

ORIGINAL ARTICLE

Risk Factors for Major Adverse Cardiac Events Outcomes in Post Percutaneous Coronary Intervention during Index Admission

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ABSTRACT

Introduction: Patients with ST-segment elevation myocardial infarction (STEMI) often undergo percutaneous coronary intervention (PCI) procedures during their index hospitalisation. However, some factors may increase the risk of major adverse cardiac event (MACE) outcomes after delaying PCI. We aimed to determine the risk factors for MACE outcomes in acute STEMI patients who had PCI during their index admission. **Methods:** In this retrospective single-center study, the medical records of STEMI patients who had PCI during their index hospitalisation in our facility were retrieved. At 30 days and six months post-PCI, demographic characteristics, clinical presentation, coronary risk factors, and the rate of MACE outcome were recorded and analysed. **Results:** This study included 91 STEMI patients. At 30 days and six months post-PCI, the rate of MACE was 10.5% and 8.0% respectively. At 30 days post-PCI, gender ($p = 0.025$), systolic blood pressure ($p = 0.005$) and heart rate ($p = 0.003$) were all associated with MACE outcomes. At six months, systolic blood pressure ($p = 0.017$), heart rate ($p = 0.003$), and previous coronary artery disease (CAD) ($p = 0.014$) were all associated with MACE. **Conclusion:** In acute STEMI patients, female gender, systolic blood pressure, heart rate, and a history of CAD are the risk factors for MACE outcomes after the PCI during the index admission. However, this is only single center study with short follow up period. Therefore, multi centers study and longer follow up period could provide better understanding on the factors associated with delayed PCI. *Malaysian Journal of Medicine and Health Sciences* (2023) 19(4):130-138. doi:10.47836/mjmh19.4.20

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INTRODUCTION

Acute Coronary Syndrome (ACS) is a serious complication of atherosclerotic coronary artery disease. Three main categories of ACS were ST-elevation myocardial infarction (STEMI), Non-STEMI and unstable angina (1). Acute STEMI remains a main health issue globally. STEMI accounts for about 25% to 40% of all acute myocardial infarctions (2). In Europe, STEMI had an annual incidence rate of 58 per 100,000 in 2015 (3). While in Malaysia scenario, STEMI was responsible for 10.6%, 12.3%, and 17.9% of the in-hospital, 30-day, and 1-year mortality respectively (4). Reperfusion therapy is the principal treatment for STEMI patients. It can be done pharmacologically (administration of fibrinolysis) or mechanically (involving coronary intervention) (2). The mortality rate of STEMI patients has been reduced due to the extensive use of reperfusion therapy (3, 4).

Primary percutaneous coronary intervention (primary PCI) is used to treat STEMI patients who have not been priorly treated with fibrinolytics (3). Immense evidence has shown that mechanical reperfusion is better than fibrinolytic therapy (5). In a prospective cohort study, primary PCI was the most frequently used treatment for STEMI and associated with low total in-hospital mortality (6). The time that it takes to restore reperfusion in patients with STEMI is critical because the time loss is equivalent to myocardial loss (7). The best way to treat STEMI is to begin reperfusion therapy as soon as possible (within the first 12 hours after the symptoms onset) (2), and this approach has been shown to improve the clinical outcomes (8). Meanwhile, the longer time is taken to receive treatment once arriving at the hospital which has increased the mortality in STEMI patients (9). Additionally, PCI was helping to reduce cost in the management of STEMI patients in Japan. PCI was found to be more cost-effective than pharmacotherapy approach with a cost-effectiveness probability of 99.9% (10).

Major Adverse Cardiac Events (MACE) can be defined

as a combined clinical endpoint that signifies the effectiveness and safety outcomes of certain interventions, especially in cardiology. The components of MACE include all-cause mortality, cardiac death, myocardial infarction, repeated coronary revascularization, stroke, hospitalization due to heart failure, or coronary artery bypass grafting (11). Globally, the prevalence of MACE post-PCI was varied from one study to another. A pooled data from prospective randomised stent trials showed that 1-year MACE rate was 7.9% while the overall 5-year rate of MACE was 16.1% (12). Separated by gender, the MACE rate for men and women at 30-day after PCI were 3.6% and 4.2% respectively, and increased to 17.7% and 18.9% for men and women, respectively after 5 years (13). In Malaysia, the available data demonstrated that the MACE rate at 30-day post-PCI was 10.7% in non-diabetic STEMI patients and 13.8% in diabetic STEMI patients respectively (14). MACE outcomes contribute to the increase of illness and death of coronary artery disease (CAD) patients after the percutaneous coronary intervention (PCI) procedure. Thus, the risk factors associated with MACE need to be identified and treated as early as possible to reduce the mortality rate (15).

Although primary PCI is the preferred reperfusion approach, its availability may be limited (16). In some areas, mainly in developing countries, early revascularization by pharmacoinvasive or PCI remains the main challenge. As a result, many STEMI patients missed it (17). Alternatively, delayed PCI becomes the preferred option, and the delay may contribute to the occurrence of MACE outcomes post-PCI. This will have a huge impact on the patients' quality of life. A study found that the combined endpoints of mortality, ischemic events, reinfection, and the need for revascularization were significantly higher in delayed PCI group as compared to early PCI group at 30 days (30.9% vs. 8.5%) and six months (50.6% vs. 25.6%) post-PCI (18). Nevertheless, factors such as diabetes, heart failure, and older age increased the risk for MACE outcomes in ACS patients (19). Hence, it is critical to identify what factors that predict MACE outcomes in acute STEMI patients who had PCI procedures during their index admission. The assessment of risk factors, clinical characteristics, and PCI outcomes will provide valuable information for effective prevention and control strategies, which will improve the management of STEMI patients post-PCI. Therefore, the current study aimed to determine the risk factors of MACE outcomes for STEMI patients who underwent PCI during the index admission.

MATERIALS AND METHODS

This retrospective single-center study was performed at a tertiary governmental university hospital. The Human Research Ethics Committee of Universiti Sains Malaysia has approved this study's protocol (USM/JEPeM/18040202). The researchers retrieved the medical files of all STEMI patients who were 18 years of age or

older, admitted with or without fibrinolytic therapy, and treated by PCI during index admission from January 2013 to March 2018. Data collection focused on the demographic characteristics, clinical presentation, coronary risk factors, coronary angiography parameters, and the outcomes of PCI. The information was gathered using a standard data collection form. Only STEMI diagnoses that were documented in the patients' medical records were included in this study. A diagnosis of STEMI was made based on the symptoms, electrocardiogram changes, and cardiac biomarker measurement. STEMI was then confirmed if at least two out of these criteria occurred (20, 21). Meanwhile, STEMI diagnoses that treated by a primary PCI strategy or underwent PCI after discharge from the hospital were excluded.

End point and study definition

The primary end point was the rate of MACE at 30 days and six months for STEMI patients' post-PCI. Secondary end point was the determination and association of the risk factors in STEMI patients with MACE at 30 days and six months post-PCI. STEMI was defined as a clinical syndrome characterized by the presence of myocardial ischemic symptoms and associated with persistent electrocardiographic ST-segment elevation and/or subsequent raising of the cardiac enzymes (22). PCI during index admission was referred to the implementation of PCI after 48 hours and up to 28 days after the onset of STEMI, and during the same hospitalisation of patients (23). The 48-hour cut-off was selected based from the previous studies (24, 25). MACE outcomes were defined as the occurrence of one or more of the following: cardiac death, recurrent myocardial infarction, stroke, rehospitalisation due to heart failure, or repeated coronary revascularization (11). The MACE outcomes were recorded 30 days and six months after PCI by reviewing the patients follow-up notes and by phone calls.

Statistical analysis

All statistical analyses were carried out with the IBM® Statistical Package for Social Science (SPSS®) version 24 software (IBM®; Armonk, New York, United States). Continuous variables were presented as mean (standard deviation, SD) while categorical variables were summarised by frequency and percentage. The Simple Logistic Regression (SLogR) analysis was performed to identify variables that could be associated with the MACE outcome. The absence and presence of MACE were coded as '0' and '1' respectively. Clinically relevant variables and variables from the SLogR analysis (p -value < 0.25) were identified. The identified variables were included in the Multiple Logistic Regression (MLogR) analysis for variable selection in the final model of MLogR. The variable selection was performed with conditional, backward, and forward stepwise procedures. Only variables with p -value < 0.05 from these procedures were selected as final variables, and included in the final model of MLogR. The final model

was then performed with the enter method in order to find the association of the final variables with the MACE outcomes. Significant analysis was determined by a 2-sided p-value of less than 0.05. The model fitness was evaluated using the area under the Receiver Operation Characteristic (ROC) curve. The model was considered fit when there was more than 0.8 (80%) area under the ROC curve with a p-value less than 0.05.

RESULTS

Between January 2013 and March 2018, a total of 168 STEMI patients were screened. Seventy-seven out of them were excluded. The reasons for the exclusion were due to the patients were treated by primary PCI (two patients) and undergone PCI after discharge (75 patients). Finally, 91 patients were enrolled in this study.

Demographic and medical background

The mean (SD) age of all patients was 55.80 (11.0) years, and 85.7% of the patients were male. Meanwhile, the mean body mass index (BMI) for all patients was 25.9 (4.9) kg/m². The mean (SD) systolic and diastolic blood pressure (BP) were 134.84 (28.22) and 82.43 (22.14) mmHg respectively. In this study, more than half of the patients were smokers. The main risk factors were hypertension, dyslipidaemia, and diabetes mellitus. Moreover, our study population also had previous coronary artery disease (CAD), atrial fibrillation, cerebrovascular accident, angioplasty, and chronic kidney disease (CKD). During their admission, the majority of our patients were classified as Killip class I. The most common type of STEMI was the anterior, followed by the inferior. The angiographic findings revealed that nearly half of all patients had single-vessel disease, followed by two-and three-vessel disease. The majority of the patients had achieved Thrombolysis In Myocardial Infarction (TIMI) flow grade 3 after PCI. The majority of patients received fibrinolysis as STEMI treatment, followed by PCI. In terms of in-hospital and discharge medications, patients received adenosine di-phosphate (ADP) inhibitors, aspirin, beta-blockers, angiotensin-converting enzyme inhibitors (ACEI) and statins as medications (Table I).

Clinical outcomes and factors associated with MACE outcomes

At 30 days after PCI, the overall MACE rate was 10.5%, and at six months, it was 8.0%. Rehospitalization due to heart failure was the most common post-PCI clinical outcome at both time points. Meanwhile, upper gastrointestinal bleeding was the cause of the reported major bleeding (Table II).

From the SLogR analysis, at 30 days post-PCI, significant association was seen between variables of gender, systolic BP, and heart rate with MACE outcomes. Meanwhile, at six months post PCI, only heart rate had shown a significant association with MACE

Table I: Demographic and medical background of STEMI patients.

Variables	Mean (SD)	Frequency (%)
Age (years)	55.80 (11.0)	
BMI (kg/m ²)	25.9 (4.9)	
Systolic BP (mmHg)	134.84 (28.22)	
Diastolic BP (mmHg)	82.43 (22.14)	
Heart rate (bpm)	79.07 (24.66)	
DNT (min)	81.97 (172.38)	
Gender		
Male		78 (85.7)
Female		13 (14.3)
Coronary risk factors		
Smoking		55 (64.7)
Hypertension		42 (46.2)
Dyslipidaemia		34 (37.4)
Diabetes Mellitus		33 (36.3)
Previous CAD		11 (12.1)
History of CKD		10 (11.0)
History of AF		2 (2.2)
History of CVA		1 (1.1)
Previous angioplasty		2 (2.2)
Previous CABG		0 (0.0)
Killip Class		
I		47 (51.6)
II		21 (23.1)
III		7 (7.7)
IV		13 (14.3)
STEMI Location		
Anterior		56 (61.5)
Inferior		33 (36.3)
Lateral		1 (1.1)
Posterior		1 (1.1)
Diseased Vessels		
1VD		45 (49.5)
2VD		35 (38.5)
3VD		11 (12.1)
TIMI Flow Post-PCI		
0		0 (0.0)
1		0 (0.0)
2		2 (2.2)
3		88 (97.8)
Medications during hospitalisation and at discharge		
Fibrinolysis		79 (86.8)
Aspirin		91 (100.0)
ADPI		86 (97.7)
ACEI		57 (64.0)
Beta-Blockers		38 (42.7)
Statin		72 (80.9)

BMI: Body mass index, BP: Blood pressure, DNT: Door to needle time, CAD: Coronary artery disease, CKD: Chronic kidney disease, AF: Atrial fibrillation, CVA: Cerebrovascular accident, CABG: Coronary artery bypass grafting, VD: Vessel diseased, TIMI: Thrombolysis in myocardial infarction, ADPI: Adenosine di-phosphate receptor inhibitors, ACEI: Angiotensin converting enzyme.

outcomes (Table III). In addition to the significant SLogR parameters, we identified parameters that had a p-value of less than 0.25 (from SLogR analysis) and also clinically relevant parameters. Age, diastolic BP, hypertension, dyslipidemia, diabetes mellitus, and door to needle time

Table II: MACE outcomes at 30 days and 6 months follow up

Variables	30 Days Post-PCI	6 Months Post-PCI
MACE	9 (10.5)	6 (8.0)
Mortality	2 (2.2)	2 (2.5)
Stroke	2 (2.4)	1 (1.4)
Reinfarction	1 (1.1)	0 (0.0)
Rehospitalisation due to HF	9 (10.5)	6 (8.1)
Repeated revascularization		
PCI	1 (1.2)	0 (0.0)
CABG	0 (0.0)	0 (0.0)
Major bleeding	1 (3.4)	1 (1.4)

Value presented as frequency (%). MACE: Major adverse cardiac event, HF: Heart failure, PCI: Percutaneous coronary intervention, CABG: Coronary artery bypass grafting.

(DNT) were the parameters with a p-value less than 0.25. The history of smoking, previous CAD, and CKD were identified as the clinically relevant parameters. All these parameters were then analysed in the MLogR analysis.

The results of MLogR showed that at 30 days post PCI, female gender, systolic BP, and heart rate at admission had significant associations with MACE outcomes. At six months, the systolic BP, heart rate, and previous CAD history were all significantly associated with MACE outcomes (Table IV). The area under the ROC curve was applied to evaluate the final model fitness for factors that were significantly associated with MACE outcome. There was good model fitness, fulfilled model assumptions, and no problems with multicollinearity or interaction. At 30 days after PCI, the area under the ROC curve was 0.945 (94.5%), $p < 0.001$ (Fig. 1), and at six months after PCI, it was 0.925 (92.5%), $p = 0.001$ (Fig. 2). The results indicated excellent discriminant ability for this model.

DISCUSSION

In this retrospective single-center study, smoking, being overweight or obese, hypertension, dyslipidaemia, and diabetes mellitus were all prevalent in our study participants. Meanwhile, female gender, low systolic BP, high heart rate, and previous CAD were the significant risk factors of MACE outcomes.

Patients in the current study had a mean age of 55.80 (11.0) years. There were younger than patients from other countries and studies, where the average age of STEMI patients was over 60 years (26-28). The early onset of STEMI among our patients could be explained due to a higher prevalence of smoking, an established coronary risk factor. Smoking constituted 64.7% of our STEMI patients. This is slightly higher than data from the NCVD-ACS registry which demonstrated that 51.7% of STEMI patients were current smokers (4). Meanwhile, the smokers' percentage in the Global Registry of Acute Coronary Events (GRACE) registry was 56.7% (28). In term of gender, the majority (85.7%) of patients in this study were males. This is in accordance

Table III: Simple logistic regression analysis at 30 days and 6 months

Variables	30 Days Post-PCI		6 Months Post-PCI	
	Crude Odds Ratio (95% CI)	p-value	Crude Odds Ratio (95% CI)	p-value
Age	1.04 (0.97, 1.12)	0.200	1.08 (0.98, 1.20)	0.111
Systolic BP	0.96 (0.93, 0.99)	0.015	0.97 (0.94, 1.01)	0.219
Diastolic BP	0.97 (0.93, 1.01)	0.146	0.99 (0.95, 1.03)	0.740
Heart rate	1.02 (1.00, 1.05)	0.048	1.03 (1.00, 1.06)	0.048
DNT (min)	1.00 (1.000, 1.008)	0.059	0.99 (0.98, 1.01)	0.718
TIMI	0.00 (0.00,)	0.999	0.00 (0.00,)	0.999
Gender				
Male	1.00		1.00	
Female	12.50 (2.71, 57.56)	0.001	4.44 (0.68, 28.69)	0.119
Smoking				
No	1.00		1.00	
Yes	2.04 (0.47, 8.87)	0.341	1.39 (0.21, 9.00)	0.725
Hypertension				
No	1.00		1.00	
Yes	0.35 (0.003, 1.52)	0.165	0.12 (0.01, 1.09)	0.060
Dyslipidaemia				
No	1.00		1.00	
Yes	0.30 (0.07, 1.30)	0.108	0.30 (0.05, 1.76)	0.184
Diabetes Mellitus				
No	1.00		1.00	
Yes	0.36 (0.08, 1.47)	0.155	0.19 (0.03, 1.12)	0.067
Previous CAD				
No	1.00		1.00	
Yes	1.19 (0.13, 10.58)	0.873	0.22 (0.03, 1.46)	0.119
History of CKD				
No	1.00		1.00	
Yes	0.92 (0.10, 8.40)	0.947	0.56 (0.05, 5.54)	0.624
Fibrinolysis				
No	1.00		1.00	
Yes	0.83 (0.09, 7.42)	0.873	1.52 (0.15, 14.76)	0.716
ADPI				
No	1.00		1.00	
Yes	0.00 (0.00)	1.000	0.00 (0.00)	1.000
ACEI				
No	1.00		1.00	
Yes	1.48 (0.36, 5.98)	0.581	1.55 (0.29, 8.27)	0.604
Beta-blocker				
No	1.00		1.00	
Yes	1.42 (0.33, 6.11)	0.636	0.68 (0.12, 3.63)	0.655
Statin				
No	1.00		1.00	
Yes	1.18 (0.22, 6.27)	0.845	2.15 (0.35, 13.04)	0.404

BP: Blood pressure, DNT: Door to needle time, TIMI: Timing in myocardial infarction, CKD: Chronic kidney disease, CAD: Coronary artery disease, ADPI: Adenosine di-phosphate receptor inhibitors, ACEI: Angiotensin converting enzyme inhibitors.

Table IV: Factors associated with MACE outcome at 30 days and 6 months post-PCI

Variables	Crude Odds Ratio ^a (95% CI)	Adjusted Odds Ratio ^b (95% CI)	p-value ^b
30 Days Post-PCI			
Gender	1.00	1.00	
Male	4.44 (0.68, 28.69)	10.91 (1.35, 87.80)	0.025
Female			
Systolic BP (mmHg)	0.97 (0.94, 1.01)	0.92 (0.87, 0.97)	0.005
Heart rate (bpm)	1.03 (1.00, 1.06)	1.09 (1.03, 1.16)	0.003
6 Months Post-PCI			
Systolic BP (mmHg)	0.97 (0.94, 1.01)	0.93 (0.88, 0.98)	0.017
Heart rate (bpm)	1.03 (1.00, 1.06)	1.08 (1.02, 1.14)	0.003
Previous CAD	1.00	1.00	
No			
Yes	0.22 (0.03, 1.46)	27.41 (1.97, 380.21)	0.014

^aSimple logistic regression, ^bMultiple logistic regression, CI: Confidence interval, BP: Blood pressure, CAD: Coronary artery disease.

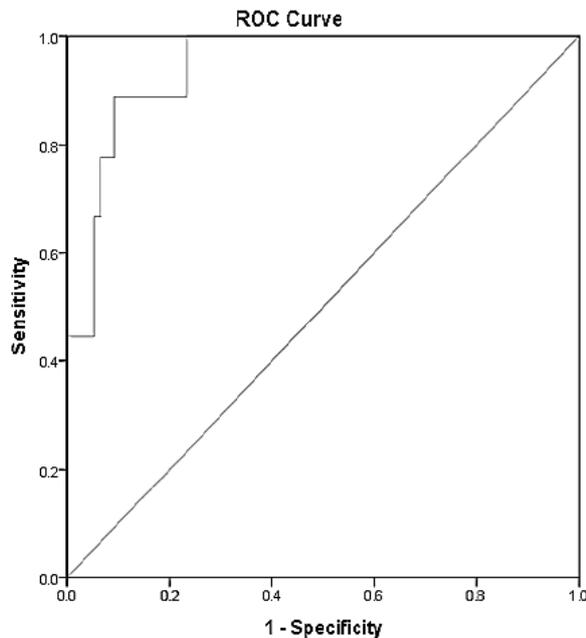


Figure 1: The Receiver Operation Characteristic (ROC) curve of the final model fitness for the associated factors with MACE outcome at 30 days post-PCI. Area under the ROC curve was 0.945 (94.5%) and $p < 0.001$ indicated excellent discriminant ability for this model.

with our National Cardiovascular Disease Database-Acute Coronary Syndrome (NCVD-ACS) registry, which revealed that 86.9% of all patients were male (4). Similarly, 70% of STEMI patients in the Romanian STEMI registry were male (26). The average body mass index (BMI) for patients in the current study was 25.9 (4.9) kg/m². The value was similar to that of the NCVD-ACS registry, in which the mean was 26.0 kg/m² (4).

Comorbidities, namely hypertension, dyslipidaemia, and diabetes mellitus, were commonly reported risk

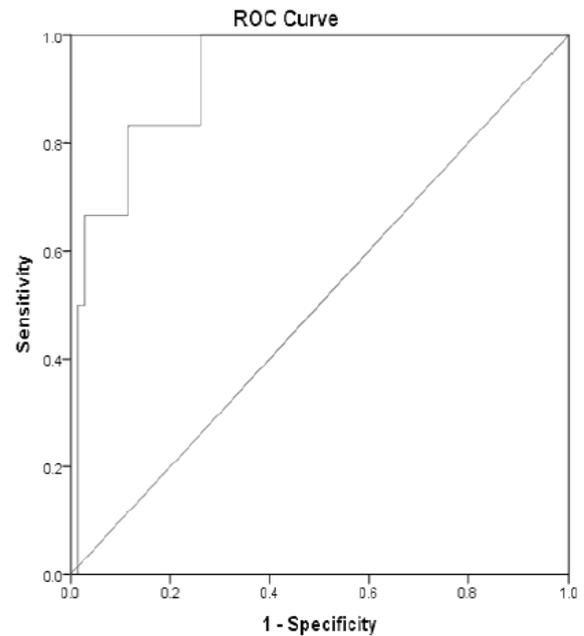


Figure 2: The Receiver Operation Characteristic (ROC) curve of the final model fitness for the associated factors with MACE outcome at six months post-PCI. Area under the ROC curve was 0.925 (92.5%) and $p = 0.001$ indicated excellent discriminant ability for this model.

factors in our STEMI patients. The percentages of our STEMI patients who had hypertension, dyslipidaemia, and diabetes mellitus were 46.2%, 37.4%, and 36.3% respectively. In the local scenario, 38.0% of patients were diagnosed with diabetes mellitus, 36.1% with hypertension, and 28.8% with dyslipidaemia as reported in the NCVD-ACS registry (4). In the GRACE registry, the percentages of hypertension, dyslipidaemia, and diabetes mellitus were 57.8%, 43.6%, and 23.3% respectively (28). In short, these comorbidities were common and had significant impact on STEMI patients. Hypertensive STEMI patients had more cardiovascular risk factors and a more complicated clinical course of MI than those who did not have hypertension (29). Hypertensive patients who had PCI, recorded a higher long-term mortality rate than non-hypertensive patients (30). Meanwhile, dyslipidaemia emerged as an independent predictor of STEMI in patients without chest pain (31). Moreover, diabetes mellitus was linked to in-hospital and annual mortality of STEMI patients (32, 33). A study pooled patient-level data from 21 randomized PCI trials demonstrated that, diabetes mellitus were independent predictors of MACE 5 years following PCI. Besides, diabetes mellitus and hyperlipidaemia were found to be the independent predictors for all-cause death after 5 years of PCI (13).

At 30 days and at six months after PCI, the overall MACE rate was 10.5% and 8.0% respectively. There were various MACE rates that have been reported previously. Data taken from Korea Acute Myocardial Infarction Registry revealed that MACE rate at 2-year follow up

for different group of STEMI patients who underwent delayed PCI was ranged from 13.4% to 17.9% (34). In a patient-level pooled data from prospective randomised stent trials, 1-year MACE rate was 7.9% while the overall 5-year rate of MACE was 16.1% (12). In Malaysian context, our finding was similar to a reported data from The Asia Pacific Evaluation of Cardiovascular Therapies (ASPECT) collaboration. The ASPECT data revealed that, the MACE rate at 30-day post-PCI was 10.7% in non-diabetic STEMI patients and 13.8% in diabetic STEMI patients respectively (14).

Our study found that after 30 days post PCI, MACE outcomes were significantly associated with the female gender, low systolic BP, and high heart rate at patients' admission. At six months post-PCI, a significant association was seen between systolic BP, heart rate, and the history of CAD with MACE outcomes. Female patients had a higher odds of having MACE outcomes by 10.9 times than male patients. An observational study on the sex differences in ACS conducted in our country may explain these findings. In that study, older female patients were diagnosed with more comorbidities, and tended to refuse treatments (35). Another study stated that female CAD patients (including STEMI) recorded a higher rate of MACE than male patients after a year of undergoing PCI (36). According to individual patient data pooled analysis from randomised PCI trials at 30 days and 5 years showed that the rate of MACE was significantly higher in women than men (4.2% vs. 3.6% and 18.9% vs. 17.7% respectively). Women also showed higher rate of all-cause death, cardiac death and ischemia-driven target lesion revascularization as compared to men at 5-year follow-up. Furthermore, in multivariable analysis, female gender was found to be an independent predictor of MACE (13).

This study showed a reverse relationship between systolic BP and MACE outcomes. With an increased of one mmHg of systolic BP, the likelihood of having MACE is reduced by 8% and 7% at 30 days and six months post-PCI respectively. Hemodynamic instability (low systolic BP and rapid heart rate) during admission is an important predictor for in-hospital and short-term mortality after STEMI events (37-39). Previous findings have demonstrated that low systolic BP at the patient's presentation was associated with in-hospital MACE (40). While in the GRACE registry, the chances of having in-hospital mortality were 1.4 times higher with a decrease of 20 mmHg in the systolic BP (28). Furthermore, in STEMI patients who underwent primary PCI, the systolic BP < 100 mmHg independently predicts 1-year mortality (41). Lower at admission systolic BP (< 105 mmHg) of STEMI patients who underwent primary PCI was associated with a higher risk of both all-cause death and cardiac death (42). In a study among ACS patients (including STEMI), the mean pre-procedural systolic BP in group with MACE was significantly lower than group without MACE, indicating that lower systolic BP was

associated to the occurrence of MACE (43). Our study exhibited similar finding where mean systolic BP at admission of our patients with MACE at 30 days post-PCI was significantly lower than patients without MACE [112.3 (23.8) vs. 137.8 (27.2) mmHg, $p = 0.009$].

Increased of one bpm heart rate in our patients indicated that they were 1.09 and 1.08 times more likely to develop MACE at 30 days and six months post-PCI respectively. Similarly, in the GRACE registry, the possibility of having in-hospital mortality was increased 1.3 times with every 30 bpm rise in heart rate (28). In addition, for every 10 bpm increases in heart rate, the likelihood of mortality in a year increases by 1.18 times (44). Meanwhile, STEMI patients with heart rate ≥ 80 bpm at admission also had higher mortality rates for general and cardiac death after undergoing primary PCI (42). In line with this, the mean heart rate at admission in our patients who developed MACE was more than 80 bpm, and significantly higher compared to patients without MACE at 30 days [92.4 (24.3) vs. 75.2 (23.0) bpm, $p = 0.037$] and six months [96.0 (26.1) vs. 74.9 (22.53), $p = 0.033$] post-PCI.

At six months post-PCI, MACE was more likely to occur in patients with CAD history by 27.41 times as compared to patients without CAD history. MACE outcomes has been more common in patients with CAD when comparing to control without cardiovascular disease by at least 1.4 fold and is commonly noticed within 30 days of primary PCI (45). Additionally, presentation of coronary artery disease (acute or chronic) has been considered as an important variable affecting patient survival after undergoing PCI (46).

The current study has some limitations. One of the limitations was that only a single-centre experience was considered in this study. Furthermore, because the data was obtained retrospectively from the patients' records, it was possible that some variables were recorded incorrectly or that some variables were missing. There also no cut off values for systolic BP and heart rate were investigated in this study. Thus, no reference value for systolic BP and heart rate can be recommended. Nevertheless, our study offered a new sight on the local knowledge that was limited on the risk factors for MACE outcomes post-PCI during the index admission. Multi centres studies, longer follow up periods and identifying the ideal cut off value for certain variable such as blood pressure and heart rate are the promising areas that need to be focused on. This will offer sufficient evidences regarding the safety of delayed PCI strategy, as well as to minimise the MACE outcomes in patients who undergo PCI during their index admission.

CONCLUSION

At 30 days post-PCI, the factors of female gender, systolic BP, and heart rate were all significant predictors for MACE outcomes. At six months, systolic BP, heart rate,

and history of CAD were significant factors associated with MACE outcomes. In other words, these factors were significant in affecting the risk of STEMI patients having MACE outcomes after PCI. Therefore, these factors could be considered for PCI during the index admission for STEMI patients who were unable to receive early PCI.

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REFERENCES

1. Kumar A, Cannon CP. Acute coronary syndromes: diagnosis and management, part I. *Mayo Clin Proc.* 2009;84(10):917-38. doi: 10.1016/S0025-6196(11)60509-0.
2. O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2013;61(4):e78-e140. doi: 10.1016/j.jacc.2012.11.019.
3. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J.* 2018;39(2):119-77. doi: 10.1093/eurheartj/ehx393.
4. Wan Ahmad WA. (Ed). Annual report of the NCVD-ACS registry, 2014 - 2015. Kuala Lumpur, Malaysia: National Cardiovascular Disease Database, 2017.
5. Pollack C Jr. Pharmacological and mechanical revascularization strategies in STEMI: integration of the two approaches. *J Invasive Cardiol.* 2008;20(5):231-8.
6. Zeymer U, Ludman P, Danchin N, Kala P, Laroche C, Sadeghi M, et al. Reperfusion therapies and in-hospital outcomes for ST-elevation myocardial infarction in Europe: the ACVC-EAPCI EORP STEMI Registry of the European Society of Cardiology. *Eur Heart J.* 2021;42(44):4536-49. doi: 10.1093/eurheartj/ehab342.
7. Rathore SS, Curtis JP, Chen J, Wang Y, Nallamothu BK, Epstein AJ, et al. Association of door-to-balloon time and mortality in patients admitted to hospital with ST elevation myocardial infarction: national cohort study. *BMJ.* 2009;338:b1807. doi: 10.1136/bmj.b1807.
8. Boden WE, Eagle K, Granger CB. Reperfusion strategies in acute ST-segment elevation myocardial infarction: a comprehensive review of contemporary management options. *J Am Coll Cardiol.* 2007;50(10):917-29. doi: 10.1016/j.jacc.2007.04.084.
9. McNamara RL, Herrin J, Wang Y, Curtis JP, Bradley EH, Magid DJ, et al. Impact of delay in door-to-needle time on mortality in patients with ST-segment elevation myocardial infarction. *Am J Cardiol.* 2007;100(8):1227-32. doi: 10.1016/j.amjcard.2007.05.043.
10. Kodera S, Morita H, Kiyosue A, Ando J, Komuro I. Cost-effectiveness of percutaneous coronary intervention compared with medical therapy for ischemic heart disease in Japan. *Circ J.* 2019;83(7):1498-1505. doi: 10.1253/circj.CJ-19-0148.
11. Kip KE, Hollabaugh K, Marroquin OC, Williams DO. The problem with composite end points in cardiovascular studies: the story of major adverse cardiac events and percutaneous coronary intervention. *J Am Coll Cardiol.* 2008;51(7):701-7. doi: 10.1016/j.jacc.2007.10.034.
12. Madhavan MV, Redfors B, Ali ZA, Prasad M, Shahim B, Smits PC, et al. Long-term outcomes after revascularization for stable ischemic heart disease. An individual patient-level pooled analysis of 19 randomized coronary stent trials. *Circ Cardiovasc Interv.* 2020;13:e008565. doi: 10.1161/CIRCINTERVENTIONS.119.008565.
13. Kosmidou I, Leon MB, Zhang Y, Serruys PW, von Birgelen C, Smits PC, et al. Long-term outcomes in women and men following percutaneous coronary intervention. *J Am Coll Cardiol.* 2020;75(14):1631-40. doi: 10.1016/j.jacc.2020.01.056.
14. Wong MYZ, Yap JLL, Chih HJ, Yan BPY, Fong AYY, Beltrame JF, et al. Regional differences in percutaneous coronary intervention outcomes in STEMI patients with diabetes: The Asia-Pacific evaluation of cardiovascular therapies (ASPECT) collaboration. *Int J Cardiol.* 2023;371:84-91. doi: 10.1016/j.ijcard.2022.10.001.
15. Tsai IT, Wang CP, Lu YC, Hung WC, Wu CC, Lu LF, et al. The burden of major adverse cardiac events in patients with coronary artery disease. *BMC Cardiovasc Disord.* 2017;17(1):1. doi: 10.1186/s12872-016-0436-7.
16. Rashid MK, Guron N, Bernick J, Wells GA, Blondeau M, Chong AY, et al. Safety and efficacy of a pharmacoinvasive strategy in ST-segment elevation myocardial infarction: A patient population study comparing a pharmacoinvasive strategy with a primary percutaneous coronary intervention strategy within a regional system. *JACC: Cardiovasc Interv.* 2016;9(19): 2014-20. doi: 10.1016/j.jcin.2016.07.004.
17. Eagle KA, Goodman SG, Avezum A, Budaj A, Sullivan CM, Lypez-Sendyn J, et al. Practice variation and missed opportunities for reperfusion in ST-segment-elevation myocardial infarction:

- findings from the Global Registry of Acute Coronary Events (GRACE). *Lancet*. 2002;359(9304):373-7. doi: 10.1016/S0140-6736(02)07595-5.
18. Scheller B, Hennen B, Hammer B, Walle J, Hofer C, Hilpert V, et al. Beneficial effects of immediate stenting after thrombolysis in acute myocardial infarction. *J Am Coll Cardiol*. 2003;42(4):634-41. doi: 10.1016/s0735-1097(03)00763-0.
 19. Okkonen M, Havulinna AS, Ukkola O, Huikuri H, Pietilä A, Koukkunen H, et al. Risk factors for major adverse cardiovascular events after the first acute coronary syndrome. *Ann Med*. 2021;53(1):817-23. doi: 10.1080/07853890.2021.1924395.
 20. Clinical Practice Guidelines. Management of Acute ST Segment Elevation Myocardial Infarction (STEMI) 2019, 4th Edition. National Heart Association of Malaysia.
 21. Antman EM, Hand M, Armstrong PW, Bates ER, Green LA, Halasyamani LK, et al. 2007 Focused update of the ACC/AHA 2004 guidelines for the management of patients with ST-elevation myocardial infarction: A report of the American College of Cardiology/American Heart Association task force on practice guidelines. *Circulation*. 2008;117(2):296-329. doi: 10.1161/CIRCULATIONAHA.107.188209.
 22. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, et al. ESC Committee for Practice Guidelines (CPG). Third universal definition of myocardial infarction. *Eur Heart J*. 2012;33(20):2551-67. doi: 10.1093/eurheartj/ehs184.
 23. Zheng W, Yu CM, Liu J, Xie WX, Wang M, Zhang YJ, et al. Patients with ST-segment elevation of myocardial infarction miss out on early reperfusion: when to undergo delayed revascularization. *J Geriatr Cardiol*. 2017;14(8):524-31. doi: 10.11909/j.issn.1671-5411.2017.08.006.
 24. Bodn V, Rumiz E, Merlos P, Nunez J, Lypez-Lereu MP, Monmeneu JV, et al. One-week and 6-month cardiovascular magnetic resonance outcome of the pharmacoinvasive strategy and primary angioplasty for the reperfusion of ST-segment elevation myocardial infarction. *Revista Española de Cardiología (English Edition)*. 2011;64(2): 111-20. doi: 10.1016/j.rec.2010.10.010.
 25. Kanamasa K, Nakabayashi T, Hayashi T, Inoue Y, Ikeda A, Morii H, et al. Percutaneous transluminal coronary angioplasty performed 24-48 hours after the onset of acute myocardial infarction improves chronic-phase left ventricular regional wall motion. *Angiology*. 2000;51(4):281-8. doi: 10.1177/000331970005100402.
 26. Cretu DE, Udroui CA, Stoicescu CI, Tatu-Chitoiu G, Vinereanu D. Predictors of in-hospital mortality of ST-segment elevation myocardial infarction patients undergoing interventional treatment. An analysis of data from the RO-STEMI registry. *Maedica (Bucur)*. 2015;10(4):295-303.
 27. Chew DP, French J, Briffa TG, Hammett CJ, Ellis CJ, Ranasinghe I, et al. Acute coronary syndrome care across Australia and New Zealand: the SNAPSHOT ACS study. *Med J Aust*. 2013;199(3):185-91. doi: 10.5694/mja12.11854.
 28. Granger CB, Goldberg RJ, Dabbous O, Pieper KS, Eagle KA, Cannon CP, et al. Predictors of hospital mortality in the global registry of acute coronary events. *Arch Intern Med*. 2003;163(19):2345-53. doi: 10.1001/archinte.163.19.2345.
 29. Rembek M, Goch A, Goch J. The clinical course of acute ST-elevation myocardial infarction in patients with hypertension. *Kardiol Pol*. 2010;68(2):157-63.
 30. Bundhun PK, Wu ZJ, Chen MH. Impact of modifiable cardiovascular risk factors on mortality after percutaneous coronary intervention: A systematic review and meta-analysis of 100 studies. *Medicine (Baltimore)*. 2015;94(50):e2313. doi: 10.1097/MD.0000000000002313.
 31. Pong JZ, Ho AFW, Tan TXZ, Zheng H, Pek PP, Sia CH, et al. ST-segment elevation myocardial infarction with non-chest pain presentation at the Emergency Department: Insights from the Singapore Myocardial Infarction Registry. *Intern Emerg Med*. 2019;14(6): 989-97. doi: 10.1007/s11739-019-02122-3.
 32. Radomska E, Sadowski M, Kurzawski J, Gierlotka M, Poloński L. ST-segment elevation myocardial infarction in women with type 2 diabetes. *Diabetes Care*. 2013;36(11):3469-75. doi: 10.2337/dc13-0394.
 33. Park KH, Ahn Y, Jeong MH, Chae SC, Hur SH, Kim YJ, et al. Different impact of diabetes mellitus on in-hospital and 1-year mortality in patients with acute myocardial infarction who underwent successful percutaneous coronary intervention: results from the Korean Acute Myocardial Infarction Registry. *Korean J Intern Med*. 2012;27(4):180-8. doi:10.3904/kjim.2012.27.2.180.
 34. Ki YJ, Kang J, Yang HM, Woo Park K, Kang HJ, Koo BK, et al. Immediate compared with delayed percutaneous coronary intervention for patients with ST-segment-elevation myocardial infarction presenting ≥ 12 hours after symptom onset is not associated with improved clinical outcome. *Circ Cardiovasc Interv*. 2021;14(5):e009863. doi: 10.1161/CIRCINTERVENTIONS.120.009863.
 35. Lee CY, Hairi NN, Wan Ahmad WA, Ismail O, Liew HB, Zambahari R, et al. Are there gender differences in coronary artery disease? The Malaysian National Cardiovascular Disease Database - Percutaneous Coronary Intervention (NCVD-PCI) Registry. *PLoS One*. 2013;8(2):e72382. doi: 10.1371/journal.pone.0072382.
 36. Guo Y, Yin F, Fan C, Wang Z. Gender difference in clinical outcomes of the patients with coronary artery disease after percutaneous coronary intervention: A systematic review and meta-analysis. *Medicine*

- (Baltimore). 2018;97(30):e11644. doi: 10.1097/MD.00000000000011644.
37. Alexander KP, Newby LK, Cannon CP, Armstrong PW, Gibler WB, Rich MW, et al. Acute coronary care in the elderly, part I: Non-ST-segment-elevation acute coronary syndromes: a scientific statement for healthcare professionals from the American Heart Association Council on Clinical Cardiology: in collaboration with the Society of Geriatric Cardiology. *Circulation*. 2007;115(19):2549-69. doi: 10.1161/CIRCULATIONAHA.107.182615.
 38. Bueno H, Betriu A, Heras M, Alonso JJ, Cequier A, Garcia EJ, et al. Primary angioplasty vs. fibrinolysis in very old patients with acute myocardial infarction: TRIANA (TRatamiento del Infarto Agudo de miocardio eN Ancianos) randomized trial and pooled analysis with previous studies. *Eur Heart J*. 2011;32(1):51-60. doi: 10.1093/eurheartj/ehq375.
 39. Claessen BE, Kikkert WJ, Engstrom AE, Hoebbers LP, Damman P, Vis MM, et al. Primary percutaneous coronary intervention for ST elevation myocardial infarction in octogenarians: trends and outcomes. *Heart*. 2010;96(11):843-7. doi: 10.1136/hrt.2009.185678.
 40. Chen X, Li M, Jiang H, Li Y, Mo J, Lin P, et al. STEMI outcomes in Guangzhou and Hong Kong: Two-centre retrospective interregional study. *PLoS One*. 2016;11(3):e0149981. doi: 10.1371/journal.pone.0149981.
 41. Caretta G, Passamonti E, Pedroni PN, Fadin BM, Galeazzi GL, Pirelli S. Outcomes and predictors of mortality among octogenarians and older with ST-segment elevation myocardial infarction treated with primary coronary angioplasty. *Clin Cardiol*. 2014;37(9):523-9. doi:10.1002/clc.22313.
 42. Bordejevic DA, Caruntu F, Mornos C, Olariu I, Petrescu L, Tomescu MC, et al. Prognostic impact of blood pressure and heart rate at admission on in-hospital mortality after primary percutaneous intervention for acute myocardial infarction with ST-segment elevation in western Romania. *Ther Clin Risk Manag*. 2017;13:1061-68. doi:10.2147/TCRM.S141312.
 43. Labib S, Kassem HH, Kandil H. Peri-procedural blood pressure changes and their relationship with mace in patients undergoing percutaneous coronary intervention: a cross-sectional study. *Integr Blood Press Control*. 2020;13:187-95. doi: 10.2147/IBPC.S268848.
 44. Montalescot G, Dallongeville J, Van Belle E, Rouanet S, Baulac C, Degrandart A, et al. STEMI and NSTEMI: are they so different? 1 year outcomes in acute myocardial infarction as defined by the ESC/ACC definition (the OPERA registry). *Eur Heart J*. 2007;28(12):1409-17. doi: 10.1093/eurheartj/ehm031.
 45. Khoury H, Lavoie L, Welner S, Folkerts K. The Burden of Major Adverse Cardiac Events and Antiplatelet Prevention in Patients with Coronary or Peripheral Arterial Disease. *Cardiovasc Ther*. 2016;34(2):115-24. doi: 10.1111/1755-5922.12169.
 46. Farhadian M, Dehdar Karsidani S, Mozayanimonfared A, Mahjub H. Risk factors associated with major adverse cardiac and cerebrovascular events following percutaneous coronary intervention: a 10-year follow-up comparing random survival forest and Cox proportional-hazards model. *BMC Cardiovasc Disord* 21, 38 (2021). doi:10.1186/s12872-020-01834-1.