Peer reviewed article

Long-term survival and functional outcome of unselected patients undergoing percutaneous coronary intervention for acute myocardial infarction

Pablo Anabitarte[a,b,], David J. Kurz[a,*], Irene Stettler[a], Barbara Naegeli[a,c], Osmund Bertel[a,c], Juergen Frielingsdorf[a,d], Dominik Maurer[a,c], Edwin Straumann[a,c]*

[a] Division of Cardiology, Department of Internal Medicine, Triemli Hospital, Zurich, Switzerland
[b] Division of Cardiology, Department of Internal Medicine, Kantonsspital, Aarau, Switzerland
[c] Klinik im Park, Cardiovascular Centre, Zurich, Switzerland
[d] Department of Internal Medicine, Kantonsspital, Winterthur, Switzerland

Summary

Background: Percutaneous coronary intervention (PCI) is the most effective reperfusion modality in patients with acute myocardial infarction (MI). Data concerning long-term survival and functional outcome are sparse.

Methods: One thousand consecutive patients treated by emergency PCI were systematically analysed in a single-centre registry. Multivariate predictors of in-hospital mortality, post-discharge mortality and late functional capacity were identified.

Results: Follow-up was completed for 978 patients. The median clinical follow-up length was 3.2 years. In-hospital and post-discharge mortality were 7.6% and 7.3%, respectively. Annualised post-discharge mortality remained stable over time at 2% per year. Independent predictors of in-hospital death were cardiogenic shock, TIMI flow <3 after PCI, left ventricular ejection fraction <40%, age and time to patent artery >6 h. Independent predictors of post-discharge mortality were TIMI flow after PCI <3, prior MI, elevated glucose levels at admission, and increasing age. In contrast, cardiogenic shock, time to patent artery and left ventricular ejection fraction <40% were not independently associated with post-hospital death. At late follow-up, 47% of patients had normal functional capacity and 49.1% were in New York Heart Association functional class II. Predictors of impaired functional capacity at follow-up were age, gender, smoking habits and multivessel coronary disease.

Conclusions: Post-discharge mortality after PCI for acute MI was 2% per year. Significant differences exist between predictors of in-hospital and post-discharge mortality. The functional capacity of surviving patients was remarkably good, even when presented in cardiogenic shock.

Key words: acute myocardial infarction; PCI; mortality; outcome; functional capacity

Introduction

Optimal management of acute myocardial infarction (MI) depends on early and complete restoration of coronary artery patency. Individual trials comparing fibrinolytic therapy with primary percutaneous coronary intervention (PCI) and a meta-analysis of 23 randomised trials have demonstrated primary PCI to be superior to fibrinolytic therapy, both with regard to short-term mortality [1, 2], as well as additional short-term outcome measures [3]. Current guidelines recommend primary PCI as the treatment of choice for ST-elevation MI when this can be performed by an experienced team within two hours, irrespective of need for hospital transfer, and in the case of cardiogenic shock for all patients. For Non-ST-elevation MI, urgent PCI is recommended in moderate to high risk cases [4]. Following thrombolysis, the long-term benefit has been proven to be sustained over more than 20 years [5]. In contrast, long-term follow-up data of patients with acute MI treated by urgent PCI is restricted to two trials comparing thrombolytic therapy with primary angioplasty [6–8], and one other registry [9].

The purpose of this analysis was to assess short and long-term mortality after PCI for acute MI, and to identify predictors of death and functional outcome at late follow-up.

* equal contributions

No conflict of interest in relation to this article.

Methods

Patients

Characteristics of the Triemli registry, which was initiated in 1995, have been reported previously [10]. In this registry, all patients undergoing PCI within 24 hours following the onset of symptoms were prospectively included. The registry consisted of patients undergoing primary or rescue PCI, which includes failed thrombolytic therapy or a failed primary conservative strategy.

Patients were classified as having an acute MI, if a rise of CK and CK-MB more than double the upper limit of normal was present, and at least one of the two following criteria were fulfilled: (1) persistent chest pain suggestive for MI of at least 30 minutes duration, (2) ST elevation of at least 1 mm in at least two consecutive leads or left bundle branch block. Concomitant medical treatment with anti-platelet agents, beta-blockers, ACE inhibitors and statins followed published ACC/AHA guidelines.

Cardiogenic shock was defined as systolic blood pressure persistently (>30 min) below 90 mmHg despite adequate volume replacement, in combination with clinical signs of hypoperfusion and/or urinary output below 20 ml/hour [11].

Serum levels of the myocardial biomarkers CK and CK-MB were measured after 4, 8, 12, and 24 hours.

Long-term follow-up was performed by contacting patients directly as previously described [10]. In a minority of cases in which patients could not be reached, survival status was obtained from census and registry offices. In addition to survival status, physical capacity was assessed from a structured questionnaire sent to all patients. Functional status at follow-up was quantified with the New York Heart Association (NYHA) classification system [12].

Endpoints

The endpoints were in-hospital mortality, mortality during the follow-up period after hospital discharge, and functional class at late follow-up. For post-discharge mortality, cardiac death was defined as death due to heart failure, recurrent MI or sudden death.

Statistical analysis

Statistical analysis was performed using SPSS 12.4. Continuous variables are expressed as means ± 1 SD. The survival curves were constructed by using life table analysis. Categorical variables, potentially predictive for death, were tested first by chi-square test. The following categorical variables were used: age >75 years, gender, known diabetes mellitus, glucose levels >11 mmol/l, previous MI, primary PCI, anterior MI, multivessel disease, TIMI flow <3 before PCI, time from onset of symptoms to patent artery >6 hours, peak CK >2000 IU/l, left ventricular ejection fraction <40%, cardiogenic shock, and TIMI flow <3 after PCI.

A stepwise forward selection procedure for in-hospital and post-hospital death was performed for Cox regression models. The following covariates were tested: age, gender, history of diabetes mellitus, glucose levels at admission as a continuous variable (mmol/l), prior MI, anterior MI, ST-elevation MI, multivessel disease, left ventricular ejection fraction <40%, TIMI flow before and after revascularization, rescue PCI, time to patent coronary artery, peak CK, smoking habits, and cardiogenic shock at presentation.

Predictors of impaired functional capacity (NYHA >1) at late follow-up were tested for significance using a logistic regression model with the same variables.

Results

Patient characteristics

One thousand consecutive patients with acute MI and treated with direct or rescue PCI within 24 hours following the onset of symptoms were included in this analysis. Patient characteristics upon admission are given in table 1. At the initial coronary angiography, the TIMI flow in the infarct-related artery was ≤1 in most patients (77%). After PCI, TIMI 3 flow was present in 91% and TIMI 2 flow in 6%.

Table 1

Patient characteristics.

	N = 978
Mean age (years)	60 ± 12
Age >75 years (%)	11
Female gender (%)	19
History of Diabetes mellitus (%)	17
History of hypertension (%)	47
Previous smokers / Current smokers (%)	21 / 45
Mean cholesterol level (mmol/l)	5.5 ± 1.2
Family history of coronary disease (%)	33
Prior myocardial infarction (%)	15
Anterior myocardial infarction (%)	44
Cardiogenic shock at PCI (%)	15
Mean left ventricular ejection fraction (%)	51 ± 14
1 / 2 / 3 vessel disease (% of patients)	36 / 27 / 37
TIMI flow ≤1 before PCI (%)	77

In-hospital and post-discharge mortality

Survival status was obtained from 978 of patients included in the registry. From this sample, 22 patients, mainly tourists and migrants who had been denied right of asylum, remained unavailable for follow-up. The median follow-up time was 3.2 years (interquartile range: 2.0 to 5.0 years). In-hospital mortality was 7.6%, with the rate for patients with and without cardiogenic shock at presentation being 38.4% and 2.7%, respectively. Post-discharge mortality was 7.3%, resulting in a mortality rate of 2.0% per year. The death rate after discharge remained constant during the entire follow-up period (fig. 1). In almost half (44%) of the post discharge fatalities, death was not of cardiovascular origin, and was mainly caused by cancer-related death (n = 18). Use of guideline recommended medical treatment at late follow-up was as follows: 96% of patients were on platelet inhibition or anticoagulation, 78% on

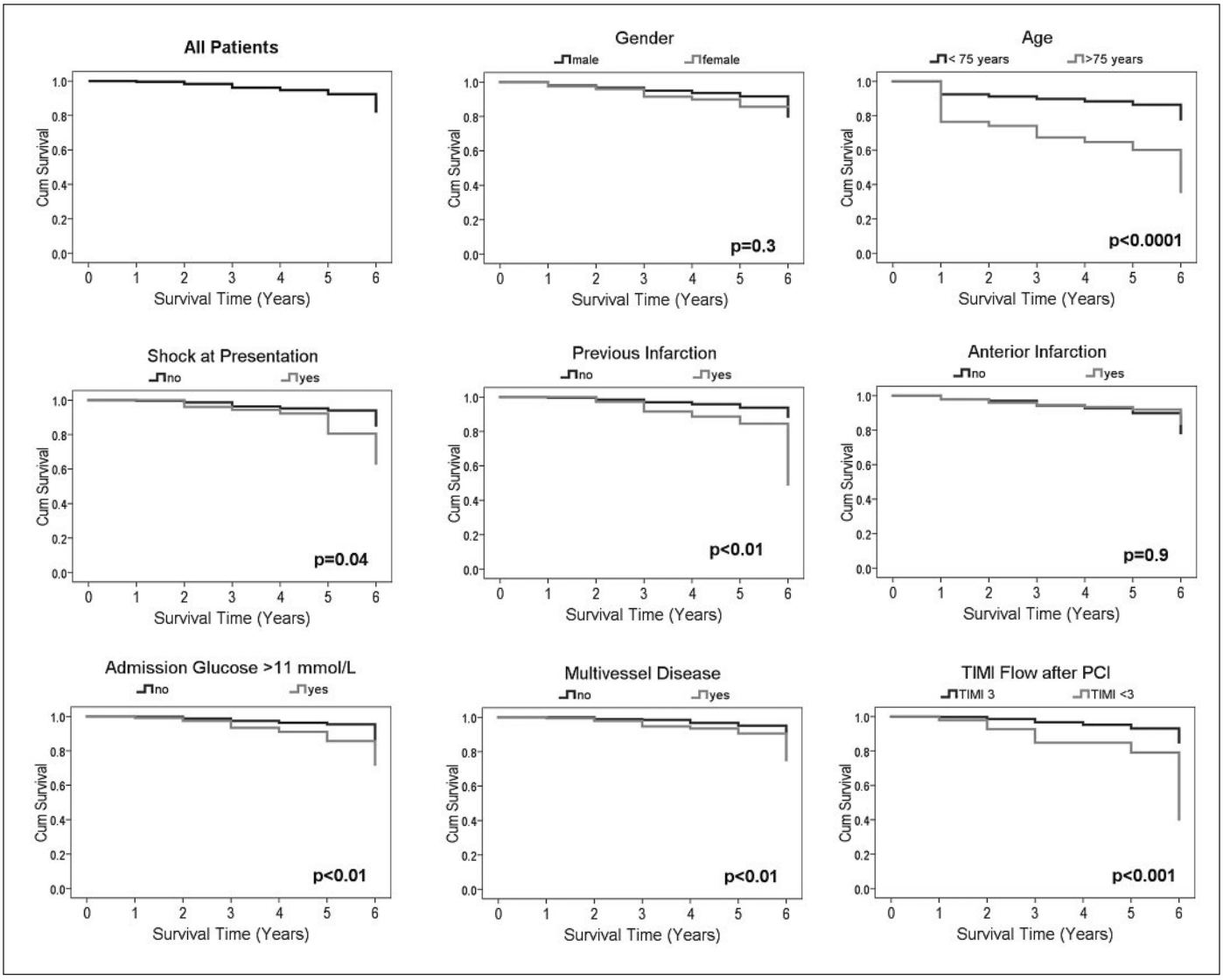

Figure 1

Post-discharge life table analyses for all patients, and pair wise comparisons of survival according to age, gender, history of previous infarction, shock at presentation, anterior infraction, glucose levels at hospital admission, multi-vessel disease, and the presence of TIMI 3 flow after PCI.

beta-blockers, 87% on statins, and 59% on ACE-inhibitors or angiotensin II receptor blockers.

Predictors of in-hospital and post-discharge mortality

Variables with significant impact on in-hospital death rate, following Cox regression analysis, are depicted in table 2a. Cardiogenic shock, followed by glucose level on admission (>11 mmol/l) and TIMI flow < 3 after PCI showed the strongest associations with in-hospital death. Interestingly, anterior MI was not a predictor for death (p = 0.20).

After hospital discharge, age, cardiogenic shock and prior MI were the strongest predictors for death (table 2b). Again, anterior MI was not associated with a negative outcome (p = 0.1).

Multivariate predictors of in-hospital and post-discharge mortality are given in table 3a and table 3b. As expected, cardiogenic shock was the strongest independent predictor for in-hospital mortality (HR 8.86, p <0.001). However, after discharge this parameter was no longer independently predictive for death. Glucose level on admission (HR 1.07 per mmol/l, p <0.001), age (HR 1.05 per year, p <0.001), TIMI flow <3 after PCI (HR 3.01, p = 0.002) and a history of prior MI at presentation (HR 2.18, p = 0.004) were independent predictors for death at late follow-up.

Predictors of late functional capacity

No functional impairment (NYHA class I) was present in 47% of all patients after a median follow-up of 3.2 years. From the sample, 49.1% complained of dyspnoea NYHA II, while only a small number of patients were severely impaired (NYHA class III: 3.9%, class IV: 0%). When the above-mentioned covariates were entered in a logistic regression model, the resulting predictors of impaired functional capacity (NYHA >1) at final follow-up were female gender, increasing age (per year), smoking habit, and multivessel coronary disease (table 4). However, the discriminatory capacity of the model was poor, with only 60% of cases being predicted correctly in a receiver operator characteristic analysis (c-statistic 0.6).

Table 2a

Non-adjusted risk of in-hospital death (N = 978).

	%	HR[1])	95% CI	p
Cardiogenic shock	15	20.0	11.8; 33.6	<.001
Glucose level at admission >11 mmol/l	31	5.3	3.2; 8.7	<.001
TIMI flow after PCI <3	8	7.2	4.5; 11.8	<.001
Known Diabetes mellitus	17	3.5	2.2; 5.5	<.001
LVEF <40%	19	3.3	2.6; 4.3	<.001
Multivessel disease	36	2.7	1.5; 4.9	<.001
Age >75 years	11	2.7	1.6; 4.0	<.001
Female gender	19	2.2	1.4; 3.6	.001
Peak CK >2000 UI/l	47	2.0	1.1; 3.6	.002
Symptom onset to patent artery >6 h	43	2.0	1.2; 3.3	.01
Previous myocardial infarction	15	1.9	1.1; 3.3	.01
Anterior MI	44	1.3	0.9; 2.1	.2
Primary PCI	69	1.0	0.6; 1.6	.9
TIMI flow before PCI <3	10	1.0	0.5; 2.0	.9

[1]) Hazard Ratio
Cox regression analysis

Table 2b

Non-adjusted risk of post-discharge death (N = 978).

	%	HR[1])	95% CI	p
Age >75 years	11	4.3	2.5; 7.5	<.001
Cardiogenic shock	15	2.8	1.6; 5.0	<.001
Previous myocardial infarction	15	2.7	1.6; 4.7	<.001
Glucose level at admission >11 mmol/l	31	2.1	1.3; 3.4	.003
TIMI flow after PCI <3	8	3.3	1.6; 6.6	.004
Known Diabetes mellitus	17	1.9	1.1; 3.3	.02
Multivessel disease	36	2.0	1.1; 3.4	.02
Anterior MI	44	0.7	0.4; 1.1	.1
Female gender	19	1.5	0.8; 2.7	.1
Peak CK >2000 UI/l	47	1.2	0.8; 2.0	.4
Symptom onset to patent artery >6 h	43	1.1	0.6; 1.9	.6
TIMI flow before PCI <3	10	1.1	0.5; 2.8	.8
LVEF <40%	19	1.0	0.7; 1.5	.8
Primary PCI	69	0.9	0.5; 1.6	.8

[1]) Hazard Ratio
Cox regression analysis

Table 3a

Independent predictors of in-hospital death.

	HR[1])	95.0% CI	p
Cardiogenic shock at presentation	8.86	4.88; 16.08	<.001
TIMI flow <3 after PCI	4.61	2.67; 7.96	<.001
LVEF below 40%	3.10	1.76; 5.46	<.001
Symptom onset to patent artery >6 h	2.19	1.28; 3.74	.004
Age (per year)	1.03	1.01; 1.6	.006

Table 3b

Independent predictors of post-discharge death.

	HR[1])	95.0% CI	p
Admission glucose level (per 1 mmol/l)	1.07	1.04; 1.11	<.001
Age (per 1 year)	1.05	1.02; 1.07	<.001
TIMI flow <3 after PCI	3.01	1.48; 6.13	.002
Previous MI	2.18	1.28; 3.72	.004

[1]) Hazard Ratio
Cox regression analysis

Table 4

Independent predictors of functional impairment (NYHA >1) at late follow-up.

	OR[1])	95.0% CI	p-value
Female gender	2.22	1.47; 3.33	<.001
Age (per one year)	1.02	1.01; 1.03	.005
Smoking	1.62	1.07; 2.45	.023
Multivessel disease	1.40	1.03; 1.91	.033

[1]) Odds Ratio
logistic regression model

Discussion

In this study, the results and predictors of late outcome and functional capacity of patients with acute MI treated with emergency PCI were reported. Post discharge mortality during long-term follow-up was 7.3%, equalling an annual mortality rate of 2.0% without excess mortality during the early post-discharge period (figure 1). Predictors of late mortality were glucose levels at hospital admission, age, TIMI flow <3 after PCI, and a history of prior MI, which all had a major independent impact on long-term survival (table 3). For instance, a one mmol/l increase in glucose concentration at hospital entry increased the hazard rate by 7.3%, a one year increase in age raised it by 4.7%, a history of a prior MI doubled the risk, and incomplete restoration of flow in the infarct-related artery (TIMI flow <3) increased the post-discharge mortality risk threefold.

As shown in table 3, there were important differences between predictors of in-hospital mortality and post-discharge mortality. In-hospital mortality (7.6%) was similar to that reported from other cohorts and randomised trials [2], and was largely driven by mortality of patients presenting with cardiogenic shock. This patient subgroup, which represented 15% of the current cohort, had a hospital mortality rate of 38.4%, compared to only 2.7% in patients without shock. Not surprisingly, cardiogenic shock at the time of PCI was the strongest independent predictor of in-hospital death (HR 8.86, 95% CI 4.88–16.08). The over-representation of patients in cardiogenic shock results from the high proportion of these patients transferred from other hospitals for rescue PCI [13]. The results do not reflect the general trend of decreasing incidence in cardiogenic shock over the last years in Switzerland [14].

Other factors independently contributing to early mortality were age, TIMI flow <3 after PCI, left ventricular ejection fraction < 40%, and time to patent artery >6 hours after onset of symptoms. These predictors are in line with previous reports [15, 16]. Remarkably, 3 of the 4 strongest predictors of in-hospital death, namely cardiogenic shock at presentation, time to patent artery, and left ventricular ejection fraction <40%, did not independently contribute to post-discharge mortality.

Other studies have shown that the survival benefit of direct PCI in patients with acute MI seems to be maintained during the follow-up period [6, 7, 17]. However, follow-up data beyond 1 year and contemporary data including possible benefits from recent progress in medical therapy and PCI techniques are sparse. Parodi et al. reported a five-year overall mortality rate of 20% in a registry similar to ours [9]. In the randomised Zwolle trial, mortality was 22% after eight years when patients were treated by primary PCI, compared to 31% when treated by fibrinolysis [8]. In the current registry, overall mortality was 14.4% after a median follow-up period of 3.2 years with a constant death rate of 2% per year after hospital discharge. Prompt initiation and long-term maintenance of guideline-adherent medical treatment and secondary prevention measures may have contributed to this beneficial outcome.

Little is known about the long-term functional outcome of MI survivors in the modern era. In the current study, functional capacity was remarkably well maintained at late follow-up, with the vast majority of patients having no or only mild impairment (47% in NYHA class I, 49.1 % in NYHA class II). Survival bias, that increased mortality in patients with impaired functional capacity, will have contributed to this result [18]. The authors are unaware of other studies reporting the predictors of impaired functional capacity after PCI for MI. The current analysis showed that female gender, increasing age, smoking habit and multivessel disease were the only independent predictors of decreased late functional capacity, while shock and decreased left ventricular function at admission did not contribute significantly to the model (table 4). Our observation that patients with shock complicating acute MI generally do well after discharge, is in line with the one year results from the SHOCK trial, which found that 87% of patients in the revascularisation group had no or only mild impairment of physical capacity [19]. Unfortunately, the final model predicted only 60% of patients correctly and was thus not sufficiently reliable for clinical use.

Study limitations

The data presented here were derived from a prospective single centre registry. Therefore they may be less universally valid than data derived from a multi-centre study. However this registry represents patients uniformly treated by PCI within 24 hours of acute MI symptom onset under real world conditions.

More than half of the cohort was referred from other hospitals for emergency PCI. Although this has been shown not to influence our results [13], referral patterns may have brought in a selection bias towards patients with more severe disease. This is reflected by the rather high proportion of patients in cardiogenic shock at presentation.

The definition of MI has changed during the observation time and now depends on the release of cardiac troponin [20]. This may have an impact on our data, as patients with minor myocardial necrosis reflected by troponin elevation without significant increase in CK-MB levels were not included in the registry.

Conclusion

In patients undergoing emergency PCI for acute MI post-discharge mortality rates are low at about 2% per year. The study found considerable differences between the predictors of in-hospital and post-discharge mortality. Notably, cardiogenic shock, time to patent artery, and left ventricular ejection fraction <40% were associated with in-hospital, but not post-discharge death. In surviving patients, functional capacity was remarkably good. Although independent predictors of impaired functional status (>NYHA I) could be identified, predictive accuracy was poor.

Statistical analyses were performed by C. Schmidhauser, La Volta Statistics, Zurich, Switzerland.

Correspondence:
Pablo Anabitarte
Department of Internal Medicine
Division of Cardiology
Cantonal Hospital
Tellstrasse
CH-5001 Aarau
Switzerland
E-Mail: pablo.anabitarte@ksa.ch

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