The incidence and timing of major arrhythmias following successful primary angioplasty for acute myocardial infarction

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Angioplasty, primary; Arrhythmias; Myocardial infarction.

Background. **The potential benefits of direct percutaneous transluminal coronary angioplasty (PTCA) on malignant arrhythmias in the hospital phase of acute myocardial infarction have not yet been established.**

Methods. **We prospectively investigated the incidence and timing of major arrhythmias occurring during direct PTCA and within 24 hours of mechanical reperfusion in 90 consecutive patients with acute myocardial infarction undergoing successful direct PTCA within 12 hours of symptom onset.**

Results. **Ventricular fibrillation and complete atrioventricular block occurred exclusively during direct PTCA and both resolved in the catheterization laboratory. Holter monitoring showed that ventricular tachyarrhythmias, such as runs of more than 3 extrasystoles, were detectable only during the first 8 hours after direct PTCA.**

Conclusions. **In our group of patients undergoing successful direct PTCA, no in-hospital life-threatening arrhythmias occurred after this procedure.**

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Introduction

Over the past decade the management of acute myocardial infarction (AMI) has changed to a more aggressive approach: i.e. the restoration of antegrade flow in the infarct-related artery (IRA) by means of direct percutaneous transluminal coronary angioplasty (D-PTCA)[1-3].

Mechanical reperfusion is an established treatment for AMI and has been shown to achieve higher rates of TIMI grade 3 flow and lower rates of recurrent ischemia, reinfarction, stroke, and death than thrombolytic therapy[4-6].

Nevertheless, the potential benefits of D-PTCA on malignant arrhythmias during the hospital phase of AMI have not been completely established[7,8]. We therefore prospectively investigated the incidence and timing of major arrhythmias occurring during D-PTCA and within 24 hours of successful mechanical reperfusion by means of this procedure performed within 12 hours of symptom onset in 90 consecutive patients with AMI.

Methods

Study population. Ninety unselected consecutive patients with AMI were enrolled between September 2000 and March 2001. All patients were referred to our catheterization laboratory for D-PTCA within 12 hours of symptom onset. AMI was defined as typical chest pain lasting > 20 min and associated with ST-segment elevation ≥ 1 mm in two contiguous leads or with new complete left bundle branch block. The study population was unselected because patients were referred to the catheterization laboratory exclusively on the basis of their diagnosis and of the time elapsing since symptom onset. Any other criterion such as age, sex, Killip class, and infarct location was not considered.

All patients included in the study gave their informed consent to the procedure and underwent coronary angiography and D-PTCA of the IRA. A 24-hour Holter recording was started immediately after D-PTCA. The study protocol, which was approved by the local Ethics Committee, was in accordance with the declaration of Helsinki.

Procedural technique. Coronary angiography and angioplasty were performed using standard techniques, usually through a percutaneous femoral approach. Before PTCA a 70 IU/kg i.v. bolus of unfractionat-

ed heparin was administered, followed by additional weight-adjusted doses, in order to maintain an activated clotting time ≥ 250 s throughout the procedure. All patients were also treated with 500 mg of aspirin. Treatment with glycoprotein IIb/IIIa inhibitors was at the operator's discretion.

D-PTCA was attempted only at the site of the culprit lesion with the exception of patients with cardiogenic shock who received the most complete revascularization possible.

An optimal angiographic result was defined as residual stenosis < 30% associated with TIMI grade 3 flow. A TIMI grade 2 flow as well as a residual stenosis of 30-50% were considered a suboptimal result. An unsuccessful D-PTCA was defined as a procedure resulting in a TIMI grade 0 or 1 flow or in a residual stenosis > 50%. TIMI flow rates have been derived from a blinded core laboratory reviewing our cine-angiograms[9]. The left ventricular ejection fraction was determined angiographically in 72 (80%) patients and at echocardiography in 18 (20%).

Continuous ECG monitoring of the cardiac rhythm was performed throughout the procedure and arrhythmias were defined in accordance with the recommendations of Topol[10].

Holter monitoring. All patients underwent 24-hour Holter monitoring, starting immediately after D-PTCA. Holter recording using bipolar leads (CM1 and CM5) was scanned by means of a computer-based system (Elatec 3.0, ELA Medical, Segrate-MI, Italy); the beat morphology and timing were adjusted by one of the authors.

Ventricular arrhythmias were classified using Lown's classification[11]: grade 0, no premature ventricular complexes; grade 1, < 30 premature ventricular complexes/hour; grade 2, > 30 premature ventricular complexes/hour; grade 3, multiform premature ventricular complexes; grade 4A, couplets; grade 4B, a run of ventricular tachycardia (≥ 3 consecutive premature ventricular complexes). Lown grades ≥ 3 were considered as complex ventricular arrhythmias.

Clinical data recorded during the coronary care unit (CCU) and hospital stays (mean total time 6.7 ± 2.02 days) were collected in a dedicated database. Blood samples for creatine phosphokinase (CPK) measurements were drawn every 6 hours during the first 48 hours. The peak CPK values were recorded in the database.

For each patient the behavior of the arrhythmias was observed during D-PTCA, during the patients' CCU stay, in the 24 hours following the procedure, and then until discharge. A control group was not considered because at our institution since 1996 we have adopted the policy of treating all AMI patients with D-PTCA.

Statistical analysis. Statistical analysis was performed using a computer software (Statistical Package for Social Sciences for Windows, release 11.01, SPSS Inc., Chicago, IL, USA). Data were collected in dichotomous variables and analyzed using the Kendall Tau-b test; continuous variables were analyzed for variance followed by the Bonferroni post-test as appropriate, or the Tamhane test if the values of the measured clinical parameters were not normally distributed. A p value < 0.05 was required for statistical significance. Results are expressed as mean ± SD.

Results

Clinical and procedural characteristics. Table I shows the clinical characteristics of the study population. At the time of admission to the catheterization laboratory, the majority of patients (94%) were in Killip class I or II, whereas 6 patients (6%) were in Killip class III or IV: 3 presented with acute pulmonary edema and 3 with cardiogenic shock necessitating the administration of inotropic agents and the insertion of an intra-aortic balloon pump. The mean time to revascularization was 5.07 ± 5.8 hours, being < 4 hours for the majority of patients (55.1%). The infarct location was anterior in 42 patients (47%), inferior in 42 (47%), and lateral in 6 patients (6%).

D-PTCA was successful in all patients and none died in the catheterization laboratory or during hospitalization. Table II shows the procedural and angiographic data including the IRA, coronary disease ex-

Table I. Patient characteristics.

No. patients	90
Age (years)	61 ± 13
Sex	
Women	22 (24%)
Men	68 (76%)
Current smokers	51 (56%)
Arterial hypertension	42 (46%)
Family history	31 (34%)
Hypercholesterolemia	30 (33%)
Diabetes mellitus	13 (14%)
Previous unstable angina	24 (26%)
Previous stable angina	16 (18%)
Previous AMI	7 (8%)
AMI location	
Anterior	42 (47%)
Lateral	6 (6%)
Inferior	42 (47%)
Time to revascularization (hours)	5.07 ± 5.8
0-2	5 (5%)
2-4	43 (48%)
4-6	7 (19%)
6-12	20 (22%)
> 12	5 (6%)
Killip class before intervention	
I	72 (81%)
II	12 (13%)
III	3 (3%)
IV	3 (3%)

AMI = acute myocardial infarction.

Table II. Procedural data.

Infarct-related artery	
Left anterior descending artery	42 (47%)
Circumflex artery	16 (18%)
Right coronary artery	32 (35%)
No. coronary arteries with > 75% stenosis	
1	39 (43%)
2	29 (32%)
3	22 (25%)
PTCA with stent	89 (99%)
Angiojet system	1 (1%)
Patients treated with GP IIb/IIIa inhibitors	56 (62%)
Abciximab	28 (31%)
Tirofiban	27 (30%)
Eptifibatide	1 (1%)
Left ventricular ejection fraction < 45%	27 (30%)
Average duration of PTCA (min)	54 ± 9
Successful PTCA	90 (100%)
TIMI flow before the procedure	
3	2 (2%)
2	7 (8%)
0-1	81 (90%)
TIMI flow after the procedure	
3	89 (99%)
2	1 (1%)
1	0
Mortality during PTCA	0
Hospital mortality	0

GP = glycoprotein; PTCA = percutaneous transluminal coronary angioplasty.

tension, and ejection fraction. Twenty-four percent of patients had three-vessel disease and ejection fraction was < 45% in 27 patients (30%).

One or more stents were implanted in 89 patients (99%), and 56 patients (62%) received glycoprotein IIb/IIIa inhibitors in the catheterization laboratory. No differences were observed in the timing and incidence of arrhythmias on the Holter recordings of patients who received glycoprotein IIb/IIIa inhibitors compared to those who did not.

During D-PTCA (Table III), immediately after the reopening of the IRA by means of a guidewire or balloon inflation, bradyarrhythmias were recorded in 11.1% of patients and complete atrioventricular block requiring temporary pacemaker insertion in 8.8%. Six patients out of 90 (6.6%) developed ventricular fibrillation (VF) during D-PTCA immediately after the reopening of the IRA and were successfully treated by DC-shock.

Complete atrioventricular blocks and VF were detectable only in patients with inferior AMI. Both brady- and tachyarrhythmias occurred exclusively in patients who were in Killip class I.

Clinical course during the 24 hours following direct percutaneous transluminal coronary angioplasty. Figures 1 and 2 show the incidence of arrhythmias during D-PTCA and during the following 24 hours. The occurrence of both brady- and tachyarrhythmias significantly declined after D-PTCA. All complete atrioven-

Table III. Arrhythmias during percutaneous transluminal coronary angioplasty and acute myocardial infarction (AMI) location.

Bradyarrhythmias	
All	10 (11%)
CAVB	8 (9%)
Bradycardia < 50 b/min	2 (2%)
Anterior or lateral AMI with CAVB	0
Inferior AMI with CAVB	8 (19%)
Tachyarrhythmias	
All	11 (12%)
VF	6 (7%)
Atrial fibrillation	5 (5%)
Anterior or lateral AMI with VF	0
Inferior AMI with VF	6 (14%)

CAVB = complete atrioventricular block; VF = ventricular fibrillation.

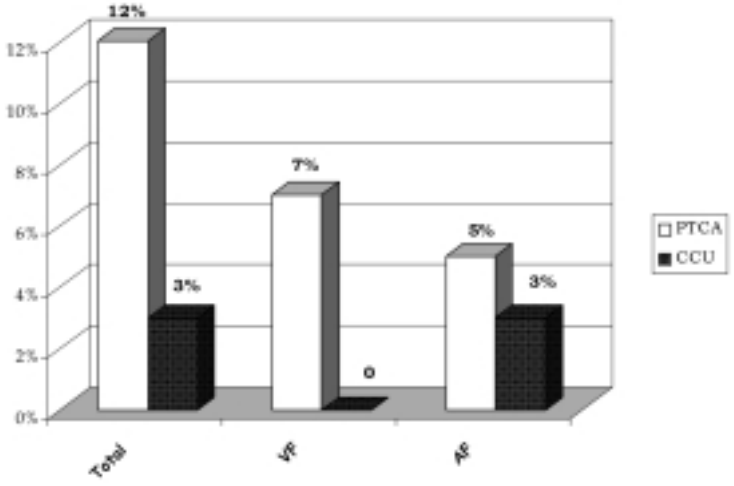

Figure 1. *The incidence of arrhythmias during direct percutaneous transluminal coronary angioplasty (PTCA) for the 90 patients included in the study. AF = atrial fibrillation; CCU = coronary care unit; VF = ventricular fibrillation.*

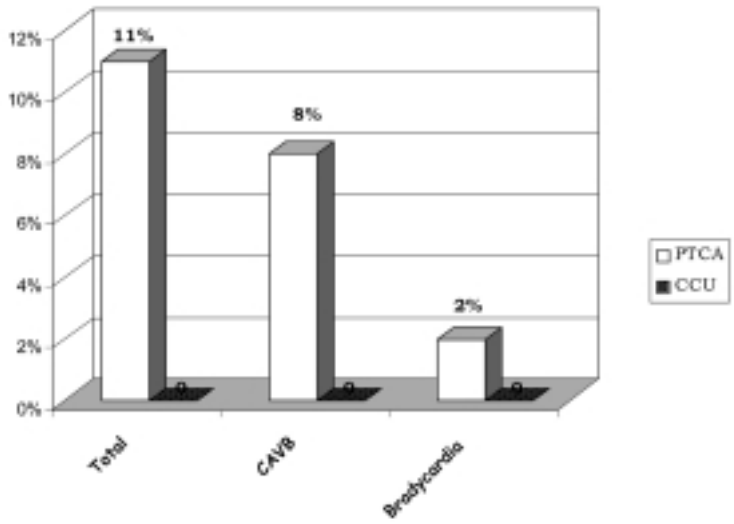

Figure 2. *The incidence of arrhythmias during the 24 hours following direct percutaneous transluminal coronary angioplasty (PTCA) for the 90 patients included in the study. CAVB = complete atrioventricular block; CCU = coronary care unit.*

tricular blocks resolved in the catheterization laboratory before the end of the procedure and no patient presented with VF or sustained ventricular tachycardia after the reopening of the IRA.

During the first 24 hours following D-PTCA (Holter monitoring) 14 patients were placed on beta-blockers (15.5%) and 7 patients on amiodarone (7.7%) because of paroxysmal atrial fibrillation. No significant differences in the incidence of bradyarrhythmias (0.6 ± 0.03 vs 0.8 ± 0.05, p = NS) and ventricular arrhythmias (≥ 3 beats 1.1 ± 0.7 vs 0.9 ± 0.8, p = NS) were found between the patients who were on amiodarone or beta-blockers and those who were not.

Eight patients (8.8%) developed complications in the CCU: 3 subjects (3.3%) treated with glycoprotein IIb/IIIa inhibitors presented with a major cardiovascular event (one cardiac tamponade, successfully treated with pericardiocentesis and one hemoperitoneum treated with blood transfusion). One patient, submitted to intra-aortic counterpulsation, presented with a common iliac artery thrombosis, successfully treated with rheolytic thrombectomy performed using the Angiojet system (Possis, Minneapolis, MN, USA). Five patients (5.5%) presented with minor bleeding at the site of the femoral artery puncture. No reocclusions and no ischemic recurrences were observed.

Twenty-four-hour Holter monitoring. Five patients were in atrial fibrillation, while 85 were in sinus rhythm. Table IV shows the incidence of ventricular arrhythmias recorded at 24-hour Holter monitoring: most patients (53%) had isolated, monomorphic ventricular extrasystoles, while Lown IVa arrhythmias were documented in 23/90 (26%) patients and Lown IVb arrhythmias in 19/90 (21%).

However, the patients included in Lown class IVb had only short runs of ventricular extrasystoles (4 to 6 beats in 9 patients, from 6 to 8 beats in 8 patients, and 9 beats in 2 patients). Besides, ventricular tachyarrhythmias, such as runs of more than 3 extrasystoles, were observed exclusively during the first 8 hours after D-PTCA (Fig. 3). No bradyarrhythmias were detected at 24-hour Holter monitoring.

Table IV. Ventricular tachyarrhythmias during coronary care unit stay.

Lown class	
I-III	48 (53%)
IVa	23 (26%)
IVb	19 (21%)
No. repetitive ventricular complexes in patients with class IVb arrhythmias (n=19)	
4-6	9 (48%)
6-8	8 (42%)
9	2 (10%)

Non-parametric test and ANOVA post-test result analysis. The infarct location significantly correlated with the incidence of brady- and tachyarrhythmias which were more frequent in case of inferior AMI (p = 0.004 and p = 0.047, respectively) than for anterior or lateral AMI.

The IRA significantly correlated with the CPK levels (p = 0.048) and with ejection fraction (p = 0.021): in particular, left anterior descending artery occlusion was associated with higher peak serum CPK levels and with a lower ejection fraction. The number of diseased vessels did not influence any of the variables considered.

The brady- and tachyarrhythmias detected at 24-hour Holter monitoring after D-PTCA did not show any correlation with the arrhythmias observed in the catheterization laboratory, with the IRA, with the time to reperfusion, and with ejection fraction.

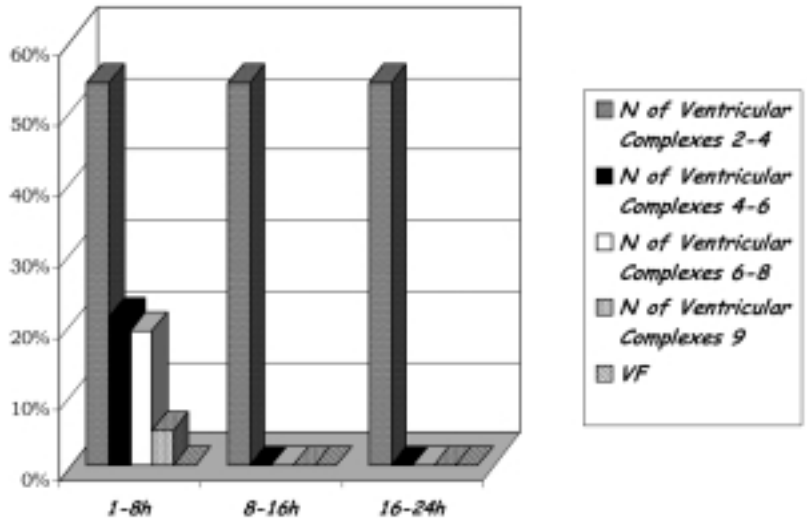

Figure 3. *The temporal distribution of arrhythmias during the 24 hours following direct percutaneous transluminal coronary angioplasty for the 90 patients included in the study. VF = ventricular fibrillation.*

Discussion

In our study group AMI patients submitted to successful reopening of the IRA by means of D-PTCA did not present with any life-threatening arrhythmias during hospitalization. VF and complete atrioventricular block occurred exclusively during D-PTCA and both resolved in the catheterization laboratory. Nevertheless, the Holter recordings showed that ventricular premature beats (isolated as well as short runs) were frequent throughout the 24 hours following D-PTCA, although their clinical relevance seemed limited. These findings deserve further consideration.

Arrhythmias during direct percutaneous transluminal coronary angioplasty. *Ventricular fibrillation.* The incidence of VF (6.6%) observed in the present study is consistent with that reported in previous studies on D-PTCA[1,2] and on thrombolysis[12,13], but the timing and the setting of this arrhythmia are peculiar. In fact, in our patients, this arrhythmia was observed only during the first hour of hospitalization and exclusively in the catheterization laboratory, immediately after the reopening of the IRA. This temporal distribution of VF suggests that the myocardial injury due to the faster reperfusion actively achieved by means of the mechanical reopening of the IRA can itself be responsible for VF. The link between VF and the restoration of blood flow after coronary occlusion has been previously described in several reports based on experimental models[12-17]. Reperfusion induces a rapid re-expansion of the extracellular compartment, the washout of the extracellular K^+ and H^+ and the recovery of excitability in the presence of persistent cellular uncoupling. The latter phenomenon contributes to the heterogeneity of electrical properties, to the slowing of impulse conduction, and the propagation of delayed afterdepolarizations and thus to the initiation of arrhythmias by a reentrant mechanism[12].

Moreover, it cannot be ruled out that the intracoronary injection of radiographic contrast agents[1], together with the intracoronary infusion of cold fluids (such as saline and medications)[16] that are themselves potentially arrhythmogenic, may have contributed to the development of VF in our patients.

In our study group, all patients who developed VF during D-PTCA showed a right coronary artery occlusion. In none of these patients was the infundibular artery cannulated. The relation between the right coronary artery and life-threatening arrhythmias has been described by Huang et al.[18] who documented a higher incidence of VF in patients without AMI undergoing PTCA of the right coronary artery. These authors concluded that the smaller caliber of the right coronary artery ostium may play an important role in the development of this arrhythmia. However, the reason(s) for the higher incidence of VF in patients with occlusion of the right coronary artery have so far not been completely understood.

Complete atrioventricular block. The incidence of complete atrioventricular block (8.8%) observed in our study group and its association with inferior AMI is consistent with what observed in previous reports on D-PTCA[1]. Interestingly, all complete atrioventricular blocks observed during the procedure resolved in the catheterization laboratory, within approximately 1 hour, without recurrences or *de novo* onsets during hospitalization. Complete atrioventricular block in the setting of inferior AMI is known to be due to hypoperfusion of the atrioventricular nodal artery and it usually involves the supra-Hissian atrioventricular junction[19]: in these patients, the transient nature of the complete atrioventricular block is probably due to the

relative resistance of the conduction system to ischemia.

Our data show that D-PTCA itself is able to shorten the duration of complete atrioventricular block, probably because it rapidly relieves the ischemic burden on the atrioventricular nodal junction[20]. Moreover, D-PTCA reduces the incidence of late-onset complete atrioventricular block by decreasing the incidence of ischemic recurrences and of reocclusion of the IRA[4,5,21].

The complete resolution of atrioventricular blocks by the end of the procedure allows the early removal of temporary pacemakers in the catheterization laboratory, thereby possibly reducing the occurrence of in-hospital complications such as infections, ventricular perforation, and ventricular arrhythmias.

Life-threatening arrhythmias in the 24 hours following percutaneous transluminal coronary angioplasty and during hospital course. No life-threatening arrhythmias (such as sustained ventricular tachycardia and/or VF, or advanced bradyarrhythmias, such as complete atrioventricular blocks) were observed during the CCU stay neither in the few patients treated with beta-blockers or amiodarone nor in the remaining ones who were not on these agents.

It is conceivable that our patients showed a low arrhythmic risk profile after D-PTCA and at the time of admission to the CCU. In particular, they had overcome the risk of life-threatening arrhythmias due to both the acute ischemic event (that is the occlusion of the culprit artery at the onset of the AMI, mainly during the prehospital phase), and to reperfusion (that is the reopening of the IRA during the procedure in the catheterization laboratory). Moreover, because stents were implanted in most patients (89/90, 99%), and glycoprotein IIb/IIIa inhibitors were administered to 56/90 patients (62%), the risk of reocclusion could be considered low in agreement with previously reported data[6,22,23]. In particular, none of the patients included in our study presented with ischemic recurrences or reocclusion of the treated artery. Thus, a successful D-PTCA without reocclusion of the IRA and the absence of ischemic recurrences are the main factors accounting for the lack of life-threatening arrhythmias occurring in the CCU in our population.

Therefore, our data suggest that D-PTCA, systematically performed in all patients with AMI in accordance with the policy at our institution, is able to modify both the clinical characteristics of subjects admitted to CCUs and, consequently, the "daily work" of these units. In fact, intensive CCUs were instituted in the early '60s in order to reduce the cardiac mortality of patients with AMI by preventing and treating VF[24]. The results of the present investigation strongly suggest that the use of D-PTCA in patients with AMI renders arrhythmic and ischemic complications a rare event, whereas other clinical problems, such as hemorrhagic and vascular events, may still occur[1,22,23].

Arrhythmias recorded at 24-hour Holter monitoring. Following D-PTCA, 21% of patients presented with class IVb ventricular arrhythmias, which showed a peculiar temporal distribution. While couples of ventricular extrasystoles were detectable throughout the whole recording period, runs of ventricular extrasystoles (> 3 beats) were observed only during the first 8 hours after the procedure. Besides, no patient presented with long runs[8] of ventricular extrasystoles (> 10 beats), and sequences of repetitive ventricular beats (< 10 beats) did not affect the patient's clinical course and early outcome. This finding strongly suggests that the pro-arrhythmic effect of reperfusion is limited in time (to a few hours after the procedure) probably because the restoration of an effective blood flow progressively reduces the reperfusion injury. This temporal distribution of class IVb ventricular arrhythmias could make do that a shorter period (12 hours) of cardiac rhythm monitoring is necessary after a successful D-PTCA thus allowing for early discharge from the CCU. Moreover, this finding suggests that patients referred from hospitals where D-PTCA is not available may be safely transferred back within a few hours, with a low arrhythmic risk profile[25].

Few data are available on the incidence and prognostic significance of non-sustained ventricular tachycardia in patients submitted to D-PTCA. In the prethrombolytic era, non-sustained ventricular tachycardia was related to an increased late mortality[26,27]. However, the prognostic value of non-sustained ventricular tachycardia was questioned after the advent of fibrinolysis[28]. Recently Schwab et al.[8] observed, in Holter recordings performed 10-30 days after AMI treated with D-PTCA, that non-sustained ventricular tachycardia is not a predictor of the overall and cardiac mortality but that it is associated with arrhythmic morbidity at long-term follow-up. However, in previous reports[8,26-28] Holter monitoring was performed before discharge and not during the first 24 hours when the occurrence of an arrhythmia holds a different prognostic significance.

A possible limitation of the present paper is represented by the small number of patients included. For this reason, the relevance of our results cannot be established with certainty until further studies including larger cohorts of AMI patients submitted to D-PTCA are performed.

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