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Markers of Myocardial Reperfusion as Predictors of Left Ventricular Function Recovery in Acute Myocardial Infarction Treated with Primary Angioplasty

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Summary

Background: Myocardial blush grade (MBG), corrected TIMI frame count (cTFC), and ST-segment reduction are indices of myocardial reperfusion.

Hypothesis: We evaluated their predictive value for left ventricular (LV) function recovery by gated single-photon emission computed tomography (SPECT) after acute myocardial infarction (AMI) treated with primary percutaneous coronary intervention (PCI).

Methods: In 40 patients with AMI, gated SPECT was performed at admission and repeated 7 and 30 days after PCI. Left ventricular function recovery was defined as an increase ≥ 10 points in SPECT LV ejection fraction from baseline to 1 month. The MBG, cTFC, and ST-segment elevation index 1 h after PCI were determined to evaluate reperfusion.

Results: Twenty-four patients (Group 1) had LV function recovery and 16 (Group 2) did not. A significant correlation was found between LV function recovery and MBG ($r = 0.66$; $p = 0.0001$), and ST-segment elevation index at 1 h ($r = -0.55$; $p = 0.0001$), but not with cTFC. Univariate predictors of LV function recovery were MBG ($p = 0.0003$) and ST-segment elevation index 1 h after intervention ($p = 0.0026$), but not cTFC. In a multivariate analysis, MBG was the only predictor of LV function recovery. Myocardial blush grade ≥ 2 and ST-segment elevation index reduction had the same accuracy (88%) for predicting LV function recovery. Lower accuracy (75%) was shown by fast cTFC (< 23 frames). Myocardial blush grade ≥ 2 showed the better negative likelihood ratio, and ST-segment elevation index reduction had the higher positive likelihood ratio in predicting LV function recovery.

Conclusions: Myocardial blush grade was the best parameter for prediction of LV function recovery: MBG ≥ 2 and ST-segment elevation index reduction showed good accuracy in predicting LV function recovery. The cTFC failed to be a significant predictor.

Key words: acute myocardial infarction, gated tomography, primary coronary angioplasty

Introduction

Myocardial salvage and left ventricular (LV) function recovery are the main goals of reperfusion therapy in acute myocardial infarction (AMI). There is substantial interest in parameters assessing reperfusion with the potential to predict LV function and clinical outcome. Some reperfusion parameters can be obtained by myocardial contrast echocardiography, Doppler flow wire, myocardial scintigraphy, and magnetic resonance imaging; however, their application is difficult and time consuming.[1–4] On the other hand, the resolution of ST-segment elevation,[5, 6] the angiographic myocardial blush grade (MBG),[6, 7] and the corrected Thrombolysis In Myocardial Infarction (TIMI) frame count (cTFC)[8] are early and easily obtainable during the acute stage of AMI treated with primary coronary intervention (PCI) .

In this study, we evaluated and compared the value of MBG, cTFC, and ST-segment elevation index as predictors of significant LV function recovery in AMI treated with PCI. Left ventricular function recovery was assessed in terms of myocardial salvage, LV ejection fraction, and volumes quantified by gated single-photon emission computed tomographic imaging (SPECT) scintigraphy with technetium-99m sestamibi.[9, 10]

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Methods

Patient Population

From April to September 2003, 45 consecutive patients with AMI were enrolled. They presented with chest pain lasting ≥ 30 min and < 6 h, and persistent ST-segment elevation > 0.1 mV in at least two contiguous leads. Exclusion criteria were previous AMI or other heart disease, conditions precluding the evaluation of ST-segment changes, and evidence of reinfarction or restenosis of the culprit vessel during follow-up. The protocol was approved by the institutional ethics committee. All patients gave informed consent.

Study Protocol

All patients received 500 mg of aspirin, heparin (bolus of 60 U/Kg, up to a maximum of 5000 U, followed by a 24-h infusion of 7U/Kg/h), clopidogrel (300 mg), and abciximab standard dose. Prior to PCI, patients received an intravenous injection of 30 mCi of technetium 99m sestamibi. Gated SPECT was performed after intervention, within 6 h from the injection of the radionuclide. Gated SPECT was repeated 7 and 30 days after treatment.

All patients received clopidogrel (75 mg daily for 4 weeks), and aspirin (100 mg daily indefinitely).

Invasive Procedure and Angiographic Evaluation

Coronary angiography was performed by the femoral approach. All patients underwent primary stenting of the infarct-related artery (IRA) according to standard technique.

Initial and postprocedural flow in the IRA were graded according to TIMI classification.[11] Final cTFC and MBG of the IRA were assessed blindly, as previously described.[7, 8] Myocardial blush grades 0 and 1 indicated failed myocardial reperfusion, whereas MBG 2 and 3 showed successful myocardial reperfusion.[12] Fast TIMI 3 flow was defined as a cTFC < 23 frames.[13] Quantitative coronary angiography (QCA) was performed by an automatic edge detection system (Siemens Acom Quantcor QCA, Munich, Germany). Procedural success was defined as residual stenosis < 20% and TIMI grade 3 flow.[6]

Electrocardiographic Data

ST-segment elevation index, before and 1 h after PCI, was calculated as previously described.[5] Reduction in ST-segment elevation index was defined as a ≥ 50% decrease 1 h after recanalization of the IRA.

Radionuclide Studies

The automated geometric method for the measurement of LV ejection fraction, end-diastolic and end-systolic LV volumes, and perfusion defect size has been described elsewhere.[10] This method allowed to calculate the following: size of perfusion defects as a percentage of the left ventricle on admission, at 7 and 30 days; degree of the myocardial salvage as a percentage of the left ventricle, calculated as the difference between the initial and 7-day perfusion defects; and salvage index, calculated as the ratio of myocardial salvaged and the initial perfusion defect.[9] Left ventricular function recovery was calculated as the difference between 1 month and baseline SPECT LV ejection fraction.

Definitions

A significant LV function recovery was defined as an increase ≥ 10 points in SPECT LV ejection fraction from baseline to 1 month.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for Social Sciences 8.0 software (SPSS Inc., Chicago, Ill., USA). Discrete data are summarized as frequencies, whereas continuous data are expressed as mean ± standard deviation (SD). Fisher's exact test or Kruskal-Wallis one-way analysis of variance were used for comparison of categorical variables. Two-tailed Student's *t*-test was used to verify differences between continuous variables (normally distributed according to the Shapiro-Wilks test). Univariate and multivariate analyses were used to evaluate whether MBG, cTFC, and ST-segment elevation index 1 h after intervention predicted LV function recovery. Accuracy, sensitivity, specificity, positive and negative likelihood ratios of MBG ≥ 2, fast cTFC, and ST-segment elevation index reduction at 1 h for prediction of LV function recovery were also calculated. The positive likelihood ratio was calculated as sensitivity divided by 1 minus specificity and the negative likelihood ratio as 1 minus sensitivity divided by specificity. A p value of < 0.05 was considered significant.

Results

The initial radionuclide study could not be performed in five patients because of hemodynamic instability; thus, the final study group included 40 patients. Of these, 24 had significant LV function recovery (Group 1) and 16 did not (Group 2). These groups were homogeneous with respect to baseline characteristics (Table I). Only the peak creatine kinase level was significantly higher in Group 2.

Scintigraphic Evaluation

Table II shows the results of serial scintigraphic scans. The extent of the perfusion defect on admission was similar between the two groups, while at 7 and 30 days it was significantly smaller in Group 1. Thus, salvage index was significantly higher in Group 1 as a result of a greater degree of myocardial salvage. In the entire study cohort, a significant correlation was found between salvage index and LV function recovery ($r = 0.84$; $p = 0.0001$). As shown in Table II, LV function recovery in Group 1 was mostly the result of a significant reduction

TABLE I Baseline characteristics of the patients

	Group 1 (n = 24)	Group 2 (n = 16)	p Value
Age (years)	62 ± 10	62 ± 15	0.96
Male sex	19 (79.2)	14 (87.5)	0.8
Weight (kg)	73 ± 8	71 ± 9	0.42
Diabetes	4 (16.7)	4 (25)	0.81
Hypertension	10 (41.7)	8 (50)	0.85
Hyperlipidemia	10 (41.7)	8 (50)	0.85
Current smoker	12 (50)	8 (50)	0.75
Killip class ≥2	4 (16.7)	3 (18.7)	0.8
Symptom onset to recanalization (min)	237 ± 171	228 ± 159	0.85
Admission to balloon inflation (min)	71 ± 30	77 ± 31	0.53
Intra-aortic balloon counterpulsation	1 (4.2)	4 (24)	0.14
Peak creatine kinase (U/l)	1990 ± 1729	3429 ± 2197	0.026
Infarct artery			0.99
Left anterior descending	10 (41.7)	7 (43.8)	0.85
Right coronary artery	11 (45.8)	7 (43.8)	0.85
Circumflex artery	3 (12.5)	2 (12.4)	0.63
Multivessel disease	11 (68.7)	9 (37.5)	0.11

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

TABLE II Scintigraphic results

	Group 1 (n = 24)	Group 2 (n = 16)	p Value
Size of initial perfusion defect, % of left ventricular	31.3 ± 13.8	35.9 ± 16.8	0.35
Size of perfusion defect after 7 days, % of left ventricular	10.7 ± 10.2	28.6 ± 14.5	0.0001
Degree of myocardial salvage, % of left ventricular	20.5 ± 7.5	7.3 ± 5	0.0001
Salvage index	0.71 ± 0.1	0.23 ± 0.1	0.0001
Size of perfusion defect after 1 month, % of left ventricular	8.6 ± 9	24 ± 13	0.0001
Scintigraphic left ventricular ejection fraction (%)			
Before procedure	38.5 ± 7	35.8 ± 9.4	0.3
After 7 days	49.5 ± 11.3	40.9 ± 11	0.02
After 1 month	59.2 ± 7.1	39.3 ± 10.5	0.0001
Scintigraphic left ventricular volumes (ml)			
End – diastolic			
Before procedure	117 ± 55	156 ± 145	0.24
After 7 days	110 ± 49	138 ± 62	0.12
After 1 month	101 ± 38	135 ± 69	0.06
End – systolic			
Before procedure	74 ± 45	108 ± 130	0.24
After 7 days	61 ± 44	87 ± 63	0.13
After 1 month	42 ± 22	86 ± 65	0.004

Values are presented as mean ± standard deviation.

in end-systolic volume at 30 days (from 74 ± 45 to 42 ± 22 ml; p = 0.003).

Reperfusion Parameters

Angiographic and electrocardiographic results are summarized in Table III. Procedural success was achieved in 37 patients (92.5%) with a similar rate in the two groups. Twenty patients (50%) had MBG 3, 7 patients (17.5%) MBG 2, and 13 patients (32.5%) MBG 1. Twenty-two patients (55%) had fast cTFC and 25 patients (62.5%) had ST-segment elevation index reduction. Left ventricular function recovery was achieved in 23 patients (85.2%) with MBG ≥ 2 after the procedure versus 1 (7.7%) with MBG 0–1 (p = 0.0001); in 18 patients (81.8%) with fast cTFC versus 6 (33.3%) with cTFC > 23 (p = 0.005); and in 22 patients (88%) with ST-segment

TABLE III Angiographic characteristics and procedural data

	Group 1 (n = 24)	Group 2 (n = 16)	p Value
Reference vessel diameter (mm)	3.06 ± 0.4	2.9 ± 0.5	0.24
Initial minimal luminal diameter (mm)	0.08 ± 0.14	0.06 ± 0.08	0.6
Initial extent of stenosis (%)	98 ± 4.4	97.4 ± 4.1	0.66
Final minimal luminal diameter (mm)	3.06 ± 0.4	2.9 ± 0.5	0.27
Final extent of stenosis (%)	2.8 ± 2.4	1.9 ± 3.1	0.31
Length of stented segment (mm)	15.8 ± 5.8	14.5 ± 5.6	0.49
Multiple infarct artery lesions (%)	9 (37.5)	2 (12.5)	0.17
Procedural time (min)	15.9 ± 5.2	14.7 ± 7	0.54
Baseline TIMI flow 3	3 (12.5)	2 (12.5)	0.63
Postprocedure TIMI flow 3	23 (95.8)	14 (87.5)	0.71
Myocardial blush grade			0.0001
0–1	1 (4.2)	12 (75)	
2	6 (25)	1 (6.2)	
3	17 (70.8)	3 (18.8)	
Corrected TIMI frame count (frames)	21.8 ± 10.2	27.6 ± 11	0.096
Corrected TIMI frame count < 23 frames	18 (75)	4 (25)	0.005
ST-segment elevation index at 1 h (mm)	0.42 ± 0.38	1.36 ± 0.98	0.0001
ST-segment elevation index reduction	22 (91.7)	3 (18.8)	0.0001

Values are presented as mean ± SD or n (%).
Abbreviations: TIMI = Thrombolysis In Myocardial Infarction, SD = standard deviation.

elevation index reduction versus 2 (13.3%) without ST-segment elevation index reduction (p = 0.0001).

Prediction of Left Ventricular Function Recovery

There was a significant correlation between LV function recovery and MBG (r = 0.66; p = 0.0001) (Fig. 1A), and ST-segment elevation index at 1 h (r = −0.55; p = 0.0001) (Fig. 1B); on the other hand, no correlation was found with cTFC (r = −0.33; p = 0.1) (Fig. 1C).

Univariate predictors of LV function recovery were MBG (odds ratio [OR] 7, 95% confidence interval [CI] 2.5–20.1; p = 0.0003) and ST-segment elevation index 1 h after intervention

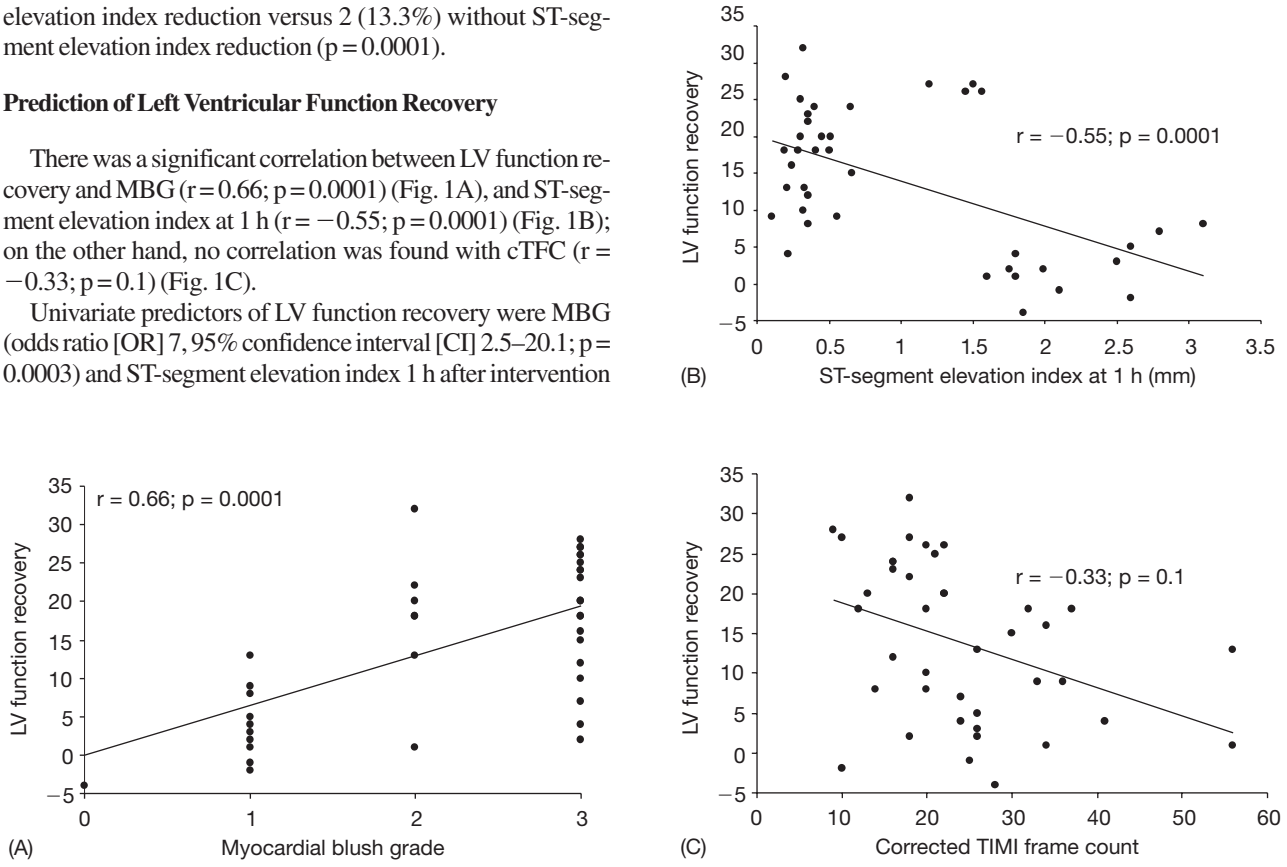

FIG. 1 Correlation between left ventricular (LV) function recovery and myocardial blush grade (A), ST-segment elevation index at 1 h after intervention (B), and corrected Thrombolysis In Myocardial Infarction (TIMI) frame count (C). LV = left ventricular.

(OR 1.05, 95% CI 1.01–1.08; p = 0.0026), but not cTFC (OR 0.94, 95% CI 0.88–1.01; p = 0.1). In a multivariate analysis including all reperfusion parameters, MBG was the only predictor of LV function recovery.

Myocardial blush grade ≥ 2 and ST-segment elevation index reduction had the same accuracy (88%) for prediction of LV function recovery with a sensitivity of 96 and 92%, respectively, and a specificity of 75 and 81%, respectively; the positive likelihood ratios were 3.8 and 4.9, respectively, and the negative likelihood ratios 0.055 and 0.1, respectively. Fast cTFC showed lower accuracy (75%), with sensitivity and specificity 75%; the positive and negative likelihood ratios were 3 and 0.33, respectively.

Discussion

To our knowledge, and starting from functional data obtained by serial scintigraphic examinations, this is the first study that evaluated the predictive value for LV functional recovery of early invasive and noninvasive markers of reperfusion after AMI .

The main findings were: (1) MBG was the best of the analyzed parameters for prediction of significant LV function recovery; (2) MBG ≥ 2 showed the best negative likelihood ratio while ST-segment elevation index reduction had the highest positive likelihood ratio in predicting LV function recovery; and (3) cTFC did not show a significant correlation with LV function recovery.

Previous Studies

Recent studies have demonstrated that myocardial perfusion may remain impaired even after achievement of TIMI 3 flow without residual stenosis, possibly because of microcirculatory damage. Impaired myocardial reperfusion after AMI is associated with a greater infarct size, poorer LV function, higher rate of congestive heart failure, and higher mortality.[1]

Angiographic MBG, cTFC, and ST-segment elevation index are parameters easily obtainable to evaluate myocardial reperfusion.[5–8] Myocardial blush is related to the enzymatic infarct size, the extent of ST-segment elevation resolution, LV function, and long-term mortality in patients with AMI after primary PCI,[7] as well as to the final infarct size and the degree of myocardial salvage assessed by scintigraphy.[12, 14] The cTFC has been suggested to be an independent predictor of functional recovery, in-hospital, and 1-month clinical outcome.[8, 13] ST-segment elevation persistence despite a patent IRA is a predictor of higher in-hospital and long-term mortality,[5] while its early resolution after reperfusion correlates with myocardial salvage, final infarct size, and 6-month mortality.[15]

In this study, LV function recovery was more often observed in patients with a better myocardial reperfusion as assessed by MBG and ST-segment elevation index 1 h after PCI.

Prediction of Left Ventricular Function Recovery

Previous studies revealed a closed correlation between recovery of perfusion and recovery of contraction in the infarct area.[6] In this study, MBG was the most powerful predictor for significant LV function recovery and the only significant parameter at multivariate analysis. The cTFC failed to be a significant predictor for LV function recovery. The MBG ≥ 2 showed the best negative likelihood ratio. Accordingly, the lack to achieve MBG ≥ 2 at the end of intervention was the greater negative predictor for significant LV function recovery. On the other hand, ST-segment elevation index reduction showed the highest positive likelihood ratio, thus representing the best positive predictor for LV function recovery.

A possible explanation for the different predictive values of the reperfusion parameters evaluated in the present study stands in their intrinsic pathophysiologic nature.[16] The cTFC is mainly influenced by the epicardial flow and, similar to TIMI flow grade, can be expected to be a weak predictor of myocardial reperfusion and LV function recovery. Conversely, the MBG is more strongly related to coronary microvascular flow and can be expected to be a better predictor of LV function recovery. Finally, the ST-segment resolution is a functional index of the electrical activity of the jeopardized myocardium. Accordingly, it is conceivable that it can represent the best positive predictor when compared with cTFC and MBG.

Study Limitation

The small patient population is the most important limitation of the study. Moreover, no prognostic data were available, and therefore we are unable to establish whether the higher degree of myocardial salvage implies a better clinical outcome. Because of some degree of systematic underestimation of LV ejection fraction measured with gated SPECT, the relationship between LV ejection fraction and infarct size using this approach could be slightly different from what has been observed using contrast ventriculography or echocardiography.

Conclusion

The myocardial blush grade (MBG) was the most powerful predictor of LV function recovery: MBG ≥ 2 and ST-segment elevation index reduction had good accuracy; MBG ≥ 2 showed the best negative likelihood ratio, while ST-segment elevation index reduction had the highest positive likelihood ratio in predicting LV function recovery. The cTFC failed to be a significant predictor.

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