Short- and Long-Term Recovery of Left Ventricular Function Predicted at the Time of Primary Percutaneous Coronary Intervention in Anterior Myocardial Infarction

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OBJECTIVES	The aim of this study was to determine predictors of left ventricular (LV) function recovery at the time of primary percutaneous coronary intervention (PCI).
BACKGROUND	Angiographic, intracoronary Doppler flow, and electrocardiographic variables have been reported to be predictors of recovery of LV function after acute myocardial infarction (MI). We directly compared the predictive value of Thrombolysis In Myocardial Infarction (TIMI) flow grade, corrected TIMI frame count (cTfc), myocardial blush grade, coronary Doppler flow velocity analysis, and resolution of ST-segment elevation for recovery of LV function in patients undergoing primary PCI for acute MI.
METHODS	We prospectively studied 73 patients who underwent PCI for an acute anterior MI. Recovery of global and regional LV function was measured using an echocardiographic 16-segment wall motion index (WMI) before PCI, at 24 h, at one week, and at six months. Directly after successful PCI, coronary flow velocity reserve (CFR), cTfc, TIMI flow grade, and myocardial blush grade were assessed.
RESULTS	Mean global and regional WMI improved gradually over time from 1.86 ± 0.23 before PCI to 1.54 ± 0.34 at six-month follow-up ($p < 0.0001$) and from 2.39 ± 0.30 before PCI to 1.87 ± 0.48 at six-month follow-up ($p < 0.0001$), respectively. Multivariate analysis revealed CFR as the only independent predictor for global and regional recovery of LV function at six months.
CONCLUSIONS	Doppler-derived CFR is a better prognostic marker for LV function recovery after anterior MI than other currently used parameters of myocardial reperfusion. (J Am Coll Cardiol 2004;43:534–41) © 2004 by the American College of Cardiology Foundation

Early restoration of perfusion after myocardial infarction (MI) reduces mortality, limits infarct size, and preserves left ventricular (LV) function (1–3). The primary objective of reperfusion therapy is not only to restore epicardial vessel patency but also to reperfuse tissue in order to maintain myocyte integrity and function and, thus, LV function. At present, it is unclear which diagnostic method in the acute phase of MI accurately predicts the recovery of LV function. Electrocardiographic (ECG) determinants such as ST-segment deviation resolution (4) and (in)direct measurements of microvascular function after reperfusion therapy may indicate recovery of LV function (5,6). Angiographic predictors include Thrombolysis In Myocardial Infarction (TIMI) flow grade (2,7,8), corrected TIMI frame count (cTfc) (9), and myocardial blush grade as surrogates for tissue reperfusion (10). Coronary flow velocity reserve (CFR) obtained by digital subtraction cine-angiography significantly correlated with regional myocardial function at follow-up in the setting of acute MI (5). Both Doppler-

derived CFR and blood flow velocity pattern may indicate LV function recovery (11–13).

The purpose of this study was to identify early determinants (at the time of reperfusion) of recovery of LV function by a direct comparison of the aforementioned parameters in patients with acute MI treated with primary percutaneous coronary intervention (PCI).

METHODS

Patient selection. We studied 100 consecutive patients presenting with a first, acute, anterior MI treated with primary PCI. Acute MI was defined as chest pain lasting more than 30 min in conjunction with persistent ST-segment elevation in the precordial leads. Exclusion criteria were cardiogenic shock defined as systolic blood pressure below 90 mm Hg despite conservative measurements, previous anterior MI, previous coronary artery bypass grafting, prior LV ejection fraction <40%, LV hypertrophy (interventricular septum or posterior wall >12 mm), absence of thoracic windows for echocardiography, three-vessel coronary artery disease, TIMI grade 2 or 3 flow at time of initial angiography, or unsuccessful PCI defined as no antegrade flow and/or >50% residual stenosis in the infarct-related artery (IRA). All patients gave informed consent to the

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Abbreviations and Acronyms

APV	=	average peak flow velocity
CFR	=	coronary flow velocity reserve
cTfc	=	corrected TIMI frame count
ECG	=	electrocardiogram/electrocardiographic/electrocardiography
IRA	=	infarct-related artery
LAD	=	left anterior descending
LV	=	left ventricle/left ventricular
MI	=	myocardial infarction
PCI	=	percutaneous coronary intervention
TIMI	=	Thrombolysis In Myocardial Infarction
WMI	=	wall motion score index

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study before the procedure. The institutional review board had approved the study protocol.

Primary angioplasty and Doppler flow measurements. Primary PCI was performed within 6 h after the onset of symptoms via 6F sheath in the femoral artery, according to standard clinical practice with provisional stent implantation. Coronary angiography was performed at the end of PCI for off-line flow analyses. Five to 10 min after successful PCI, blood flow velocity was measured with a 0.014 inch Doppler wire (FloWire, Jomed, Ulestraten, The Netherlands) distal to the lesion. Coronary flow velocity reserve was determined as the ratio of adenosine (20 μg intracoronary), induced hyperemic average peak flow velocity (APV), and baseline APV. Flow velocities were recorded continuously on videotape (FloMap, Jomed). Coronary flow velocity reserve was also measured in an angiographically normal (diameter stenosis <30%) reference artery at the end of the procedure. A 12-lead ECG was performed before and at the end of PCI to evaluate ST-segment deviation.

Concomitant medical therapy. All patients were treated with aspirin 300 mg orally and heparin 5,000 IU intravenously before the procedure. An additional 2,500 IU heparin intravenously was administered if the procedure lasted more than 90 min. According to the protocol, patients subsequently received unfractionated heparin for 48 h, aspirin 100 mg daily, and ticlopidine 250 mg or clopidogrel 75 mg once daily after stent placement. Captopril was administered within 24 h after PCI and uptitrated if possible to 25 mg three times a day, metoprolol 50 mg twice a day, uptitrated if possible. Statin treatment was started the day after admission irrespective of serum cholesterol values.

LV function evaluation and follow-up. Two-dimensional echocardiography was performed immediately before primary PCI with a commercially available imaging system (Philips SONOS 2500, 2.0/2.5 MHz transducer). Data was stored on videotape. Echocardiographic evaluation of the LV function was repeated at day one, at one week, and at six months follow-up. After five weeks, a gated radionuclide ventriculography was performed. At six months follow-up, coronary angiography was repeated to assess vessel patency and/or restenosis. At six months, all patients were evaluated

for major events, defined as death from all causes, non-fatal reinfarction, repeat PCI, or coronary artery bypass grafting.

Data extraction. The sum of ST-segment elevations was measured manually 80 ms after the end of the QRS complex (J-point) in leads I, aVL, and V_1 through V_6. Resolution of ST-segment elevation was expressed as a percentage of the initial ST-segment elevation. Resolution of >70% was defined as indicative for good myocardial reperfusion (14).

Collateral flow to the IRA was graded before PCI, according to Rentrop's classification (15). The TIMI flow and myocardial blush were graded (7,10), and cTfc was measured (9) off-line. The rate–pressure product was defined as the product of heart rate and systolic blood pressure at the end of the procedure. Doppler flow velocity spectra were analyzed off-line to determine the following parameters: diastolic APV, diastolic deceleration time with a cutoff value of 600 ms (11), average antegrade systolic flow velocity with a cutoff value of 6.5 cm/s (11), the calculated ratio of mean diastolic-to-systolic flow velocity and early systolic retrograde flow velocity defined as retrograde peak velocity ≥10 cm/s, and duration ≥60 ms as previously described (16).

A 16-segment model was used to determine systolic LV function (17). All segments with a good delineation of the endocardium were scored: 1 = normal, 2 = hypokinesis, 3 = akinesis, 4 = dyskinesis. Global wall motion score index (WMI) was calculated by summation of the scores divided by the number of analyzed segments. Nine segments were used to calculate regional WMI: basal and mid-anteroseptal; mid-septal; apico-septal; apico-lateral; basal-, mid-, and apico-anterior; and apico-inferior—usually representing the perfusion territory of the left anterior descending [LAD] artery.

Recovery of global and regional LV function was defined as the difference in global and, respectively, regional WMI before PCI and that at specific time points at follow-up.

Statistical analysis. The study cohort consisted of patients who had an uneventful follow-up with an analyzable six-month follow-up echocardiography. The primary end point was recovery of LV function at six months, as defined above. Variables are presented as percentage of number of patients. Continuous variables are expressed as mean ± SD. Normally distributed variables were tested by two-tailed Student t test for paired or unpaired data, as appropriate, or by one-way analysis of variance (ANOVA) for more than two independent groups of data. The categorical variables were compared by chi-square or Fisher exact test where appropriate. Changes in global and regional WMI were tested by ANOVA for repeated measures. A p value <0.05 was considered statistically significant. Regression lines were obtained by least squares regression method. After determining univariate predictors of recovery of LV function and ejection fraction, multivariate stepwise linear regression

Table 1. Baseline and Clinical Characteristics and Univariate Predictors for Regional LV Function Recovery

	n = 73 %	Regional LV Function Recovery					
		1 Day Mean (±SD)	p Value	1 Week Mean (±SD)	p Value	6 Months Mean (±SD)	p Value
Age ≥ 55 yrs			NS		NS		NS*
Yes	45	0.11 (0.28)		0.32 (0.35)		0.54 (0.55)	
No	55	0.06 (0.23)		0.34 (0.38)		0.49 (0.42)	
Male gender			0.13		0.06		NS*
Yes	84	0.06 (0.24)		0.29 (0.35)		0.49 (0.46)	
No	16	0.19 (0.30)		0.51 (0.39)		0.63 (0.54)	
Hypertension			NS		NS		NS*
Yes	26	0.02 (0.29)		0.28 (0.33)		0.36 (0.41)	
No	74	0.09 (0.24)		0.36 (0.37)		0.53 (0.47)	
Smoking			NS		NS		NS
Yes	60	0.09 (0.24)		0.33 (0.37)		0.42 (0.45)	
No	40	0.04 (0.27)		0.33 (0.34)		0.55 (0.48)	
Hypercholesterolemia			NS		0.15		NS
Yes	29	0.05 (0.22)		0.44 (0.41)		0.52 (0.52)	
No	71	0.09 (0.26)		0.30 (0.31)		0.48 (0.43)	
Diabetes mellitus			NS		NS		NS
Yes	8	−0.07 (0.19)		0.11 (0.24)		0.40 (0.73)	
No	92	0.09 (0.26)		0.35 (0.36)		0.49 (0.44)	
Positive family history			NS		NS		NS
Yes	49	0.09 (0.28)		0.39 (0.43)		0.51 (0.46)	
No	51	0.06 (0.24)		0.28 (0.27)		0.43 (0.45)	
Beta blocker			NS		NS		NS
Yes	14	0.09 (0.26)		0.30 (0.38)		0.37 (0.36)	
No	86	0.08 (0.25)		0.34 (0.37)		0.52 (0.49)	
Calcium antagonist			NS		NS		NS
Yes	9	0.09 (0.18)		0.30 (0.35)		0.65 (0.56)	
No	91	0.08 (0.26)		0.33 (0.38)		0.48 (0.46)	
Aspirin			NS		0.02		NS
Yes	10	0.19 (0.15)		0.71 (0.17)		0.70 (0.45)	
No	90	0.06 (0.26)		0.30 (0.37)		0.48 (0.47)	
ACE inhibitor			0.12		NS		NS
Yes	6	−0.11 (0.34)		0.21 (0.58)		0.41 (0.58)	
No	94	0.09 (0.24)		0.34 (0.36)		0.50 (0.47)	
Statin			NS		0.08		NS
Yes	10	0.03 (0.31)		0.59 (0.35)		0.68 (0.61)	
No	90	0.08 (0.25)		0.31 (0.37)		0.49 (0.45)	
Preinfarct angina			NS		0.14		NS
Yes	63	0.11 (0.26)		0.39 (0.40)		0.54 (0.47)	
No	37	0.03 (0.23)		0.25 (0.23)		0.44 (0.48)	
Time to arrival <2.0 h			NS		NS		NS
Yes	54	0.07 (0.27)		0.28 (0.42)		0.47 (0.43)	
No	46	0.10 (0.24)		0.39 (0.30)		0.57 (0.53)	
Time to reperfusion <3.0 h			NS		0.1		0.08
Yes	55	0.10 (0.24)		0.39 (0.33)		0.60 (0.53)	
No	45	0.06 (0.27)		0.25 (0.40)		0.41 (0.38)	
Global WMI before PCI <1.9			NS		NS		NS
Yes	56	0.07 (0.30)		0.30 (0.39)		0.51 (0.50)	
No	44	0.11 (0.18)		0.37 (0.34)		0.51 (0.45)	
Regional WMI before PCI <2.4			0.11		0.02		NS
Yes	45	0.000 (0.29)		0.21 (0.34)		0.46 (0.45)	
No	55	0.16 (0.20)		0.42 (0.36)		0.56 (0.50)	

*Variables with a p value <0.15 were submitted to multivariate analysis for LV function recovery evaluation.
ACE = angiotensin-converting enzyme; LV = left ventricular; PCI = percutaneous coronary intervention; WMI = wall motion index.

analysis was applied to univariate variables with a significance level lower than 0.15. Qualitative variables were coded as 1 when the property was present and as 0 when absent. Statistical analysis was performed with SPSS version 10.0.7 (SPSS Inc., Chicago, Illinois).

RESULTS

Clinical events. One patient died of a hemorrhagic stroke three days after primary PCI, and one patient of end-stage kidney failure with progressive heart failure at 147 days'

Table 2. Angiographic, Doppler, and Procedural Characteristics and Univariate Predictors for Regional LV Function Recovery

	n = 73 %	Regional LV Function Recovery					
		1 Day Mean (±SD)	p Value	1 Week Mean (±SD)	p Value	6 Months Mean (±SD)	p Value
Single-vessel disease			0.07		0.06		0.12*
Yes	78	0.11 (0.26)		0.37 (0.39)		0.56 (0.46)	
No	22	−0.02 (0.19)		0.16 (0.23)		0.35 (0.51)	
Location of occlusion			NS		NS		NS*
Before septal	15	0.11 (0.20)		0.28 (0.20)		0.57 (0.43)	
Between septal and diagonal	43	0.03 (0.21)		0.30 (0.27)		0.44 (0.49)	
Distal to first diagonal	42	0.11 (0.30)		0.38 (0.50)		0.58 (0.51)	
Collaterals			NS		NS		NS*
No collaterals	40	0.07 (0.24)		0.26 (0.33)		0.51 (0.48)	
Rentrop grade 1	47	0.09 (0.25)		0.39 (0.42)		0.54 (0.51)	
Rentrop grade 2	13	0.08 (0.30)		0.26 (0.21)		0.44 (0.41)	
Rentrop grade 3	0						
Stent implantation			NS		NS		NS
Yes	62	0.09 (0.26)		0.31 (0.39)		0.45 (0.52)	
No	38	0.09 (0.25)		0.35 (0.35)		0.56 (0.45)	
Abciximab			NS		NS		NS
Yes	18	0.09 (0.23)		0.20 (0.21)		0.52 (0.46)	
No	82	0.09 (0.26)		0.35 (0.38)		0.52 (0.48)	
TIMI flow after PCI			0.06		0.07		NS
Grade 1	1	−0.5		−0.5		0.06	
Grade 2	20	0.07 (0.20)		0.30 (0.29)		0.45 (0.44)	
Grade 3	79	0.09 (0.25)		0.34 (0.37)		0.54 (0.49)	
cTfc after PCI			NS		NS		NS
>40	43	0.05 (0.25)		0.30 (0.35)		0.52 (0.47)	
30–40	31	0.10 (0.25)		0.39 (0.42)		0.58 (0.42)	
<30	26	0.11 (0.27)		0.29 (0.33)		0.42 (0.56)	
Myocardial blush grade after PCI			0.08		NS		NS
Grade 1	4	−0.13 (0.50)		−0.08 (0.59)		0.24 (0.20)	
Grade 2	39	0.02 (0.23)		0.30 (0.33)		0.43 (0.47)	
Grade 3	57	0.13 (0.23)		0.36 (0.37)		0.59 (0.49)	
Rate-pressure product <10,000			0.11		NS		0.1
Yes	61	0.12 (0.28)				0.59 (0.49)	
No	39	0.02 (0.20)				0.40 (0.46)	
CFR LAD			NS		0.06		<0.0001
<1.50	33	0.04 (0.28)		0.24 (0.27)		0.26 (0.41)	
1.50–1.75	41	0.11 (0.25)		0.28 (0.41)		0.53 (0.48)	
>1.75	26	0.11 (0.22)		0.50 (0.37)		0.81 (0.39)	
Baseline APV LAD (cm/s)			NS		NS		NS
<15	27	0.06 (0.27)		0.25 (0.41)		0.55 (0.51)	
15–20	33	0.08 (0.26)		0.31 (0.25)		0.45 (0.40)	
>20	40	0.11 (0.24)		0.40 (0.41)		0.55 (0.52)	
Hyperemic APV LAD (cm/s)			NS		0.13		NS
<25	34	0.04 (0.28)		0.22 (0.36)		0.46 (0.52)	
25–35	32	0.07 (0.25)		0.31 (0.29)		0.50 (0.40)	
>35	34	0.14 (0.23)		0.44 (0.42)		0.59 (0.51)	
Diastolic deceleration time <600 ms			NS		NS		NS
Yes	55	0.08 (0.28)		0.31 (0.39)		0.51 (0.44)	
No	45	0.09 (0.25)		0.37 (0.37)		0.55 (0.56)	
Average systolic flow velocity <6.5 cm/s			NS		NS		NS
Yes	31	0.02 (0.23)		0.26 (0.35)		0.57 (0.47)	
No	69	0.11 (0.22)		0.39 (0.36)		0.59 (0.44)	
Diastolic-systolic velocity ratio <3			0.12		NS		0.03
Yes	62	0.12 (0.24)		0.40 (0.41)		0.67 (0.47)	
No	38	0.03 (0.18)		0.25 (0.23)		0.42 (0.36)	
Systolic retrograde flow velocity ≥10 cm/s			0.008		0.02		0.03
Yes	30	−0.03 (0.30)		0.17 (0.34)		0.33 (0.43)	
No	70	0.14 (0.21)		0.40 (0.36)		0.59 (0.49)	
CFR reference vessel			NS		NS		NS
<2.0	16	0.11 (0.22)		0.40 (0.46)		0.34 (0.44)	
2.0–2.8	64	0.07 (0.28)		0.31 (0.37)		0.54 (0.48)	
>2.8	19	0.11 (0.21)		0.35 (0.30)		0.57 (0.50)	
ST-resolution >70%			NS		NS		NS
Yes	55	0.12 (0.31)		0.30 (0.36)		0.55 (0.40)	
No	45	0.05 (0.21)		0.38 (0.44)		0.48 (0.54)	

*Variables with a p value <0.15 were submitted to multivariate analysis for LV function recovery evaluation.

APV = average peak flow velocity; CFR = coronary flow velocity reserve; cTfc = corrected TIMI frame count; LAD = left anterior descending coronary artery; LV = left ventricular; PCI = percutaneous coronary intervention; TIMI = Thrombolysis In Myocardial Infarction.

Table 3. Recovery of Global and Regional Left Ventricular Function

	Global WMI	p Value*	Regional WMI	p Value*
Before PCI	1.86 (0.23)	0.0001	2.39 (0.30)	0.0001
Recovery† at one day	0.03 (0.22)		0.09 (0.25)	
Recovery† at one week	0.20 (0.28)		0.33 (0.37)	
Recovery† at six months	0.32 (0.34)		0.52 (0.48)	

*p value obtained in analysis of variance for repeated measurements; †recovery defined as WMI before PCI minus WMI at specific time points. Values are given as means ± SD.

PCI = percutaneous coronary intervention; WMI = wall motion index.

follow-up. One patient underwent coronary artery bypass grafting at day 89. Eight patients underwent repeat PCI (4 patients showed target lesion restenosis, 1 acute stent closure at day 14, and 3 patients underwent non-LAD coronary artery repeat PCI). Six patients with significant restenosis at six months' follow-up were excluded from the analysis because of possible influences on LV function recovery. Ten patients with an uncomplicated clinical course at follow-up refused a reangiography. The remaining 73 of the initial 100 patients constitute the study cohort and were analyzed in the present study.

Baseline characteristics. Baseline clinical characteristics are shown in Table 1. Angiographic, Doppler, and procedural characteristics are shown in Table 2. Mean age of the analyzed patients was 54 ± 12 years. Mean summated ST-segment elevation before PCI was 26.5 ± 14.8 mV and after the procedure 7.9 ± 6.1 mV resulting in 18.6 ± 12.2 mV absolute ST-segment resolution. The relative resolution was 70.2 ± 23.0%. Mean time between reperfusion and second ECG was 106 ± 30 min.

Mean cTfc in the LAD coronary artery after PCI was 44 ± 21 and in the reference vessel 29 ± 12. A significant association existed between TIMI flow grade and cTfc (r = −0.72, p < 0.0001), TIMI flow grade and myocardial blush grade (r = 0.45, p < 0.0001), and cTfc and myocardial blush grade (r = −0.53, p < 0.0001).

At the end of the PCI procedure, mean CFR in the LAD coronary artery was 1.62 ± 0.37 (range, 1.0 to 2.6), with a mean baseline APV of 20.1 ± 8.5 cm/s and a mean hyperemic APV of 32.0 ± 14.1 cm/s. The mean reference vessel CFR was 2.43 ± 0.53. In the LAD coronary artery, mean diastolic deceleration time was 635 ± 382 ms, mean average systolic flow velocity 9.9 ± 8.4 cm/s, mean diastolic-to-systolic flow velocity 4.2 ± 6.2, and mean early systolic retrograde flow velocity 6.3 ± 11 cm/s. Baseline APV in the LAD coronary artery showed fair correlations with TIMI flow grade (r = 0.31, p = 0.007) and cTfc (r = −0.54, p < 0.0001). No association was found between baseline APV and myocardial blush grade. A fair correlation existed between baseline APV and ST-segment resolution (r = −0.40, p = 0.003). Hyperemic APV in the LAD coronary artery was associated with TIMI flow grade (r = 0.35, p = 0.003), cTfc (r = −0.50, p < 0.0001), myocardial blush grade (r = 0.25, p = 0.04), and with ST-segment resolution (r = 0.29, p = 0.04). There was no significant correlation between CFR and any of the angiographic

parameters or between CFR and ST-segment resolution. Mean peak CK-MB was 486 ± 255 μg/l.

Recovery of global and regional LV function. A progressive improvement of short-term and long-term global and regional LV function was documented (Table 3). All baseline variables were used to identify univariate predictors for short-term and long-term global (data not shown) and regional (Tables 1 and 2) LV function recovery.

The relation between CFR and LV function recovery is plotted in Figure 1. All patients with a CFR ≥2.0 immediately after primary PCI showed improvement of LV function (Fig. 1A). No relation existed between angiographic parameters and recovery of LV function (Fig. 1B, 1C, and 1D).

Coronary flow velocity reserve of the LAD coronary artery directly after primary PCI was the only independent predictor in multivariate analysis of global (Table 4) and regional (Table 5) LV function recovery at six months. Global and regional LV function recovery at one week were predicted by clinical, echocardiographic, angiographic, and Doppler-derived variables (Tables 4 and 5). Independent predictors of short-term LV function improvement were not similar to those predicting long-term improvement (Tables 4 and 5).

LV ejection fraction. Mean ejection fraction at five weeks' follow-up was 47 ± 13%. Multivariate regression analysis revealed CFR in the LAD coronary artery and early systolic retrograde flow velocity as independent predictors of ejection fraction at five weeks (coefficient of constant, 14.6; coefficient of CFR, 15.7; 95% confidence interval, 5.8 to 25.5; p = 0.003; coefficient of systolic retrograde flow, −10.0; 95% confidence interval, −18.0 to −2.1; p = 0.01).

DISCUSSION

In our homogenously selected group of patients with a first anterior acute MI, Doppler-derived CFR obtained directly after primary PCI was the only independent predictor of long-term global and regional recovery of LV function. Thrombolysis In Myocardial Infarction flow grading predicted global recovery of LV function at one week, but not at other time points. No other angiographic parameter after primary PCI predicted LV function recovery. To our knowledge, this is the first study that directly compared CFR with other prognostic variables for LV function recovery at six months after primary PCI.
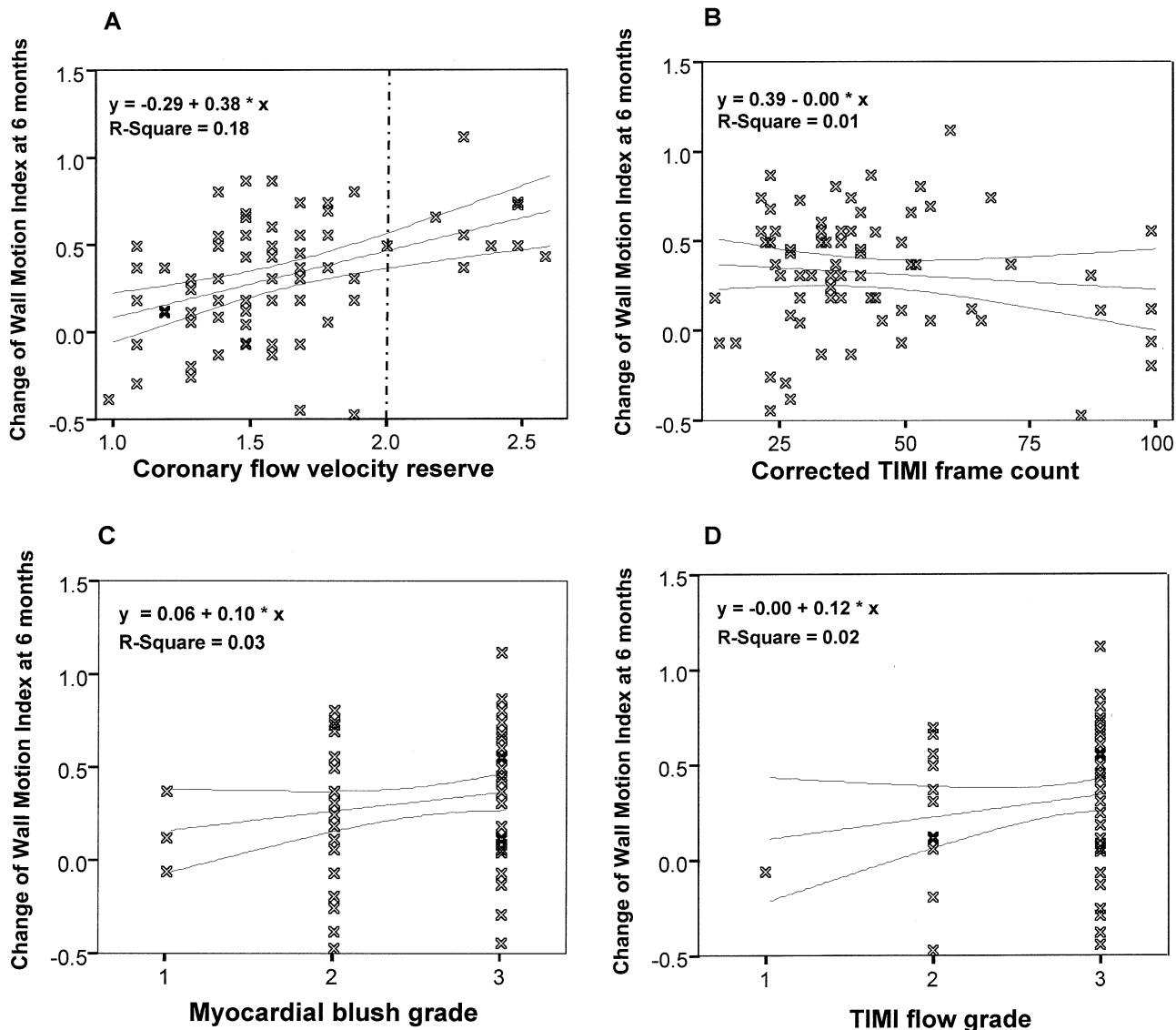
Figure 1. Relation between six-month change in global wall motion index (WMI) and coronary flow velocity reserve after percutaneous coronary intervention **(A)** and change in WMI as a function of corrected Thrombolysis In Myocardial Infarction (TIMI) frame count, **(B)** myocardial blush grade **(C)**, and TIMI flow grade **(D)**. The regression lines and 95% confidence intervals are shown. Change in WMI >0 reflects improvement of left ventricular function after six months.

ST-segment resolution and LV function recovery. In contrast with earlier studies (14,18,19), we could not demonstrate a relation between ST-segment recovery and ejection fraction nor between ST-segment recovery and improvement of LV function. Our results are in accordance with the results of Poli et al. (19) as they found, with respect to six-month functional recovery, no additional prediction of ST-segment resolution next to myocardial blush grade. ST-segment resolution is proposed as a marker of microvascular reperfusion (20). However, in our study, no relation existed between ST-segment resolution and CFR, although it was associated with baseline and hyperemic APV. In previous studies, ST-segment resolution was slower in patients with anterior MI than with non-anterior MI. This may explain the absence of association between ST resolu-

tion and CFR in our study in patients with only anterior MI.

Angiographic parameters in relation to LV function recovery. Our current knowledge on factors influencing LV function recovery after acute MI is based on angiographic studies. In large, multicenter studies evaluating thrombolysis, TIMI flow grading appeared to be of clinical use for risk stratification (2,8,21). In our study, TIMI flow after PCI showed a weak correlation with LV function recovery at one week (r = 0.30, p = 0.015), and myocardial blush grade was weakly correlated with regional function recovery at one day (r = 0.27, p = 0.02). Our study consisted of non-high-risk patients (excluding shock, low ejection fraction, previous anterior MI, and excluding cardiac events on follow-up). This may be the reason for a

Table 4. Multivariate Predictors of Recovery of Global Left Ventricular Function*

	Coefficient	95% CI	p Value
Recovery at one day			
Constant	−0.076		
Early systolic retrograde flow velocity <10 cm/s	0.16	0.04–0.27	0.007
Recovery at one week			
Constant	−0.88		
Statin use	0.21	0.007–0.40	0.042
Global WMI before PCI ≥1.9	0.18	0.06–0.30	0.005
Single-vessel disease	0.19	0.04–0.34	0.012
TIMI flow grade	0.17	0.04–0.30	0.011
CFR after PCI	0.09	0.004–0.17	0.039
Recovery at six months			
Constant	−0.004		
CFR after PCI	0.17	0.06–0.27	0.002

*Recovery defined as WMI before PCI minus WMI at specific time points.
CFR = coronary flow velocity reserve; CI = confidence interval; PCI = percutaneous coronary intervention; WMI = wall motion index; TIMI = Thrombolysis In Myocardial Infarction.

Table 5. Multivariate Predictors of Recovery of Regional Left Ventricular Function*

	Coefficient	95% CI	p Value
Recovery at one day			
Constant	−0.44		
Regional WMI before PCI ≥2.4	0.18	0.06–0.29	0.004
Single-vessel disease	0.17	0.03–0.31	0.016
Early systolic retrograde flow velocity <10 cm/s	0.16	0.40–0.29	0.011
Recovery at one week			
Constant	−0.47		
Aspirin use	0.20	−0.07–0.47	0.148
Statin use	0.34	0.08–0.61	0.012
Regional WMI before PCI ≥2.4	0.25	0.08–0.41	0.004
Single-vessel disease	0.27	0.07–0.46	0.008
Early systolic retrograde flow velocity <10 cm/s	0.22	0.04–0.39	0.015
Recovery at six months			
Constant	−0.02		
CFR after PCI	0.28	0.14–0.41	<0.0001

*Recovery defined as WMI before PCI minus WMI at specific time points.
CFR = coronary flow velocity reserve; CI = confidence interval; PCI = percutaneous coronary intervention; WMI = wall motion index.

diminished ability to detect a relationship between angiographic parameters and LV function recovery, whereas CFR is a potent predictor of LV function recovery in these patients.

Doppler-flow parameters in relation to LV function recovery. In our study, CFR was the only independent predictor of long-term global and regional LV function recovery. Coronary flow velocity reserve after PCI predicted not only the change in LV function over six months but also the ventriculographic ejection fraction at five weeks that is associated with long-term mortality. Coronary flow velocity reserve as a predictor being superior to the other parameters of myocardial perfusion may be explained by the direct way of interrogating the microvascular bed, thereby more accurately reflecting microvascular integrity and function.

Iwakura et al. (16) demonstrated altered coronary flow velocity patterns as the appearance of systolic retrograde flow, diminished systolic antegrade flow, and rapid deceleration of diastolic flow in patients with the no-reflow phenomenon after reperfusion therapy. These flow velocity patterns appeared to be inversely related with in-hospital (22) and with one-month recovery of LV function (11). This is in accordance with our findings that absence of early systolic retrograde flow immediately after primary PCI was associated with recovery of global and regional LV function at one-day follow-up and with regional LV function improvement at one week. At five weeks, systolic retrograde flow, next to CFR, independently correlated with ejection fraction. However, long-term LV function changes were not predicted by altered coronary flow velocity patterns in contrast with CFR. Surprisingly, CFR was not assessed in the aforementioned studies. Although altered flow patterns after primary PCI could predict in-hospital complications and mortality (23), it is unclear if these flow patterns can predict also long-term mortality.

Study limitations. This study was designed to evaluate prognostic parameters obtained during primary PCI on LV

function recovery. The present study indicates that CFR is a good prognostic parameter for LV function recovery, although larger studies are needed for evaluation of Doppler-derived parameters to predict mortality.

In this study we did not perform intracoronary pressure measurements with microvascular resistance calculations. Combined and repeated coronary flow and pressure assessment in the early and late phase of MI may give more insight into changes in microvascular resistance in relation to LV function recovery.

Clinical implications. Our study suggests that CFR immediately after primary PCI can predict LV function recovery. This finding is relevant for selection of patients that may benefit from adjunctive therapies aiming at improving tissue reperfusion and, hence, recovery of LV function.

Conclusions. Percutaneous coronary intervention in patients with acute MI reduces infarct size and preserves LV function. Preservation of the microvascular function, and thus, of the integrity of myocardial tissue, is the pivotal factor influencing recovery of LV function after primary PCI. This study demonstrates that Doppler-derived CFR better predicts recovery of LV function than the commonly reported angiographic and clinical parameters.

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