

Prognostic factors of in-hospital mortality in all comers with ST elevation myocardial infarction undergoing primary percutaneous coronary intervention

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ABSTRACT

Background The prognostic factors of in-hospital mortality in all comers and unselected patients with ST elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI) have not been well established.

Objective To identify the predictive factors of in-hospital mortality in patients with STEMI undergoing primary PCI in a tertiary heart centre.

Methods Between January 2008 and December 2011, all patients with STEMI undergoing primary PCI were retrospectively included in this study. Baseline characteristics and angiographic data were reviewed and recorded. The study endpoint was all-cause in-hospital mortality.

Results Of the 541 patients included in the study, 63 (11.6%) died during hospitalisation. Cardiogenic shock at admission was recorded in 301 patients (55.6%) and 424 patients (78%) had multivessel disease. Median door-to-device time was 65 min. After adjustment for baseline variables, the factors associated with in-hospital mortality included age >60 years (OR 2.98, 95% CI 1.17 to 7.05; $p=0.01$), left ventricular ejection fraction <40% (OR 2.53, 95% CI 1.20 to 5.36; $p=0.02$), and final TIMI flow grade 0/1 (OR 20.55, 95% CI 3.49 to 120.94; $p=0.001$).

Conclusions Age, left ventricular function and final TIMI flow are significant predictors of adverse outcomes in unselected patients with STEMI undergoing primary PCI.

INTRODUCTION

Primary percutaneous coronary intervention (PCI) is the reperfusion therapy of choice in patients with acute ST elevation myocardial infarction (STEMI), provided it can be performed in a PCI-capable hospital within the recommended time lines.^{1–3} Improvements in the PCI technique and adjunctive pharmacological therapy have led to lower mortality when compared to thrombolytic therapy alone.^{4–5} The predictors of mortality, either short- or long-term, have been reported; however, most clinical trials of primary PCI excluded STEMI patients at high risk from cardiogenic shock and heart failure.^{6–8} Furthermore most of those studies were performed in areas where the availability of a catheterisation laboratory was not an obstacle to treatment. The objective of this study was to identify the predictors of in-hospital mortality in unselected patients with STEMI in a tertiary heart centre, because the results might differ from previous studies.

PATIENTS AND METHODS

This was a retrospective study performed at a single tertiary heart centre in Northeast Thailand. The data included all STEMI patients who underwent primary PCI within 12 hours of symptom onset between January 2008 and December 2011. Patients who underwent rescue PCI and a pharmaco-invasive strategy were excluded from the study. The baseline characteristics recorded included: medical history, vital signs, laboratory results, electrocardiographic findings, cardiac biomarkers, left ventricular ejection fraction (LVEF), door to device time, and angiographic findings. All angiographic features and procedural outcomes were reviewed by two investigators (SK and CW). Discrepancies in interpretation were resolved by consensus. The degree of stenosis was quantitated by visual analysis and significant stenosis was considered present when the narrowing of the coronary artery was >70%. The final epicardial TIMI was graded as previously described by the TIMI (Thrombolysis in Myocardial Infarction) group.^{9–10} The study was performed in accordance with the Declaration of Helsinki and the institutional ethics committee approved the use of data for this study and analysis.

Definitions

STEMI was defined as: (1) angina chest pain lasting >30 min with ST elevation ≥ 1 mm in two consecutive precordial or limb leads; or (2) angina chest pain lasting >30 min with new left bundle branch block. Cardiogenic shock at admission was defined as: (1) systolic blood pressure <90 mm Hg for 30 min despite adequate fluid therapy; (2) requirement for vasopressor infusion or intra-aortic balloon pump to maintain systolic blood pressure >90 mm Hg; and (3) signs of poor tissue perfusion. Left ventricular function was assessed by echocardiography and left ventricular systolic dysfunction was defined as LVEF <40%. Renal dysfunction was defined as creatinine concentration >1.5 mg/dL at admission. Anaemia was defined as haemoglobin concentration <10 g/dL. Death included all causes of in-hospital death.

Statistics

Continuous variables were presented as mean \pm SD, while categorical variables were described as frequencies and percentages. Differences between the patient groups for categorical variables were examined using the χ^2 or Fisher exact test or the z test. Differences in the continuous variables between groups were assessed using the Student's t -test,



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Mann-Whitney U test, or Wilcoxon rank sum test, where appropriate. A univariate logistic model was used to examine the relationship between all clinical meaningful variables and in-hospital mortality. After each variable was tested independently in a univariate regression model, those that achieved a value of $p < 0.25$ (and were clinically meaningful) were selected for testing in a multivariable logistic regression. ORs and 95% CIs were used to illustrate the association between potential variables and in-hospital mortality. A two-sided p value < 0.05 was considered statistically significant. Stata V.10.0 was used to perform all statistical analyses (Stata Corp, College Station, Texas, USA).

RESULTS

Baseline characteristic

Between January 2008 and December 2011, 541 patients presenting with STEMI underwent primary PCI within 12 hours were included in the study. Of these 541 patients, 63 (11.6%) died during hospitalisation. Death was due to cardiac causes in 58 patients (92%) and non-cardiac causes in five patients (8%). Table 1 summarises the baseline characteristic of all the patients. The study population was predominately male (69%), with an average age of 63 years, and about one-third were diabetic. The mean total cholesterol and high density lipoprotein cholesterol values at admission were 189 mg/dL and 38.9 mg/dL, respectively. Cardiogenic shock at admission was recorded in 301 patients (55.6%) and intra-aortic balloon pump was used in 39% of all patients. About 95% of the patients received dual

antiplatelet (aspirin and clopidogrel) therapy and only 20% of the patients received β -blockers or ACE inhibitors during hospitalisation. The in-hospital mortality rate in patients with admission cardiogenic shock was 76%. Compared with the patients in the survival group, patients in the non-survival group were older, more likely to be female, non-smokers, have an LVEF $< 40\%$, be in cardiogenic shock at admission, exhibit renal dysfunction at admission, be anaemic, and have higher concentrations of admission troponin and plasma glucose.

Coronary angiographic features and procedural outcomes

Table 2 shows the coronary angiographic features and procedural outcomes. The median door-to-device time was 65 min and ~80% of the patients underwent PCI within 90 min after admission. Coronary angiography showed that 78% of the patients ($n=424$) had multivessel disease and the most commonly treated lesions were in the left anterior descending artery. The right coronary artery was found to be the infarct-related artery in 44% of all patients. There was no difference in number of vessel disease and the treated lesion between the survival and non-survival group. Thrombus aspiration was performed in 55% of all patients, and intracoronary glycoprotein IIb/IIIa was administered in 50% of all patients. Coronary stenting was performed in 86% of all patients. About 22% of the patients received drug eluting stents. Most of the infarct-related arteries were restored after PCI and the final TIMI grade 2/3 flow was achieved in 96.5% of the patients. The overall incidence of the no reflow phenomenon was 2.2%.

Table 1 Baseline characteristic of the study patients

Variables	Overall (n=541)	Survive (n=478)	Death (n=63)	p Value
Age, years (mean \pm SD)	63.5 \pm 12.1	62.6 \pm 12.0	69.8 \pm 10.8	0.001
Male (n, %)	375 (69.3)	344 (71.9)	31 (49.2)	0.001
BMI, kg/m ² (mean \pm SD)	23.3 \pm 3.9	23.4 \pm 3.8	23.0 \pm 3.7	0.482
Pulse rate (mean \pm SD)	80.8 \pm 22.9	80.4 \pm 21.7	84.3 \pm 30.6	0.213
Diabetes mellitus (n, %)	163 (30.1)	139 (29.8)	24 (38.1)	0.152
Hypertension (n, %)	198 (36.6)	171 (35.7)	27 (42.8)	0.290
Smoking (n, %)	192 (35.4)	181 (37.8)	11 (17.4)	0.001
Previous CAD (n, %)	42 (7.7)	35 (7.3)	7 (11.1)	0.340
Killip classification				
Class I (n, %)	145 (26.8)	137 (28.6)	8 (12.7)	0.004
Class II (n, %)	80 (14.8)	73 (15.2)	7 (11.1)	
Class III (n, %)	15 (2.7)	15 (3.14)	0 (0)	
Class IV (n, %)	301 (55.6)	253 (52.9)	48 (76.2)	
Cardiogenic shock at admission (n, %)	301 (55.6)	253 (52.9)	48 (76.1)	0.001
Creatinine > 1.5 mg/dL (n, %)	127 (23.4)	102 (21.34)	25 (39.68)	0.001
Haemoglobin < 10 g/dL (n, %)	75 (13.8)	56 (11.7)	19 (30.1)	0.001
Admission troponin T, ng/mL (mean \pm SD)	4.6 \pm 7.5	4.3 \pm 6.9	6.9 \pm 10.7	0.011
Admission plasma glucose, mg/mL (mean \pm SD)	199.5 \pm 111.3	191.6 \pm 104.7	256.7 \pm 138.8	0.001
Total cholesterol, mg/mL (mean \pm SD)	189.8 \pm 75.0	191.3 \pm 73.7	172.4 \pm 89.5	0.279
LVEF $< 40\%$ (n, %)	123 (22.7)	99 (20.7)	24 (38.0)	0.001
Median door-to-device time (min)	65	65	60	0.734
Door-to-device time > 90 min	119 (22.0)	108 (22.5)	11 (9.2)	0.331
Length of hospital stay (day) (mean \pm SD)	5.2 (5.9)	5.5 (6.1)	2.7 (1.8)	0.001
In-hospital medication				
ASA (n, %)	522.0 (96.5)	464.0 (97.0)	58.0 (92.0)	0.617
Clopidogrel (n, %)	513.0 (94.8)	455.0 (95.1)	58.0 (92.0)	0.237
β -blocker (n, %)	123.0 (22.7)	122.0 (25.8)	1.0 (1.6)	0.001
ACEI (n, %)	101.0 (18.6)	99.0 (18.2)	2.0 (3.4)	0.001

ACEI, ACE inhibitor; ASA, acetylsalicylic acid (aspirin); BMI, body mass index; CAD, coronary artery disease; LVEF, left ventricular ejection fraction.

Table 2 Angiographic and procedural characteristics

Variables	Overall (n=541)	Survive (n=478)	Death (n=63)	p Value
Single vessel disease (n, %)	117 (21.6)	97 (20.2)	20 (31.7)	0.262
Double vessel disease (n, %)	167 (30.8)	151 (31.5)	16 (25.4)	0.611
Triple vessel disease (n, %)	257 (47.5)	230 (48.1)	27 (42.8)	0.605
Left main disease (n, %)	54 (9.9)	46 (9.6)	8 (12.7)	0.444
Infarct related vessel=LAD (n, %)	266 (49.1)	236 (49.3)	30 (47.6)	0.856
Infarct related vessel=RCA (n, %)	241 (44.5)	213 (44.5)	28 (44.4)	0.990
Reference vessel diameter, mm (mean±SD)	3.26±0.08	3.29±0.09	3.00±0.08	0.277
Stented implanted (n, %)	468.0 (86.5)	421.0 (88.1)	47.0 (74.6)	0.003
Number of stent (mean±SD)	1.33 (0.6)	1.34 (0.6)	1.23 (0.5)	0.259
DES (n, %)	121.0 (22.3)	113.0 (23.6)	8.0 (12.7)	0.549
Use of thrombus aspiration (n, %)	302 (55.8)	271 (56.6)	31 (49.2)	0.261
Glycoprotein IIb/IIIa inhibitor administered (n, %)	267 (49.3)	239 (50.0)	28 (44.4)	0.407
Initial TIMI flow grade 0/1 (n, %)	336.0 (62.1)	293.0 (61.3)	43.0 (68.3)	0.248
Final TIMI flow grade 0/1 (n, %)	19 (3.5)	9 (1.8)	10 (15.8)	0.293

DES, drug eluting stent; LAD, left anterior descending artery; RCA, right coronary artery; TIMI, Thrombolysis in Myocardial Infarction.

In-hospital outcomes

Univariate and multivariate analysis

In the univariate analysis (table 3), in-hospital mortality was independently related to: age >60 years, female sex, LVEF <40%, cardiogenic shock at admission, renal dysfunction at admission, haemoglobin <10 g/dL, admission troponin, admission plasma glucose, reference vessel diameter, stent implantation, and final TIMI grade 0/1. After adjustment for baseline variables (table 4) in-hospital mortality was related to: age >60 years (OR 2.98, 95% CI 1.17 to 7.05), LVEF <40% (OR 2.53, 95% CI 1.20 to 5.36), and final TIMI grade 0/1 (OR 20.55, 95% CI 3.49 to 120.94).

Table 3 Univariate analysis

Variables	OR	95% CI	p Value
Age >60 years	3.47	1.81 to 6.68	0.001
Female sex	2.63	1.49 to 4.64	0.001
BMI	0.97	0.91 to 1.04	0.482
Pulse rate	1.00	0.99 to 1.02	0.213
Diabetes mellitus	1.49	0.82 to 2.64	0.152
Hypertension	1.33	0.75 to 2.34	0.289
Smoking	0.33	0.15 to 0.66	0.001
Previous CAD	1.58	0.67 to 3.71	0.420
Cardiogenic shock at admission	2.82	1.50 to 5.57	0.001
Creatinine >1.5 mg/dL	2.42	1.33 to 4.33	0.001
Haemoglobin <10 g/dL	3.30	1.69 to 6.27	0.001
Admission troponin T	1.03	1.00 to 1.06	0.015
Admission plasma glucose	1.04	1.002 to 1.006	0.001
LVEF <40%	3.01	1.60 to 5.62	0.001
Door-to-device time >90 min	0.71	0.32 to 1.44	0.330
Triple vessel disease	0.57	0.30 to 1.06	0.077
Infarct vessel=LAD	0.93	0.55 to 1.56	0.790
Infarct vessel=RCA	0.99	0.59 to 1.68	0.980
Reference vessel diameter	0.59	0.36 to 0.96	0.035
Stented implanted	0.39	0.21 to 0.80	0.001
Use of glycoprotein IIb/IIIa inhibitor	0.80	0.45 to 1.40	0.400
Use of thrombus aspiration	1.13	0.65 to 1.98	0.651
Final TIMI flow grade 0/1	9.83	3.39 to 28.48	0.001

BMI, body mass index; CAD, coronary artery disease; LAD, left anterior descending artery; LVEF, left ventricular ejection fraction; RCA, right coronary artery; TIMI, Thrombolysis in Myocardial Infarction.

DISCUSSION

The present study found that: (1) age >60 years, LVEF <40%, and final TIMI flow are related to in-hospital mortality; and (2) in-hospital mortality is high in unselected patients with STEMI transferred to the tertiary heart centre.

Although previous studies identified risk factors for short- and long-term outcomes for patients with ST elevation, it is unknown whether these can be generalised to all patients in modern daily practice. The emergence of primary PCI has dramatically improved outcomes for patients with STEMI in the last decade.^{11–12} The improvement in vessel patency and the higher rate of TIMI flow, and the reduction of fatal haemorrhagic stroke, are the key reasons for the success of primary PCI. Moreover, in-hospital mortality has consistently declined over the last decade. Age and LVEF are the most consistent predictors of mortality in STEMI since the introduction of aspirin and thrombolytic therapy.^{13–15} Recent clinical trials have moreover combined the clinical and angiographic information for identifying the predictors of mortality in STEMI. Impaired LV systolic function remains a dominant predictor of cardiovascular events among STEMI patients undergoing PCI.^{7–16–19}

Mounting evidence demonstrates that about half of patients with STEMI have multivessel coronary artery disease.^{20–21} The incidence of multivessel coronary artery disease in the

Table 4 Multivariate analysis

Variables	OR	95% CI	p Value
Age >60 years	2.98	1.17 to 7.05	0.01
Female sex	1.33	0.60 to 2.92	0.48
Smoking	0.69	0.27 to 1.81	0.46
Cardiogenic shock at admission	1.78	0.82 to 3.87	0.14
Creatinine >1.5 mg/dL	0.81	0.37 to 1.81	0.62
Haemoglobin <10 g/dL	2.19	0.97 to 4.93	0.06
Admission troponin T	0.99	0.95 to 1.04	0.83
Admission plasma glucose	1.00	1.000 to 1.006	0.01
LVEF <40%	2.53	1.20 to 5.36	0.02
Triple vessel disease	1.86	0.73 to 4.72	0.19
Reference vessel diameter	0.99	0.69 to 1.42	0.97
Stented implanted	0.85	0.31 to 2.37	0.77
Final TIMI flow grade 0/1	20.55	3.49 to 120.94	0.001

LVEF, left ventricular ejection fraction; TIMI, Thrombolysis in Myocardial Infarction.

present study is ~78%, which is relatively high compared to previous studies.^{21 22} Although several studies have reported that a greater degree of coronary artery disease is associated with a worse prognosis in these patients, multivessel coronary artery disease was not an independent risk factor of in-hospital mortality in the present study. This indicates that primary PCI of the infarct-related artery may be sufficient to reduce in-hospital mortality.

System delays to reperfusion are correlated with higher rates of mortality and morbidity.² Door-to-device time is critical and key to preserving the jeopardised muscle.^{3 23} Although the majority of the patients (78%) in the present study underwent primary PCI within 90 min or less, a significant number of patients (22%) still had a door-to-device time >90 min. The causes of in-hospital delay may due to the patient preparation process, including the blood sample draw process, electrocardiographic and echocardiographic examination, and resuscitation therapy in the emergency room. The skip emergency room strategy may reduce the door-to-device time and probably improve patient outcomes.

A key to the success of primary PCI in patients with STEMI is patency of the infarct related artery after revascularisation therapy.⁴ TIMI grade has been accepted as the gold standard for evaluating patency of the epicardial artery. Most of the patients in the present study (96.5%) achieved TIMI flow grade 2/3 and the overall incidence of no-reflow phenomenon was 2.2%. Thrombus aspiration was performed in 55% of the patients and intracoronary glycoprotein IIb/IIIa inhibitor was administered in 49% of them.

The in-hospital mortality (11.6%) was higher than that reported in previous clinical trials.^{24 25} Shihara *et al*²² reported in-hospital and 1-year mortality rates of 7.1% and 10.9%, respectively. The high mortality rate in the present study may be attributable to the high proportion of patients with cardiogenic shock transferred to our heart centre. The non-high risk and stable patients were probably treated at local hospitals and transferred for risk stratification after the event.

The definition of cardiogenic shock and the difference of the study population may contribute to the higher prevalence of cardiogenic shock in this study compared to previous studies.^{26 27} The incidence of acute myocardial infarction complicated by cardiogenic shock in a single community hospital reported by Goldberg *et al*²⁶ was 7.1% and the in-hospital mortality was 71.7%. Awad *et al*²⁷ reported that the incidence of cardiogenic shock in the Global Registry of Acute Coronary Events (GRACE) registry was 4.6% and the overall mortality rate was 59.4%. The haemodynamic criteria for cardiogenic shock, including pulmonary capillary wedge pressure and cardiac index information, were not available in the present study; therefore, other possible causes of hypotension including hypovolaemic shock, right ventricular infarction, and hypotension secondary to bradycardia could not be absolutely excluded. However, in the present study, most of the patients with admission cardiogenic shock (70.4%) required intra-aortic balloon pump therapy to support their haemodynamic status, and may represent the high-risk STEMI population who required intensive cardiac care and early coronary interventions.

Risk stratification in patients with STEMI is crucial for guiding therapy and managing patient risk. The risk score and multivariable model derived from clinical trials comprised highly selected populations but may not include all patients in daily clinical practice.²⁸ Differences in treatment strategy and the availability of coronary intervention may result in different outcomes. A TIMI risk score for STEMI is clinically useful for

triaging and managing fibrinolytic-eligible patients, but may not be suitable for those undergoing a revascularisation procedure in PCI-capable hospitals.¹³ The CADILLAC risk score defined seven risk factors (age >65 years, Killip class 2/3, LVEF <40%, anaemia, renal insufficiency, triple vessel disease, and TIMI flow grade) that accurately predict short- and long-term outcomes in patients with STEMI undergoing primary PCI.¹⁷ The CADILLAC risk score was derived from two clinical trials that excluded patients with cardiogenic shock at presentation. The GRACE risk score—a multivariable logistic regression model derived from patients with non-ST elevation and ST elevation acute coronary syndrome enrolled in GRACE—has not been verified for patients with STEMI undergoing primary PCI.²⁹ Sanguanwong *et al*,³⁰ using data from the Thai Acute Coronary Syndrome Registry (TACSR), reported that age ≥75 years, diabetes, shock, and cardiac arrhythmias were predictors of in-hospital mortality in patients with STEMI. The total mortality rate in TACSR was 17% and primary PCI was performed in 22.24% of all patients. Recently, the ALPHA score defined five variables (age, heart rate, systolic blood pressure, access site, and anterior localisation of the infarction) that were associated with 30-day mortality in patients with STEMI treated with primary PCI.³¹ The ALPHA score could be calculated without the need for ventriculography and blood tests.

Limitations

There are several limitations of the present study that should be acknowledged. First, the retrospective observational study design is subject to bias. Second, single centre operator experience should be taken into account. Third, patients who underwent rescue PCI and a pharmaco-invasive approach—as recommended by the current guideline—were excluded. Finally, the diagnosis of admission cardiogenic shock might be overestimated in this present study due to the lack of haemodynamic criteria for cardiogenic shock.

CONCLUSION

This study demonstrates that age >60 years, LVEF <40%, and final TIMI grade 0/1 are significant predictors of in-hospital

Key messages

What is already known about this subject?

Aging and left ventricular function are predictors of short- and long-term mortality in patients with ST elevation acute coronary syndrome in randomised controlled trials.

What does this study add?

The present study adds important information on very high-risk patients with ST elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention in a tertiary heart centre. The proportion of patients with cardiogenic shock is higher than those reported in previous studies. The present study demonstrated that age, left ventricular ejection fraction, and final TIMI flow were associated with in-hospital mortality.

What might this impact on clinical practice?

The results of this study support the use of intensive treatment in high-risk patients with STEMI to improve the clinical outcomes.

mortality in unselected patients with STEMI undergoing primary PCI. Our findings highlight the importance of LV function assessment before primary PCI, and suggest that optimal restoration of myocardial reperfusion during the PCI procedure is essential for improving patient outcomes.

Contributors SK: initiated the study design. CW and BP: provided the statistical analysis. All authors contributed to refinement of the study protocol, data collection and approved the final manuscript.

Competing interests None declared.

Ethics approval Khon Kaen University Ethics Committee.

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Data sharing statement The raw data will be provided on request at: sonkia@kku.ac.th.

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