Myocardial Perfusion Grade After Late Infarct Artery Recanalization Is Associated With Global and Regional Left Ventricular Function at One Year

Analysis From the Total Occlusion Study of Canada-2

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Background—Whether myocardial perfusion grade (MPG) following late recanalization of infarct-related arteries (IRAs) predicts left ventricular (LV) function recovery beyond the acute phase of myocardial infarction (MI) is unknown.

Methods and Results—The Total Occlusion Study of Canada-2 enrolled stable patients with a persistently occluded IRA beyond 24 hours and up to 28 days post-MI. We studied the relationship between the initial MPG and changes in LV function and volume as well as the change in MPG from immediate post-percutaneous coronary intervention (PCI) to 1 year in 139 PCI patients with thrombolysis in myocardial infarction grade 3 epicardial flow post-PCI and with paired values grouped into impaired or good MPG groups (MPG 0/1 or MPG 2/3). MPG 0/1 patients were more likely to have received thrombolytic therapy and to have a left anterior descending IRA. They had lower blood pressure and LV ejection fraction (LVEF) and a higher heart rate and systolic sphericity index at baseline. Changes in the MPG 0/1 and MPG 2/3 groups from baseline to 1 year were LVEF, 3.3±9.0% and 4.8±8.9% (P=0.42); LV end-systolic volume index (LVESVI), −1.1±9.2 and −4.7±12.3 mL/m^2 (P=0.25); LV end-diastolic volume index (LVEDVI), 0.08±19.1 and −2.4±22.2 mL/m^2 (P=0.67); and SDs/chord for infarct zone wall motion index (WMI), 0.38±0.70 and 0.84±1.11 (P=0.01). By covariate-adjusted analysis, post-PCI MPG 0/1 predicted lower WMI (P<0.001), lower LVEF (P<0.001), and higher LVESVI (P<0.01) but not LVEDVI at 1 year. Of the MPG 0/1 patients, 60% were MPG 2 or 3 at 1 year.

Conclusions—Preserved MPG is present in a high proportion of patients following late PCI of occluded IRAs post-MI. Poor MPG post-PCI frequently improves MPG over 1 year. MPG graded after IRA recanalization undertaken days to weeks post MI is associated with LV recovery, indicating that MPG determined in the subacute post-MI period remains a marker of viability.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00025766.

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Key Words: acute coronary syndrome ■ myocardial infarction ■ myocardial reperfusion ■ angioplasty ■ coronary artery disease

Timely recanalization and sustained patency of the infarct-related artery (IRA) are major determinants of left ventricular (LV) function and survival after acute myocardial infarction (MI). Patients with normal epicardial flow in the IRA (thrombolysis in myocardial infarction [TIMI] grade 3) but reduced tissue-level perfusion as quantified by TIMI myocardial perfusion grade (MPG) immediately following acute reperfusion with fibrinolysis or primary or rescue percutaneous coronary intervention (PCI)[1] have longer ischemic times, larger infarcts, worse global and regional LV systolic function, and increased mortality.[2,3] These observations suggest that MPG marks microvascular integrity and is thereby a surrogate for myocardial viability in the acute phase of MI.[4–7]

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In contrast to the extensively documented benefit of early recanalization, routine late recanalization (beyond 24 hours) after symptom onset is not well supported by evidence[8,9] and is not guideline recommended. Until recently, late PCI for persistent occlusion generally has been performed on the basis of the late open artery hypothesis.[10] The extent to which effective microvascular reperfusion can be achieved by PCI performed after the acute phase and whether it is followed by regional or global functional recovery of the LV are unknown. The Occluded Artery Trial (OAT)[9] was a multicenter randomized controlled trial that evaluated the benefit of PCI in addition to optimal medical therapy compared with optimal medical therapy alone in patients beyond the first 24 hours and up to 28 days after MI onset. The Total Occlusion Study of Canada-2 (TOSCA-2) was a National Heart, Lung, and Blood Institute-funded angiographic ancillary study of OAT with coprimary end points of IRA patency at 1 year and change in LV ejection fraction (EF) from baseline to 1 year.[8] Paired coronary and LV angiograms were obtained at baseline and 1 year post-PCI (n=332), providing a unique opportunity to evaluate the association between MPG at baseline (following successful PCI) and global and regional functional recovery at 1 year follow-up and to examine the stability of perfusion grade over time.

Methods

Study Population

The primary results of TOSCA-2[8] as well as the study design[11] and results[9] of the parent OAT have been published. Inclusion criteria for TOSCA-2 and OAT included a documented index MI and an occluded IRA (TIMI flow grade 0 or 1) in addition to 1 of 2 high-risk criteria: (1) proximal occlusion or (2) LVEF <50%. Important exclusion criteria included a clinical indication for revascularization (significant angina, severe inducible ischemia, left main or triple-vessel disease), serum creatinine >2.5 mg/dL, severe valvular disease, New York Heart Association (NYHA) class III or IV heart failure, or cardiogenic shock at the time of screening. Inclusion criteria for the MPG analysis included OAT treatment assignment to the PCI group with subsequent successful PCI of IRA with post-PCI antegrade TIMI 3 flow. Finally, baseline, post-PCI, and 1-year follow-up coronary angiograms suitable for MPG analysis and analyzable LV angiograms were required.

Data Collection

Baseline characteristics were recorded from the time of index MI to the time of randomization. Qualifying coronary and LV angiograms performed after the first 24 hours and up to 28 days post-MI as well as post-PCI and follow-up angiograms performed after 1 year were submitted for quantitative analysis performed in a dedicated core angiographic laboratory. LV volumes, LVEF, regional wall motion, and sphericity index were calculated as described previously.[12–14]

PCI

Protocol PCI of the IRA with routine stenting was performed within 24 hours of randomization. All patients received aspirin and either ticlopidine or clopidogrel beginning the day of the procedure or earlier. Anticoagulation with heparin during PCI to a target activated clotting time of ≥250 seconds was recommended. Use of glycoprotein IIb/IIIa inhibitors was encouraged.

MPG

The MPG substudy was prospectively planned, and participating centers were instructed with respect to technique for obtaining immediate post-PCI and 1-year follow-up angiograms optimized for MPG analysis, generally requiring a longer cine-angiographic recording focusing on the myocardial segment likely to demonstrate blush. MPG was graded semiquantitatively by 2 independent core laboratory readers (V.J., T.S.) trained to use standard TIMI MPG criteria[1] and blinded to clinical data and timing and sequence of angiography. In case of discrepancies, angiograms were re-read independently by both readers, and any remaining discrepancies were resolved by a third reader (G.B.J.M.). Post-PCI and follow-up angiograms also were evaluated for residual thrombus and evidence of distal embolization. The present analysis was limited to patients with post-PCI TIMI flow grade 3 because it is technically difficult to grade myocardial blush when the epicardial vessel is poorly opacified and, moreover, abnormalities of MPG might no longer reflect microvascular function if flow were restricted proximally. We have recently published a reproducibility study that included the TIMI MPG method in an angiographic core laboratory where we found a high degree of interobserver reproducibility when MPG was dichotomized to 0 or 1 versus 2 or 3.[15] Because of the relatively small number of patients in the present study and the inherent difficulties in MPG grading, we prospectively defined grouping of MPG to 0 or 1 (MPG 0/1) versus 2 or 3 (MPG 2/3).

Statistical Analysis

Categorical variables are expressed as frequencies and percentages and continuous variables as mean±SDs. Categorical variables were compared using χ^2 test or, alternatively, Fisher exact test if expected frequency for any cell in a 2×2 table was <5. The Wilcoxon 2-sample test was used to compare time intervals from index MI to baseline angiography, randomization, and PCI. Independent-sample t test was used to compare other continuous variables that were normally distributed. Within-group changes over time were compared using a paired t test of the difference, and between-group differences were compared with 2-sample t tests. The prespecified level of significance for all secondary analyses of OAT was $P<0.01$, whereas $P\geq0.01$ and <0.05 were considered to indicate a trend toward statistical significance.

Effects of impaired post-PCI MPG (MPG 0/1) on 1-year LVEF, wall motion index (WMI), LV end-systolic volume index (LVESVI), and LV end-diastolic volume index (LVEDVI) were examined in an unadjusted as well as a covariate-adjusted linear regression model. All baseline covariates that were tested for are listed in Table 1 of the main OAT publication.[9] Adjustments were made for other baseline covariates, with $P<0.05$ on multiple linear regression using backward elimination. WMI was adjusted for baseline WMI, days to randomization, body mass index (BMI), and new Q waves. LVEF was adjusted for baseline LVEF, heart rate, BMI, and new Q waves. LVESVI was adjusted for baseline LVESVI, no family history, NYHA class >I at presentation, and left anterior descending artery (LAD) as the IRA.

Results

Distribution of MPG

Of the 381 patients enrolled in TOSCA-2, 195 were assigned to PCI, and of these, 186 had angiograms potentially suitable for baseline MPG analysis. The 9 angiograms that were excluded had cine-angiographic recordings that were too short for analysis. The distribution of post-PCI TIMI flow grade in these 186 patients was grade 0 in 12 (6.5%), grade 1 in 6 (3.2%), grade 2 in 11 (5.9%), and grade 3 in 157 (84.4%). The distribution of MPG, evaluated in all 157 patients with TIMI flow grade 3, was MPG 0 in 25 (15.9%), MPG 1 in 8 (5.1%), MPG 2 in 77 (49.0%), and MPG 3 in 47 (29.9%). Baseline clinical characteristics of the MPG 0/1 and MPG 2/3 groups are provided in Table 1, and angiographic and procedural characteristics are provided in Table 2. Of these 157 evaluable patients, 142 also had MPG and global and regional LV functional parameters suitable for analysis at 1-year follow-up. Paired analyses were available for 139 patients (post-PCI and 1 year).

Table 1. Baseline Clinical Characteristics by Post-PCI MPG

Characteristic	Post-PCI MPG 0/1 (n=33)	Post-PCI MPG 2/3 (n=124)	*P*
Male sex, %	78.8	85.5	0.350
Age, y	54.6±9.2	57.4±10.5	0.174
BMI, kg/m^2	28.6±4.5	27.6±4.1	0.21
Diabetes	24.2	16.9	0.336
Hypertension	48.5	50.8	0.813
Hyperlipidemia	48.5	58.9	0.285
Family history of CAD	42.4	48.4	0.542
Current-smoker	42.4	31.5	0.236
Prior angina	12.1	21.8	0.216
Prior MI	6.1	13.7	0.368
Interval from MI to baseline angiogram, d	5 (4, 8)	5 (3, 9)	0.566
Interval from MI to randomization, d	9 (5, 17)	10 (6, 20)	0.512
Interval from MI to PCI, d	10 (5, 18)	10 (7, 20)	0.507
Interval from baseline angiogram to PCI, d	3 (0, 9)	2 (0, 12)	0.939
Heart rate, beats/min	74.9±12.1	67.4±10.9	0.001
Systolic blood pressure, mm Hg	108.4±16.5	119.3±15.1	0.0004
Diastolic blood pressure, mm Hg	66.9±9.7	72.1±10.8	0.014
Fibrinolytic therapy during first 24 h of index MI	45.4	16.9	<0.001
ST elevation >0.1 mV	72.7	59.8	0.175
ST depression >0.1 mV	36.4	30.3	0.508
New Q waves	63.4	65.3	0.860
Maximum pre-PCI total CK divided by ULN	10.1±6.2*	7.1±7.3†	0.048
Maximum pre-PCI CK MB divided by ULN	23.4±26.6	11.8±14.3	0.123
Maximum pre-PCI TNI divided by ULN	172.4±152.0	271.4±713.6	0.253
Maximum pre-PCI TNT divided by ULN	229.5±215.9	50.6±50.3	0.138
Killip class >1 during index MI	9.1	10.5	0.999
NYHA class >I at randomization	9.1	6.4	0.700

Data are presented as mean±SD, median (interquartile range), or percentage. CAD indicates coronary artery disease; CK, creatine kinase; TNI, troponin I; TNT, troponin T; ULN, upper limit of the local laboratory normal.

*n=27.

†n=104.

Table 2. Angiographic and Procedural Characteristics by Post-PCI MPG

Characteristic	Post-PCI MPG 0/1 (n=33)	Post-PCI MPG 2/3 (n=124)	*P*
Pre-PCI coronary angiography			
LAD IRA	54.6	21.8	<0.001
Circumflex IRA	21.2	9.7	
RCA IRA	24.2	68.5	
IRA TIMI flow grade 0 to 1	100.0	98.4	1.000
Collaterals present	72.3	95.1	<0.001
Single-vessel disease	87.9	81.4	0.385
Pre-PCI LV angiography			
Infarct segment regional WMI SD/chord	−3.2±0.7	−2.9±1.0	0.177
LVEF	42.6±11.6	50.6±8.7	<0.001
LVESVI	39.8±20.1	31.3±14.3	0.08
LVEDVI	69.7±27.3	63.6±24.7	0.34
Diastolic sphericity index	31.0±5.3	30.8±6.4	0.862
Systolic sphericity index	25.3±6.1	22.9±5.5	0.035
Mitral regurgitation present	28.1	35.8	0.414
Procedural characteristics and post-PCI angiography			
Residual thrombus	9.1	2.4	0.108
Distal embolization	3.0	8.9	0.462
Post-PCI residual % diameter stenosis	29.8±17.6	27.8±14.3	0.507
Post-PCI minimal luminal diameter, mm	2.2±0.6	2.3±0.5	0.097
Glycoprotein IIb/IIIa inhibitors used	90.9	83.1	0.27
Stent implanted	100.0	99.2	1.000

Data are presented as mean±SD or percentage. RCA indicates right coronary artery.

Univariate Correlates of Impaired MPG Post-PCI

At baseline, patients with MPG 0/1 had evidence of larger infarcts, lower systolic blood pressure and LVEF, and a trend to a larger LVESVI and higher peak creatine kinase compared with patients with MPG 2/3. They also were more likely to have an occluded LAD and to have been treated with fibrinolytic therapy for the index MI and less likely to have angiographically visible collaterals. Glycoprotein IIb/IIIa inhibitors were used in a majority of cases, with no difference between groups (Tables 1 and 2). These baseline findings are similar to those reported for the larger cohort of 261 OAT ancillary study patients in whom baseline MPG was measured.[16]

Optimal Medical Treatment

Both MPG groups had high rates of optimal medical therapy during hospital stay, at discharge, and at 1-year follow-up, with no differences observed between the groups (Table 3).

Changes in LV Size and Function Over 1 Year

As a group, patients with MPG 2/3 showed significant improvement at follow-up in measures of global contractility, including LVEF and LVESVI. In contrast, those with MPG 0/1 showed no improvement. The more demanding between-group comparison testing for differential effects of post-PCI MPG on these LV parameters, however, was not significant (Figure A and B). Regional contractility of the infarct zone as expressed by the wall motion score improved in both MPG groups at follow-up, but the degree of wall motion improvement observed in the MPG 2/3 group was significantly greater than that observed in the MPG 0/1 group (Figure D). No significant change or

Table 3. Use of Medical Therapies at Discharge and at 1 Year (by MPG)

	Discharge			1-Year Follow-Up		
	MPG 0/1 (n=30)	MPG 2/3 (n=109)	*P*	MPG 0/1 (n=29)	MPG 2/3 (n=106)	*P*
Discharge						
Aspirin	29 (96.7)	108 (99.1)	0.39	28 (96.6)	100 (94.3)	1.00
Thienopyridines (clopidogrel or ticlopidine)*	30 (100.0)	108 (99.1)	1.00	9 (31.0)	29 (27.4)	0.70
Aspirin or thienopyridine	30 (100.0)	109 (100.0)	NA	28 (96.6)	103 (97.2)	1.00
Aspirin plus thienopyridine	29 (96.7)	107 (98.2)	0.52	9 (31.0)	26 (24.5)	0.48
Warfarin	5 (16.7)	4 (3.7)	0.02	…	…	…
One or more of aspirin, warfarin, thienopyridine	30 (100.0)	109 (100.0)	NA	…	…	…
Two or more of aspirin, warfarin, thienopyridine	30 (100.0)	107 (98.2)	1.00	…	…	…
β-blocker	28 (93.3)	97 (89.0)	0.73	28 (96.6)	89 (84.0)	0.12
ACE inhibitor or ARB	29 (96.7)	94 (86.2)	0.19	28 (96.6)	92 (86.8)	0.19
Spironolactone	4 (13.3)	2 (1.8)	0.02	4 (13.8)	6 (5.7)	0.22
Lipid-lowering agent	28 (93.3)	92 (84.4)	0.37	28 (96.6)	93 (87.7)	0.30

Data are presented as no. (%). ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocking agent.
*Only clopidogrel for 1-year follow-up.

difference was noted within or between MPG groups for LVEDVI (Figure C). We also observed a significantly lower systolic sphericity index at 1 year in the MPG 2/3 (0.206) versus the MPG 0/1 (0.240) group ($P=0.008$).

Changes in MPG Over 1 Year

Of the 109 MPG 2/3 group patients, 18 (17%) had MPG 0 or 1 at 1 year (Table 4). Binary restenosis in the IRA was observed in 16 (88.9%) of these patients and in 27 (29.7%) of 91 patients in whom MPG remained 2 or 3 ($P<0.0001$). Mean diameter stenosis was 82.5±22.8% versus 43.9±20.4% ($P<0.0001$) in these 2 groups. Of the post-PCI MPG 0/1 group, 60% had MPG 2 or 3 at 1 year. Among the 30 MPG 0/1 group patients with angiographic follow-up, restenosis was observed in 9 (50%) of the 18 with MPG 2 or 3 at 1 year and 3 (25%) of 12 with persistent MPG 0 or 1 ($P=0.17$).

Independent Correlates of LV Size and Function at 1 Year (by Post-PCI MPG)

On multivariable analysis (Table 5) post-PCI MPG 0/1 predicted lower WMI ($P=0.0002$) and LVEF ($P=0.0008$) and a higher LVESVI ($P=0.0056$) at 1 year.

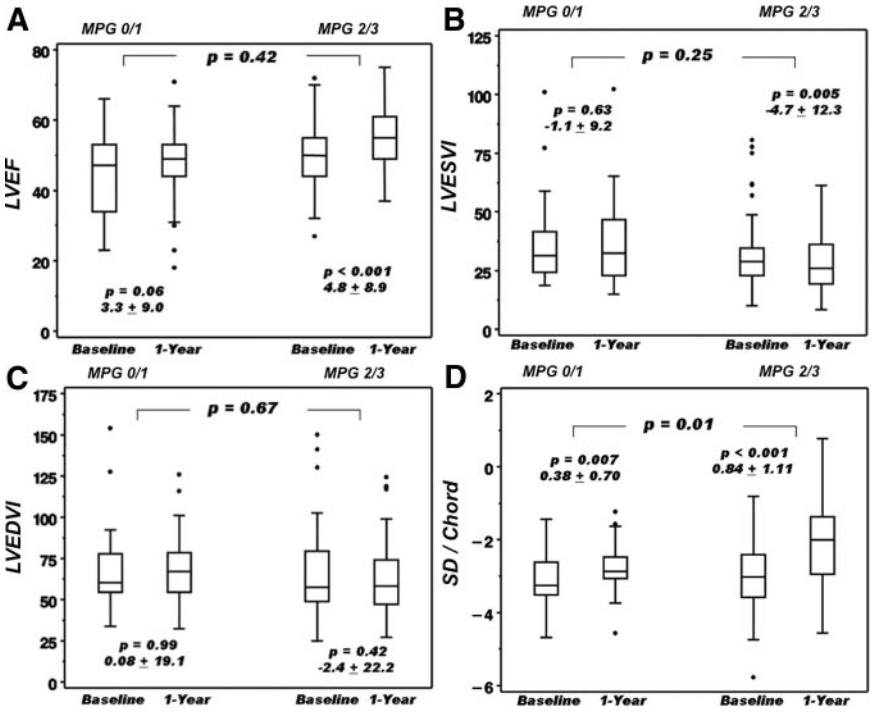

Figure. Comparison of baseline (post-PCI) and follow-up at 1 year of LVEF (A). LVESVI (B), LVEDVI (C), and target region wall motion (SD/chord) (D) between groups (MPG 0/1 versus MPG 2/3) (paired data). Values are given for change within group and *P* values for within-group and between-group comparisons. ED indicates end diastolic; ES, end systolic.

Table 4. Changes in MPG Over 1 Year

	1-Year MPG		
Post-PCI MPG	MPG 0/1	MPG 2/3	Total
MPG 0/1	12 (40)	18 (60)	30 (22)
MPG 2/3	18 (17)	91 (83)	109 (78)
Total	30 (22)	109 (78)	139 (100)

Data are presented as no. (%). $P=0.006$ for changes.

Discussion

This study addresses the ability of MPG to discriminate among patients with successful PCI of occluded infarct arteries and those who will have favorable changes in LV function from those who will not. To our knowledge, this study is the first to address the association between MPG and global and regional recovery of LV function following late recanalization of the IRA after MI and to describe MPG at 1-year follow-up.

The study population was uniformly selected and uniquely suited to test MPG as a predictor of LV recovery post-MI. OAT-enrolled, stable patients with occluded IRAs underwent recanalization with PCI/stent. We selected only patients with normal epicardial flow immediately post-PCI after a median occlusion time of 10 days. Notably, 79% of our cohort demonstrated MPG 2 or 3. Extending the results of studies examining acute reperfusion cohorts, preserved MPG was significantly associated with better indices of LV systolic function at 1 year (Figure). We also observed that MPG improved significantly from post-PCI to follow-up at 1 year.

Distribution of MPG

Our results are consistent with a large study of early recanalization by primary PCI with good epicardial and microvascular flow in 1190 (76.9%) of 1548 patients.[17] In a recent publication on thrombus aspiration in the setting of acute MI, 75% to 82% of patients had myocardial blush grade 2 or 3.[18] Both of these studies used myocardial blush grade,[17] which, although it uses somewhat different criteria, is angiographically and conceptually similar to the MPG system used in the present study. The results are comparable to the 79% prevalence following successful late recanalization after the first 24 hours and up to 28 days post-MI in the present study.

Table 5. Effects of Post-PCI MPG 0/1 Versus Post-PCI MPG 2/3 on LV Outcome Measures at 1 Year

Variable	Parameter Estimate	SEM	T	*P*
Unadjusted				
Infarct segment regional WMI (n=118)	−0.67	0.23	−2.90	0.0045
LVEF (n=126)	−8.86	1.92	−4.60	<0.0001
LVESVI (n=76)	7.23	3.14	2.30	0.023
LVEDVI (n=76)	4.66	5.34	0.87	0.39
Covariate adjusted				
Infarct segment regional WMI	−0.71	0.18	−3.89	0.0002
LVEF	−5.75	1.67	−3.43	0.0008
LVESVI	7.16	2.50	2.86	0.0056
LVEDVI	4.49	4.81	0.93	0.35

WMI adjusted for baseline WMI, days to randomization, BMI, and new Q waves. LVEF adjusted for baseline EF %, heart rate, BMI, and new Q waves. LVESVI adjusted for baseline LVESVI, no family history, NYHA class >I, and LAD culprit. LVEDVI adjusted for baseline LVEDVI, baseline LVEF, and LAD culprit.

Several factors may be responsible for the high rates of preserved MPG following late PCI in the present study. We selected only patients with TIMI 3 flow post-PCI, as explained in the Methods section. Stents were implanted in nearly all (99.4%) patients, and angiographic evidence of residual thrombus and distal embolization was seen only in a very small number of patients. Finally, the myocardial edema and microvascular plugging by aggregates of leukocytes and platelets, typical of acute MI, may have begun to resolve in many of our patients. Rochitte and colleagues[19] showed that the extent of microvascular obstruction increases over the first 48 hours after experimental acute MI and reperfusion in canines. The same group reported that the peak extent of microvascular obstruction occurs 2 days after reperfusion and is unchanged at 9 days.[20] Using coronary Doppler ultrasound, Hozumi and coworkers,[21] reported a short deceleration time of diastolic flow velocity (DDT), a measure of microvascular resistance, 1 day after IRA recanalization, indicating poor runoff in the microcirculation. Interestingly, they found significantly longer DDT, indicating lower microvascular resistance, 1 and 2 weeks after acute IRA recanalization in a group with viable myocardium and a group with nonviable myocardium in the region of interest. In both groups, the DDT normalized by 2 weeks after recanalization. The authors postulated that after the first 2 days following reperfusion, there is a gradual recanalization of the occluded microvessels, causing a progressive decrease in coronary resistance, even in areas without viable myocardium. In support of this hypothesis, we observed an increase in the number of patients showing MPG 2 or 3 at 1 year compared with post-PCI. In light of these data, it seems clear that poor blush can improve, indicating that it does not always imply irreversible necrosis of the microvasculature even if the subtended myocardium is substantially infarcted. The change in MPG from good to worse is associated with severe restenosis in the IRA, suggesting that parts of the microcirculation in areas with scar tissue may occlude spontaneously over time in the presence of severe restenosis, even if the epicardial artery remains patent with TIMI 3 flow. Alternatively, assessment of MPG in the presence of a severe upstream stenosis, particularly in a previously infarcted region, may be unreliable.

Functional Recovery in the Context of TOSCA-2 Results

In TOSCA-2, significant improvement in LVEF was observed at 1 year in both medically treated and PCI patients of about the same magnitude as in the MPG 2/3 group in the present substudy (4.8±8.9%).[8] The MPG 0/1 subgroup likely had more densely infarcted myocardium and microvascular derangement as evidenced by the significantly lower LVEF and larger volumes just a few days post-MI. As already stated, however, it does not appear that, if poor myocardial perfusion represents a larger infarct and microvascular derangement, this derangement is entirely irreversible. In addition, improvement in LVEF ap-

peared to be attenuated in the MPG 0/1 subgroup but was not significantly different from the MPG 2/3 subgroup, and the target regional wall motion score significantly increased in the MPG 0/1 subgroup, which means that there is some viability retained, even with poor blush immediately post-PCI.

Rather, early poor perfusion may represent a larger extent of injury causing microvascular dysfunction and early ventricular dilation that has potential for recovery over time. This notion is further supported by the OAT nuclear ancillary study[22] in which improvement in LVEF over 1 year was predicted by baseline infarct zone viability.

Infarct Size and MPG

Patients with baseline clinical and angiographic features of larger infarct size subsequently exhibited impaired MPG following PCI in agreement with previous studies, suggesting that infarct size is closely related to microvascular obstruction despite restoration of epicardial patency.[23,24] Infarct size was shown to be a major determinant of reflow following release of coronary occlusion in an experimental model of coronary occlusion and recanalization.[24] We found fewer collaterals, significantly more LAD occlusions, and a greater likelihood of unsuccessful fibrinolytic therapy in the MPG 0/1 group. These findings are similar to those reported for the larger cohort of 261 OAT ancillary study patients in whom baseline MPG was measured[16] and in correspondence with data published by Kandzari et al[26] from a study of primary percutaneous revascularization in acute MI, showing that anterior infarction is associated with greater impairment of LVEF, less frequent collateral flow, and diminished reperfusion success as measured by MPG.

We reported in our previous publication[16] that failed fibrinolytic therapy was significantly associated with impaired MPG following late recanalization of occluded IRAs by PCI. The association was no longer significant when adjusted for multiple variables that correlate with infarct size, suggesting that impaired post-PCI MPG in patients with failed fibrinolytic therapy is mainly related to larger infarct size, and we may speculate that fibrinolytic therapy is preferentially administered to more critically ill patients. Thus, the higher frequency of impaired MPG in patients with LAD occlusion may be related to larger infarcts in these patients. Absence of collaterals, noted more often with LAD occlusion, may have further contributed to higher frequency of impaired MPG in this subset.

Limitations

Myocardial perfusion as assessed by contrast angiography is semiquantitative and might be considered a difficult parameter to adjudicate. However, we have recently published a reproducibility study that included the TIMI MPG method in an angiographic core laboratory.[15] We found a high degree of interobserver reproducibility when MPG was dichotomized to 0 or 1 versus 2 or 3; thus, we prospectively defined the grouping as MPG 0/1 versus MPG 2/3. The study population in TOSCA-2 was relevant to examining the benefit of routine late PCI compared with medical therapy alone in patients with occluded IRAs post-MI, and the results cannot be extrapolated to all patients undergoing late PCI after MI. We analyzed MPG only in the subset of this population with antegrade TIMI 3 flow after late IRA recanalization. Follow-up coronary angiography may reflect ascertainment bias, with sicker patients not returning. Therefore, it is unknown whether the reported findings in a subset of patients extend to the entire cohort.

Conclusions

Preserved MPG is present in the majority of patients with MI with normal epicardial flow following late PCI recanalization of their occluded IRA. Impaired baseline MPG is associated with unfavorable LV indices, whereas preserved baseline MPG in our cohort is associated with segmental and global LV recovery. This observation extends prior analyses undertaken in acute MI settings and is consistent with favorable MPG marking retained viability within the infarct zone. Finally, patients with poor baseline MPG frequently show MPG improvement and significantly, but modestly improved wall motion over 1 year and, thus, a relative lack of LV functional improvement. These data suggest that microvascular integrity and myocardial viability can be disengaged from each other in the chronic post-MI phase and warrant further study.

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CLINICAL PERSPECTIVE

The extent to which effective microvascular perfusion can be achieved by percutaneous coronary intervention (PCI) performed after the acute phase of a myocardial infarction (MI) and whether the magnitude of microvascular perfusion affects left ventricular (LV) recovery is unknown. The Total Occlusion Study of Canada-2, an ancillary study of the 2166-patient Occluded Artery Trial, enrolled 381 stable patients with a persistently occluded infarct-related artery (IRA) days to weeks post-MI to PCI or medical therapy alone. Change in myocardial perfusion grade (MPG) was determined from immediate post-PCI to 1 year follow-up (157 patients), and the relationship between initial MPG and LV function and volume was assessed in 139 patients. Preserved MPG was present in the majority of patients with normal epicardial flow following late PCI recanalization of the IRA. Impaired baseline MPG was associated with unfavorable LV indices, whereas preserved baseline MPG was associated with segmental and global LV recovery. Patients with poor baseline MPG frequently showed MPG improvement and significantly, but only modestly improved wall motion over 1 year. Thus, microvascular integrity and myocardial viability can be disengaged from each other in the chronic post-MI phase, but subgroups of stable patients with areas of viable myocardium might benefit from late recanalization. Preserved MPG immediately post-PCI may be associated with LV recovery.