Cardiac death and heart failure following primary angioplasty in extensive myocardial infarction: incremental prognostic value of clinical, functional and angiographic data

Elena Corrada, Riccardo Bigi*, Paola Colombo, Irene Bossi, Anna Maria De Biase, Antonio Mafrici, Oberdan Parodi*, Silvio Klugmann

*Cardiothoracic and Vascular Department "A. De Gasperis", *Institute of Clinical Physiology, National Research Council, Niguarda Ca' Granda Hospital, Milan, Italy*

Key words:
Angioplasty, primary; Heart failure; Myocardial infarction; Prognosis.

Background. **The incidence of late severe heart failure after primary angioplasty is not clear and few data are available about the clinical prognostic predictors of this event. The aims of our study were a) to evaluate the incidence of cardiac death and heart failure after an extensive acute myocardial infarction treated with primary angioplasty, and b) to identify, among clinical, ECG, functional, and angiographic variables, the outcome predictors and their incremental prognostic value.**

Methods. **Two hundred and thirty-three patients with ST-segment elevation in ≥ 4 leads, without cardiogenic shock, underwent primary angioplasty within 12 hours of symptom onset and were prospectively followed up for a median of 21 months for the combined endpoint of cardiac death and heart failure. The effects of clinical, ECG, functional, and angiographic data on the combined endpoint were evaluated using Cox's analysis. Separate models were developed including all variables of a given model plus significant variables of previous models to reproduce the usual clinical information flow.**

Results. **Twelve (5%) deaths and 23 (10%) heart failures occurred. Diabetes (hazard ratio [HR] 6.46, 95% confidence interval [CI] 1.99-20.98) and peak creatine kinase-MB (HR 1.002, 95% CI 1.001-1.004 per unit increment), wall motion score index (HR 1.46, 95% CI 0.35-6.15 per 0.1 unit increment), and TIMI flow grade < 3 after angioplasty (HR 5.35, 95% CI 2.04-14.02) were the only significant and independent prognostic indicators. ECG information did not improve the model, whilst functional and angiographic data provided incremental prognostic value over clinical information.**

Conclusions. **At mid-term follow-up, extensive acute myocardial infarction patients undergoing primary angioplasty have a moderate heart failure event rate. The integrated evaluation of data routinely available from diagnostic work-up allows accurate prediction of the outcome; functional and angiographic data provide incremental prognostic information over clinical and ECG variables.**

(Ital Heart J 2004; 5 (12): 912-918)

Received June 15, 2004; revision received October 22, 2004; accepted October 25, 2004.

Address:

Dr.ssa Elena Corrada

Via S. Mirocle, 9
20138 Milano
E-mail: elena.corrada@fastwebnet.it

In the last few years, primary percutaneous transluminal coronary angioplasty (PPTCA) has been increasingly used for the management of patients with ST-segment elevation acute myocardial infarction (AMI). At present, a large body of evidence demonstrates its superiority to systemic thrombolysis in reducing the incidence of mortality, non-fatal reinfarction, recurrent ischemia, need for revascularization and stroke[1-3]. However, heart failure (HF) still remains the most important cause of death following an extensive AMI[4,5]. Although the theoretical concept of a more effective myocardial salvage in patients undergoing PPTCA supports the presumption of a better preserved left ventricular function over time, the occurrence of HF in these patients has not been extensively evaluated in prognostic studies. Thus, the effectiveness of PPTCA in reducing the overall event rate related to extensive myocardial damage is not well defined. Moreover, few data are available about the prognostic value of the integrated evaluation of the clinical, ECG, functional and angiographic variables routinely obtainable from the usual diagnostic work-up, and about their incremental power in predicting the adverse outcome.

The aim of this study was 2-fold: 1) to assess the timing and incidence of cardiac death and acute HF in patients with extensive AMI (≥ 4 leads involved) undergoing PPTCA; 2) to identify, among the more common and easily obtainable clinical, ECG, functional, and angiographic variables, the most powerful predictors of the combined endpoint of death and acute HF and to evaluate their incremental prognostic value.

Methods

Patient population. The initial study population of 720 patients consecutively admitted to our Department from January 1999 to June 2001 with an established diagnosis of ST-segment elevation AMI[6] was considered for inclusion using the following criteria: a) typical characteristics of extensive AMI, identified by ST-segment elevation in ≥ 4 leads on the admission ECG)[7]; b) PPTCA performed within 12 hours of symptom onset; c) no cardiogenic shock; d) no severe comorbidity (valvular or congenital heart disease, malignancy, severe hepatic or renal failure, coagulation disorders).

On the basis of these criteria, 233 patients (32%) were included in the study and underwent prospective follow-up.

Coronary angiography and percutaneous transluminal coronary angioplasty. Coronary angiography was performed in accordance with standard acquisition guidelines. Multivessel disease was defined as ≥ 50% stenosis in ≥ 2 major epicardial vessels. The blood flow to the culprit vessel was evaluated and scored using the Thrombolysis in Myocardial Infarction (TIMI) flow grading scale[8].

PPTCA was performed with the conventional technique, and coronary stents were used without restrictions. The infarct-related artery was the only target of the procedure; however, further procedures were performed in case of severe proximal lesions. The decision to administer platelet glycoprotein IIb/IIIa receptor inhibitors was taken by the treating cardiologist. Intraaortic counterpulsation was performed in case of hemodynamic instability.

Electrocardiographic and echocardiographic examination. Standard 12-lead ECG was recorded in the emergency room and 90 min after PPTCA. AMI was classified as anterior, lateral and inferior accordingly. QRS distorsion was defined as a J point ≥ 50% R-wave voltage in leads with a QR pattern or as the absence of the S-wave in leads with an RS pattern[9]. Post-PPTCA ST-segment resolution was defined as a reduction > 50% in the summative ST-segment elevation in comparison with the basal ECG[10].

Standard echocardiographic images were obtained at the time of admission. Left ventricular volumes were derived using the Simpson's rule. For semiquantitative assessment, the left ventricular wall was divided into 16 segments[11] and scored using a 4-point scale (where 1 = normal, 2 = hypokinetic, 3 = akinetic, and 4 = dyskinetic); a wall motion score index, representing the ratio between the sum of the scores and the number of visualized segments, was calculated.

Follow-up. Follow-up information was obtained by prospectively determined visits at our outpatient clinic, from discharge reports of other hospitals in case of emergency admission and by telephone interview with the patient, his/her close relative or referring physician. The study combined endpoints were cardiac death and acute HF requiring new hospital admission and defined as systemic volume-overload HF, acute pulmonary edema, and low-output HF syndrome[12]. Death was defined as cardiac if strictly related to proven cardiac causes (fatal reinfarction, acute HF or malignant arrhythmias) or if sudden and unexpected when occurring outside the hospital. Patients undergoing revascularization were censored at the time of the procedure.

Statistical analysis. Continuous variables are expressed as means ± SD and categorical variables as percentages. Differences between the groups with and without the combined endpoint were compared using the Student's t-test or χ^2 test, as appropriate. The effects of clinical (age, history of diabetes, hypertension, coronary artery disease, prodromic syndrome, leukocyte count, heart rate and Killip class on admission, and symptom-to-hospital time), ECG (AMI location, number of ST-segment elevation leads, maximal ST-segment elevation, QRS distorsion, resolution of ST-segment elevation), functional (peak creatine kinase-MB mass, and echocardiographic left ventricular volumes, wall motion score index and ejection fraction), angiographic (multivessel disease, pre- [0 vs 1-3] and post- [0-2 vs 3] PTCA TIMI flow grade), and procedural (use of platelet glycoprotein IIb/IIIa receptor inhibitors, stenting, symptom-to-balloon time) variables on the combined endpoint were evaluated using Cox's proportional-hazard regression analysis according to a stepwise forward procedure[13]. Four separate prognostic models were developed including clinical, ECG, functional and angiographic plus procedural variables respectively. Cox's analysis was performed with all variables of a given model plus all variables from the antecedent model identified as independent, with each model reflecting the total accumulation of information available to the clinician at that point. At each step a significance of 0.1 was required for the variable to be entered into the model. The χ^2 value was calculated from the log likelihood ratio. A significant increase in the global χ^2 value of the model after the addition of further variables indicated an incremental prognostic value.

The area under the receiver-operating-characteristic curve method[14] was used to select the cut-off value of the continuous variables providing the most accurate prediction of event-free survival.

The log-rank test was used to compare the Kaplan-Meier event-free survival curves. Statistical significance was settled at a p value < 0.05. The SPSS statistical package (release 10.0 for Microsoft Windows, SPSS Inc., Chicago, IL, USA) was used.

Results

Baseline characteristics. The principal clinical, ECG, functional, and angiographic data of the study population are shown in table I.

Follow-up. Follow-up information (Table II) was available for 230/233 (99%) patients. During a median follow-up of 21 months (range 0-40 months, interquartile range 16-30 months), the combined endpoint of death and acute HF was observed in 33 (14%) patients. In particular, 12 (5%) died and 23 (10%) were hospitalized because of acute HF (systemic volume-overload HF in 11, acute pulmonary edema in 10, and low-output HF syndrome in 2 patients). Among the latter, 2 died.

Death occurred during the initial hospitalization in 6 (50%) and after discharge in the remaining 6 patients; in 9 of 12 (75%) cases it occurred within 6 months of the index acute event. Causes of death were cardiogenic shock (6 patients, 50%), low-output HF syndrome necessitating hospitalization (2 cases, 17%) and sudden death (4 patients, 33%).

HF occurred during the first 6 months in 15 (65%) and after the first year in the remaining 8 (35%) patients.

Table I. Baseline characteristics of the patient population.

Age (years)	59 ± 12
Age > 75 years	24 (10%)
Sex (M/F)	185 (79%)/48 (21%)
Diabetes	36 (15%)
Hypertension	103 (44%)
Prior myocardial infarction	36 (15%)
Prior coronary artery bypass graft	8 (3%)
Prior PTCA	19 (8%)
Anterior AMI location	161 (69%)
Killip class 2-3	45 (19%)
No. leads with ST-segment elevation	5.2 ± 1.7
Post-PTCA resolution of ST-segment elevation > 50%	165 (71%)
Symptom-to-admission time (min)	144 ± 167
Symptom-to-balloon time (min)	272 ± 185
Multivessel coronary disease	118 (51%)
Left ventricular ejection fraction (%)	42.9 ± 9.7

AMI = acute myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty.

Table II. Clinical follow-up (median 21 months).

Follow-up completed	230 (99%)
Combined endpoint	33 (14%)
Death	12 (5%)
During hospitalization	6 (2.5%)
During follow-up	6 (2.5%)
Acute heart failure	23 (10%)
Reinfarction	10 (4%)
Target vessel revascularization	36 (15%)

Death or HF was associated with reinfarction in 6 (18%) cases. In addition, among the patients without the endpoint, 4 (2%) presented with non-fatal reinfarction and 36 (15%) underwent revascularization procedures (bypass surgery in 5, angioplasty in 26 and both in 5).

Outcome prediction and survival analysis. The patients with and without the combined endpoint of death and acute HF differed with regard to age, diabetes history, anterior infarct location, heart rate, and Killip class > 1 on admission, peak creatine kinase-MB level, left ventricular volumes, ejection fraction and wall motion score index, symptom-to-balloon time > 4 hours, and post-PTCA TIMI flow grade < 3 (Table III).

However, after adjusting for the most significant covariate, diabetes (hazard ratio [HR] 6.46, 95% confidence interval [CI] 1.99-20.98), peak creatine kinase-MB levels (HR 1.0021, 95% CI 1.001-1.004 per unit increment), wall motion score index (HR 1.46, 95% CI 0.35-6.15 per 0.1 unit increment), and final TIMI flow < 3 (HR 5.35, 95% CI 2.04-14.02) were the only independent predictors of outcome at multivariate analysis (Table IV).

Receiver-operating-characteristic curve analysis indicated 289 μg/l and 1.94 as the cut-off values of creatine kinase-MB levels and wall motion score index as being predictive of the cumulative endpoint of death and acute HF with the best sensitivity and specificity (sensitivity 59 and 72%, specificity 73 and 71% respectively).

The relative power of the four prognostic models in predicting outcome is shown in figure 1: the addition of the ECG to the clinical variables did not significantly add power, whilst the functional and angiographic variables provided an incremental prognostic value (χ^2 increment +71 and +108%, respectively).

The overall and event-free survival in the study population is reported in figure 2. In addition, the event-free survival according to the multivariate predictors of outcome is reported in figure 3. Clinical, functional and angiographic data may help to distinguish low-risk subjects, who have an excellent event-free survival, from those at higher risk.

Discussion

The results of this study demonstrate that at the medium-term follow-up patients with an extensive AMI and no cardiogenic shock undergoing PPTCA have a low cardiac mortality and a moderate incidence of rehospitalization because of acute HF. Diabetes, the markers of extensive necrosis and functional impairment, and a postprocedural TIMI flow < 3 in the infarct-related vessel are independent predictors of the combined endpoint of death and HF in these patients. Finally, functional and angiographic data provide in-

Table III. Characteristics of the patients with and without events at follow-up.

	Events (n=33)	No events (n=200)	p
Clinical variables			
Age (years)	63.3 ± 12.1	58.1 ± 12.1	< 0.05
Age > 75 years	7 (21%)	17 (8%)	NS
Female sex	8 (24%)	40 (20%)	NS
Diabetes	10 (30%)	26 (13%)	< 0.05
Hypertension	14 (42%)	89 (45%)	NS
Prodromic syndrome	15 (45%)	70 (35%)	NS
Previous AMI	5 (15%)	31 (15%)	NS
Previous coronary artery bypass graft	1 (3%)	7 (4%)	NS
Heart rate on admission (b/min)	90 ± 17	78 ± 16	< 0.001
Killip class > 1	15 (45%)	30 (15%)	< 0.001
Leukocyte count	12 383 ± 4744	11 644 ± 4403	NS
Symptom-to-admission time (min)	195 ± 158	136 ± 198	NS
ECG variables			
Anterior AMI	28 (85%)	133 (67%)	< 0.05
No. ST-segment elevation leads	5.8 ± 1.9	5.1 ± 1.7	NS
Maximal ST-segment elevation (mm)	6.2 ± 3.8	5.5 ± 3.2	NS
QRS distorsion on the admission ECG	17 (57%)	74 (39%)	NS
Post-PTCA resolution ST-segment elevation > 50%	21 (63%)	144 (72%)	NS
Functional variables			
Wall motion score index	2.1 ± 0.4	1.8 ± 0.3	< 0.0001
Left ventricular end-diastolic volume (ml)	123 ± 39	105 ± 29	< 0.02
Left ventricular end-systolic volume (ml)	80 ± 33	59 ± 22	< 0.0005
Left ventricular ejection fraction (%)	37.4 ± 9.1	44 ± 9	< 0.0005
Peak creatine kinase-MB (μg/l)	431 ± 366	264 ± 296	< 0.01
Angiographic and procedural variables			
Multivessel disease	20 (60%)	98 (49%)	NS
Pre-PTCA TIMI flow grade 0	25 (81%)	142 (72%)	NS
Post-PTCA TIMI flow grade < 3	16 (53%)	40 (20%)	< 0.0005
Symptom-to-balloon time (min)	345 ± 204	261 ± 181	< 0.05
Symptom-to-balloon time > 4 hours	19 (59%)	72 (36%)	< 0.05
Stenting	27 (83%)	182 (91%)	NS
Platelet glycoprotein IIb/IIIa inhibitors	17 (52%)	136 (68%)	NS

AMI = acute myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty.

Table IV. Significant outcome predictors at multivariate analysis.

	HR (95% CI for OR)	p
Diabetes	6.46 (1.99-20.98)	0.002
Peak CK-MB	1.0021* (1.001-1.004)	0.001
WMSI	1.46** (0.35-6.15)	0.001
Final TIMI flow < 3	5.35 (2.04-14.02)	0.001

CI = confidence interval; CK = creatine kinase; HR = hazard ratio; OR = odds ratio; WMSI = wall motion score index. * per unit increment; ** per 0.1 unit increment.

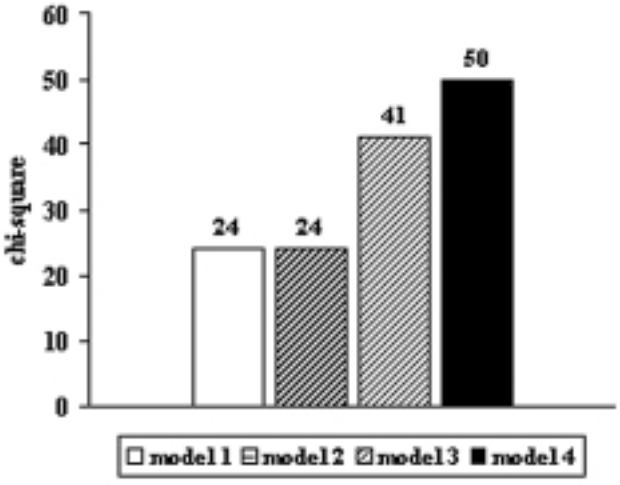

Figure 1. *Global χ^2 analysis of the four prognostic models. The addition of functional and angiographic variables adds incremental prognostic value (χ^2 increases 71 and 108%, respectively).*

cremental prognostic information over clinical and ECG variables.

Comparison with previous studies. An overall mortality ranging from 6.2 to 12.6% has been reported in studies with 1- to 3-year follow-up after PPTCA[15-17]. In keeping with the results of the majority of previous studies, even in the present study the mortality rate was

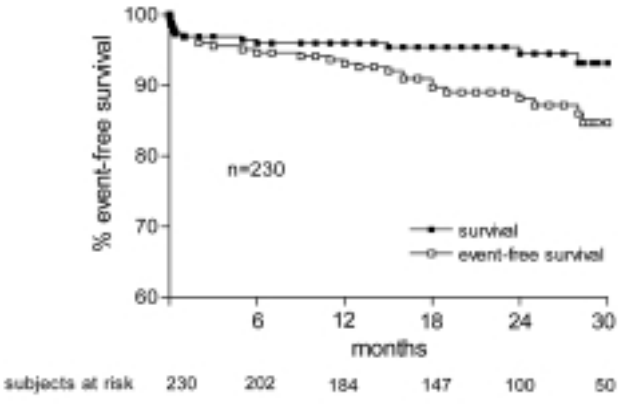

Figure 2. *Overall and event-free survival in the study population.*

low. On the other hand, comparison is more difficult when dealing with HF, due to relevant differences in terms of the population characteristics, endpoint definition and treatment. HF after myocardial infarction is reported to occur in 14 to 51% of patients and to be associated with up to a 5-fold increase in the 1-year mortality following AMI[4]. Generally, it is secondary to recurrent ischemia or reinfarction and/or extensive left ventricular dysfunction. PPTCA proved to achieve a relevant reduction in the incidence of reinfarction[1-3] and a greater myocardial salvage[18-21] as compared to systemic thrombolysis. Therefore, it is expected to assure a better preservation of the left ventricular function over time. However, the occurrence of HF has been underscored in prognostic studies addressing the use of PPTCA. Bolognese et al.[21,22] recently reported a 7-8% cardiac mortality and a 5% rehospitalization rate due to HF during a 5-year follow-up after PPTCA. Zijlstra et al.[23] found a lower 5-year mortality (13 vs 24%) and HF (7 vs 20%) rate among patients undergoing PPTCA as compared to those receiving intravenous streptokinase. In the study by Waldecker et al.[24] 5% of patients died of cardiac causes whilst 1.5% of them were in NYHA class IV within 3 years of PPTCA. However, only Bolognese considered HF as a primary endpoint.

Different clinical, functional and angiographic prognostic indicators were identified in previous studies addressing PPTCA[15-17,21-26]. Bolognese et al.[21,22] found age, left ventricular end-diastolic volume and microvascular dysfunction as being predictive of the long-term cumulative endpoint of death, HF and reinfarction. Other studies, where only subgroups of patients had undergone PPTCA, identified age, female gender, diabetes, hypertension, history of coronary artery disease, anterior AMI, left bundle branch block, peak creatine kinase-MB levels, heart rate on admission, and a reduced ejection fraction as being predictive of HF[4,5,27].

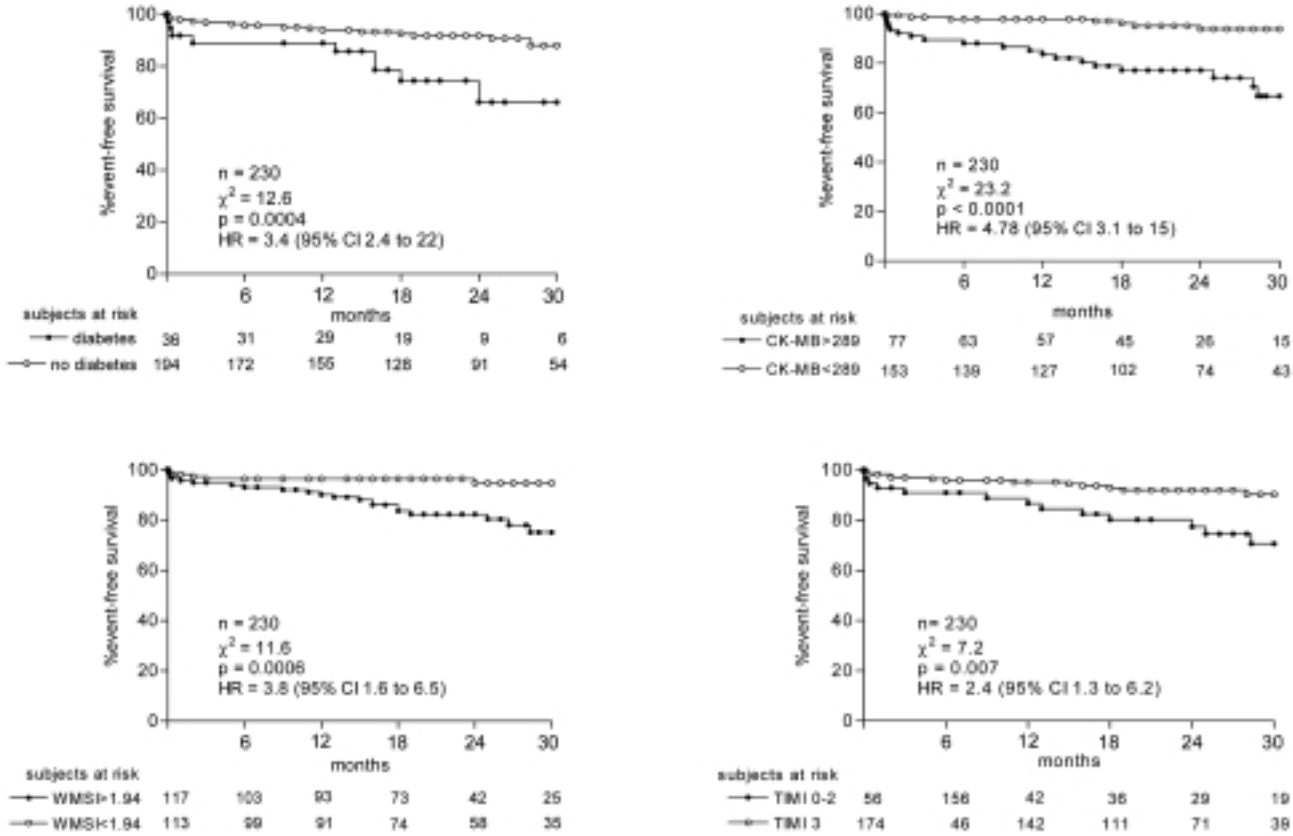

Figure 3. *Event-free survival according to the multivariate predictors of outcome. CI = confidence interval; CK = creatine kinase; HR = hazard ratio; WMSI = wall motion score index.*

However, important methodological differences among these studies render them difficult to compare. Distinguishing points of our study are the inclusion of patients with features of increased risk (such as an extensive AMI, a high prevalence of the anterior location and multivessel disease, a late presentation, and a suboptimal PPTCA result) but no cardiogenic shock at admission, a strict definition of HF (minimizing the likelihood of incorrect endpoint classification), and the frequent use of coronary stenting and platelet glycoprotein IIb/IIIa inhibitors. These issues are of pivotal importance in defining the clinical setting where the additional prognostic yield of PPTCA is expected to be most rewarding.

Outcome prediction. Diabetes, markers of myocardial and functional damage, and unsuccessful recanalization were independent predictors of outcome in this study, thus demonstrating an important prognostic interaction among the different and complementary features of the patient's profile. Moreover, the stepwise prognostic model allowed us to evaluate whether incremental information could be obtained by the addition of each individual block of variables. In particular, the addition of ECG data failed to improve the predictive capability of the model. Conversely, functional as well as angiographic information was able to achieve further prognostic discrimination.

The fact that in the present study age was not an independent predictor of an adverse outcome is probably due to the low number of patients aged ≥ 75 years: the presence of severe comorbidities and a significant delay (> 12 hours) in hospital admission were the main reasons for exclusion from PPTCA at our Institution.

We found that ECG data did not have a significant prognostic power: this could be explained by our selection criteria that included only patients with ST-segment elevation in ≥ 4 leads, by the possible underevaluation of ST-segment elevation resolution in patients with a longer symptom-to-balloon time and by the definition of ST-segment resolution (resolution > 50%).

In our study, the symptom-to-balloon time was not an independent outcome predictor; we believe that this was probably due to the stronger prognostic power conveyed by different but related variables, such as markers of myocardial necrosis and functional damage.

In conclusion, despite an acceptably low early and late cardiac mortality, patients with an extensive AMI undergoing PPTCA have a not negligible incidence of acute HF during follow-up. An early integrated evaluation of clinical, functional and angiographic data may permit us to distinguish low-risk subjects (who have an excellent event-free survival), from those at higher risk, for whom close follow-up surveillance, continuous optimization and titration of the pharmacological treatment and/or alternative therapies and revascularization strategies are warranted.

References

1. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. Lancet 2003; 361: 13-20.
2. Weaver WD, Simes RJ, Betriu A, et al. Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review. JAMA 1997; 278: 2093-8.
3. Zahn R, Schiele R, Schneider S, et al, for the Maximal Individual Therapy in Acute Myocardial Infarction (MITRA) and the Myocardial Infarction Registry (MIR) Study Groups. Primary angioplasty versus intravenous thrombolysis in acute myocardial infarction: can we define subgroups of patients benefiting most from primary angioplasty? J Am Coll Cardiol 2001; 37: 1827-35.
4. Hellermann JP, Jacobsen SJ, Gersh BJ, Rodeheffer RJ, Reeder GS, Roger VL. Heart failure after myocardial infarction: a review. Am J Med 2002; 13: 324-30.
5. Spencer FA, Meyer TE, Gore JM, Goldberg RJ. Heterogeneity in the management and outcomes of patients with acute myocardial infarction complicated by heart failure: the National Registry of Myocardial Infarction. Circulation 2002; 105: 2605-10.
6. Gillum RF, Fortmann SP, Prineas RJ, Kottke TE. International diagnostic criteria for acute myocardial infarction and acute stroke. Am Heart J 1984; 108: 150-8.
7. Mauri F, Franzosi MG, Maggioni AP, Santoro E, Santoro L. Clinical value of 12-lead electrocardiography to predict the long-term prognosis of GISSI-1 patients. J Am Coll Cardiol 2002; 39: 1594-600.
8. The Thrombolysis in Myocardial Infarction (TIMI) trial: phase I findings. The TIMI Study Group. N Engl J Med 1985; 312: 932-6.
9. Birnbaum Y, Herz I, Scalovsky S, et al. Prognostic significance of the admission electrocardiogram in acute myocardial infarction. J Am Coll Cardiol 1996; 27: 1128-32.
10. de Lemos JA, Braunwald E. ST segment resolution as a tool for assessing the efficacy of reperfusion therapy. J Am Coll Cardiol 2001; 38: 1283-94.
11. Schiller NB, Shah PM, Crawford M, and the American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. J Am Soc Echocardiogr 1989; 2: 358-67.
12. Felker GM, Adams KF, Konstam MA, O'Connor CM, Gheorghiade M. The problem of decompensated heart failure: nomenclature, classification, and risk stratification. Am Heart J 2003; 145 (Suppl): S18-S25.
13. Cox DR. Regression model and life tables. J R Statist Soc Series B 1972; 34: 187-220.
14. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology 1982; 143: 29-36.
15. Hannan EL, Racz MJ, Arani DT, Ryan TJ, Walford G, McCallister BD. Short and long-term mortality for patients undergoing primary angioplasty for acute myocardial infarction. J Am Coll Cardiol 2000; 36: 1194-201.
16. Shihara M, Tsutsui H, Tsuchihashi M, Tada H, Kono S, Takeshita A, for the Japanese Coronary Intervention Study (JCIS) Group. In hospital and one-year outcomes for patients undergoing percutaneous coronary intervention for acute myocardial infarction. Am J Cardiol 2002; 90: 932-6.
17. Nunn CM, O'Neill WW, Rothbaum D, et al, for the Primary Angioplasty in Myocardial Infarction I Study Group.

Long-term outcome after primary angioplasty: report from the Primary Angioplasty in Myocardial Infarction (PAMI-I) trial. J Am Coll Cardiol 1999; 33: 640-6.
18. de Boer MJ, Suryapranata H, Hoorntje JC, et al. Limitation of infarct size and preservation of left ventricular function after primary coronary angioplasty compared with intravenous streptokinase in acute myocardial infarction. Circulation 1994; 90: 753-61.
19. Sheiban I, Fragasso G, Rosano GM, et al. Time course and determinants of left ventricular function recovery after primary angioplasty in patients with acute myocardial infarction. J Am Coll Cardiol 2001; 38: 464-71.
20. Ottervanger JP, van't Hof AW, Reiffers S, et al. Long-term recovery of left ventricular ejection fraction after primary angioplasty for acute myocardial infarction. Eur Heart J 2001; 22: 785-90.
21. Bolognese L, Neskovic AN, Parodi G, et al. Left ventricular remodeling following primary coronary angioplasty: patterns of left ventricular dilation and long-term prognostic implications. Circulation 2002; 106: 2351-7.
22. Bolognese L, Carrabba N, Parodi G, et al. Impact of microvascular dysfunction on left ventricular remodeling and long-term clinical outcome after primary coronary angioplasty for acute myocardial infarction. Circulation 2004; 109: 1121-6.
23. Zijlstra F, Hoorntje JC, de Boer MJ, et al. Long-term benefit of primary angioplasty as compared with thrombolytic therapy for acute myocardial infarction. N Engl J Med 1999; 341: 1413-9.
24. Waldecker B, Waas W, Haberbosch W, Voss R, Heizmann H, Tillmanns H. Long-term follow-up after direct percutaneous transluminal coronary angioplasty for acute myocardial infarction. J Am Coll Cardiol 1998; 32: 1320-5.
25. Haager PK, Christott P, Heussen N, Lepper W, Hanrath P, Hoffmann R. Prediction of clinical outcome after mechanical revascularization in acute myocardial infarction by markers of myocardial reperfusion. J Am Coll Cardiol 2003; 41: 532-8.
26. De Luca G, van't Hof AW, de Boer MJ, et al. Impaired myocardial perfusion is a major explanation of the poor outcome observed in patients undergoing primary angioplasty for ST-segment-elevation myocardial infarction and signs of heart failure. Circulation 2004; 109: 958-61.
27. Ali AS, Rybicki BA, Alam M, et al. Clinical predictors of heart failure in patients with first acute myocardial infarction. Am Heart J 1999; 138: 1133-9.