.3) | — |
| Lateral wall | 2 (2.9) | 2 (5.4) | 0 | 0 | — |
| Inferior wall | 19 (27.9) | 6 (16.2) | 8 (42.1) | 5 (41.7) | — |
| **Presentation details** | | | | | |
| Time to presentation (d) | 11.59 ± 8.5 | 12.43 ± 9.04 | 11.94 ± 8.59 | 8.75 ± 6.37 | 0.432 |
| TIMI score | 6.07 ± 2.72 | 6.27 ± 3.04 | 5.58 ± 2.43 | 6.25 ± 2.14 | 0.654 |
| Killip class | 1.62 ± 0.65 | 1.54 ± 0.61 | 1.53 ± 0.7 | 2 ± 0.6 | 0.077 |
| Thrombolysis | 34 (50) | 19 (51.4) | 9 (47.4) | 6 (50) | 0.961 |

TIMI = Thrombolysis in Myocardial Infarction

Data are presented as mean ± SD or as number and percentage. $P < 0.05$ was considered statistically significant.

**TABLE III.** Angiographic Characteristics of Index Myocardial Infarction

| Variable | **Overall** (N=68) | **Group 1** (n=37) | **Group 2** (n=19) | **Group 3** (n=12) | ***P* Value** |
|---|---|---|---|---|---|
| **Culprit coronary artery** | | | | | 0.012 |
| Left anterior descending | 48 (70.6) | 30 (81.1) | 11 (57.9) | 7 (58.3) | |
| Left circumflex | 10 (14.7) | 5 (13.5) | 5 (26.3) | 0 | |
| Right | 10 (14.7) | 2 (5.4) | 3 (15.8) | 5 (14.7) | |
| **Angiographic characteristics** | | | | | |
| Percent stenosis in infarct-related artery | | | | | 0.796 |
| 100 | 25 (36.8) | 14 (37.8) | 8 (42.1) | 3 (25) | |
| 99 | 10 (14.7) | 5 (13.5) | 4 (21.1) | 1 (8.3) | |
| 90–95 | 26 (38.2) | 14 (37.8) | 6 (31.6) | 6 (50) | |
| <90 | 7 (10.3) | 4 (10.8) | 1 (5.3) | 2 (16.7) | |
| Baseline TIMI flow | | | | | 0.345 |
| TIMI 0/1 | 41 (60.3) | 24 (64.9) | 12 (63.2) | 5 (41.7) | |
| TIMI 2/3 | 27 (39.7) | 13 (35.1) | 7 (36.8) | 7 (58.3) | |
| Final TIMI Flow | | | | | 0.005 |
| TIMI 2 | 7 (13.2) | 2 (5.4) | 2 (10.5) | 5 (41.7) | |
| TIMI 3 | 59 (86.8) | 35 (94.6) | 17 (89.5) | 7 (58.3) | |

TIMI = Thrombolysis in Myocardial Infarction

Data are presented as number and percentage. $P < 0.05$ was considered statistically significant.

patients with severely reduced viability ($P=0.03$). Body mass index and laboratory values of blood sugar and lipids (samples taken while fasting) were similar in the 3 groups except for low-density-lipoprotein-cholesterol levels, which were highest in the group with severely reduced viability. Nearly 80% of the patients were male, which might be considered a selection bias.

Left ventricular ejection fraction (LVEF), LV end-diastolic volume (LVEDV), and LV end-systolic volume (LVESV) were calculated with the aid of an automated software program.[19] The use of gated SPECT for the determination of LVEF and volumes has been extensively validated.[20-22] Wall-motion scores (WMS) were quantified via the standard 17-segment model, which assigned scores for wall motion ranging from normal (4) to akinetic (0). All analyses were performed independently for both the baseline scan and the follow-up (done 6 months later).

### Statistical Analysis

Patients' clinical and MI characteristics, both at baseline and at hospital discharge, were evaluated as proportions or as mean ± SD. Their distributions among the groups were compared by means of $\chi^2$ or Fisher exact tests. For comparing continuous variables in the 3 groups, one-way analysis of variance and post hoc analysis (the Bonferroni method) were used to determine significance in different groups. The endpoints of LV remodeling (LVEDV, LVESV, LVEF, and WMS) were evaluated by looking at changes from baseline to 6 months. Two-sided 2-group *t* tests were performed in comparing those changes from baseline to 6 months. To evaluate the influence of the magnitude of viability on the extent of LV remodeling, we compared the 6-month LV volumes and LVEFs with our original findings in regard to baseline viability. Bivariate correlation was performed by the Pearson method, with 2-tailed significance. A *P* value <0.05 was specified as significant. All analyses were performed with SPSS 16.0 software (IBM Corporation; Armonk, NY).

## Results

Group 1 patients (mildly reduced viability) numbered 37; Group 2 patients (moderately reduced viability) numbered 19; and Group 3 patients (severely reduced viability) numbered 12. Of all the patients finally entering the paired analysis, nearly 60% had TIMI 0 or 1 flow in the IRA, while the remaining 40% had either TIMI 2 or 3 flow in the IRA and significant stenosis. At the end of 6 months, more than 85% of enrolled patients achieved TIMI 3 flow. The distribution of preprocedural baseline TIMI flow was not significantly different among the 3 groups that we studied. In contrast, the percentage of patients who did not achieve final TIMI 3 flow was significantly higher in Group 3.

### Relation of Baseline Viability to Left Ventricular Remodeling at 6 Months

At baseline, the percentage of viable myocardium in the IRA territory was 48.44% ± 24.84% in the overall population, and 68% ± 10.66%, 34.63% ± 7.95%, and 10% ± 7.33% in Groups 1, 2, and 3, respectively ($P < 0.001$). The baseline LVEFs were not significantly different among the 3 groups. Table IV shows the LV remodeling indices, which include the LV volume indices,

**TABLE IV.** Left Ventricular Volume Indices, Ejection Fractions, and Wall-Motion Scores in the Overall Cohort and 3 Groups

| Variable | **Overall** (N=68) | **Group 1** (n=37) | **Group 2** (n=19) | **Group 3** (n=12) | ***P* Value** (intergroup) |
|---|---|---|---|---|---|
| **LVEDV** (mL) | | | | | |
| Baseline | 124 ± 29.8 | 123 ± 27.7 | 117.7 ± 27 | 138.5 ± 38 | 0.158 |
| 6 mo | 118.3 ± 30.7 | 118.3 ± 28.7 | 110.6 ± 27.6 | 132.5 ± 38.7 | 0.155 |
| Change | –5.6 ± 10.1 | –4.7 ± 8.9 | –7.1 ± 11.1 | –6.0 ± 12.8 | 0.712 |
| *P* value (of change) | <0.001 | 0.003 | 0.012 | 0.133 | — |
| **LVESV** (mL) | | | | | |
| Baseline | 67.7 ± 26.2 | 68.4 ± 20.5 | 59.8 ± 24 | 79.4 ± 40.2 | 0.128 |
| 6 mo | 61.5 ± 24.5 | 62.8 ± 20.5 | 52.3 ± 22.5 | 73 ± 34.5 | 0.066 |
| Change | –6.2 ± 7.1 | –5.5 ± 4.3 | –7.5 ± 8.3 | –6.4 ± 11.1 | 0.625 |
| *P* value (of change) | <0.001 | <0.001 | 0.001 | 0.074 | — |
| **LVEF** | | | | | |
| Baseline | 0.47 ± 0.12 | 0.45 ± 0.09 | 0.50 ± 0.14 | 0.46 ± 0.16 | 0.293 |
| 6 mo | 0.49 ± 0.13 | 0.48 ± 0.11 | 0.54 ± 0.14 | 0.48 ± 0.16 | 0.172 |
| Change | 0.03 ± 0.02 | 0.03 ± 0.03 | 0.04 ± 0.05 | 0.02 ± 0.05 | 0.412 |
| *P* value (of change) | <0.001 | <0.001 | 0.006 | 0.336 | — |
| **Wall-motion score** | | | | | |
| Baseline | 20.5 ± 1.8 | 20.1 ± 1.7 | 20.3 ± 1.6 | 21.8 ± 2 | 0.011 |
| 6 mo | 19 ± 1.5 | 18.6 ± 1.5 | 18.6 ± 1.1 | 20.3 ± 1.5 | 0.001 |
| Change | –1.5 ± 1 | –1.5 ± 0.9 | –1.7 ± 1.1 | –1.5 ± 1.2 | 0.75 |
| *P* value (of change) | <0.001 | <0.001 | <0.001 | 0.002 | — |

LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume

Data are presented as mean ± SD. $P < 0.05$ was considered statistically significant.

the LVEFs, and the WMSs in the overall cohort and 3 study groups at baseline and at the 6-month follow-up. Group 3 had larger mean LVEDVs and LVESVs and lower LVEFs at baseline and at 6 months, in comparison with Groups 1 and 2, but this difference was not statistically significant. However, the WMS was significantly higher in Group 3.

At follow-up, there was significant reduction in the LVEDV and LVESV and improvement in the LVEF in the overall cohort. However, this improvement was in the groups with mildly reduced and moderately reduced viability, not in the group with severely reduced viability. Even the group with severely reduced viability had a trend toward improvement in LVESV, but not in LVEDV or LVEF. However, the WMS improved comprehensively, regardless of the extent in viability. In patients with either TIMI 0/1 or TIMI 2/3 flow in the IRA at baseline, there was reduction in the LVESV and LVEDV at follow-up, together with incremental improvement in LVEF. In other words, the extent of improvement in LV indices was not different between groups with preprocedural TIMI 0/1 and preprocedural TIMI 2/3 flow.

### Influence of Clinical Variables on Remodeling

None of the baseline characteristics of age, TIMI score, presence or absence of conventional risk factors, early postinfarction LV volumes, or angiographic values was significantly associated with the degree of quantitative changes in ventricular volume at follow-up.

## Discussion

The beneficial effects of early opening of an occluded IRA within the window period after MI are established, but the relevance of late opening of the IRA has been controversial.[23,24] The OAT trial does not support the late-open-artery hypothesis.[6] However, across the globe, even late presenters receive percutaneous coronary intervention (PCI) in real-life situations.[9,25] This issue is of larger importance in India, where timely presentation with acute STEMI remains unlikely.[3] Although the thrust of management no doubt will always be toward reduction of "total ischemic time,"[26] patients in the larger subgroup that presents late warrant a clearer evaluation of the effects on LV function of successful, albeit late, revascularization. The main findings of our study are twofold. First, revascularization of the IRA improves LV function, even if done late. Second, the extent of that improvement relates to the magnitude of viable myocardium in the IRA territory.

Several small studies have documented improvement in LV function after delayed PCI of the culprit vessel in acute MI—the delay ranging from 18 days[27] to 6 weeks.[28] A few studies, such as Thrombolysis and Angioplasty in Myocardial Infarction-6 (TAMI-6),[29] do not support this finding and suggest that any improvement in LV function seen at one month is eventually lost by 6 months. The credibility of this observation, however, is reduced by the considerable restenosis rate in the TAMI-6 PCI group. Although it has been postu-

lated that the improvement in LV function was due to the residual viable myocardium, very few studies before this one have documented the extent of myocardial viability present in the IRA territory.

It was earlier believed that if necrosis is extensive, preserved blood flow in the infarct zone cannot, independent of myocardial salvage, prevent remodeling.[30] Our study reiterates this concept, in that the extent of improvement in LV indices was not different between groups with preprocedural TIMI 0/1 and preprocedural TIMI 2/3 flow. However, the latest American College of Cardiology Foundation/American Heart Association guidelines[31] recommend delayed PCI in the setting of late presentation of acute STEMI in stable patients whose patent IRAs show significant stenosis (class II indication); in contrast, delayed PCI is not recommended in late-presentation patients whose IRAs are occluded (class III indication).

Although our study concludes that a benefit of improvement in LV remodeling indices cannot be judged by baseline TIMI flow, we think that preprocedural evaluation of the extent of viability can help discern which patients will experience an improvement in LV function.[32,33] It has been proposed that, when infarct size is comparable, a transmural infarct leads to infarct expansion,[34-36] and the extent of improvement varies inversely with the thickness of the surviving myocardium.[35,37] Various imaging techniques have been used in the attempt to quantify the amount of viable myocardium: dobutamine stress echocardiography,[38] changes in the redistribution of thallium at rest,[39] and dobutamine stress cardiac magnetic resonance imaging.[40-42] Using technetium-99m sestamibi SPECT–MPI, we ourselves quantify viable myocardium on the basis of its proportion in the IRA territory.

Table V outlines the important results of our study in comparison with results from the main clinical trials that evaluated the interaction between the magnitude of myocardial viability and the extent of ventricular remodeling in the setting of successful late revascularization of IRA after MI. Our results are consistent with the results of these studies, although neither dealt specifically with the issue of the amount of viable myocardium that might influence the remodeling response of the ventricle in this setting. Our method of quantifying the residual viable myocardium in the IRA territory as a *proportion* is both unique and easily reproducible. We concluded that patients who, upon quantitative analysis, have more than 20% viable myocardium in the IRA territory experience a remodeling benefit, even when successful revascularization is performed late.

Although regional wall motion also improves in a comprehensive manner, global function improves in patients who have moderately or mildly reduced viability. This benefit in remodeling could translate into better clinical outcomes and prognosis.[43]

An important angiographic observation from our study was that no preprocedural angiographic characteristic, including occlusive or nonocclusive IRA or baseline TIMI flow, correlated with improvement in LV function. In contrast, failure to achieve postprocedural TIMI 3 flow was more prevalent in patients with severely reduced preprocedural viability, which implies that failure to achieve postprocedural TIMI 3 flow is possibly a surrogate marker of reduced viability and of poor outcome.

### Limitations of the Study

The arbitrary assignment of vascular territory by means of a polar plot could be a limitation, but the use of the total size of the nonviable region mitigates that limitation, because none of the subjects had any prior infarction. Another potential limitation of our study is its lack of a medical control arm, whereby stable patients who presented late after MI could have been treated medically with guideline-directed therapy and their LV indices compared at follow-up with the indices of patients undergoing successful PCI. It is therefore dif-

**TABLE V.** Comparison with Earlier Viability Studies

| Variable | TOAT–CMR[14] (n=26) | OAT–NUC[15] (n=61 PCI + 63 MED) | Our Study (n=68; PCI Arm Only) |
|---|---|---|---|
| LVEDV | With increasing viability, does not improve in PCI or MED arm. | With increasing viability, does not improve, regardless of PCI or MED. | With increasing baseline viability, improves with PCI. |
| LVESV | With increasing viability, improves in PCI arm but not in MED arm. | With increasing viability, shows a trend toward improvement, although nonsignificant, regardless of PCI or MED. | With increasing baseline viability, improves with PCI. |
| LVEF | With increasing viability, improves in PCI arm but not in MED arm. | With increasing viability, shows a trend toward significant improvement, regardless of PCI or MED. | With increasing baseline viability, improves significantly with PCI. |

LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; MED = medical therapy; OAT–NUC = Occluded Artery Trial–Nuclear Viability Ancillary Study; PCI = percutaneous coronary intervention; TOAT–CMR = Total Open Artery Trial–Cardiac Magnetic Resonance

ficult to say whether medical therapy alone would have yielded similar improvement in LV function. Further, the improvement that we found in LV function might not result in improved clinical outcomes; this would need to be investigated in larger randomized trials that apply similar methods for the quantitative evaluation of viability. In addition, our number of patients in Group 3 is so small that our failure to achieve statistical significance in that group might be the result of sample size, rather than magnitude of effect.

### Conclusion

The most important message from this study is that successful revascularization of the IRA in patients who present late after an initial MI results in significant improvement in LVEDV, LVESV, and LVEF, except among patients with severely reduced myocardial viability (less than 20% viability in the IRA territory). This study, for the first time, quantitatively illuminates the important interaction of the amount of viable myocardium that is associated with functional improvement after late successful revascularization of the IRA.

This highly reproducible technique lends considerable weight to our contention that viability plays a significant role in the open-artery hypothesis: unless the patient has evidence of severely reduced viability in the IRA territory, he or she can be offered revascularization with the intent of improving LV function. This is a more scientific approach to such patients than is the outright refusal of revascularization on the basis of clinical outcome data alone. In this context, SPECT–MPI can be used as an adjunctive guide in choosing patients for revascularization.

## References


1. Muller-Nordhorn J, Binting S, Roll S, Willich SN. An update on regional variation in cardiovascular mortality within Europe. Eur Heart J 2008;29(10):1316-26.
2. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med 2006;3(11): e442.
3. Xavier D, Pais P, Devereaux PJ, Xie C, Prabhakaran D, Reddy KS, et al. Treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. Lancet 2008;371(9622):1435-42.
4. Kim CB, Braunwald E. Potential benefits of late reperfusion of infarcted myocardium. The open artery hypothesis. Circulation 1993;88(5 Pt 1):2426-36.
5. Horie H, Takahashi M, Minai K, Izumi M, Takaoka A, Nozawa M, et al. Long-term beneficial effect of late reperfusion for acute anterior myocardial infarction with percutaneous transluminal coronary angioplasty. Circulation 1998;98(22): 2377-82.
6. Hochman JS, Lamas GA, Buller CE, Dzavik V, Reynolds HR, Abramsky SJ, et al. Coronary intervention for persistent occlusion after myocardial infarction. N Engl J Med 2006;355(23):2395-407.
7. Williams DO, Braunwald E, Knatterud G, Babb J, Bresnahan J, Greenberg MA, et al. One-year results of the Thrombolysis in Myocardial Infarction investigation (TIMI) Phase II Trial. Circulation 1992;85(2):533-42.
8. SWIFT trial of delayed elective intervention v conservative treatment after thrombolysis with anistreplase in acute myocardial infarction. SWIFT (Should We Intervene Following Thrombolysis?) Trial Study Group. BMJ 1991;302 (6776):555-60.
9. Braunwald E. The open-artery theory is alive and well--again. N Engl J Med 1993;329(22):1650-2.
10. Braunwald E. Myocardial reperfusion, limitation of infarct size, reduction of left ventricular dysfunction, and improved survival. Should the paradigm be expanded? Circulation 1989;79(2):441-4.
11. Mortara A, Specchia G, La Rovere MT, Bigger JT Jr, Marcus FI, Camm JA, et al. Patency of infarct-related artery. Effect of restoration of anterograde flow on vagal reflexes. ATRAMI (Automatic Tone and Reflexes After Myocardial Infarction) Investigators. Circulation 1996;93(6):1114-22.
12. Steg PG, Thuaire C, Himbert D, Carrie D, Champagne S, Coisne D, et al. DECOPI (DEsobstruction COronaire en Post-Infarctus): a randomized multi-centre trial of occluded artery angioplasty after acute myocardial infarction. Eur Heart J 2004;25(24):2187-94.
13. Silva JC, Rochitte CE, Junior JS, Tsutsui J, Andrade J, Martinez EE, et al. Late coronary artery recanalization effects on left ventricular remodelling and contractility by magnetic resonance imaging. Eur Heart J 2005;26(1):36-43.
14. Bellenger NG, Yousef Z, Rajappan K, Marber MS, Pennell DJ. Infarct zone viability influences ventricular remodelling after late recanalisation of an occluded infarct related artery. Heart 2005;91(4):478-83.
15. Udelson JE, Pearte CA, Kimmelstiel CD, Kruk M, Kufera JA, Forman SA, et al. The Occluded Artery Trial (OAT) Viability Ancillary Study (OAT-NUC): influence of infarct zone viability on left ventricular remodeling after percutaneous coronary intervention versus optimal medical therapy alone. Am Heart J 2011;161(3):611-21.
16. Maes AF, Borgers M, Flameng W, Nuyts JL, van de Werf F, Ausma JJ, et al. Assessment of myocardial viability in chronic coronary artery disease using technetium-99m sestamibi SPECT. Correlation with histologic and positron emission tomographic studies and functional follow-up. J Am Coll Cardiol 1997;29(1):62-8.
17. Canty JM Jr, Fallavollita JA. Chronic hibernation and chronic stunning: a continuum. J Nucl Cardiol 2000;7(5):509-27.
18. Travin MI, Bergmann SR. Assessment of myocardial viability. Semin Nucl Med 2005;35(1):2-16.
19. Germano G, Kiat H, Kavanagh PB, Moriel M, Mazzanti M, Su HT, et al. Automatic quantification of ejection fraction from gated myocardial perfusion SPECT. J Nucl Med 1995; 36(11):2138-47.
20. Achtert AD, King MA, Dahlberg ST, Pretorius PH, LaCroix KJ, Tsui BM. An investigation of the estimation of ejection fractions and cardiac volumes by a quantitative gated SPECT software package in simulated gated SPECT images. J Nucl Cardiol 1998;5(2):144-52.
21. Iskandrian AE, Germano G, VanDecker W, Ogilby JD, Wolf N, Mintz R, Berman DS. Validation of left ventricular volume measurements by gated SPECT 99mTc-labeled sestamibi imaging. J Nucl Cardiol 1998;5(6):574-8.
22. Mochizuki T, Murase K, Tanaka H, Kondoh T, Hamamoto K, Tauxe WN. Assessment of left ventricular volume using ECG-gated SPECT with technetium-99m-MIBI and technetium-99m-tetrofosmin. J Nucl Med 1997;38(1):53-7.
23. Yousef ZR, Redwood SR, Bucknall CA, Sulke AN, Marber MS. Late intervention after anterior myocardial infarction: effects on left ventricular size, function, quality of life, and

exercise tolerance: results of the Open Artery Trial (TOAT Study). J Am Coll Cardiol 2002;40(5):869-76.
24. Sadanandan S, Buller C, Menon V, Dzavik V, Terrin M, Thompson B, et al. The late open artery hypothesis--a decade later. Am Heart J 2001;142(3):411-21.
25. Deyell MW, Buller CE, Miller LH, Wang TY, Dai D, Lamas GA, et al. Impact of National Clinical Guideline recommendations for revascularization of persistently occluded infarct-related arteries on clinical practice in the United States. Arch Intern Med 2011;171(18):1636-43.
26. Lamas GA, Hochman JS. Where does the Occluded Artery Trial leave the late open artery hypothesis? Heart 2007;93(11): 1319-21.
27. Pizzetti G, Belotti G, Margonato A, Cappelletti A, Chierchia SL. Coronary recanalization by elective angioplasty prevents ventricular dilation after anterior myocardial infarction. J Am Coll Cardiol 1996;28(4):837-45.
28. Dzavik V, Beanlands DS, Davies RF, Leddy D, Marquis JF, Teo KK, et al. Effects of late percutaneous transluminal coronary angioplasty of an occluded infarct-related coronary artery on left ventricular function in patients with a recent (<6 weeks) Q-wave acute myocardial infarction (Total Occlusion Post-Myocardial Infarction Intervention Study [TOMIIS]--a pilot study). Am J Cardiol 1994;73(12):856-61.
29. Topol EJ, Califf RM, Vandormael M, Grines CL, George BS, Sanz ML, et al. A randomized trial of late reperfusion therapy for acute myocardial infarction. Thrombolysis and Angioplasty in Myocardial Infarction-6 Study Group. Circulation 1992;85(6):2090-9.
30. Chareonthaitawee P, Christian TF, Hirose K, Gibbons RJ, Rumberger JA. Relation of initial infarct size to extent of left ventricular remodeling in the year after acute myocardial infarction. J Am Coll Cardiol 1995;25(3):567-73.
31. O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: developed in collaboration with the American College of Emergency Physicians and Society for Cardiovascular Angiography and Interventions. Catheter Cardiovasc Interv 2013;82(1):E1-27.
32. Kaul S. There may be more to myocardial viability than meets the eye. Circulation 1995;92(10):2790-3.
33. Bolognese L, Cerisano G, Buonamici P, Santini A, Santoro GM, Antoniucci D, Fazzini PF. Influence of infarct-zone viability on left ventricular remodeling after acute myocardial infarction. Circulation 1997;96(10):3353-9.
34. Eaton LW, Weiss JL, Bulkley BH, Garrison JB, Weisfeldt ML. Regional cardiac dilatation after acute myocardial infarction: recognition by two-dimensional echocardiography. N Engl J Med 1979;300(2):57-62.
35. Pirolo JS, Hutchins GM, Moore GW. Infarct expansion: pathologic analysis of 204 patients with a single myocardial infarct. J Am Coll Cardiol 1986;7(2):349-54.
36. Jugdutt BI. Nitrates and left ventricular remodeling. Am J Cardiol 1998;81(1 Suppl):57A-67A.
37. Alhaddad IA, Kloner RA, Hakim I, Garno JL, Brown EJ. Benefits of late coronary artery reperfusion on infarct expansion progressively diminish over time: relation to viable islets of myocytes within the scar. Am Heart J 1996;131(3):451-7.
38. Rizzello V, Biagini E, Schinkel AF, Bountioukos M, Boersma E, Vourvouri EC, et al. Comparison of functional recovery of mildly hypokinetic versus severely dysfunctional left ventricular segments after revascularization in patients with ischemic cardiomyopathy. Am J Cardiol 2004;93(4):394-8.
39. Faraggi M, Montalescot G, Sarda L, Heintz JF, Doumit D, Drobinski G, et al. Spontaneous late improvement of myocardial viability in the chronic infarct zone is possible, depending on persistent TIMI 3 flow and a low grade stenosis of the infarct artery. Heart 1999;81(4):424-30.
40. Rogers WJ Jr, Kramer CM, Geskin G, Hu YL, Theobald TM, Vido DA, et al. Early contrast-enhanced MRI predicts late functional recovery after reperfused myocardial infarction. Circulation 1999;99(6):744-50.
41. Geskin G, Kramer CM, Rogers WJ, Theobald TM, Pakstis D, Hu YL, Reichek N. Quantitative assessment of myocardial viability after infarction by dobutamine magnetic resonance tagging. Circulation 1998;98(3):217-23.
42. Coletta C, Sestili A, Seccareccia F, Rambaldi R, Ricci R, Galati A, et al. Influence of contractile reserve and inducible ischaemia on left ventricular remodelling after acute myocardial infarction. Heart 2003;89(10):1138-43.
43. Bigi R, Desideri A, Bax JJ, Galati A, Coletta C, Fiorentini C, Fioretti PM. Prognostic interaction between viability and residual myocardial ischemia by dobutamine stress echocardiography in patients with acute myocardial infarction and mildly impaired left ventricular function. Am J Cardiol 2001;87(3):283-8.