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Effects of abciximab on microvascular integrity and left ventricular functional recovery in patients with acute infarction treated by primary coronary angioplasty

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Received 30 April 2002; accepted 8 May 2002

KEYWORDS

Contrast
echocardiography;
primary PTCA;
myocardial infarction;
platelet inhibitors;
coronary
microcirculation

Aim To investigate the effect of abciximab on microvascular integrity and left ventricular (LV) functional recovery in patients with acute myocardial infarction (MI) treated by primary coronary angioplasty (PTCA).

Methods and results Thirty-one patients (27 males; age 39–76 years) with first, acute MI (<6 h after onset) were randomized to receive either abciximab + primary PTCA (n = 17) or primary PTCA alone (n = 14). Baseline characteristics of the two groups were similar. Myocardial reperfusion was studied shortly after PTCA by corrected TIMI frame count (cTFC) and intracoronary myocardial contrast echocardiography (MCE), after 48 h by intravenous MCE using intermittent, harmonic power Doppler, and after 1 month by intravenous MCE and 99 mTc-tetrofosmin SPECT. The patients treated with abciximab showed a shorter cTFC (23±4 vs 30±9 frames; $P<0.05$), a more preserved microvascular integrity shortly after PTCA (77% vs 55%; $P<0.01$), after 48 h (86% vs 50%; $P<0.005$) and at 1-month follow-up (86% vs 54% by MCE, $P<0.001$, and 68% vs 60% by SPECT, $P<0.005$) than patients treated with PTCA alone. Abciximab patients also showed a better recovery of LV function, as demonstrated by greater reduction in wall motion score index (1.4±0.3 vs 1.5±0.2; $P<0.05$) and increase in LV ejection fraction (53±7% vs 48±5%; $P<0.001$).

Conclusions Abciximab improves microvascular perfusion and LV functional recovery in primary PTCA.

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Introduction

The achievement of early and adequate reperfusion is of top priority in patients with acute myocardial infarction (MI). In patients admitted with

ST-segment elevation adequate coronary recanalization, documented by a TIMI III flow 90 min after hospitalization, was achieved in 50% to 75% of patients managed medically^{1–5} and in 79% to 90% of those treated by primary percutaneous transluminal coronary angioplasty (PTCA).^{6–8} Despite the recanalization of the epicardial infarct related artery, microvascular damage (referred to as no- or

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low-reflow phenomenon) has been documented in 14% to 30% of patients with TIMI III flow; this event is consistently associated with impaired recovery of left ventricular (LV) contractile function and poor clinical outcome.^{9–14} The first line of treatment in acute infarction patients is therefore to guarantee—in addition to coronary recanalization—an adequate reperfusion at the level of coronary microcirculation.

To preserve microvascular integrity in the infarct related myocardium, new therapeutic strategies have been proposed in adjunction to primary PTCA. Specifically, verapamil has been shown to reduce TIMI II flow probably by reversing coronary microvascular spasm,¹⁵ and adenosine has recently been demonstrated to improve myocardial reperfusion by its multifactorial action on leukocytes, platelets and other mediators.¹⁶ Due to the role of platelet aggregation and possible thrombus embolism on the no-reflow phenomenon, glycoprotein IIb/IIIa receptor antagonists have been postulated as one of these adjunctive treatments. In particular, abciximab has been shown to enhance coronary blood flow in primary PTCA patients and to improve functional recovery by its action on platelets, leukocytes and probably on micro embolisms.^{17–20} With these considerations in mind, this study was undertaken to investigate the effect of abciximab on microvascular integrity and LV functional recovery in patients with acute MI treated by primary PTCA.

Methods

Study population

The study was performed in 31 patients with acute MI treated by primary PTCA (27 males, mean age 57 years, range 39–76). Inclusion criteria were: continuous chest pain of more than 30 min, ST-segment elevation ≥ 0.2 mV in at least two contiguous leads, admission within 6 h from the onset of symptoms, occlusion of the infarct related artery with the appearance of fresh thrombus, and a good acoustic echocardiographic window in the supine position.

Exclusion criteria were: previous MI, previous coronary artery bypass graft surgery, cardiogenic shock, multivessel coronary disease or $>50\%$ left main stenosis, significant valvular disease, age more than 80 years and any counterindication to platelet glycoprotein IIb/IIIa receptor antagonists or primary PTCA.

The study complies with the Declaration of Helsinki. The protocol was approved by the Ethical

Committee of the University of Pisa. All patients gave formal written consent before the procedure.

Study protocol

Before PTCA, patients were treated with aspirin, intravenous nitrates and a 5000 IU bolus of unfractionated heparin. Coronary arteriography was performed by the femoral approach. Immediately after coronary arteriography patients, if eligible, were randomized to receive either abciximab plus heparin (group A) or only heparin (group B). Group A patients received a bolus of abciximab ($0.25 \text{ mg} \cdot \text{kg}^{-1}$) followed by a 12-h infusion ($0.125 \mu\text{g} \cdot \text{min}^{-1}$); during PTCA an adjunctive bolus of heparin was administered according to body weight ($70 \text{ IU} \cdot \text{kg}^{-1}$) and to ACT (Activated clotting time) monitoring (included between 250 and 300 s). After the procedure no more heparin was given and the activated partial thromboplastin time (aPTT) was monitored for the following 12 h. Group B patients were treated only with a heparin bolus during PTCA (according to body weight and ACT between 250 and 300 s), followed by a continuous intravenous infusion of unfractionated heparin ($10 \text{ IU} \cdot \text{kg/h}^{-1}$) for 24 h; the infusion was titrated every 6 h as needed to maintain aPTT between 50 and 70 s. All patients received a coronary stent (Multilink, NIR or GFX) and were treated with aspirin 300 mg daily plus ticlopidine 250 mg twice a day, reduced to 250 mg daily after 1 week. Beta-blockers and angiotensin-converting enzyme inhibitors, if not contraindicated and well tolerated, were routinely administered to all patients independently of randomization. The success of primary PTCA was defined as achievement of a residual stenosis $<30\%$ of diameter reduction with TIMI flow grade 3, together with disappearance of ST elevation and chest pain.

Immediately after PTCA, a 2D echocardiogram and intracoronary myocardial contrast study were performed. After 48 h a transthoracic 2D echocardiogram with intravenous contrast administration and harmonic power Doppler imaging (HPDI) was performed. At 1-month follow-up all patients underwent a 2D echo with intravenous contrast administration and a stress and rest $^{99\text{m}}\text{Tc}$ -tetrafosmin SPECT.

Clinical and metabolic data

All patients were screened for ECG changes; to assess the extent of microvascular reperfusion, serial ST-segment analysis on a 12-lead ECG recording just before and 30 to 60 min after coronary

intervention was done by one observer blinded to clinical data. A decline of ST-segment elevation—exceeding 50% of initial value—was the electrocardiographic criterion of microvascular reperfusion.²¹ Creatinine kinase (CPK) and creatinine-kinase-MB (CK-MB) values were assessed every 6 h during the first day and then every day before discharge, unless clinical events suggested further measurements. Adverse clinical events (including death, ventricular arrhythmias, re-infarction, recurrent angina, target lesion revascularization and heart failure) were evaluated during hospital stay and at the 30-day follow-up.

Bleeding was defined according to the criteria of the Thrombolysis in Myocardial Infarction trial²²; major bleeding was defined as a decrease in the haemoglobin level of $5 \text{ g} \cdot \text{dl}^{-1}$, intracranial haemorrhage or cardiac tamponade, and minor bleeding was defined as a decrease in the haemoglobin level of more than $3 \text{ g} \cdot \text{dl}^{-1}$ from an identified site, spontaneous gross haematuria, haematemesis, haemoptysis or puncture site bleeding.

Echocardiographic and echo contrast follow-up

2D echo and intracoronary MCE

At the end of PTCA, a radiographic non ionic, low osmolar contrast medium (iopromide), the same as utilized for angiography, was sonicated to generate microbubbles according to a standardized protocol²³; these microbubbles have a mean diameter of $8 \mu\text{m}$.²⁴ Eight microlitres of the sonicated medium were manually injected in the coronary artery related to the infarcted area. After the injection, the catheter was removed from the coronary ostium and any contrast agent remaining in the catheter was withdrawn. Echocardiographic images were obtained by using a commercial scanner (Sonos 5500, Agilent Technologies, USA), equipped with a 2.5–3.75 MHz transducer. With the patient lying down in the supine position the probe was oriented to obtain apical four-, five- and two-chamber views of the heart. Before contrast injection, the echocardiographic images were recorded to identify the asynergic area and to quantify both LV ejection fraction (EF) and wall motion score index (WMSI); after contrast administration the images were recorded to document myocardial enhancement until its disappearance. Gain setting controls were maintained constant during data acquisition; the images were stored on a Super VHS videotape for further evaluation.

Forty-eight h and 1-month 2D echo and MCE

After 48 h each patient underwent myocardial contrast echocardiography using Levovist (Schering AG, Berlin, Germany), a galactose-based agent containing microbubbles with an average diameter of 3–4 μm . The safety of Levovist and its lack of adverse effects on haemodynamics, LV function, and pulmonary gas exchange have been demonstrated.²⁵ Levovist powder (4 g) was reconstituted by adding 8 ml of sterile water to give a concentration of $400 \text{ mg} \cdot \text{ml}^{-1}$. It was administered intravenously as a slow bolus (first 2 ml over a period of 4 s), followed by a slow infusion (remaining 8 ml over a period of 2 min). Contrast agent injection was followed by a 5 ml saline flush.

Harmonic power Doppler was performed with the same scanner and with a transducer transmitting and receiving at a mean frequency of 1.8 and 3.6 MHz, respectively; the dynamic range of this system is 40 dB. The mechanical index was set as high as possible to favour microbubble resonance and destruction. Images were triggered to the peak of the T wave, every fourth cardiac cycle. End-systolic triggering was chosen because the myocardial wall segments are thicker and LV cavity size smaller, resulting in less contrast attenuation. To avoid artifacts related to cardiac motion the endsystolic triggering was carefully tuned. The acquisition of MCE images started just before contrast injection and was continued until contrast effect in the myocardium had dissipated. Echo images were acquired in the apical views utilized during the first registration with intracoronary MCE.

Ultrasound system gains were optimized at the beginning of the study and held constant during subsequent image acquisitions. To minimize the misinterpretation of artifacts, HPDI images were displayed on a split screen, in which the first ultrasound exposure results in microbubble stimulation and the second in bubble destruction. The images were stored digitally on a magneto optical disk and on super VHS videotape.

Single photon emission computed tomography

All patients underwent a myocardial perfusion SPECT study according to a stress and rest protocol. About 1 h after the i.v. administration of 740 MBq of ^{99}Tc -Tetrofosmin under resting conditions, SPECT images were acquired by using a dual detector gamma camera (Optima NT ELGEMS) equipped with LEHR (low emission high resolution) collimators.

Thirty-two views of 60 s each, over an orbit of 180°, were acquired from the 45° RAO (right anterior oblique) to the 45° LPO (left posterior oblique) projection on a matrix of 64×64 pixels (6 mm pixel size). The energy window used was 20% centred on the 140 KeV photo peak of ⁹⁹Tc. Tomographic reconstruction was performed with filtered back-projection using a low pass Butterworth filter with a cut-off frequency of 0.4 cycles/cm and order 10. No attenuation or scatter correction was used. Transaxial slices (1 pixel thick) were then re-oriented along the vertical and horizontal long axes and the short axis of the left ventricle.

Image interpretation

The corrected TIMI frame count (cTFC) was calculated for the infarct-related artery according to the technique described by Gibson and coworkers²⁶ after the first balloon inflation and after stent deployment.

In echocardiographic analysis, the LV myocardium was divided according to a 16-segment model; the wall motion of each segment was scored according to a 5-point scale, where 1 is normal, 2 is hypokinetic, 3 is akinetic, 4 is dyskinetic and 5 is aneurismal.²⁷ The WMSI was obtained averaging the scores of the visualized LV segments. In each patient left ventricular ejection fraction (LVEF) was calculated by using the modified Simpson's rule.

Myocardial contrast enhancement was assessed by dividing LV myocardium according to the same 16-segment model and assigning to each segment a score of 0 (no enhancement), 0.5 (heterogeneous or subepicardial enhancement) or 1 (homogeneous contrast effect). For each patient a perfusion score index was calculated by averaging the contrast scores of the segments within the area at risk, defined as the LV area showing wall motion abnormalities at the first echocardiographic study.²⁸ The analysis of 2D echocardiograms, of intracoronary and intravenous contrast studies was performed by two independent observers, blinded to the clinical history and SPECT data, and twice by the same observer.

The reading of 2D echocardiograms, of intracoronary and intravenous contrast studies was performed separately for every patient.

Horizontal and vertical long-axis views by SPECT imaging were also interpreted by two independent observers. All the observers were blind to the treatment. For semi-quantitative analysis, short axis slices from the first apical to the last basal slice were used for generating a two-dimensional

volume-weighted polar map. This map was divided into 16 segments, to be as close as possible to the echocardiographic analysis. The segment with the highest mean tracer uptake was then normalized to 100% and the activity within the other segments was expressed as a percentage of peak activity. According to other authors^{29,30} segmental 99 mTc-tetrofosmin activity was classified as mild to moderately abnormal if it was <75% and >55% of the peak value and as severely abnormal if it was <55% of the peak value.

Statistical analysis

Categorical data are presented as absolute values and percentages, whereas continuous data are summarized as mean value±SD. Chi-squared and Fisher's exact tests were used for comparison of categorical variables as appropriate. Comparison of continuous variables was performed by means of Student's t-test or Wilcoxon rank-sum test, as appropriate. Linear regression analysis was performed to identify correlation between cTFC and MCE score. *P* values <0.05 were considered statistically significant.

Results

A total of 36 patients with acute MI treated by primary PTCA were screened; five of these patients were excluded due to inadequate acoustic window on the cardiac catheterization table. Thus, 31 patients were enrolled into the study: 17 patients were randomized to abciximab (group A) and 14 to control treatment (group B). The two groups were not statistically different as to age, sex distribution, prevalence of diabetes mellitus, time elapsed from symptom onset to first balloon inflation, degree of ST-segment elevation at admission, prevalence of anterior infarction and LAD involvement (Table 1).

Clinical course

The clinical course was similar among the two groups (Table 2). One patient from group A and another from group B had post-infarction angina; one patient from group A and four from group B had life threatening ventricular arrhythmias. A decline in ST segment elevation exceeding 50% of the initial value was observed 30 to 60 min after completion of PTCA in 11 patients (65%) from group A and in six patients (43%) from group B (*P*=0.2). The two groups were also similar as to the development of Q waves, as well as to peak CPK and CK-MB

Table 1 Baseline characteristics of patients. Values are not significant

Characteristic	All patients (n = 31)	Group A (n = 17)	Group B (n = 14)
Age	57±10	57±9	58±12
Sex (M/F)	27/4	14/3	13/1
Diabetes	4 (13%)	2 (12%)	2 (14%)
Time to PTCA (min)	223±129	210±141	238±116
ST segment elevation (mm)	5.5±2	5.7±2.1	5.3±1.7
Anterior wall infarction	20 (64%)	13 (76%)	7 (50%)
Infarct-related artery			
LDA	20 (64.5%)	13 (76%)	7 (50%)
RCA	9 (29%)	4 (24%)	5 (36%)
LCx	2 (6.5%)	—	2 (14%)
Left ventricular ejection fraction	46.7±4.6	47.5±6	45.7±5
Wall motion score index	1.77±0.24	1.78±0.27	1.77±0.2

LAD = left anterior descending artery; RCA = right coronary artery; LCx = left circumflex artery; LIMA = left internal mammary artery; PTCA = percutaneous transluminal coronary angioplasty.

Table 2 Clinical course. Values are not significant

Characteristic	All patients (n = 31)	Group A (n = 17)	Group B (n = 14)
Peak creatine kinase	3033±2134	3052±2072	3014±2218
Peak creatine kinase-MB	238±172	235±171	240±175
Q wave myocardial infarction	29 (93%)	16 (94%)	13 (92%)
Ventricular arrhythmias	5 (16%)	1 (6%)	4 (28%)
Post-infarction angina	2 (6%)	1 (6%)	1 (7%)
Target lesion reintervention	1 (3%)	0	1 (7%)
Major bleeding	0	0	0
Minor bleeding	3 (9%)	2 (12%)	1 (7%)

release. No patient had major bleeding complications, while minor bleeding (at access site) occurred in two patients treated with abciximab and in one in the control group ($P = ns$). During the 30-day follow-up, no patient of the abciximab group and one of the control group underwent target lesion reintervention ($P = ns$).

Angiographic data

During coronary angiography the presence or absence of collateral circulation was evaluated and no patients showed an angiographic Rentrop score ≥ 1 .

The interventional procedures were all successful and all the stents were successfully deployed. As shown in Fig. 1, the cTFC after first balloon inflation was similar in both groups (33 ± 12 in group A vs 37 ± 9 frames in group B, $P = 0.24$); after stent deployment cTFC decreased, and reached lower values in abciximab treated patients (23 ± 4 in group A vs 30 ± 9 frames in group B, $P < 0.05$).

Myocardial perfusion: patients analysis

Immediately after PTCA and stenting, microvascular integrity was more preserved in abciximab

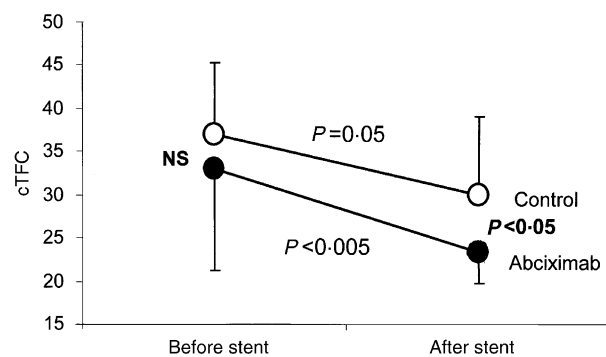


Fig. 1 Correct TIMI frame count (cTFC) after balloon and after coronary stenting in patients treated with abciximab (●) and in the control group (○).

treated patients: the perfusion score index was higher in group A patients (0.85 ± 0.10) than in those of group B (0.72 ± 0.16 ; $p = 0.014$). Two days after PTCA, and at 1-month follow-up, abciximab patients still showed a higher perfusion score index than control patients ($P < 0.05$) (Fig. 2).

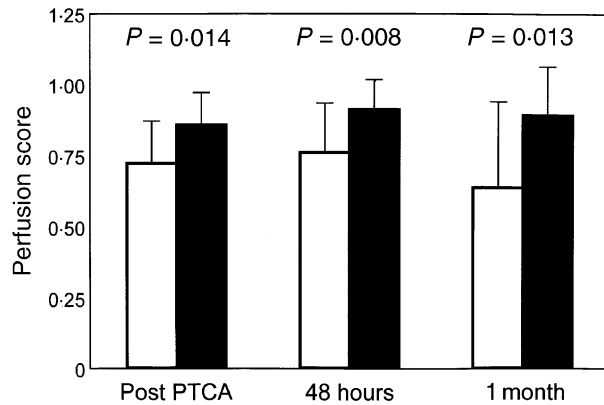


Fig. 2 Contrast perfusion scores in control (□) and abciximab patients (■) after PTCA, at 48 h and at 1 month follow-up.

Myocardial perfusion: segments analysis

A total of 171 myocardial segments were evaluated within the asynergic area. Myocardial perfusion was assessed in all these 171 segments by intracoronary contrast echocardiography shortly after PTCA. Due to attenuation artifacts, a blooming effect or inadequate contrast enhancement, myocardial perfusion was not assessable in 16 of these segments (9%) by the contrast study performed after 48 h and in 13 of these segments (8%) after the 1-month study. Shortly after PTCA, homogeneous contrast enhancement occurred more frequently in segments of group A (76/98 segments = 78%) than in those of group B (40/73 segments = 55%; $P < 0.01$). Similarly, intravenous MCE 48 h later showed preserved microvascular integrity (score 1) within the asynergic area more frequently in group A (77/90 segments = 86%) than B (38/65 segments = 58%, $P < 0.005$). The same results were confirmed at the 1-month follow-up (normal perfusion in 84/97 segments = 87% of group A vs 33/61 segments = 54% of group B; $P < 0.001$; Fig. 3). Fig. 4 shows the concordance of perfusion between intracoronary MCE and intravenous MCE at 1 month in a patient with an anterior myocardial infarction. The analysis of SPECT data at rest confirmed a greater recovery of microcirculation in abciximab ($68 \pm 19\%$) than in control patients ($60.5 \pm 21\%$; $P < 0.005$), as revealed by the significant difference in the proportion of normally perfused, mild-to-moderately hypoperfused and severely hypoperfused segments in the two groups ($P < 0.05$ by Chi-square). In fact, patients treated with abciximab showed a lower incidence (30%) of severe perfusion defects than the control group (39%) and a greater proportion of normally perfused segments (40% vs 25%). In any of the patients myocardial scintigraphy was positive for ischaemia.

The results of canonical correlation analysis demonstrated that post-stenting cTFC was significantly and inversely related to the perfusion score index in the infarct area at intracoronary MCE ($r = -0.42$; $P = 0.017$), at 48 h ($r = -0.49$; $P = 0.005$) and at 1 month intravenous MCE ($r = -0.48$; $P = 0.006$).

On both SPECT and contrast echocardiography interpretation, the two observers were in agreement in 92% of the segments analysed; the intra-observer agreement was 93%. Scoring both myocardial contrast enhancement and tetrofosmin activity on a 3-point scale, the two methods were in agreement in 48% of segments. Scoring myocardial perfusion as normal or abnormal, an agreement was present in 56% of segments ($k = 0.26$).

LV functional recovery

Immediately after PTCA, global and regional LV functions were similar in the two groups. At 30-day follow-up, LV function improved in both groups, but to a greater extent in group A than B. Specifically, the WMSI of group A patients decreased from 1.78 ± 0.27 to 1.36 ± 0.30 ($P < 0.001$), while that of group B decreased from 1.75 ± 0.20 to 1.52 ± 0.20 ($P < 0.05$, Fig. 5, top panel). Accordingly, LVEF improved in both groups, being an increment higher in group A (from $48 \pm 6\%$ to $53 \pm 7\%$; $P < 0.001$) than in group B patients (from $46 \pm 4\%$ to $48 \pm 5\%$; $P = 0.17$).

Discussion

This study demonstrates that abciximab is able to preserve microvascular integrity and to facilitate the recovery of LV function in patients with acute MI treated by primary PTCA.

Microvascular integrity after primary PTCA

The goal of treatment in acute MI is not only recanalization of the epicardial infarct related artery, but also adequate reperfusion of the coronary microcirculation.³¹ Even patients with good contrast runoff (TIMI 3 flow) can have different outcome and LV functional recovery in relation to post-reperfusion microvascular damage.^{11,12} This reperfusion injury is a multifactorial phenomenon involving platelet aggregation, leukocyte plugging, endothelial dysfunction and coronary micro-embolism.^{18,19} Some of these mechanisms could be prevented by new therapies, adjunctive to primary PTCA. In this study we evaluated the influence of

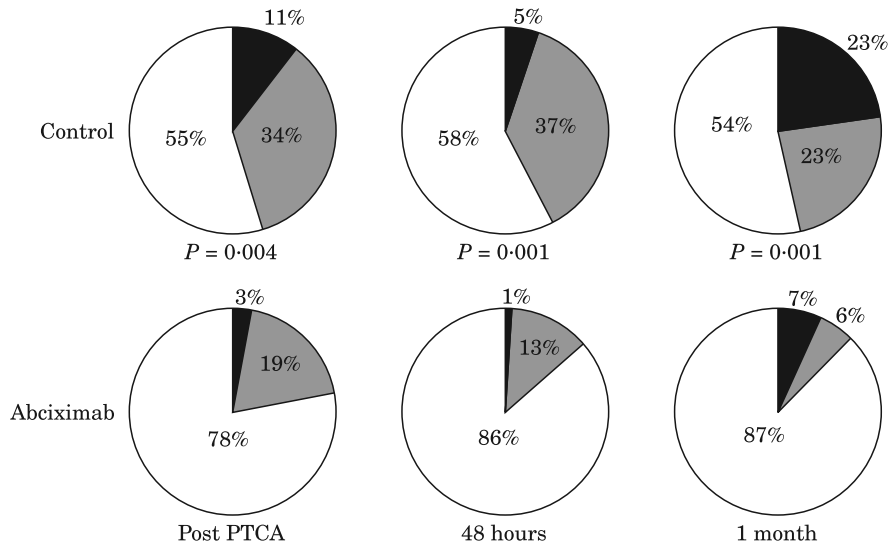


Fig. 3 Distribution of myocardial contrast perfusion scores in control and abciximab patients shortly after PTCA, at 48 h and at 1 month follow-up. ■ = score zero; ■ = score 0.5; □ = score 1.

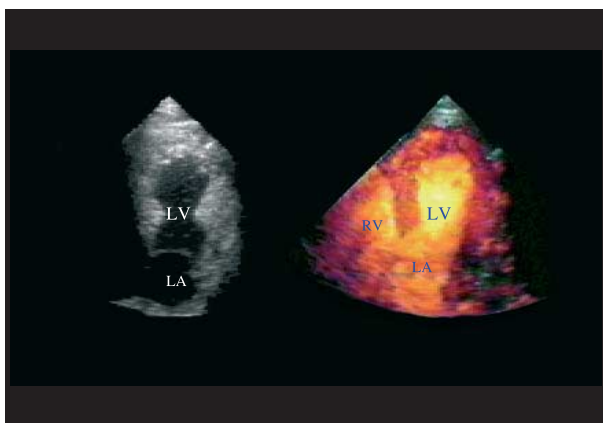


Fig. 4 Example of concordance between intravenous contrast echocardiography and intravenous contrast echocardiography. The left panel shows an intracoronary contrast study performed shortly after PTCA in a patient with anterior infarction; the right panel shows an intravenous contrast examination performed after 1 month in the same patient. Both studies show a good reperfusion of anterior wall (LV = left ventricle; LA = left atrium; RV = right ventricle).

abciximab on reperfusion injury in a highly selected and homogeneous patient population.

Diagnostic tools to identify microvascular damage

Many diagnostic indicators have been proposed to investigate coronary microcirculation after reperfusion. Resolution of ST-segment elevation is a non-invasive, inexpensive predictor of mortality in huge patient populations,³² but it lacks sensitivity.

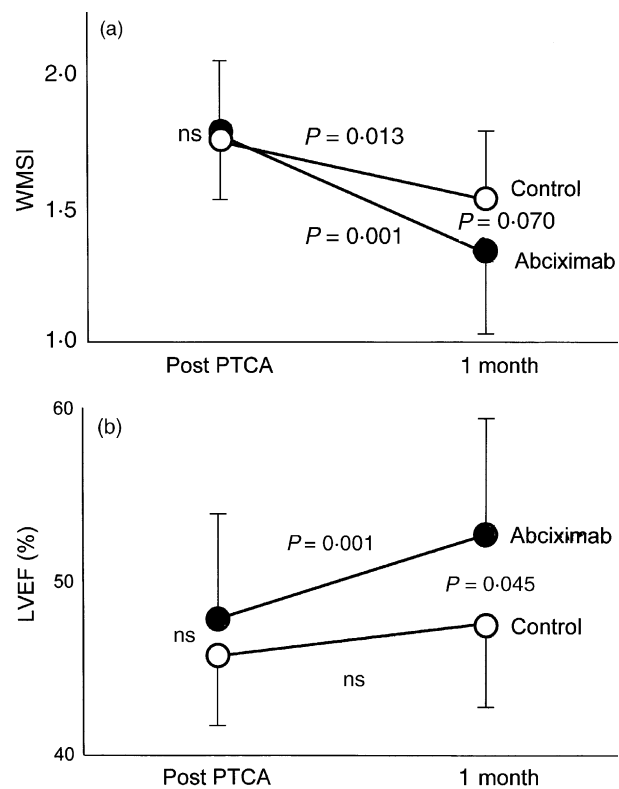


Fig. 5 Changes in echocardiographic left ventricular wall motion score index (WMSI) (a) and ejection fraction (LVEF) (b) from acute conditions to 1 month follow-up in group A (●) and in Group B (○).

Angiographic parameters such as cTFC and angiographic blush score^{33,34} can risk-stratify patients with acute MI, although they are invasive and not

easily repeatable. Doppler derived coronary flow velocity reserve relates to recovery of myocardial contractile function³⁵ and the wave forms are predictive of functional recovery³⁶; however, this technique is again invasive. MCE provides direct and immediate information on coronary microcirculation, is able to detect the changes occurring after reperfusion and to unmask perfusion abnormalities even in patients with TIMI 3 flow^{10–14}; however, MCE is limited as far as feasibility and artifacts are concerned. Nuclear perfusion is accurate, but rarely utilized in the acute setting. For these reasons, we investigated the effects of abciximab on myocardial perfusion with an integrated approach using cTFC, MCE and SPECT.

Therapeutic effects on no-reflow

A variety of therapies, adjunctive to PTCA, have been proposed to improve reperfusion in acute MI. Specifically, verapamil, adenosine and nicorandil have been shown to reduce the 'no-reflow' phenomenon in man.^{15,16,37} More recently, platelet glycoprotein IIb/IIIa inhibitors have been utilized to improve outcome of patients with acute MI treated with PTCA. Although the impact of abciximab on acute coronary syndromes has been demonstrated in several studies,^{38,39} the real benefit of this drug during primary PTCA and stenting is still debated.^{40,41} Abciximab is supposed to prevent reocclusion of the epicardial infarct related artery and to reduce reperfusion injury by interfering with platelet aggregates, leukocyte plugging and reducing microembolism due to stent deployment. The recent French experience in the ADMIRAL trial has proven that abciximab is able to improve myocardial perfusion after primary PTCA with stent deployment especially if administered prior to the procedure, while the most recent results of the CADILLAC trial underline the importance of stents in primary PTCA without confirming the advantage of platelet inhibitor therapy. However, in this last trial a crossover to abciximab was allowed when no reflow occurred. Neumann and coworkers¹⁷ showed an increase in coronary peak flow velocity in AMI patients treated with abciximab but did not observe changes in coronary flow reserve, suggesting a higher number of functional segments in treated patients. We evaluated the effect of this adjunctive treatment on reperfusion and we focused our attention mainly on coronary microcirculation and LV functional recovery. The population was highly selected, and patients with previous infarction or receiving thrombolysis before PTCA were not included. Furthermore, a high percentage of anterior infarction patients was enrolled, and a

homogeneous interventional procedure was carried out: only one vessel was treatable and no devices were used except for stent deployment.

It has been suggested that stents are able to improve epicardial flow and to reduce the risk of acute and late restenosis, but to some extent they are responsible for the no-reflow phenomenon by microembolism of the plaque thrombus. We analysed whether this event could be reduced by abciximab pretreatment. After balloon dilatation all subjects showed a similar cTFC; however, after stenting, patients treated with abciximab had a significantly lower cTFC than the control group (Fig. 2). This observation underlines the role of the platelet inhibitor in reducing microembolization caused by stent deployment, thus preserving microvascular integrity (demonstrated by both MCE and SPECT) and favouring LV functional recovery.

Study limitations

A major limitation of this study is related to the small number of patients enrolled. Intracoronary MCE in patient with acute MI is limited by the short time window for data collection, the acute clinical setting and organization problems. Furthermore, the acoustic window is often limited in patients lying on the cardiac catheterization table. Due to the above limitations, contrast echo studies in acute infarction rarely involve a huge patient population. The method used for the assessment of perfusion by MCE immediately after PTCA, after 48 h and at 1 month was different. However, the accuracy of intracoronary MCE has been demonstrated in several studies, and the substantial agreement between intracoronary and intravenous MCE in AMI patients has been recently underlined.⁴² Additionally, contrast echo images were not quantified and a fixed triggering interval was utilized.⁴³ These limitations could be overcome by using new technologies based on real time myocardial perfusion,^{44,45} that were not available at the time of the study. Collateral circulation was not evaluated in this study, the sonicated radiographic contrast medium was injected only in the infarct related artery. Collateral circulation was also not assessable by coronary arteriography, as no patient showed an angiographic Rentrop score ≥ 1 . Finally, although substantial agreement between the different techniques existed when each of them acted as its own control, the agreement between myocardial contrast enhancement and SPECT data was limited. The ability of myocardial contrast enhancement to predict tracer uptake varies widely in the different studies, ranging from a

limited^{46,47} to a good agreement.^{48–51} This study shows a limited correlation between contrast echocardiography and SPECT. This discrepancy is probably due to the intrinsic differences between the two techniques, to the difficulties in comparing various perfusion territories by these two approaches or in different cut-off values utilized to define reduced myocardial tracer uptake in the different studies.

Conclusions

In patients with acute MI treated by primary PTCA abciximab is able to preserve microvascular integrity, as demonstrated early by angiographic contrast run-off and intracoronary MCE and later by intravenous MCE and SPECT. The effect of abciximab on coronary microcirculation favours the recovery of LV function occurring in the first month after the acute infarction. Larger studies are needed to support these conclusions.

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