JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 3, NO. 4, 2010

ISSN 1936-8798/10/$36.00
PUBLISHED BY ELSEVIER INC.
DOI: 10.1016/j.jcin.2010.01.011

CVN Interview

Complete Percutaneous Revascularization for Multivessel Disease in Patients With Impaired Left Ventricular Function

Pre- and Post-Procedural Evaluation by Cardiac Magnetic Resonance Imaging

Sharon W. Kirschbaum, MD,*† Tirza Springeling, MD,*† Eric Boersma, MSc, PhD,*
Adriaan Moelker, MD, PhD,† Wim J. van der Giessen, MD, PhD,*
Patrick W. Serruys, MD, PhD,* Pim J. de Feyter, MD, PhD,*†
Robert-Jan M. van Geuns, MD, PhD*†

Rotterdam, the Netherlands

Objectives The aim of this study was to investigate the effect of complete, incomplete, and unsuccessful revascularization by percutaneous coronary intervention (PCI) on left ventricular ejection fraction (EF) in patients with multivessel disease and impaired left ventricular function and assess the diagnostic accuracy of cardiac magnetic resonance imaging (MRI) for improvement in EF.

Background The effect of PCI for multivessel coronary artery disease on long-term myocardial function and the predictive value of cardiac MRI on global function are incompletely investigated.

Methods Cardiac MRI was performed in patients with multivessel disease before and 6 months after complete revascularization (n = 34) or incomplete revascularization (n = 22) or in patients without successful revascularization (n = 15). For the prediction of recovery of EF, wall thickening was quantified on cine images at rest and during 5- and 10-μg/kg/min dobutamine. The transmural extent of infarction was quantified on delayed enhancement cardiac MRI.

Results The EF improved significantly after complete revascularization (46 ± 12% to 51 ± 13%; $p < 0.0001$) but did not change after incomplete (49 ± 11% to 49 ± 10%; $p = 0.88$) or unsuccessful revascularization (49 ± 13% to 47 ± 13%; $p = 0.11$). Sensitivity, specificity, positive and negative predictive value for the prediction of improvement in EF of >4% after PCI were 100%, 75%, 74%, and 100%, respectively, for dobutamine-cardiac MRI and 70%, 77%, 70%, and 77%, respectively, for delayed enhancement-cardiac MRI.

Conclusions Complete revascularization for multivessel coronary artery disease improves EF, whereas EF did not change in patients after incomplete or unsuccessful revascularization. Improvement in EF can be predicted by performing cardiac MRI before PCI. (J Am Coll Cardiol Intv 2010;3:392–400) © 2010 by the American College of Cardiology Foundation

From the Departments of *Cardiology and †Radiology, Erasmus Medical Center, Rotterdam, the Netherlands.
Manuscript received September 28, 2009; revised manuscript received January 4, 2010, accepted January 8, 2010.

Coronary atherosclerosis is the most common cause of heart failure in the western world (1). Several studies have shown that a coronary artery bypass graft (CABG) for multivessel coronary atherosclerosis improved ejection fraction (EF) in the presence of viable tissue (2–4). Nowadays, percutaneous coronary intervention (PCI) is increasingly used as a revascularization strategy instead of CABG, because both therapies have the same outcome in terms of survival and rates of myocardial infarction, as long as the extent of disease is not too extensive (Syntax score <33) (5). Percutaneous coronary intervention might result in incomplete revascularization due to extensive disease or when the vessel is not attempted in patients with regional systolic dysfunction which is thought to be irreversible. Incomplete revascularization has a lower event free survival than complete revascularization (6,7). Most events are due to repeated interventions, but also a lower survival rate is associated with incomplete revascularization, which is not fully understood. We hypothesized that complete revascularization in patients with multivessel disease and depressed EF better improves EF as compared with incomplete revascularization.

See page 401

In this study we evaluated the effect of complete, incomplete, or unsuccessful revascularization by PCI on EF in patients with multivessel coronary artery disease and LV dysfunction and whether improvement in EF after successful PCI can be predicted by performing cardiac magnetic resonance imaging (MRI) before PCI.

Methods

Patient population. Patients with multivessel coronary artery disease and LV wall motion abnormalities who were referred for PCI—on the basis of the discretion of the physician using the information of patient history, risk factors, and additional noninvasive stress testing if performed–were prospectively approached for enrolment in this study. Inclusion criteria were: 1) significant stenosis in at least 2 vessels; 2) sinus rhythm; and 3) abnormalities in wall motion on contrast ventriculography or echocardiography. Exclusion criteria were: 1) myocardial infarction within the last 3 months; 2) atrial fibrillation; 3) contraindications for magnetic resonance studies; 4) inability to give reliable informed consent; 5) known allergy to gadolinium-based contrast material; and 6) unstable coronary artery disease.

The institutional review board of the Erasmus Medical Center in Rotterdam approved the study, and all patients gave written informed consent.

Cardiac MRI protocol. A 1.5-T scanner with a dedicated 8-element phased-array receiver coil was used for imaging (Signa CV/i, GE Medical systems, Milwaukee, Wisconsin). Cine cardiac MRI was performed with a steady-state free-precession technique (FIESTA). Pulse sequence details have been published previously (8). To cover the entire ventricle, 10 to 12 short-axis slices were planned in the 4- and 2-chamber views (gap 2 mm). Dobutamine was infused at 5 and 10 μg/kg/min for 5 min at each dosage with an intravenous catheter, which was placed in the antecubital vein. Functional imaging was repeated during dobutamine infusion with the same long-axis imaging planes as at rest; for the short-axis only 3 slices were acquired. The 3 slices covered the basal, mid, and apical parts of the LV. During the test the patients were monitored with electrocardiographic leads for rhythm control, and blood pressure was measured at every 3-min interval. Criteria for ending the dobutamine-cardiac MRI examination were: 1) development of a new wall motion abnormality; 2) fall of systolic blood pressure of >40 mm Hg; 3) marked hypertension >240/120 mm Hg; 4) severe chest pain; 5) ventricular arrhythmias or new atrial arrhythmias; or 6) intolerable side effects of dobutamine.

Delayed enhancement (DE) cardiac MRI was performed 20 min after infusion of gadolinium-diethyltriaminepentaacetic acid (0.2 mmol/kg intravenously, Magnevist, Schering, Germany). A gated breath-hold T1-inversion recovery gradient-echo sequence was used as described previously (8). The slice locations of the delayed enhanced images were copied from the cine-images.

Definitions and data analysis. All conventional angiograms before PCI were evaluated by 2 observers, and lesions were scored visually (<50%, 50% to 99%, or 100%). A stenosis was considered significant if the diameter stenosis was >50%. Multivessel disease was defined as the presence of a significant lesion in at least 2 epicardial vessels in different perfusion territories. A chronic total occlusion (CTO) was classified as a complete occlusion for more than 3 months as obtained from either the clinical history of prolonged anginal chest pain or the date of the diagnostic angiogram before PCI. Revascularization was defined as complete when all significant stenoses defined on conventional angiogram were successfully treated. Revascularization was defined as incomplete when not all significant lesions but at least 1 was successfully treated. Revascularization was defined as unsuccessful when all significant lesions remained untreated. All cardiac magnetic resonance images were transferred to a Microsoft Windows-based personal computer for analysis with CAAS-MRV (version 3.2.1, Pie Medical Imaging, Maastricht, the Netherlands).

Abbreviations and Acronyms

ANOVA = analysis of variance
AUC = area under the receiver-operator characteristic curve
CTO = chronic total coronary occlusion
DE = delayed enhancement
DES = drug-eluting stent(s)
EF = ejection fraction
LV = left ventricle/ventricular
LVEF = left ventricular ejection fraction
MRI = magnetic resonance imaging
NYHA = New York Heart Association
PCI = percutaneous coronary intervention
TEI = transmural extent of infarction

JACC: CARDIOVASCULAR INTERVENTIONS, VOL. 3, NO. 4, 2010
APRIL 2010:392–400

This software uses the additional information of the long-axis to limit the extent of volumes at the base and apex of the heart. The EF was determined by subtracting end-systolic endocardial volume from the end-diastolic endocardial volume and dividing this number by the end-diastolic endocardial volume. Papillary muscles and trabeculations were considered as being part of the blood pool volume. A 17-segment model, excluding the apex, was used to analyze the myocardial wall in each patient. The LV segments were determined, according to the place of the stenosis and left or right dominance, as being perfused by a vessel with a significant lesion or a vessel with a nonsignificant lesion (9). Segmental wall-thickening was defined as a percentage increase of LV wall thickness during systole compared with diastole. We studied the effect of revascularization on global function and regional function. To study the effect of revascularization on regional myocardial function, segments in the perfusion territory of a significant lesion (related to anatomy on conventional angiogram) were analyzed. Myocardial segments were considered dysfunctional if wall thickening was <45% (10,11). Two viability indexes were evaluated before revascularization: 1) quantitative contractile reserve during dobutamine-cardiac MRI; and 2) transmural extent of infarction (TEI), which was calculated by dividing the hyper enhanced area by the total area in 16 segments and expressed as a percentage. The TEI was divided into 5 groups: 0%, 1% to 25%, 25% to 50%, 50% to 75%, and >75% infarct transmurality/segment, and segmental wall thickening was quantified for each group. A cutoff value of TEI <25% was used to predict functional recovery after revascularization (10,12,13). For quantitative contractile reserve during dobutamine-cardiac MRI a cutoff value of 7% was used (Kirschbaum MD, unpublished data that are under review, 2009). The percentage of dysfunctional but viable segments/patient was defined as the sum of all dysfunctional but viable segments divided by the total number of segments (n = 16). The angiograms and cardiac MRI data were analyzed in a random order with the investigator blinded to the clinical information and the previous results.

Biochemistry. Troponin T was measured 6 h after the procedure. If troponin T was above the upper limit of normal (0.02 μg/l) serial blood samples were taken every 6 h until maximum troponin T was identified. A diagnosis of an enzymatic periprocedural infarction was made according to the guidelines (European Society of Cardiology/American College of Cardiology/American Heart Association) if troponin T was >3× the upper limit of normal (14). Troponin T was quantified with Electro Chemi Luminescence Immuno Assay (ECLIA) on an Elecsys type 2010 (Roche Diagnostics, Almere, the Netherlands).

Statistical analysis. Continuous data are expressed as mean value ± 1 SD, whereas dichotomous data are expressed as numbers and percentages. Differences in baseline characteristics among patients undergoing complete, incomplete, or unsuccessful revascularization were evaluated with chi-square tests, Fisher exact tests, 1-way analysis of variance (ANOVA), or Kruskal-Wallis test where appropriate. The number of segments/patient perfused by a significant lesion was tested with 1-way ANOVA. Post hoc analysis was performed with Bonferroni correction. The changes in left ventricular ejection fraction (LVEF) and volumes within each group were tested with paired Student *t* test. The change in global functional parameters among groups was tested with ANOVA or the unpaired Student *t* test. The relationship between the amount of viability/patient and the change in LVEF was analyzed with linear regression analysis. We present the observed area under the receiver-operator characteristic curves (AUC) for both predictors. Differences in sensitivity and specificity between contrasting dobutamine-cardiac MRI and DE-cardiac MRI were evaluated by McNemar tests with exact methods. All tests were performed 2-sided, and a p value of <0.05 was considered statistically significant. All analyses were performed with SPSS version 15.0.1 (SPSS, Inc., Chicago, Illinois).

Results

Patient population. Between June 2006 and January 2008, 118 patients who met the inclusion criteria were prospectively selected, of which 28 refused to participate. Of the 90

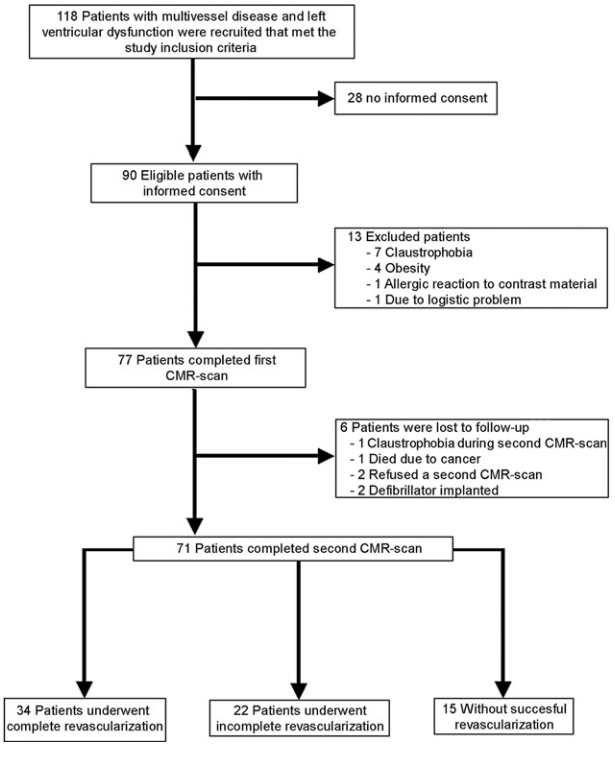

Figure 1. Flow Diagram of Patient Recruitment

Flow diagram of patient recruitment according to the Standards for Reporting of Diagnostic Accuracy statement. CMR = cardiac magnetic resonance imaging.

Table 1. Baseline Patient Characteristics

	Complete PCI (n = 34)	Incomplete PCI (n = 22)	Unsuccessful PCI (n = 15)	p Value
Age (yrs)	62 ± 9	64 ± 10	62 ± 9	0.54
Men	28 (82)	14 (64)	12 (80)	0.57
Previous MI	16 (47)	9 (41)	6 (40)	0.77
MI on DE-CMR	29 (85)	17 (77)	12 (80)	0.71
Previous PCI	6 (18)	6 (22)	7 (47)	0.10
Risk factors for coronary artery disease				
Smoking	6 (18)	4 (18)	3 (20)	0.86
Diabetes mellitus	6 (18)	2 (9)	2 (13)	0.87
Hypertension	14 (41)	10 (45)	7 (47)	0.86
Hypercholesterolemia	28 (82)	14 (64)	15 (100)	0.50
Family history	17 (50)	9 (41)	9 (60)	0.52
Medications				
ACE inhibitor	14 (41)	10 (45)	7 (47)	0.86
Beta-blocker	30 (88)	20 (91)	15 (100)	0.47
Statin	33 (97)	20 (91)	14 (93)	0.54
ASA	33 (97)	20 (91)	15 (100)	0.44
Baseline ejection fraction (%)	46 ± 12	49 ± 11	49 ± 13	0.51
Baseline end-systolic volume index (ml/m^2)	56 ± 34	52 ± 23	47 ± 23	0.10
Infarct size on DE-CMR (g)	24 ± 21	19 ± 22	25 ± 21	0.30
2-vessel disease on CAG	25 (74)	15 (69)	10 (67)	0.56
Vessel with stenosis >50%				
LAD	34 (38)	18 (38)	9 (25)	0.04
LCX	23 (26)	10 (21)	6 (17)	0.23
RCA	18 (20)	14 (29)	10 (28)	0.98
Main stem	3 (3)	0	0	0.30
Intermediate branch	0	2 (4)	2 (6)	0.64
MO	3 (3)	3 (6)	3 (8)	0.60
Diagonal 1	6 (7)	1 (2)	4 (11)	0.11
Diagonal 2	2 (2)	0	0	0.70
Total	89	48	36	
Significant lesions/patient	2.6	2.2	2.4	0.17
Chronic total occlusion	20 (59)	19 (86)	10 (67)	0.04
Syntax score	22.2 ± 9.6	22.0 ± 13.0	24.0 ± 14.1	0.90

Values are presented as n (%) or mean ± SD.

ACE = angiotensin-converting enzyme; ASA = acetylsalicylic acid; CAG = coronary angiography; DE-CMR = delayed enhancement cardiac magnetic resonance imaging; LAD = left anterior descending artery; LCX = left circumflex artery; MI = myocardial infarction; MO = marginal obtuses; PCI = percutaneous coronary intervention; RCA = right coronary artery.

patients that were included, 71 completed the study protocol. Inclusion flow chart is presented in Figure 1. The mean time interval between baseline cardiac MRI and PCI was 36 ± 36 days; clinical evidence of myocardial infarction did not occur during this time interval. In 71 patients a second cardiac MRI scan was repeated at a mean of 7 ± 1 month after PCI. All treated patients received drug-eluting stents (DES). Baseline patient characteristics are presented in Table 1. Thirty-four patients underwent complete revascularization by PCI. The left anterior descending artery was treated in 34 patients, left circumflex artery was treated in 23 patients, right coronary artery was treated in 18 patients, the main stem was treated in 3 patients, first diagonal branch was treated in 6 patients, second diagonal branch was treated in 2 patients, and the marginal obtuses were treated in 3 patients. A total of 89 vessels and 94 lesions underwent PCI with DES implantation. An average of 1.9 DES/vessel and 4.1 DES/patient were implanted with an average stent length of 21.3 mm/patient. New York Heart Association (NYHA) functional classification improved from 2.6 ± 1.1 before revascularization to 1.1 ± 0.4 at 6-month follow-up.

In patients with incomplete revascularization (n = 22), left anterior descending artery was treated in 8 patients, the first diagonal branch was treated in 1 patient, the left circumflex artery was treated in 4 patients, the marginal obtuses were treated in 1 patient, and the right coronary artery was treated in 10 patients. An average of 2.8 DES were implanted/vessel with an average stent length of 22.1

Table 2. Number of Segments/Patient Perfused by a Significant Lesion According to the Different Groups

	Complete PCI	Incomplete PCI	Unsuccessful PCI	p Value
Dysfunctional segments/patient*	5.73 ± 2.41	4.52 ± 1.12	5.14 ± 2.95	0.38
TEI <25% segments/patient	3.03 ± 1.83	2.57 ± 1.75	1.86 ± 1.35	0.12
Dobutamine responsive segments/patient	3.29 ± 1.68	2.65 ± 1.62	3.33 ± 2.42	0.45

Values are presented as mean ± SD. *Segmental wall thickening <45% at rest at baseline.
TEI = transmural extent of infarction; other abbreviations as in Table 1.

mm. The NYHA functional classification was 2.6 ± 0.7 before and changed to 1.4 ± 0.5 at 6-month follow-up. In 15 patients, PCI was not successful, mainly due to the presence of a chronic total coronary occlusion, and in some patients CABG was already rejected as a treatment option, due to comorbidity; these patients were only medically treated. The NYHA functional classification changed from 2.8 ± 0.8 at baseline and changed to 2.1 ± 1.1 at 6-month follow-up. Administration of low-dose dobutamine during cardiac MRI was well-tolerated by all patients; no serious side effects occurred. All patients with DE showed a distribution pattern extending from the endocardium, typical for ischemic heart disease.

Myocardial injury by DE-cardiac MRI and serum markers. Delayed enhancement cardiac MRI before PCI showed pre-existing myocardial damage in 85% (29 of 34) of the patients that underwent complete revascularization, in 77% (17 of 22) of the patients with incomplete revascularization, and in 87% (13 of 15) of the patients with an unsuccessful revascularization (p = 0.97). Mean infarct mass at baseline was 24 ± 21 g in patients that underwent complete revascularization, 19 ± 22 g in patients with incomplete revascularization, and 25 ± 21 g in patients with unsuccessful revascularization (p = 0.70). The number of dysfunctional segments (TEI <25%) and dobutamine responsive segments/patient showed no significant difference for the 3 groups (Table 2).

Troponin levels after procedure were elevated in 10 patients that underwent complete revascularization in which new patterns of late enhancement appeared in 3 patients and in 5 patients that underwent incomplete revascularization; none of these patients developed new patterns of DE. For the 3 patients in the complete revascularization group that developed new patterns of DE, maximum troponin levels were 0.65, 0.43, and 0.06 μg/l, and corresponding new infarct masses on DE were 6.7, 9.4, and 2.0 g, respectively. In the 3 patients with new DE, the average myocardial infarct mass changed from 11 g to 19 g. The change in infarct mass in these 3 patients did not change the total infarct size in the complete revascularization group (23.6 ± 21.7 g to 23.9 ± 22.6 g). In patients without successful revascularization, troponin levels were elevated in 3 patients, and only 1 patient developed a new infarct pattern on DE-cardiac MRI. The new infarct mass was 2 g. Total infarct mass did not change in these patients (22.0 ± 22.2 g to 20.6 ± 22.3 g).

LV function and volumes. Pre-PCI cardiac function did not differ significantly among the 3 groups (46 ± 12% vs. 49 ± 11% vs. 49 ± 13%, p = 0.51). In patients with complete revascularization by PCI, mean EF improved significantly from 46 ± 12% before revascularization to 51 ± 13% (p < 0.0001) at 6-month follow-up. The EF did not change significantly in patients after incomplete (49 ± 11% to 49 ± 10%; p = 0.88) and without successful revascularization (49 ± 13% to 47 ± 13%; p = 0.11). More detailed information is presented in Table 3.

Table 3. Functional Data at Baseline and at 6-Month Follow-Up on Left Ventricular Function

	Complete PCI (n = 34)	Incomplete PCI (n = 22)	Unsuccessful PCI (n = 15)
EF (%)			
Baseline	46 ± 12	49 ± 11	49 ± 13
6 months	51 ± 13	49 ± 10	47 ± 13
ΔEF	4 ± 5	1 ± 5	−2 ± 4
p Value	<0.0001	0.88	0.11
ESVi (ml/m^2)			
Baseline	56 ± 34	52 ± 23	47 ± 23
6 months	51 ± 37	48 ± 25	46 ± 23
ΔESVi	−5 ± 8	−4 ± 10	−1 ± 5
p Value	<0.0005	0.70	0.58
EDVi (ml/m^2)			
Baseline	99 ± 36	98 ± 22	87 ± 24
6 months	96 ± 37	91 ± 29	82 ± 24
ΔEDVi	−3 ± 10	−7 ± 15	−5 ± 9
p Value	0.11	0.74	0.07
Cardiac output			
Baseline	5.5 ± 1.0	6.1 ± 1.2	5.7 ± 1.2
6 months	6.0 ± 1.3	6.0 ± 1.4	5.1 ± 1.1
ΔCO	0.5 ± 1.2	−0.2 ± 1.0	−0.7 ± 1.1
p Value	0.02	0.79	0.10
SV			
Baseline	84 ± 16	96 ± 21	82 ± 18
6 months	88 ± 19	90 ± 22	76 ± 14
ΔSV	4 ± 15	−6 ± 17	−6 ± 15
p Value	0.13	0.29	0.16

Values are presented as mean ± SD.
CO = cardiac output; EDVi = end-diastolic volume index; EF = ejection fraction; ESVi = end-systolic volume index; SV = stroke volume; other abbreviations as in Table 1.

The improvement in EF and cardiac output in the group that underwent complete revascularization was significantly higher as compared with patients that underwent incomplete or unsuccessful revascularization (Table 4). In patients with complete revascularization the change in global parameters was not influenced by positive troponin level after PCI or whether a CTO was treated. There was a trend toward a greater improvement in EF in patients with a baseline infarct size <24 g versus patients with an infarct size of >24 g (5.4 ± 4.4% vs. 2.8 ± 5.1%; p = 0.10) (Table 4).

Global contractile function and the predictive value of cardiac MRI. The change in EF was linearly related to the extent of the LV that was dysfunctional but viable before PCI for TEI <25% (r = 0.64; p < 0.0001) (Fig. 2A) and for contractile reserve >7% (r = 0.67; p < 0.0001) (Fig. 2B).

According to the linear regression line for TEI, 4% improvement in EF corresponded to 25% of the LV that was dysfunctional but viable, which are 4 segments before revascularization. The AUC for DE-cardiac MRI to predict improvement in EF was 0.84 (95% confidence interval: 0.74 to 0.95; p < 0.0001). For dobutamine-cardiac MRI, 3 dysfunctional but viable segments/ventricle were required to achieve an improvement in EF >4%. The AUC for dobutamine-cardiac MRI to predict improvement in EF was 0.91 (95% confidence interval: 0.82 to 0.99; p < 0.0001). Dobutamine-cardiac MRI had a significant higher sensitivity (100% vs. 70%; p < 0.0001), and specificity was not different (75% vs. 77%; p = 0.80) as compared with DE-cardiac MRI. Sensitivity, specificity, positive predictive value, and negative predictive value for both viability parameters were presented in Table 5.

Regional contractile function. Segments were stratified according to the presence or absence of viability in the perfusion territory of vessels with significant lesions. Segmental wall thickening improved significantly in patients who underwent PCI if contractile reserve (positive change in segmental wall thickening >7%) was present or if TEI was <25%. Segmental wall thickening remained unchanged in patients with unsuccessful PCI regardless, if viable tissue was present (Fig. 3).

Discussion

To study the effect of multivessel PCI on depressed EF we used cardiac MRI, because it is currently accepted as the standard of reference to determine LV function (15). In addition we used both the TEI with DE-cardiac MRI and dobutamine stress cardiac MRI as potential predictors of recovery of myocardial function after PCI (12,16,17). Pre- and post-procedural DE-cardiac MRI can also detect new peri-procedural myocardial infarction during PCI that might outweigh the potential positive effect on myocardial function.

In our study we demonstrated in patients with dysfunctional myocardium referred for PCI for multivessel coronary artery disease that complete revascularization by PCI improved EF, whereas incomplete revascularization and unsuccessful revascularization did not improve EF. The extent of dysfunctional but viable myocardium/ventricle was linearly related to improvement in EF after PCI. This was reflected by the improvement in EF in patients with complete PCI in whom more dysfunctional but viable segments were revascularized than in patients with incomplete or unsuccessful PCI. The change in EF could be predicted by pre-treatment cardiac MRI where dobutamine-cardiac MRI had a higher diagnostic performance than the more widely used DE-cardiac MRI.

Table 4. Functional Data According to Different Subgroups

	n	ΔEF	ΔESVi	ΔEDVi	ΔCO	ΔSV
Complete revascularization	34	4.2 ± 4.9	−5.1 ± 7.7	−2.8 ± 10.4	0.5 ± 1.2	4.0 ± 14.3
Incomplete revascularization	22	0.7 ± 6.1	−4.3 ± 10.3	−7.4 ± 15.5	−0.1 ± 1.1	−6.5 ± 18.2
Unsuccessful revascularization	15	−1.9 ± 4.1*	−0.73 ± 4.9	−4.7 ± 9.2	−0.6 ± 1.1*	−6.2 ± 15.5
Complete revascularization						
Without CTO treatment	14	3.6 ± 5.9	−5.5 ± 7.3	−1.9 ± 8.9	0.6 ± 1.2	6.3 ± 16.9
With CTO treatment	20	4.4 ± 4.2	−4.7 ± 8.0	−3.6 ± 11.2	0.4 ± 1.2	2.0 ± 12.1
p Value		0.77	0.50	0.85	0.36	0.48
Complete revascularization						
Infarct size <24 g	17	5.4 ± 4.4	−5.6 ± 4.0	−2.7 ± 7.8	0.6 ± 1.0	6.4 ± 11.2
Infarct size >24 g	17	2.8 ± 5.1	−4.6 ± 9.8	−3.1 ± 12.4	0.4 ± 1.3	1.5 ± 16.4
p Value		0.10	0.55	0.62	0.67	0.30
Complete revascularization						
No enzymatic infarction	24	4.7 ± 4.5	−5.8 ± 8.9	−4.9 ± 10.8	0.1 ± 1.0	4.4 ± 13.4
Enzymatic infarction	10	2.9 ± 6.2	−5.6 ± 4.7	−3.3 ± 10.3	0.6 ± 1.3	0.6 ± 18.3
p Value		0.55	0.72	0.34	0.29	0.54

Values are presented as mean ± SD. *p < 0.05 as compared with the group that underwent complete revascularization.
CTO = chronic total occlusion; other abbreviations as in Table 3.

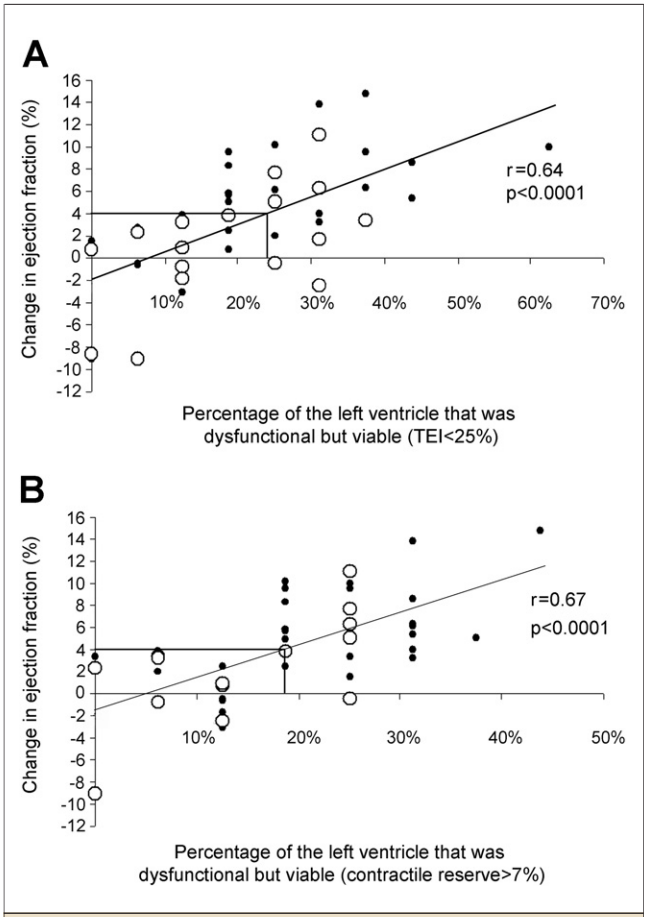

Figure 2. Prediction of Change in Ejection Fraction

The change in left ventricular ejection fraction was related to the extent of dysfunctional but viable myocardium before revascularization with delayed enhancement cardiac magnetic resonance imaging **(A)** and with dobutamine cardiac magnetic resonance imaging **(B)**. **Solid circles** = complete revascularization; **open circles** = incomplete revascularization. TEI = transmural extent of infarction.

Overall LV function. The magnitude of change of EF of 4% in patients that underwent complete PCI in the present study was relatively small but in line with previously reported data about the effect of CABG on LV function where an increase in EF of 4% to 5% was also reported (18,19). Several established clinical therapies for ischemic heart failure with a demonstrated significant impact on prognosis, such as angiotensin-converting enzyme inhibitor or beta-blocker therapy, are associated with similar improvements in LVEF (20).

The EF did not change in patients with multivessel disease followed by incomplete PCI, although segments in the perfusion territory of the significant lesion in patients with incomplete PCI were dysfunctional and viable, but apparently remaining nontreated lesions subserving dysfunctional segments might have diluted any positive effect. Not unexpectedly, an unsuccessful attempt did not improve EF. The significant increase in EF in patients that underwent complete revascularization might be a reason for the beneficial effect of complete revascularization on survival (6,7).

The PCI procedure might be associated with periprocedural myocardial infarction, which might offset the potential improvement of successful revascularization of dysfunctional but viable myocardial tissue. To account for this effect, we performed DE-cardiac MRI before and after the procedure to detect the occurrence of procedure-related myocardial infarctions. Only 3 patients with successful, complete PCI developed a peri-procedural infarction on DE-cardiac MRI; in 2 of these patients EF improved, and in the other patient EF remained the same. In the patient group with an unsuccessful attempt, 1 patient developed a peri-procedural myocardial infarction of 2 g, which is small because the mean infarct mass in these patients was 25 g. In patients with incomplete PCI no peri-procedural infarcts were detected. Therefore we can conclude that the lack of change in EF in these last 2 patient groups was not influenced by peri-procedural infarctions.

The improvement in EF in the present study was linearly related to the amount of dysfunctional but viable myocardium before revascularization ($r = 0.64$, $p < 0.001$ for DE-cardiac MRI; and $r = 0.67$, $p < 0.001$ for dobutamine), as was also shown by previously reported data by Kim et al. (12). They reported in a cohort of 41 patients undergoing revascularization by either PCI ($n = 14$) or CABG ($n = 27$) that an increasing extent of dysfunctional but viable myocardium before revascularization correlated with greater improvements in EF after revascularization ($r = 0.70$; $p < 0.001$).

Prediction of recovery of EF. Previous studies using echocardiography or nuclear imaging have shown that improvement of EF after revascularization can be predicted with a sensitivity of 57% to 84% and a specificity of 53% to 73% (21). In our study we demonstrated that the predictive power of dobutamine-cardiac MRI was higher, with a sensitivity of 100% and a specificity of 75%. However, the sensitivity with DE-cardiac MRI was lower (70%), and specificity was 77%. Several reasons might explain why dobutamine cardiac MRI had a higher diagnostic performance than DE-cardiac MRI. Dobutamine stress testing is a functional parameter; the positive inotropic effects of

Table 5. Diagnostic Accuracy for the Prediction of Improvement in Global Function

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
TEI <25%	70 (50–86)	77 (58–89)	70 (47–86)	77 (58–90)
Contractile reserve (>7%)	100 (81–100)	75 (55–89)	74 (53–88)	100 (81–100)

Values are presented as means (95% confidence intervals).
NPV = negative predictive value; PPV = positive predictive value; TEI = transmural extent of infarction.

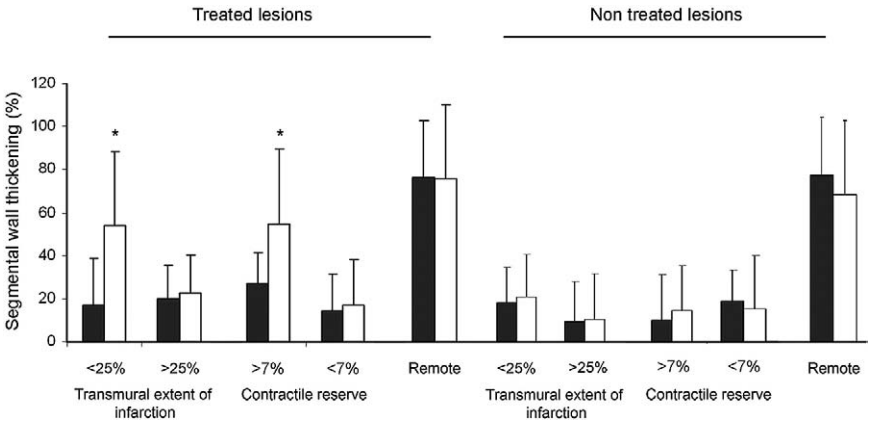

Figure 3. Segmental Wall Thickening for Dysfunctional Segments in the Perfusion Territory of a Treated Versus a Nontreated Vessel in Viable Versus Nonviable Segments

Improvement in segmental wall thickening was related to the presence of viability with magnetic resonance imaging before percutaneous coronary intervention (PCI). **Solid bars** = before PCI; **open bars** = 6 months after revascularization. *p < 0.05 versus before PCI.

dobutamine are a measure of functionality that mimics the potential effects of revascularization by improving contractile function in hypoperfused myocardium even in the absence of an increase in blood flow (22–24).

Delayed enhancement cardiac MRI is an anatomic parameter that accurately delineates the extent of infarction that will not improve after revascularization (25) but does not provide information on the extent and the functional state of the surrounding viable myocardium. The TEI is a relative value that omits the thickness of a segment and might therefore miss important information that is relevant for accurate prediction of recovery of function after revascularization therapy (13).

Study limitations. The number of patients included in this study was relatively small; nevertheless, with cardiac MRI as the gold standard for the serial assessment of cardiac function (26,27), we were able to demonstrate a significant improvement in EF. Baseline EF tended to be lower for the group that underwent complete revascularization as compared with the other 2 groups, which in theory might have influenced outcome results positively, although our results for PCI are in line with results published for CABG (18,19).

The patients in the present study had a moderately reduced EF. The results might not be applicable to patients with a severely reduced EF, because in these patients more nonviable segments might be present; however, cardiac MRI is able to detect the presence of viability that is independent of the EF. Our results might have been compromised by the occurrence of in-stent restenosis, because we did not perform late invasive coronary angiography. However, the likelihood of in-stent restenosis is low after DES implantation, and the patients that underwent complete revascularization were all symptom-free at follow-up (28).

Conclusions

Left ventricular EF improves after complete revascularization and does not change after incomplete or unsuccessful revascularization in patients with multivessel coronary artery disease and dysfunctional myocardium. The change in EF after PCI could be predicted with pre-treatment cardiac MRI, where dobutamine-cardiac MRI had a higher diagnostic performance than DE-cardiac MRI.

Reprint requests and correspondence: Dr. Robert-Jan van Geuns, Erasmus Medical Center, Thoraxcenter, Room Ba 585, P.O. Box 2040, Rotterdam, 3000 CA the Netherlands. E-mail: r.vangeuns@erasmusmc.nl.

REFERENCES

1. Gheorghiade M, Sopko G, De Luca L, et al. Navigating the crossroads of coronary artery disease and heart failure. Circulation 2006;114:1202–13.
2. Afridi I, Grayburn PA, Panza JA, Oh JK, Zoghbi WA, Marwick TH. Myocardial viability during dobutamine echocardiography predicts survival in patients with coronary artery disease and severe left ventricular systolic dysfunction. J Am Coll Cardiol 1998;32:921–6.
3. Cortigiani L, Sicari R, Desideri A, Bigi R, Bovenzi F, Picano E. Dobutamine stress echocardiography and the effect of revascularization on outcome in diabetic and non-diabetic patients with chronic ischaemic left ventricular dysfunction. Eur J Heart Fail 2007;9:1038–43.
4. Meluzin J, Cerny J, Frelich M, et al., Investigators of this Multicenter Study. Prognostic value of the amount of dysfunctional but viable myocardium in revascularized patients with coronary artery disease and left ventricular dysfunction. J Am Coll Cardiol 1998;32:912–20.
5. Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med 2009;360:961–72.

6. Hannan EL, Racz M, Holmes DR, et al. Impact of completeness of percutaneous coronary intervention revascularization on long-term outcomes in the stent era. Circulation 2006;113:2406–12.
7. van den Brand MJ, Rensing BJ, Morel MA, et al. The effect of completeness of revascularization on event-free survival at one year in the ARTS trial. J Am Coll Cardiol 2002;39:559–64.
8. Kirschbaum SW, Baks T, van den Ent M, et al. Evaluation of left ventricular function three years after percutaneous recanalization of chronic total coronary occlusions. Am J Cardiol 2008;101:179–85.
9. Pereztol-Valdes O, Candell-Riera J, Santana-Boado C, et al. Correspondence between left ventricular 17 myocardial segments and coronary arteries. Eur Heart J 2005;26:2637–43.
10. Baks T, van Geuns RJ, Duncker DJ, et al. Prediction of left ventricular function after drug-eluting stent implantation for chronic total coronary occlusions. J Am Coll Cardiol 2006;47:721–5.
11. Holman ER, Buller VG, de Roos A, et al. Detection and quantification of dysfunctional myocardium by magnetic resonance imaging. A new three-dimensional method for quantitative wall-thickening analysis. Circulation 1997;95:924–31.
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;343:1445–53.
13. Wellnhofer E, Olariu A, Klein C, et al. Magnetic resonance low-dose dobutamine test is superior to SCAR quantification for the prediction of functional recovery. Circulation 2004;109:2172–4.
14. Thygesen K, Alpert JS, White HD. Universal definition of myocardial infarction. Eur Heart J 2007;28:2525–38.
15. Bellenger NG, Davies LC, Francis JM, Coats AJ, Pennell DJ. Reduction in sample size for studies of remodeling in heart failure by the use of cardiovascular magnetic resonance. J Cardiovasc Magn Reson 2000;2:271–8.
16. Baer FM, Theissen P, Schneider CA, et al. Dobutamine magnetic resonance imaging predicts contractile recovery of chronically dysfunctional myocardium after successful revascularization. J Am Coll Cardiol 1998;31:1040–8.
17. Bove CM, DiMaria JM, Voros S, Conaway MR, Kramer CM. Dobutamine response and myocardial infarct transmurality: functional improvement after coronary artery bypass grafting—initial experience. Radiology 2006;240:835–41.
18. Gunning MG, Anagnostopoulos C, Knight CJ, et al. Comparison of 201Tl, 99mTc-tetrofosmin, and dobutamine magnetic resonance imaging for identifying hibernating myocardium. Circulation 1998; 98:1869–74.
19. Selvanayagam JB, Kardos A, Francis JM, et al. Value of delayed-enhancement cardiovascular magnetic resonance imaging in predicting myocardial viability after surgical revascularization. Circulation 2004; 110:1535–41.
20. Reffelmann T, Konemann S, Kloner RA. Promise of blood- and bone marrow-derived stem cell transplantation for functional cardiac repair: putting it in perspective with existing therapy. J Am Coll Cardiol 2009;53:305–8.
21. Schinkel AF, Bax JJ, Poldermans D, Elhendy A, Ferrari R, Rahimtoola SH. Hibernating myocardium: diagnosis and patient outcomes. Curr Probl Cardiol 2007;32:375–410.
22. Barilla F, De Vincentis G, Mangieri E, et al. Recovery of contractility of viable myocardium during inotropic stimulation is not dependent on an increase of myocardial blood flow in the absence of collateral filling. J Am Coll Cardiol 1999;33:697–704.
23. Lee HH, Davila-Roman VG, Ludbrook PA, et al. Dependency of contractile reserve on myocardial blood flow: implications for the assessment of myocardial viability with dobutamine stress echocardiography. Circulation 1997;96:2884–91.
24. Yi KD, Downey HF, Bian X, Fu M, Mallet RT. Dobutamine enhances both contractile function and energy reserves in hypoperfused canine right ventricle. Am J Physiol Heart Circ Physiol 2000;279:H2975–85.
25. 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.
26. Grothues F, Smith GC, Moon JC, et al. Comparison of interstudy reproducibility of cardiovascular magnetic resonance with two-dimensional echocardiography in normal subjects and in patients with heart failure or left ventricular hypertrophy. Am J Cardiol 2002;90: 29–34.
27. Semelka RC, Tomei E, Wagner S, et al. Normal left ventricular dimensions and function: interstudy reproducibility of measurements with cine MR imaging. Radiology 1990;174:763–8.
28. Hoye A, Tanabe K, Lemos PA, et al. Significant reduction in restenosis after the use of sirolimus-eluting stents in the treatment of chronic total occlusions. J Am Coll Cardiol 2004;43:1954–8.

Key Words: left ventricular function ■ magnetic resonance imaging ■ percutaneous coronary intervention ■ revascularization.