# Upstream High-Dose Tirofiban Does Not Reduce Myocardial Infarct Size in Patients Undergoing Primary Percutaneous Coronary Intervention: A Magnetic Resonance Imaging Pilot Study

**Address for correspondence:**
Hyeon-Cheol Gwon, MD, PhD
Division of Cardiology
Cardiac and Vascular Center
Samsung Medical Center
Sungkyunkwan University
School of Medicine
#50 Irwon-dong, Gangnam-gu
Seoul 135-710, South Korea
hcgwon@skku.edu

Young Bin Song, MD; Joo-Yong Hahn, MD; Hyeon-Cheol Gwon, MD; Jun Hyung Kim, MD; Sang Yeub Lee, MD; Yeon Hyeon Choe, MD; Seung-Hyuk Choi, MD; Jin-Ho Choi, MD; Sang Hoon Lee, MD
Cardiac and Vascular Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

ABSTRACT

*Background:* Primary percutaneous coronary intervention (PCI) is more effective than fibrinolytic therapy for ST-segment elevation myocardial infarction (STEMI), but initial treatment delay to intervention is the main limitation of this strategy. *Hypothesis:* Upstream use of high-dose tirofiban could reduce myocardial infarct size, using analysis of contrast-enhanced magnetic resonance imaging (CE-MRI).

*Methods:* Patients with STEMI within 12 hours after symptom onset were randomized to a facilitated PCI group (n = 19) or to a primary PCI group (n = 20). The primary endpoint was myocardial infarct size evaluated by the volume of delayed hyperenhancement on CE-MRI at 1 month after index procedure.

*Results:* The baseline clinical characteristics were not significantly different between the 2 groups. Although the incidence of pre-PCI thrombolysis in myocardial infarction (TIMI) flow grade 2 to 3 was significantly higher in the facilitated PCI group than in the primary PCI group (47.4% vs 15.0%, $P = 0.03$), the achievement of myocardial blush grade 2 to 3 or ST-segment resolution at 30 minutes after procedure was not significantly different between the facilitated PCI and the primary PCI group (36.8% vs 40%, $P = .84$ and 31.6% vs 20%, $P = 0.41$, respectively). Infarct size on CE-MRI was similar in the facilitated PCI group and the conventional primary PCI group (22.1% $\pm$ 11.7% vs 25.2% $\pm$ 13.2%, $P = 0.44$). At 6 months, the left ventricular ejection fraction (LVEF) on echocardiography was 52.6% $\pm$ 10.4% in the facilitated PCI group and 50.9% $\pm$ 9.8% in the primary PCI group ($P = 0.68$).

*Conclusion:* Despite the improvement of initial TIMI flow grade, the upstream use of high-dose tirofiban did not reduce myocardial infarct size measured by CE-MRI.

Tirofiban is a small nonpeptide glycoprotein (GP) IIb/IIIa inhibitor that has some advantages over abciximab regarding cost and bleeding complications.[1] However, the efficacy of adjunctive administration of tirofiban is controversial in patients undergoing primary percutaneous coronary intervention (PCI).[2] These inconsistent results may result partly from different dosage and timing of administration. A conventional dose of tirofiban showed suboptimal periprocedural platelet inhibition in patients with ST-segment elevation myocardial infarction (STEMI).[3] Several recent clinical studies demonstrated that the use of high-dose bolus tirofiban is safe and improves angiographic and clinical outcomes in patients undergoing high risk PCI.[4] The timing of administration of GP IIb/IIIa inhibitors is also an issue. Recent meta-analysis showed that early administration of GP IIb/IIIa inhibitors in STEMI appeared to improve coronary patency with favorable trends for clinical outcomes.[5] However, the impact of early administration of high-dose tirofiban has not yet been fully elucidated in patients undergoing primary PCI for STEMI.

Contrast-enhanced magnetic resonance imaging (CE-MRI) can assess myocardial infarct size with high spatial resolution and excellent reproducibility.[6] Using infarct size measurement as a surrogate endpoint allows a much smaller sample size because of its known prognostic value.[7] In this prospective, randomized pilot study, we evaluated the impact of upstream high-dose tirofiban on myocardial infarct size measured by CE-MRI in patients undergoing primary PCI.

## Methods

### Study Patients and Protocol

Patients undergoing primary PCI for STEMI were prospectively enrolled in this study. Inclusion criteria were: (1) the

The first 2 authors contributed equally to this work.
This study was supported by a grant from Cardiac and Vascular Center, Samsung Medical Center, Republic of Korea.

Received: August 14, 2008
Accepted with revision: October 29, 2008


Published online in Wiley InterScience. (www.interscience.wiley.com)
DOI:10.1002/clc.20551 

presence of chest pain for more than 30 minutes, but less than 12 hours after symptom onset; (2) ST-segment elevation more than 1 mm in 2 or more contiguous leads. Exclusion criteria were: (1) cardiogenic shock (systolic blood pressure < 80 mm Hg over 30 minutes or need for intravenous pressors or intra-aortic balloon pump); (2) previous myocardial infarction; (3) history of bleeding diathesis; (4) the use of GP IIb/IIIa inhibitors within 24 hours.

The study protocol was approved by the institutional review board at Samsung Medical Center, and informed written consent of patients was obtained before study initiation. Patients were randomly assigned to conventional primary PCI or to PCI preceded by the administration of high-dose bolus tirofiban (25μ g/kg bolus) followed by maintenance infusion of 0.15μ g/kg/min for 24 hours according to computer-based 1:1 randomization scheme in the emergency room. Because infarct location is a major determinant of infarct size, the randomization was stratified according to whether the patients had anterior or non-anterior MI. In addition to study medication, all patients received dual oral antiplatelet agents with aspirin 300 mg and clopidogrel 600 mg before PCI. Unfractionated heparin (70 units/kg) was administered intravenously before PCI, and the active clotting time was maintained at more than 300 seconds during the procedure.

### Data Collection

Twelve-lead electrocardiograms (ECGs) were obtained before and at 30 and 90 minutes after the procedure. The total ST-segment elevation was measured manually from leads exploring the infarct area as described previously.[8] The ST-segment recovery was determined by comparing ECGs recorded at prespecified time points after the procedure with ECGs obtained before PCI. ST-segment resolution was defined as a decrease in ST-segment elevation >70%. Creatine kinase (CK), its MB fraction (CK-MB), and cardiac specific troponin I were measured before and at 8, 16, 24, 36, and 48 hours after the procedure. The thrombolysis in myocardial infarction (TIMI) flow grade and myocardial blush grade (MBG) were evaluated off-line in the angiographic core laboratory by 2 blinded observers, as described previously.[9]

### Magnetic Resonance Imaging Protocol and Data Analysis

CE-MRI was performed at 1 month after the index procedure, as described previously.[10,11] A 1.5 Tesla magnetic MRI scanner (Signa CV/i, GE Healthcare, Chalfont St. Giles, UK) with a phased array cardiac coil was used. Cine MRI images were obtained using a Fast Imaging Employing Steady State Acquisition (FIESTA) system (GE Healthcare, Chalfont St. Giles, UK). For the MRI perfusion study, a dose of 0.15 mmol/kg body weight gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA; Magnevist, Schering, Berlin, Germany) was injected intravenously at a rate of 3 mL/sec after the cine MRI. A total of 6 to 7 slices were obtained at steady state to cover the whole left ventricle (LV) myocardium in a short axis view for perfusion imaging. A myocardial perfusion defect was defined visually as an area showing less or no signal enhancement of the myocardium after bolus injection on T1-weighted images of the first-pass MRI, and as indicative of the ischemic region. Delayed hyperenhancement was evaluated at 10 to 15 minutes after Gd-DTPA administration in contiguous 10 to 12 slices of 10 mm thickness (6 mm short axis slices with 4 mm gap) by use of an inversion recovery fast-gradient echo sequence, as indicative of the infarcted region.[12]

An experienced radiologist who was blinded to the clinical information analyzed the CE-MRI. The endocardial and epicardial borders were also planimetred to calculate myocardial area and summated in the same manner to calculate LV myocardial volume. The borders of the area with delayed hyperenhancement and the perfusion defect area were traced by planimetry to calculate the volume of the infarct and perfusion defect. The infarct volume was calculated from the summation of the area with delayed hyperenhancement within each segment of the short axis images, multiplied by the slice thickness to cover the whole LV.[13] The perfusion defect volume was calculated in the same manner. Myocardial infarct size and perfusion defect size were expressed as a percentage of the LV myocardial volume. The infarct transmurality for each segment was calculated by dividing the hyperenhanced area by total area of the affected myocardium in each segment. The average infarct transmurality for each patient was calculated as the average of all segments with hyperenhanced area.[14]

### Sample Size and Statistical Analysis

The expected standard deviation (SD) of myocardial infarct size was estimated to be 10%, and a difference of more than 10% would be regarded as significant. For a power of 0.80 and an alpha error of 0.05, the required estimated sample size would be 16 patients in each group. Considering the possible dropout, the final sample size was determined to be 20 patients in each group.

The Statistical Analysis Software package (SAS version 9.1, SAS Institute, Cary, NC) was used for all analyses. Continuous data were expressed as the mean ± SD or as the median and interquartile range, and categorical data as counts or percentages. Continuous variables were analyzed using an independent *t* test, and categorical variables using a Pearson's $\chi^2$ or Fisher's exact test. A value of $P < 0.05$ in the 2-tailed test was considered significant.

## Results

### Study Patients and Baseline Clinical Characteristics

A total of 40 consecutive patients were enrolled for this study. One patient with anterior infarction in the facilitated


Published online in Wiley InterScience. (www.interscience.wiley.com)
DOI:10.1002/clc.20551 

PCI group was excluded from the study because the patient did not undergo an MRI study due to hemodynamic instability after primary PCI. A total of 19 patients were finally assigned to the facilitated PCI group and 20 patients in the conventional primary PCI group were eligible for analysis. There was only 1 patient receiving abciximab due to newly developed thrombus during the intervention in the nonfacilitated PCI group. The baseline clinical characteristics were not significantly different between the 2 groups (Table 1).

### Angiographic and Procedural Data

Angiographic and procedural findings are shown in Table 2. There was no significant difference between the groups except in pre-PCI TIMI flow grade. The incidence of pre-PCI TIMI flow grade 2 or 3 was significantly higher in the facilitated PCI group compared with the primary PCI group. Coronary stents were implanted in all patients, and the diameter and length of stents used were not significantly different between the groups. Quantitative coronary angiographic analysis showed similar results between the groups.

Table 1. Baseline Characteristics

| | Facilitated PCI (n = 19) | Primary PCI (n = 20) | *P* Value |
|---|---|---|---|
| Age, years | 58.4±10.6 | 55.8±10.1 | 0.43 |
| Age≥70 years, n (%) | 4 (21.1) | 2 (10.0) | 0.41 |
| Male, n (%) | 17 (89.5) | 16 (80.0) | 0.66 |
| Medical history, n (%) Current smoker | 8 (42.1) | 10 (50.0) | 0.62 |
| Diabetes mellitus | 3 (15.8) | 5 (25.0) | 0.70 |
| Hypertension | 7 (36.8) | 6 (30.0) | 0.74 |
| Hyperlipidemia | 2 (10.5) | 7 (35.0) | 0.13 |
| On presentation | | | |
| Killip classification ≥ II, n (%) | 5 (26.3) | 7 (35.0) | 0.56 |
| Anterior infarction, n (%) | 12 (63.2) | 13 (65.0) | 0.91 |
| Left ventricular ejection fraction, % | 48.4±14.1 | 47.3±8.5 | 0.78 |
| Door-to-balloon time, min | 100±26 | 97±33 | 0.79 |
| Randomization to balloon time, min | 64±25 | 68±30 | 0.62 |
| Symptom onset-to-balloon time, min | 296±127 | 279±150 | 0.72 |

Abbreviations: PCI, percutaneous coronary intervention.

Table 2. Angiographic and Procedural Findings

| | Facilitated PCI (n = 19) | Primary PCI (n = 20) | *P* Value |
|---|---|---|---|
| Culprit vessel, n (%) Left anterior descending artery | 12 (63.2) | 13 (65.0) | 0.31 |
| Left circumflex artery | 0 | 2 (10.0) | |
| Right coronary artery | 7 (36.8) | 5 (25.0) | |
| Number of diseased vessels, n(%) | | | 0.61 |
| 1 | 11 (57.9) | 14 (70.0) | |
| 2 | 4 (21.1) | 2 (10.0) | |
| 3 | 4 (21.1) | 4 (25.0) | |
| Baseline TIMI flow grade≥2, n (%) | 9 (47.4) | 3 (15.0) | 0.03 |
| Final TIMI flow grade 3, n (%) | 17 (89.5) | 19 (95.0) | 0.61 |
| Rentrop collateral grade ≥2, n (%) | 2 (10.5) | 1 (5.0) | 0.61 |
| Visible thrombi, n (%) | 5 (26.3) | 7 (35.0) | 0 .56 |
| No reflow, n (%) | 2 (10.5) | 2 (10.0) | 0.99 |
| Stent diameter, mm | 3.3±0.4 | 3.2±0.5 | 0.60 |
| Stent length, mm | 24.8±6.2 | 24.2±8.0 | 0.77 |
| Reference diameter, mm | 3.2±0.5 | 3.0±0.5 | 0.32 |
| Lesion length, mm | 22.5±8.1 | 22.1±7.9 | 0.86 |
| Final minimal luminal diameter, mm | 2.6±0.4 | 2.5±0.5 | 0.28 |

Abbreviations: PCI, percutaneous coronary intervention; TIMI, thrombolysis in myocardial infarction.

### CE-MRI Analysis for Infarct Size

Results of CE-MRI were available in all patients (Table 3). The CE-MRI was performed at 30 days after the index procedure (median 31 d; interquartile range 27–34 d). There was no difference in interval from procedure to MRI between the groups. The LV end-diastolic volume, LV end-systolic volume, and left ventricular ejection fraction (LVEF) were similar in both groups. Infarct and perfusion defect volume were not significantly different between the groups. Our study endpoint, infarct size (percentage infarct volume) on

Table 3. Infarct Size: Analysis of CE-MRI

| | Facilitated PCI (n = 19) | Primary PCI (n = 20) | *P* Value |
|---|---|---|---|
| LVEDV (mL) | 167.7±32.3 | 150.3±44.8 | 0.17 |
| LVESV (mL) | 78.3±29.6 | 73.3±34.5 | 0.63 |
| LV ejection fraction (%) | 53.6±14.6 | 54.0±10.7 | 0.92 |
| Infarct volume (mL) | 24.0±9.7 | 30.4±22.2 | 0.25 |
| Infarct size (% of LV) | 22.1±11.7 | 25.2±13.2 | 0.44 |
| Perfusion defect volume (mL) | 2.0±4.0 | 4.1±7.3 | 0.28 |
| Perfusion defect size (% of LV) | 1.7±3.3 | 3.9±6.6 | 0.20 |
| Transmurality (%) | 75.2±18.8 | 63.0±26.3 | 0.10 |

Abbreviations: CE-MRI, contrast-enhanced magnetic resonance imaging; LV, left ventricular; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; PCI, percutaneous coronary intervention.

Table 4. Myocardial Reperfusion and Left Ventricular Function

| | Facilitated PCI (n = 19) | Primary PCI (n = 20) | *P* Value |
|---|---|---|---|
| Final myocardial blush grade ≥2, n (%) | 7 (36.8) | 8 (40.0) | 0.84 |
| ST-segment resolution>70% at 30 min, n (%) | 6 (31.6) | 4 (20.0) | 0.41 |
| ST-segment resolution>70% at 90 min, n (%) | 9 (47.4) | 6 (30.0) | 0.27 |
| Peak troponin I, ng/mL | 179.5±231.7 | 147.8±250.0 | 0.68 |
| Peak CK-MB, ng/mL | 355.7±357.6 | 245.6±196.3 | 0.24 |
| LV ejection fraction at 6-mo follow-up, % | 52.6±10.4 | 50.9±9.8 | 0.68 |

Abbreviations: LV, left ventricular; PCI, percutaneous coronary intervention.

CE-MRI, was also similar between the groups. There was a trend of larger infarct transmurality (transmural extent of infarct) in the facilitated PCI group, although it was not statistically significant.

There was no interaction between symptom onset-to-balloon time and the efficacy of facilitated PCI with high-dose tirofiban. In patients presenting within 3 hours after symptom onset, infarct size and transmurality were similar between the groups (24.8% ± 10.8% in the primary PCI group vs 17.5% ± 9.5% in the facilitated PCI group for infarct size, $P = 0.31$; 53.2% ± 23.4% vs 52.5% ± 14.2% for transmurality, $P = 0.96$). In patients presenting after 3 hours after symptom onset, infarct size and transmurality were also similar between the groups (25.2% ± 14.4% in the primary PCI group vs 23.3% ± 12.2% in the facilitated PCI group for infarct size, $P = 0.69$; 66.2% ± 27.2% vs 81.3% ± 15.0% for transmurality, $P = 0.07$).

### Myocardial Reperfusion, Peak Enzyme Levels, and Left Ventricular Function

The incidence of post-PCI MBG 2 or 3 was not significantly different (Table 4). There were no significant differences between the facilitated PCI and primary PCI group in the rates of ST-segment resolution of > 70% at 30 minutes and at 90 minutes after procedure. Peak CK-MB and troponin I level were similar between the groups. At 6-month follow-up, the LVEF on echocardiography was similar in both groups.

## Discussion

We assessed whether early administration of high-dose tirofiban might produce infarct-size reduction compared with conventional primary PCI in patients with STEMI. Our study showed that despite a higher incidence of TIMI flow grade 2 or 3 on initial angiography, the upstream use of high-dose tirofiban before primary PCI did not reduce infarct size measured by CE-MRI. Moreover, there was no significant difference in post-PCI TIMI grade, final MBG, ST-segment resolution, peak cardiac enzyme level, and follow-up LVEF between the facilitated PCI group and the conventional primary PCI group.

### Dose and Timing of Tirofiban Administration

Although GP IIb/IIIa inhibitors have significantly improved clinical outcomes after PCI, the efficacy of adjunctive treatment with tirofiban is uncertain in patients with STEMI undergoing primary PCI.[2] This may be due to dose and timing of tirofiban administration. Recent studies have shown that the conventional bolus dose of tirofiban (10 μg/kg bolus followed by a 0.15 μg/kg/min infusion) is inadequate to optimally inhibit platelet aggregation,[15] and adequate levels of platelet inhibition were obtained only with a higher dose of tirofiban in the patients with STEMI.[3] In a meta-analysis of 6 randomized trials, early administration of GP IIb/IIIa inhibitors in STEMI appeared to improve coronary patency with favorable trends for clinical outcomes.[5] Therefore, we investigated the impact of upstream high-dose bolus tirofiban followed by continuous infusion on myocardial infarct size in patients undergoing primary PCI using CE-MRI. In our study, an approach of


Published online in Wiley InterScience. (www.interscience.wiley.com)
DOI:10.1002/clc.20551 

facilitated PCI with the upstream use of high-dose bolus tirofiban showed a higher incidence of TIMI flow grade 2 or 3 on initial angiography, but the translation to a reduction in myocardial infarct size measured by CE-MRI was not observed.

### Angiographic Patency and Infarct Size

The Facilitated Intervention with Enhanced Reperfusion Speed to Stop Events (FINESSE) study was designed to test the hypothesis that facilitated PCI preceded by early treatment with the use of a combination of abciximab and half-dose reteplase or abciximab only would be more effective than primary PCI with abciximab administered in the catheterization laboratory immediately before PCI.[16] In the FINESSE study, the facilitated approach offers no clinical benefit over primary PCI in STEMI treatment, despite the improvement of initial TIMI flow grade 3. This result is concordant with our study which showed that the patency of pharmacologically induced infarct related arteries did not result in a beneficial effect on myocardial infarct size measured by CE-MRI. Although baseline patency of infarct-related artery was associated with favorable outcomes after primary PCI,[17] pharmacologically induced reperfusion of the epicardial infarct-related artery may not reflect myocardial reperfusion.

### Infarct Size Measurement by CE-MRI

Contrast-enhanced magnetic resonance imaging (CE-MRI) can assess myocardial infarct size with high spatial resolution and excellent reproducibility,[6] providing high-resolution images of first-pass perfusion defects and infarcted myocardium by means of delayed hyperenhancement.[18] Delayed hyperenhancement after contrast enables accurate delineation between the infarcted and viable myocardium, allowing the prediction of myocardial functional recovery.[19] Therefore, CE-MRI is an optimal method for assessing myocardial infarct size as surrogate endpoint for studies comparing different reperfusion strategies, and its higher accuracy allows a subsequent sample size reduction.[20] However, there has been only 1 study evaluating the effect of tirofiban using CE-MRI, which reported that pretreatment with conventional dose of tirofiban improved myocardial flow after primary PCI. In that study, infarct size and transmurality were not measured.[21] To the best of our knowledge, this is the first study to evaluate the efficacy of adjunctive treatment with tirofiban on infarct size and transmurality by CE-MRI.

### Study Limitations

Our study has several limitations. First, the sample size was relatively small. However, we calculated the sample size to have an acceptable level of statistical power. Second, we excluded patients with hemodynamic instability or a history of myocardial infarction who might benefit from a more aggressive treatment such as facilitated PCI. Finally, there was no major adverse cardiovascular event during the study follow-up period, which made it impossible to evaluate the efficacy of upstream high-dose tirofiban on clinical outcomes.

## Conclusion

This study showed that despite the improvement of initial TIMI flow grade, the upstream use of high-dose tirofiban did not result in reduction of myocardial infarct size measured by CE-MRI.

## References


1. Gunasekara AP, Walters DL, Aroney CN. Comparison of abciximab with "high-dose" tirofiban in patients undergoing percutaneous coronary intervention. *Int J Cardiol*. 2006;109:16–20.
2. van 't Hof AW, Ernst N, de Boer MJ, et al. Facilitation of primary coronary angioplasty by early start of a glycoprotein IIb/IIIa inhibitor: results of the ongoing tirofiban in myocardial infarction evaluation (On-TIME) trial. *Eur Heart J*. 2004;25:837–846.
3. Ernst NM, Suryapranata H, Miedema K, et al. Achieved platelet aggregation inhibition after different antiplatelet regimens during percutaneous coronary intervention for ST-segment elevation myocardial infarction. *J Am Coll Cardiol*. 2004;44:1187–1193.
4. Valgimigli M, Percoco G, Barbieri D, et al. The additive value of tirofiban administered with the high-dose bolus in the prevention of ischemic complications during high-risk coronary angioplasty: the ADVANCE Trial. *J Am Coll Cardiol*. 2004;44:14–19.
5. Montalescot G, Borentain M, Payot L, Collet JP, Thomas D. Early vs late administration of glycoprotein IIb/IIIa inhibitors in primary percutaneous coronary intervention of acute ST-segment elevation myocardial infarction: a meta-analysis. *JAMA*. 2004;292:362–366.
6. Thiele H, Kappl MJ, Conradi S, Niebauer J, Hambrecht R, Schuler G. Reproducibility of chronic and acute infarct size measurement by delayed enhancement-magnetic resonance imaging. *J Am Coll Cardiol*. 2006;47:1641–1645.
7. Gersh BJ, Anderson JL. Thrombolysis and myocardial salvage. Results of clinical trials and the animal paradigm—paradoxic or predictable? *Circulation*. 1993;88:296–306.
8. Claeys MJ, Bosmans J, Veenstra L, Jorens P, De Raedt H, Vrints CJ. Determinants and prognostic implications of persistent ST-segment elevation after primary angioplasty for acute myocardial infarction: importance of microvascular reperfusion injury on clinical outcome. *Circulation*. 1999;99:1972–1977.
9. van 't Hof AW, Liem A, Suryapranata H, Hoorntje JC, de Boer MJ, Zijlstra F. Angiographic assessment of myocardial reperfusion in patients treated with primary angioplasty for acute myocardial infarction: myocardial blush grade. Zwolle Myocardial Infarction Study Group. *Circulation*. 1998;97:2302–2306.
10. Hahn JY, Gwon HC, Choe YH, et al. Effects of balloon-based distal protection during primary percutaneous coronary intervention on early and late infarct size and left ventricular remodeling: a pilot study using serial contrast-enhanced magnetic resonance imaging. *Am Heart J*. 2007;153:665 e661–668.
11. Choe YH, Choo KS, Jeon ES, Gwon HC, Choi JH, Park JE. Comparison of MDCT and MRI in the detection and sizing of acute and chronic myocardial infarcts. *Eur J Radiol*. 2008;66:292–299.
12. Kim RJ, Wu E, Rafael A, et al. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. *N Engl J Med*. 2000;343:1445–1453.




Published online in Wiley InterScience. (www.interscience.wiley.com)
DOI:10.1002/clc.20551

13. Martin ET, Fuisz AR, Pohost GM. Imaging cardiac structure and pump function. *Cardiol Clin*. 1998;16:135–160.
14. Orn S, Manhenke C, Anand IS, et al. Effect of left ventricular scar size, location, and transmurality on left ventricular remodeling with healed myocardial infarction. *Am J Cardiol*. 2007;99:1109–1114.
15. Batchelor WB, Tolleson TR, Huang Y, et al. Randomized comparison of platelet inhibition with abciximab, tirofiban and eptifibatide during percutaneous coronary intervention in acute coronary syndromes: the COMPARE trial. Comparison of measurements of platelet aggregation with aggrastat, reopro, and eptifibatide. *Circulation*. 2002;106:1470–1476.
16. Ellis SG, Tendera M, de Belder MA, et al. Facilitated PCI in patients with ST-elevation myocardial infarction. *N Engl J Med*. 2008;358( ):2205–2217.
17. Stone GW, Cox D, Garcia E, et al. Normal flow (TIMI-3) before mechanical reperfusion therapy is an independent determinant of survival in acute myocardial infarction: analysis from the primary angioplasty in myocardial infarction trials. *Circulation*. 2001;104:636–641.
18. Kim RJ, Fieno DS, Parrish TB, et al. Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. *Circulation*. 1999;100:1992–2002.
19. Beek AM, Kuhl HP, Bondarenko O, et al. Delayed contrast-enhanced magnetic resonance imaging for the prediction of regional functional improvement after acute myocardial infarction. *J Am Coll Cardiol*. 2003;42:895–901.
20. Mahrholdt H, Wagner A, Holly TA, et al. Reproducibility of chronic infarct size measurement by contrast-enhanced magnetic resonance imaging. *Circulation*. 2002;106:2322–2327.
21. Steen H, Lehrke S, Wiegand UK, et al. Very early cardiac magnetic resonance imaging for quantification of myocardial tissue perfusion in patients receiving tirofiban before percutaneous coronary intervention for ST-elevation myocardial infarction. *Am Heart J*. 2005;149(564):e561–e567.


Published online in Wiley InterScience. (www.interscience.wiley.com)
DOI:10.1002/clc.20551 