

CARDIOVASCULAR MEDICINE

Five year outcome after primary coronary intervention for acute ST elevation myocardial infarction: results from a single centre experience

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Heart 2005;91:1541-1544. doi: 10.1136/hrt.2004.054692

Objectives: To analyse the five year outcome of unselected patients with acute myocardial infarction (AMI) treated by primary percutaneous coronary intervention (PCI).

Setting: High volume PCI tertiary centre.

Design and results: The study was based on a sample of 1009 consecutive patients with ST elevation AMI treated by primary PCI. The mean (SD) clinical follow up was 51 (21) months and the follow up rate was 97.8%. The overall mortality was 20% and cardiac mortality was 16%. Non-fatal reinfarction rate was 5% and additional revascularisation procedure rate was 19%. Hospitalisation for heart failure was needed by 42 patients (4%). The variables related to mortality in multivariate Cox analysis were age (hazard ratio (HR) 1.054, 95% confidence interval (CI) 1.039 to 1.069, $p < 0.0001$), cardiogenic shock (HR 2.985, 95% CI 2.157 to 4.129, $p < 0.0001$), previous myocardial infarction (HR 1.696, 95% CI 1.199 to 2.398, $p = 0.0003$), and the presence of multivessel coronary artery disease (HR 1.820, 95% CI 1.317 to 2.514, $p = 0.0003$). Each additional high risk feature was associated with a relative risk for five year death of 2.328 (95% CI 2.048 to 2.646, $p < 0.0001$).

Conclusions: The satisfactory results of routine mechanical revascularisation strategy in AMI were maintained during several years of follow up. Patients at risk of death during long term follow up may be identified by simple clinical and angiographic characteristics, such as old age, cardiogenic shock, previous myocardial infarction, and multivessel coronary artery disease. The risk of death progressively increases with the number of these high risk features.

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Accepted 17 January 2005
Published Online First
6 April 2005

Percutaneous coronary intervention (PCI) for acute myocardial infarction (AMI) is effective in decreasing mortality and adverse cardiac events.¹ Information focused on outcomes after primary PCI for AMI has increased in recent years.² However, most reported studies on long term outcome after primary PCI were based on small populations, selected cohorts, or short term follow up.³⁻⁹

The objective of this study was to analyse the five year clinical outcome of unselected patients with ST elevation AMI treated by primary PCI at a high volume PCI tertiary centre.

METHODS

Study patients

From January 1995 a routine policy of primary PCI for patients with ST elevation AMI was adopted at our institution, resulting in the treatment of more than 200 patients with ST elevation AMI a year. The population of the present study is based on 1009 consecutive patients with ST segment elevation AMI referred to our institution, within 12 hours of symptom onset, for emergency primary mechanical revascularisation from January 1995 to August 1999. Patient clinical and angiographic data were prospectively recorded and entered on to the database.

Definitions and outcome measures

Multivessel coronary artery disease (CAD) was defined as a visually assessed $\geq 70\%$ diameter stenosis of at least one major epicardial artery beyond the infarct related artery. Primary PCI success was defined as the restoration of TIMI (thrombolysis in myocardial infarction) flow grade 3 and a residual minimum stenosis $< 30\%$ at the end of the procedure. Cardiogenic shock was defined as systolic blood

pressure < 90 mm Hg for > 30 minutes (without positive inotropic agents or mechanical support) unresponsive to fluid replacement alone that was thought to be secondary to ventricular dysfunction and associated with signs of end organ hypoperfusion such as cold or diaphoretic extremities, altered mental status, or anuria.

All deaths were considered to be of cardiac origin unless a non-cardiac cause was established clinically or at necropsy. Reinfarction was defined as recurrent chest pain or the development of new ECG changes accompanied by a new rise in serum creatine kinase MB concentrations. Additional revascularisation procedures included PCI and coronary artery bypass surgery of the infarct related artery or the other coronary vessels. The diagnosis of heart failure was based on the presence of at least two of the following criteria: dyspnoea, bibasilar pulmonary rales, a third heart sound, or radiographic evidence of pulmonary congestion. After discharge from hospital, patients were referred to their private physician, who regulated treatment. All patients were asked to return to our outpatient clinic for evaluation by one of the investigators six months after discharge and annually thereafter. For those patients not returning to the clinic at the designated time follow up information was collected by telephone interview.

Statistical analysis

Continuous data are expressed as mean (SD). Baseline data were compared by means of the χ^2 test for categorical

Abbreviations: AMI, acute myocardial infarction; CAD, coronary artery disease; CI, confidence interval; HR, hazard ratio; MI, myocardial infarction; PCI, percutaneous coronary intervention; TIMI, thrombolysis in myocardial infarction

Table 1 Baseline clinical and angiographic characteristics of patients

	All (n = 1009)	Single vessel CAD (n = 511)	Multivessel CAD (n = 498)	p Value
Age (years)	63 (12)	61 (12)	65 (12)	<0.0001
Women	226 (23%)	109 (22%)	117 (23%)	0.449
Current smoking	410 (41%)	252 (49%)	158 (32%)	<0.0001
Hypertension	335 (33%)	170 (33%)	165 (33%)	0.771
Diabetes mellitus	145 (14%)	58 (11%)	87 (17%)	0.009
Cholesterolaemia >5.18 mmol/l	262 (26%)	135 (26%)	127 (26%)	0.619
Previous MI	120 (12%)	30 (6%)	90 (18%)	<0.0001
Previous PCI	31 (3%)	12 (2%)	19 (4%)	0.01
Previous bypass surgery	11 (1%)	0 (0%)	11 (2%)	0.01
Anterior infarction	525 (52%)	271 (53%)	254 (51%)	0.753
Cardiogenic shock	127 (13%)	43 (9%)	84 (17%)	<0.0001
Symptom to balloon time (min)	190 (138)	188 (95)	191 (149)	0.593
Chronic occlusion	115 (11%)	0 (0%)	115 (23%)	<0.0001
Infarct related artery				0.001
Left anterior descending	513 (51%)	273 (53%)	240 (48%)	
Right coronary	358 (35%)	174 (34%)	184 (37%)	
Circumflex	116 (11%)	59 (11%)	57 (11%)	
Left main trunk	11 (1%)	0 (0%)	11 (2%)	
Venous graft	6 (1%)	0 (0%)	6 (1%)	
TIMI flow grade 2–3	178 (18%)	91 (18%)	87 (17%)	0.854

Data are presented as mean (SD) or number (%) of patients.

CAD, coronary artery disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; TIMI, thrombolysis in myocardial infarction.

variables and unpaired *t* test for continuous variables. Survival curves were constructed by the Kaplan-Meier method and statistical differences between curves were assessed by the log rank test. Clinical and angiographic variables that were significantly different between survivors and non-survivors in the univariate model, as well as variables known to have prognostic value, were included in the Cox models for all cause mortality and cardiac mortality. A probability value of $p < 0.05$ was considered significant. Data were analysed by SPSS version 11.5 (SPSS Inc, Chicago, Illinois, USA).

RESULTS

Study population

Table 1 summarises baseline clinical and angiographic characteristics of the study patients. Overall, 498 (49%) patients had multivessel CAD. Patients with multivessel CAD were older and more often had diabetes, a previous myocardial infarction (MI), and previous revascularisation

procedures (table 1). The incidence of cardiogenic shock on admission was higher in patients with multivessel CAD than in patients with single vessel disease, despite no difference in peak creatine kinase concentrations (2496 (2299) U/l *v* 2480 (2168) U/l, $p = 0.964$).

Procedural results

Primary PCI success rate was 95%. Overall, 714 patients (71%) had infarct related artery stenting and 184 (18%) had multiple stent implantation. There were no differences in procedural success rate and stent use between patients with single vessel CAD and patients with multivessel CAD (96% *v* 94%, $p = 0.101$, and 74% *v* 70%, $p = 0.156$, respectively). Intra-aortic balloon pump was used in 130 patients (13%). The routine use of abciximab started in 1998, resulting in the administration of the drug to only 7% of the study population. Door to balloon time was 22 (15) minutes.

Long term outcome

Long term clinical follow up data were collected for all but 22 patients (follow up rate 97.8%). The mean duration of follow up was 51 (21) months (median 54 months). Overall

Table 2 Causes of death during long term follow up

Cardiac death	158 (78%)
HF	42 (21%)
Cardiogenic shock	33 (17%)
Reinfarction	22 (11%)
Sudden death	9 (4%)
Cardiac rupture	7 (3%)
Cardiac surgery	6 (3%)
Arrhythmias	2 (1%)
Unknown or undetermined	37 (18%)
Non-cardiac death	45 (22%)
Cancer	23 (11%)
Stroke	8 (4%)
Senile marasmus	4 (2%)
Pulmonary embolism	3 (1.5%)
COPD	1 (0.5%)
Aortic aneurysm rupture	1 (0.5%)
Sepsis	1 (0.5%)
Renal insufficiency	1 (0.5%)
Car accident	1 (0.5%)
Bowel infarct	1 (0.5%)
Systemic sclerosis	1 (0.5%)

Data are presented as number (%) of patients.

COPD, chronic obstructive pulmonary disease; HF, heart failure.

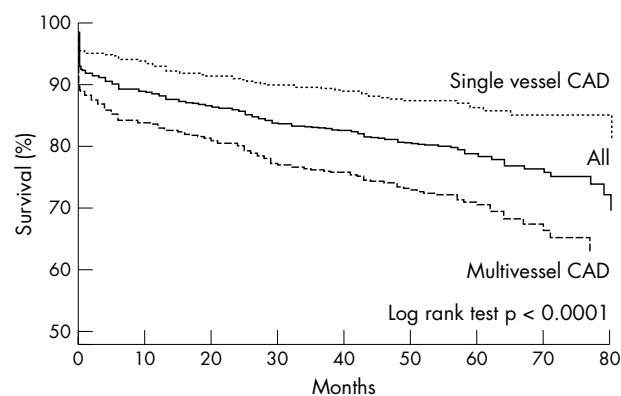


Figure 1 Kaplan-Meier survival curves for patients with single vessel (...) and multivessel coronary artery disease (CAD; ---), as well as for the overall study population (—).

Table 3 Predictors of all cause death and cardiac death

Predictor	HR (95% CI)	p Value
All cause death		
Age (years)	1.054 (1.039 to 1.069)	<0.00001
Cardiogenic shock	2.985 (2.157 to 4.129)	<0.00001
Multivessel CAD	1.820 (1.317 to 2.514)	0.0003
Previous MI	1.696 (1.199 to 2.398)	0.0003
Cardiac death		
Age (years)	1.052 (1.035 to 1.069)	<0.00001
Cardiogenic shock	3.822 (2.682 to 5.445)	<0.00001
Multivessel CAD	2.059 (1.404 to 3.019)	0.0002
Previous MI	1.921 (1.317 to 2.802)	0.0007

CI, confidence interval; HR, hazard ratio.

mortality was 20% and cardiac mortality was 16%. Table 2 summarises the causes of death. Of the 203 patients who died, one third (n = 68) died within the first 30 days after AMI (mainly in hospital). The remaining deaths occurred homogeneously over the subsequent follow up period. The annual mortality was 10.2% (6.4% within the first month) in the first year and 2.8%, 3.3%, 2.4%, 2.7%, and 4.3% in the subsequent years. Deaths of cardiac origin occurred earlier than non-cardiac deaths (mean time 15 (19) months v 36 (24) months, p < 0.0001). Annual cardiac death rate decreased during follow up: 9.3% (6.1% within the first month) in the first year and 2.4%, 2.1%, 1.5%, 1.8%, and 1.0% in the subsequent five years.

We observed a higher (but not significant) five year mortality among patients with a symptom to balloon time longer than three hours than among patients treated within three hours of symptom onset (22% v 19%, p = 0.136 by log rank). Moreover, symptom to balloon time was not independently related to long term survival in the multivariate Cox analysis.

Five year mortality was 52%, 33%, and 19% among patients with a final TIMI flow grade 0–1 (n = 21), 2 (n = 20), and 3 (n = 968), respectively (p = 0.0006 by log rank).

The non-fatal reinfarction rate was 5% and the rate of additional revascularisation procedures was 19%. Forty two patients (4%) required hospitalisation for heart failure.

Patients with multivessel CAD had higher rates of all cause mortality (28% v 12%, p < 0.0001), cardiac death (23% v 8%, p < 0.0001), revascularisation procedure (26% v 15%, p < 0.0001), and hospitalisation for heart failure (6% v 3%, p = 0.048) than did patients with single vessel disease. Non-fatal reinfarction rates were similar (6% v 5%, p = 0.700) between the two groups. Among patients with single vessel CAD, those with an anterior infarct location had a higher five year mortality (14% v 9%, p = 0.086) and rate of hospitalisation for heart failure (5% v 1%, p = 0.041) than did patients with an inferior infarct location. Figure 1 depicts long term survival curves for patients with single and multivessel CAD.

One month contrast left ventriculography (available for 779 of 941 eligible patients) showed lower left ventricular

ejection fraction in patients who presented with a previous MI at the time of the index infarction than in patients without (48.1 (16.9) v 54.6 (12.8), p = 0.0001). Five year mortality was 8.6% and 18.1% (p = 0.0001) in patients with a left ventricular ejection fraction ≥ 0.50 and < 0.50 at one month, respectively.

Multivariate Cox analysis identified the variables significantly related to mortality as age, cardiogenic shock, previous MI, and multivessel CAD (table 3).

Table 4 reports clinical event rates in relation to the number of these four high risk features. Each additional high risk feature was associated with a relative risk for five year death of 2.328 (95% confidence interval 2.048 to 2.646, p < 0.0001).

DISCUSSION

This study analysed the longest follow up ever reported of a large series of consecutive, unselected patients with ST elevation AMI treated by primary PCI at a high volume PCI tertiary centre.

One third of the deaths after the primary PCI occurred within the first month (mainly during hospital stay) and were mainly due to cardiogenic shock or refractory heart failure. After the first 30 days, mortality was stable (3–4% a year), but cardiac deaths decreased over the years, with a parallel increase in non-cardiac deaths.

Age and cardiogenic shock were found to be strong independent predictors of cardiac death after primary PCI, and these figures are consistent with previous reports.^{7 8 10}

The presence of a previous MI emerged as an independent predictor of death. This finding may be explained by the concomitant presence of multivessel CAD or by a lower left ventricular function in these patients.

The presence of multivessel CAD, even if associated with a worse baseline risk profile, was an independent predictor of all cause mortality, as well as of other adverse events. Multivessel CAD is a well known risk factor of patients with AMI undergoing conservative or lytic treatment.^{11–13} This angiographic feature is a marker of severe, diffuse, and more aggressive atherosclerotic CAD and is associated with a poor outcome. Similarly, in their pioneer study Kahn *et al*¹⁴ found a relation between the number of diseased vessels and survival after primary angioplasty.

The issue of appropriateness and timing of non-culprit lesion treatment after primary PCI is still debated.^{14 15} In this series we used to treat non-culprit lesions in the acute phase in patients with cardiogenic shock or electively with evidence of inducible ischaemia. However, the ischaemia driven strategy could not avoid the poor prognosis of patients with multivessel CAD. Recently, Corpus *et al*¹⁶ confirmed that in patients with multivessel CAD and AMI, multivessel PCI is technically feasible but is associated with higher postprocedural morbidity without a benefit in mortality. Whether a treatment strategy guided by vulnerable plaque imaging will provide effective revascularisation has not yet been determined.¹⁷

Table 4 Gradations of clinical risk and five year outcome

	Number of high risk features					p Value
	0 (n=327)	1 (n=342)	2 (n=224)	3 (n=78)	4 (n=16)	
Death	25 (7.6%)	47 (13.7%)	69 (30.8%)	49 (62.8%)	13 (81.3%)	<0.0001
Cardiac death	16 (4.9%)	31 (9.1%)	55 (24.6%)	43 (55.1%)	13 (81.3%)	<0.0001
Hospitalisation for HF	4 (1.2%)	13 (3.8%)	16 (7.1%)	7 (9.0%)	2 (12.5%)	<0.0001
Repeat MI	13 (4.0%)	18 (5.3%)	17 (7.6%)	1 (1.3%)	1 (6.3%)	0.173
Additional revascularisation	48 (14.7%)	74 (21.6%)	50 (22.3%)	14 (17.5%)	2 (12.5%)	0.085

Patients with one or more of the aforementioned high risk features (age > 70 years, cardiogenic shock, previous MI, and multivessel CAD) had a higher incidence of death and hospitalisation for heart failure in the subsequent five years than did patients without. Moreover, the risk of long term mortality and rehospitalisation progressively rose with the increase in the number of high risk features. However, reinfarction and additional revascularisation rates cannot be predicted just by the number of these high risk characteristics. In patients without high risk features a good five year outcome, with low rates of major adverse events, can be expected.

In a previous randomised trial based on 395 selected patients with AMI, primary coronary angioplasty resulted in lower five year mortality (13% v 24%, $p = 0.01$) and rate of non-fatal reinfarction (6% v 22%, $p < 0.01$) than did thrombolytic treatment with streptokinase.⁵ However, the exclusion from random selection of patients with pronounced haemodynamic instability or ECG signs of extensive infarction prevents comparison of this trial population with our patient series. Mahon *et al*,¹⁸ analysing the long term outcome of 1059 consecutive patients with AMI admitted to a tertiary centre in the thrombolytic era, found a five year survival of 50%. In this "real world" analysis only 28% of the patients included in the study received thrombolysis and 32% had pre-discharge coronary angiography.

In our primary PCI series, symptom to balloon time was not independently related to five year survival in the multivariate Cox analysis. This finding confirms that time is less important when mechanical reperfusion is used than with a pharmacological reperfusion strategy.¹⁹

Conclusions

The satisfactory results of a routine mechanical revascularisation strategy in AMI were maintained during several years of follow up. Patients at risk of death during long term follow up may be identified by simple clinical and angiographic characteristics, such as old age, cardiogenic shock, previous MI, and multivessel CAD. The risk of death progressively increases with the number of these high risk features.

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This study was supported by the ARCARD Foundation, Florence, Italy.

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