Original Article

Perfusion and kinetic variations of left ventricle after primary PCI for acute myocardial infarction: correlation between clinico-angiographic and scintigraphic parameters

E Varani[1] , M Balducelli[1], S Severi[2], A Patroncini[3], A Shoheib[1], G Vecchi[1], GR Lucchi1[2], M Aquilina[1], C Corbelli[2], R Casanova[3], A Maresta[1]

1. Catheterization Unit, Department of Cardiology, S. Maria delle Croci Hospital, Ravenna, 2. Nuclear Medicine, Ospedale per gli Infermi, Faenza, 3. Department of Cardiology, Ospedale per gli Infermi, Faenza, Italy

Background: The aim of the present study was to evaluate which of the clinico-angiographic parameters of acute ischemic extension and efficacy of reperfusion in AMI treated with primary PCI are predictive of infarct size and one month left ventricular ejection fraction (LVEF).
Patients and Method: Thirty-five patients with first AMI treated with primary PCI underwent two rest 99mTc-sestamibi gated SPECT, 4-6 days and 30-40 days after PCI. Clinical, electrocardiographic, angiographic and scintigraphic parameters for ischemic extent in acute phase, effective reperfusion, perfusional and kinetic outcome were collected.
Results: There was a significant linear correlation among indices of initial ischemic extension and early perfusion defect and infarct size, while time to treatment (symptom onset to balloon) correlated with reperfusion indices (ST resolution, corrected TIMI frame count cTFC, myocardial perfusion grade MPG) and with late functional outcomes (smaller infarct size and better LVEF). A time to treatment of <240 minutes was the most accurate predictor of effective reperfusion and functional outcome. A late LVEF ≥50% was correlated with sum of ST elevation, ST resolution, time to treatment, CK-MB peak value, early LVEF, and early and late infarct size. An improvement in LVEF in 1 month was seen in 60% of patients, who showed a shorter time to treatment and a lower cTFC.
Conclusions: Improvements of perfusion and left ventricular function were frequent one month after primary PCI in AMI. A total ischemic time ≤240 minutes and secondary ST resolution and angiographic parameters of effective reperfusion were the best indicators of infarct size, late LVEF and improvement of LVEF.

Key Words: Myocardial infarction, primary angioplasty, perfusion, gated SPECT.

Introduction

Clinical and functional outcome of acute myocardial infarction (AMI) depends on patient's age, extent and location of myocardial necrosis, infarct related artery (IRA) recanalization and presence of collateral flow[1-3].

Moreover IRA recanalization does not translate into effective tissue reperfusion in up to 30-40% of patients due to distal embolization or microvascular damage (no reflow) [4-7]. Duration of ischemia seems to determine the chance for effective reperfusion since the shorter the ischemia the better the preservation of microcirculation and of cardiac myocytes[8]. Nevertheless even short ischemic times are associated with the angiographic no-reflow phenomenon during primary PCI for AMI. The observation

Correspondence:
Aleardo Maresta
U.O. di Cardiologia, Ospedale S. Maria delle Croci
Viale Randi, 5, 48100 Ravenna
Tel. 0544-285388, Fax. 0544-285395
E-mail: ra.cardiologia@ausl.ra.it

of patients with an open IRA at the end of primary PCI but with very slow flow and extensive akinesia of left ventricle leads to ample improvement of contractility at pre-discharge echocardiogram. This prompted us to design a study in order to evaluate improvement of perfusion and kinetic indices of left ventricle during the first 4-6 weeks after treatment of AMI with mechanical reperfusion. The study also aimed to detect which of the clinico-angiographic and perfusional parameters of ischemia severity in the acute phase would predict final extension of necrosis and contractility and their subsequent improvement.

Patients and Methods

The present study comprised 35 consecutive patients (32 males, mean age 61± 11 years) with first AMI who underwent mechanical revascularization within 12 hours of symptoms onset at our Catheterizaton Laboratory from January through August 2003. The diagnosis of AMI was based on typical chest pain lasting > 30 minutes and ST segment elevation > 0.2 mV in ≥ 2 contiguous electrocardiographic leads which was subsequently confirmed by enzymatic release. Having obtained patient's written informed consent, two rest 99mTc-sestamibi gated SPECT were performed at predischarge (4-6 days after primary PCI) and after 4-6 weeks, in order to evaluate infarct size and left ventricular ejection fraction (LVEF).

Coronary angiography and angioplasty

All patients received 250 mg aspirin and 5.000 to 10.000 IU heparin intravenously before the procedure, but 28 patients were treated with GPIIb/IIIa inhibitors (25 Abciximab and 3 Tirofiban). All patients received at least one stent in the infarct related artery. After the procedure aspirin was given indefinitevely and Ticlopidine (250 mg bid) or Clopidogrel (75 mg/day) for four weeks. Coronary interventions were performed in a routine manner, using 7 Fr guiding catheters, with a frame rate of 12.5 /sec. Nitroglycerine 300-400 mcg i.c. was given before balloon inflation and before and after stent placement. The flows in IRA on the initial diagnostic angiogram and in that obtained after completion of the procedure were scored using the TIMI criteria[9]. Corrected TIMI Frame count (CTFc) and myocardial perfusion grade (MPG) were determined on the last angiogram after revascularization. As previously described[10] cTFC was obtained by counting the number of frames required for dye to reach standardized distal landmarks divided by 1.7 for the left anterior descending artery. The number of frames was then multiplied by 30 and divided by 12.5 to report a cine frame count in accordance to standard methods. The MPG was then assessed in order to describe the level of tissue perfusion. MPG grade 0 correspondend to no angiographic blush, grade 1 to angiographic stain, grade 2 to dye bright at the end of injection and grade 3 as normal ground glass appearance as previously described[11].

ECG

The first ECG with 12 leads was recorded on admission to hospital and in the coronary care unit within 1 hour after primary angioplasty (second ECG). The ST segment elevation (STE) was measured 40 msec after the J point in the 12 leads ECG. The number of ECG leads with STE (N°STE) and the sum of STE (ΣSTE) in the first ECG were used as

parameters of the jeopardized myocardium. Percentage STE resolution (STR, %) between the first and the second ECG (pre and post-PCI) was analysed in the lead with most evidenced STE.

Enzymatic analysis

Serum Creatine Kinase-MB mass was measured serially every 3 hours after admission until the peak value was obtained using one-step immunoassay based on the "sandwich principle" (Dade-Behring) and values expressed as ng/ml.

Gated SPECT

Rest 99mTc-sestamibi gated SPECT was performed on each patient 4-6 days after primary PCI and 1 month later, using a double headed Axis Picker gamma camera equipped with parallel hole collimator. Reconstructed slices were displayed by using a bulls'eye polar map and defect was delineated with a 40% blackout isocontour method related to the maximal pixel value. Infarct size was expressed as percentage of the whole myocardial area (%Black Out, B.O.); the measurement of left ventricle volumes and LVEF was performed by an automated and validated method[12]. A visual analysis of the parietal perfusion defects was expressed as number of hypoperfused segments out of a total of 20 by three experienced and blinded operators.

Table 1. Clinical, angiographic and scintigraphic parameters of the patient population.

	Mean Value	Range
Anterior myocardial infarction	14 (40%)	
N° STE (n°)	5.4±1.6	3-9
ΣSTE (mm)	15±10	2-55
STR (%)	78±22	0-100
Time to Treatment (min)	204±144	60-600
CK-MB peak (ng/ml)	242±179	25-658
CK-MB peak time (hours)	7.4±2.6	3-14
TIMI flow pre-PCI	0.5±0.8	0-3
cTFC	24±12	14-76
MPG	2.7±0.5	1-3
Early P. D.	6±3	1-12
Late P. D.	5±3	1-12
Early B.O. (%)	22±13	1-48
Late B.O. (%)	17±12	0-41
Early LVEF (%)	45±10	19-61
Late LVEF (%)	47±10	15-60

B.O.= infarct size expressed as black out; cTFC= corrected TIMI frame count; LVEF= left ventricular ejection fraction; MPG= myocardial perfusion grade; N° STE= n° of leads with ST segment elevation; P.D.= perfusion defect; ΣSTE= sum of STE in the first ECG; STR= ST segment resolution; Time to treatment= symptom onset to balloon time.

Statistical analysis

The analysed parameters were divided into three categories: indices of extension/severity of acute ischemia: infaret localization, N°STE, ΣSTE, total ischemia time from the onset of chest pain to the first balloon inflation (Time to Treatment), CK-MB peak value (CK-MB peak), early perfusion defect (Early P.D.), early infarct size (Early B.O.), early LVEF; clinico-angiographic indices of reperfusion: time of CK-MB peak (CK-MB peak time), percentage ST resolution (STR), initial and final TIMI flow grade, corrected TIMI frame count (cTFC), MPG; indices of functional outcome: late perfusion defect (Late P.D.), late infarct size (Late B.O.), late LVEF (Late LVEF), improvement of LVEF and reduction of infarct size. Continuous variables were expressed as mean ± SD and categorical data as percentage. The correlation between continuous variables was calculated using the Pearson's correlation coefficient. The comparison between groups was performed by the unpaired t-Student's test for continuous variables and Chi-square test for categorical data. The p value < 0.05 was considered statistically significant.

RESULTS

According to admission ECG, 14 patients had an anterior, 10 an inferior and 11 a postero-lateral myocardial infarction. The infarct related artwas the left anterior descending artery in 14 cases, the right coronary artery in 15 and the left circumflex in 6 cases. Of 18 patients with multivessel coronary artery disease, 7 received a two-vessel percutaneous intervention. All patients had successful stent implantation without major in-hospital complications. The mean hospital stay was 6±1 days. The mean interval between index infarction and the first rest 99mTc-sestamibi gated SPECT was 5±2 days; the interval between the first and the second gated SPECT was 29±5 days. After 1 month follow-up all patients were alive and free from angina or recurrence of MI.

Table 1 shows the mean and range values of the considered parameters in the patient population. Of note, STR≥70% was observed in 26 patients (74%); time to treatment < 240 min was present in 26 (74%), TIMI flow 0-1 before procedure was observed in 28 (80%), and TIMI flow 3 post-PCI in 33 (94%).

Table 2. Linear correlation coefficients between indices of effective reperfusion and late perfusional and kinetic parameters.

	Time to treatment	CK-MB peak time	STR	cTFC	MPG
Late P.D.	r= 0.325 p= 0.049	r= 0.078 NS	r= -0.483 p= 0.003	r= 0.056 NS	r= -0.285 p= 0.089
Late B.O.	r= 0.282 NS	r= 0.055 NS	r= -0.385 p= 0.022	r= 0.110 NS	r= -0.368 p= 0.029
Late LVEF	r= -0.316 p= 0.058	r= 0.112 NS	r= 0.300 p= 0.078	r= -0.472 p= 0.004	r= 0.577 p< 0.001

B.O.= infarct size expressed as black out; cTFC= corrected TIMI frame count; LVEF= left ventricular ejection fraction; MPG= myocardial perfusion grade; P.D.= perfusion defect; STR= ST segment resolution; Time to treatment= symptom onset to balloon time.

Table 3. Reperfusion parameters and functional outcome in patients with time to treatment within or above 240 minutes.

	Time toTreatment < = 240 min n = 26 (74%)	Time toTreatment > 240' min n = 9 (26%)	P-value
STR (%)	83±17	66±30	0.054
cTFC	22±6	33±17	0.012
MPG	2.8±0.4	2 .4±0.7	0.037
Late B.O. (%)	15±11	26±14	0.024
Late LVEF (%)	49±7	41±15	0.044

B.O.= infarct size expressed as black out; cTFC= corrected TIMI frame count; LVEF= left ventricular ejection fraction; MPG= myocardial perfusion grade; STR= ST segment resolution.

In 14 patients (40%) the infarct size expressed as percentage black out diminished in the second examination, the mean values in total population changed from 22 to 17%; LVEF increased at 1 month follow-up in 21 patients (60%) and in 12 of these patients the increase in LVEF was ≥5 points.

Linear correlation test revealed a good correspondence of initial extension parameters with each other (N° STE, Σ STE, CK-MB peak) and with indices of short-term perfusion and LV function. Total ischemic time (time to treatment) statistically correlated with indices of effective reperfusion with the exception of time of CK-MB peak (STR r= -0.543, p< 0.001, cTFC r= 0.369, p= 0.03; MPG r= -0.443, p= 0.008); correlation coefficients with late perfusion and kinetic parameters are shown in Table 2. Out of all considered parameters, time to treatment < 240 min resulted most accurately in predicting effective reperfusion and final perfusion and kinetics that showed statistically significant differences in reperfusion parameters (better STR and MPG, lower cTFC) and functional outcome (smaller infarct size and better LVEF) (Table 3).

Patients with smaller infarct size (late B.O.<15%, 20 pts) had less extensive acute phase ischemia (ΣST 12±7 vs 19±12 mm, p=0.05), lower time to treatment (165±117 vs 264±162 min, p=0.04), a smaller early and late perfusion defect (5±3 vs 8±3, p=.003 and 4±2 vs 7±3, p=0.002 respectively) and greater initial and late LVEF (48±8 vs 42±11%, p=0.05 and 51±7 vs 42±12%, p=0.02 respectively). A reduction of infarct size between initial and late SPECT was found in 14 patients (40%) who had greater initial hypoperfusion (early B.O. 28±13 vs 18±13%, p=0.03) and a trend for a lower initial and late LVEF (43±13 vs 47± 7%, p=0.36 and 44±14 vs 49±7%, p=0.18 respectively). Table 4 shows the parameters predicting late LVEF> 50%. Indices that showed significant differences in patients with amelioration of late LVEF were a shorter time to treatment (165±82 vs 271±193 min, p=0.03) and a smaller cTFC (22±6 vs 31±15, p=0.02). Prevalence of anterior myocardial infarction was higher (52 vs 27%), although not statistically significant (p=0.14), in patients with increasing LVEF.

Table 4. Clinical, angiographic and scintigraphic parameters in two patients groups divided according to late left ventricle ejection fraction.

	Late LVEF > = 50% N = 19 (54%)	Late LVEF <50% N = 16 (46%)	P-value
Anterior MI	**33%**	**50%**	**0.490**
N° STE (n°)	**5±2**	**6±1.5**	**0.119**
mm STE (mm)	**12±6**	**19±12**	**0.028**
STR (%)	**89±17**	**67±22**	**0.002**
Reperfusion Time (min)	**151±80**	**273±176**	**0.010**
CK- MB peak (ng/ml)	**183±156**	**317±177**	**0.023**
CK-MB peak time (hours)	**7.5±3**	**7.3±2**	**0.760**
Timi flow pre-PCI	**0.7±1**	**0.6±0,9**	**0.718**
cTFC	**21±5**	**24±13**	**0.294**
MPG	**2.9±0.3**	**2.6±0.5**	**0.061**
Early Pef. Defect (n°)	**4.6±2.7**	**7.8±2.6**	**0.001**
Late Perf. Defect (n°)	**3.7±2.1**	**6.43**	**0.004**
Early B.O. (%)	**15±10**	**30±13**	**<0.001**
Late B.O. (%)	**13±10**	**24±12**	**0.006**
Early LVEF (%)	**50±5**	**40±11**	**0.001**

B.O.= infarct size expressed as black out; cTFC= corrected TIMI frame count; LVEF= left ventricular ejection fraction; MPG= myocardial perfusion grade; N° STE= n° of leads with ST segment elevation; P.D.= perfusion defect; ΣSTE= sum of STE in the first ECG; STR= ST segment resolution; Time to treatment= symptom onset to balloon time.

DISCUSSION

Our cases are limited in number but rather complete in terms of ECG, biochemical markers, angiographic and scintigraphic parameters usually considered in the setting of acute myocardial infarction and reperfusion. In the era of thrombolytic therapy, various studies had underlined the significant role of clinico-enzymatic parameters in the prediction of myocardial reperfusion [13-17] The aim of our study was to evaluate in the middle-term, the correlation of these parameters with the functional outcome (infarct size, LVEF) in the setting of mechanical reperfusion .

Peak CK-MB did not represent a marker of reperfusion in this setting as it did for thrombolysis. It was early in all cases (7.4±2.6 hours, range 3-14) and did not correlate with other indices of early reperfusion or functional outcome. The quick and effective achievement of an antegrade flow with primary PCI was probably responsible for the early enzymatic peak in this population.

Final necrosis extent and late LVEF were essentially correlated with a total ischemic time < 240 minutes and with effective reperfusion as evidenced by ECG (ST segment resolution) and angiographic parameters (cTFC, MPG) which were confirmed to be predictive and reliable[18-24]. Time to reperfusion or total ischemic time was the most significant predictor of outcome in all analyses, despite the small population in our study. This confirmed its importance as already shown in more relevant studies not only on functional end points (reperfusion indexes, infarct size, LVEF) but also on

mortality[25-27].

Patients whose LVEF increased over time had shorter reperfusion time, comparable infarct size (17 vs 19%), a trend towards a lower early LVEF (44 vs 48%, p=0.24) and more often an anterior MI (52 vs 27%, p=0.14). Moreover, patients whose infarct size decreased after one month follow up, initially had larger infarct size (28 vs 18%, p=0.03) and showed a trend towards a lower initial and late LVEF. These data suggested that in patients with an early limited myocardial vulnerability, the benefit of an early optimal mechanical reperfusion is obtained immediately. This was demonstrated by a smaller infarct size and preserved LVEF at the initial SPECT without any significant difference at the follow up. However, patients with an initially more extensive jeopardized myocardium, larger infarct size and lower initial LVEF, exhibited a late improvement which was dependent on reperfusion time and efficiency as evaluated with ECG and angiographic parameters. This confirms the necessity to exert every possible effort to obtain maximum reduction in time to treatment as indicated in the ACC/AHA Guidelines[28] and eventually using appropriate interventions such as GPIIb/IIIa antagonists[29-31], adenosine[32,33], thromboaspiration devices[34,35] and filters[36] to preserve microcirculation.

The difference in infarct size between early and late scintigraphy confirms the presence of a proportion of viable myocardium able to restore its metabolic properties (stunned myocardium) and validate the practice in research studies of verifying infarct size with scintigraphy one month after reperfusion therapy for MI [37,38]. The black out index obtained with gated Tc-sestamibi SPECT was not representative of total tissue necrosis, since it indicated < 40% capacity of tracer uptake relative to normal surrounding tissue. Reversibility of black out testifies the presence of a proportion of viable myocardium with late restoration of radioisotope capture capacity. A reduction in the extent of perfusional defect associated with restoration of contractility one month after primary PCI was also demonstrated by myocardial contrast echocardiography[39, 40].

Although NMR is probably the gold standard technique to measure infarct size[41], the gated SPECT has been widely reported as a reliable quantitative method[42]. It is also clinically validated[3, 43-46], measures ventricular volumes and is a reliable, automated, reproducible and semi quantitative method for estimation of LVEF[12, 47-49]. Improvement of perfusional and kinetic parameters of left ventricle is frequent one month after primary PCI for acute myocardial infarction. Total ischemic time (time to treatment) is the best determinant of final infarct size and LVEF. Less significantly ST segment resolution and angiographic parameters of optimal reperfusion (cTFC and MPG) correlate with late absolute improvement of LVEF.

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