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Clinical predictors and outcomes of ST-elevation myocardial infarction related cardiogenic shock in the Asian population

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ABSTRACT

Background: Cardiogenic shock (CS) complicating myocardial infarction is associated with poor outcomes. Data among Asian populations are scarce. We aimed to investigate the long-term outcomes, prognostic factors, and predictors of CS among Asian ST elevation myocardial infarction (STEMI) patients.

Methods: This was a retrospective cohort study of consecutive patients undergoing primary percutaneous coronary intervention (PPCI) for STEMI within our regional STEMI network between 2015 and 2019. The long-term outcomes of those with and without CS were compared. Clinical predictors of outcomes and development of CS were investigated.

Results: A total of 1791 patients who underwent PPCI were included. Patients completed at least 2 years' follow-up with a median follow-up period of 2.6 years (IQR 1.0, 3,9). Overall, 208/1791 (11.6 %) STEMI patients developed CS. These patients were older (61.1 ± 12.5 vs 57.8 ± 12.2, P < 0.001) and mostly men (87.0 %). All-cause mortality (59.9 % vs 4.7 % P < 0.001), cardiac mortality (43.8 % vs 2.2 %, P < 0.001) and major adverse cardiovascular events (MACE) was significantly higher in the CS group (59.1 % vs 14.0 %, P < 0.001). Independent predictors of survival were higher index LVEF (adjusted hazards ratio [aHR] 0.967, 95 %CI 0.951–0.984, p < 0.001) and higher arterial pH at onset of shock (aHR 0.750, 0.626–0.897, p = 0.002). Increased serum lactate concentration independently predicts poor prognosis (aHR 1.084, 95 % CI 1.046–1.124, p < 0.001).

Conclusion: In Asian STEMI patients who underwent PPCI, CS was associated with poor outcomes. Higher LVEF on index admission was associated with better outcomes; while lactic acidosis independently predicted mortality.

1. Introduction

Cardiogenic shock (CS) is caused by severe impairment of myocardial performance resulting in diminished cardiac output, end-organ hypoperfusion and hypoxia. It is defined as a state in which ineffective cardiac output due to a primary cardiac disorder results in both clinical and biochemical manifestations of impaired tissue perfusion. This can present as severe hypotension refractory to volume resuscitation, with features of end-organ hypoperfusion requiring pharmacological or mechanical intervention [1].

CS is a continuum that extends from pre-shock to refractory shock states, with implications on timely administration of pharmacological and mechanical interventions [2]. Despite a multitude of etiologies, acute myocardial infarction (AMI) constitutes up to 81 % of all cases of CS [3]. Furthermore, CS complicates 5–10 % of AMI presentations and is the leading cause of mortality following MI [1].

Despite contemporary pharmacologic and invasive interventions, outcomes of patients with AMI complicated by CS are dismal. Hence,

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much is needed to guide risk stratification, patient selection, therapeutic strategies, and timely interventions.

Due to the paucity in data among the Asian population, we conducted a study aimed to investigate the prevalence of CS and compare the primary percutaneous coronary intervention (PPCI) procedural characteristics, immediate outcome and post-PPCI supportive care, in-hospital complications and long-term outcomes between those who developed CS and who did not among a group of patients who presented with ST-elevation myocardial infarction (STEMI) receiving contemporary STEMI treatment.

2. Methods

2.1. Study population

This was a retrospective cohort study of consecutive patients admitted with and treated with primary percutaneous coronary intervention (PPCI) between 1 July 2015 and 30 June 2019 within the Western STEMI network which provides PPCI services to three acute hospitals in Western Singapore as previously described [4,5]. All patients who underwent PPCI for STEMI were included. There were no exclusion criteria. The patients were divided into those with (CS) and without CS (non-CS) groups (Fig. 1). Ethics board approval was obtained from the National Healthcare Group Domain Specific Review Board and the requirement for informed consent was waived (Reference number 2020/00942).

We extracted patient demographics, medical history, clinical characteristics, cardiac catheterization information, in-hospital events during index admission and subsequent follow-up events from the hospital's electronic medical records. Index coronary angiographies on presentation were reviewed by three independent investigators. Patient comorbidities included both known and newly diagnosed conditions during the index admission for STEMI. STEMI was defined according to the fourth universal definition of MI [6]. CS was defined as a systolic blood pressure (SBP) less than 90 mmHg despite appropriate fluid resuscitation with clinical and biochemical evidence of end-organ damage [7], attributed to a primary cardiac disorder. Patients were stratified according to whether CS developed during index admission. Unfractionated heparin 70–100 IU/kg was administered during PPCI. Intraprocedural administration of drugs such as glycoprotein IIb/IIIa inhibitors, use of devices such as thrombectomy, balloon angioplasty, and if decision for stenting is made, choice of stent was left to the discretion of the interventional cardiologists. Only drug eluting stents (DES) were used in our center. The choice of subsequent medical therapy was left to the discretion of the treating physician.

Multivessel disease was defined as the presence of angiographic diameter stenosis of >50 % in ≥2 major coronary arteries. Coronary artery flow was assessed using the Thrombolysis in Myocardial Infarction (TIMI) frame count method[8]. Angiographic procedure success was defined as final TIMI 3 distal flow with less than 20 % vessel stenosis and no immediate mechanical complications. Thrombus burden was assessed according to the TIMI-thrombus scale [9]. Acute kidney injury was defined as an absolute increase in serum creatinine (sCr) ≥ 26.5 μmol/L or ≥1.5 fold from baseline, or urine output (UO) < 0.5 mL/kg/hr for 6 h[10]. Stroke was defined as any cerebrovascular event (hemorrhagic or non-hemorrhagic) satisfying the following criteria: 1) rapid onset of neurological deficit; 2) duration ≥24 h (unless therapeutic intervention); 3) absence of an alternative cause; 4) confirmation by neurologist/neurosurgeon.

2.2. Outcomes

The primary outcome was major adverse cardiovascular events (MACE), which consisted of a combined endpoint of all-cause mortality, unplanned repeat revascularization, myocardial infarction (MI), heart failure (HF), and stroke. Secondary outcomes included individual components of the primary outcome. Other outcomes include in-hospital events such as acute pulmonary edema (APE), atrial fibrillation (AF), ventricular tachycardia (VT) or ventricular fibrillation (VF), acute kidney injury (AKI), and all-cause mortality at 30-days.

2.3. Statistical analysis

Statistical analyses of categorical variables were performed with $\chi 2$ test and presented as frequencies with percentages. Continuous variables are presented as mean ± 1 SD and statistical analyses were performed with unpaired Student's *t*-test for normally distributed variables and Mann Whitney *U* test if otherwise. Kaplan-Meier curves were used to describe the cumulative MACE during follow-up, and the log-rank test was used to assess for any significant difference between the two groups.

Univariate and multivariate binary logistic regression analyses were performed to investigate for predictors of the development of

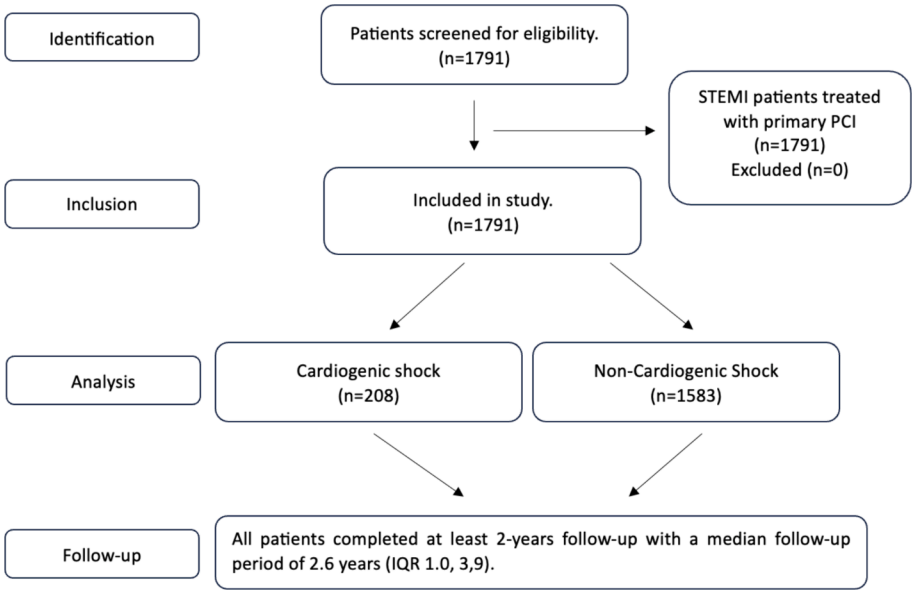

Fig. 1. STROBE Flow Diagram.

cardiogenic shock. Univariate and multivariate Cox regression analyses were performed to investigate the relationship between cardiogenic shock and MACE, and to identify the independent predictors of all-cause mortality among patients who developed cardiogenic shock. All statistical analyses were performed using IBM SPSS Statistics for Windows, V26.0 (IBM Corp, Armonk, New York, USA). A p value of < 0.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics

A total of 1791 patients who underwent PPCI were included. Patients completed at least 2 years' follow-up with a median follow-up period of 2.6 years (IQR 1.0, 3,9).

Baseline demographic, clinical characteristics and discharge medications are summarized in Supplementary Table 1. Overall, 208 (11.6 %) developed CS. Compared to patients without CS, those who developed CS were significantly older, had a higher prevalence of diabetes mellitus (DM), chronic kidney disease (CKD), previous diagnosis of HF, a longer door-to-balloon time (DTBT), and lower left ventricular ejection fraction (LVEF) during index admission. Guideline-directed medical therapy (GDMT) for post-STEMI patients such as dual antiplatelet therapy (DAPT), angiotensin-converting enzymes (ACE) inhibitors, angiotensin-receptor blockers (ARBs), beta-blockers and statins were significantly lower among the CS group compared to the non-CS group.

3.2. Procedural characteristics

Angiographic and procedural data are summarized in Supplementary Table 2. No significant differences in culprit vessel territory and prevalence of left main-triple vessel disease (LMTVD) were observed between the two groups. The use of glycoprotein 2b/3a (GP IIB/IIIA) inhibitors (29.8 % vs 26.2 %, p = 0.271), thrombectomy devices (38.0 % vs 39.4 %, p = 0.703), balloon angioplasty (92.3 % vs 93.6 %, p = 0.472) were also not significantly different between the two groups. However, coronary stenting of culprit vessel (78.8 % vs 86.5 %, p = 0.004) and post-procedure TIMI 3 flow (85.6 % vs 96.0 %, p < 0.001) was significantly lower in the CS group.

3.3. Clinical events and mortality

Compared to non-CS group, in-hospital events including acute pulmonary edema (APE), sepsis, atrial fibrillation (AF), bleeding according to the Bleeding Academic Research Consortium (BARC) criteria, ventricular tachycardia (VT), ventricular fibrillation (VF), and acute kidney injury (AKI) were markedly higher among the CS group (Table 1). 30-day mortality was significantly higher in the CS compared to non-CS group [90 (43.3 %) vs 28 (1.8 %), p < 0.001].

At 2 years, 345 patients (19.3 %) experienced MACE. Among which 183 (10.2 %) patients had died, 61 (3.4 %) patients had recurrent MI, 64 (3.6 %) patients underwent an unplanned repeat revascularization, 94 (5.2 %) patients presented with HF, and 23 (1.3 %) patients suffered from stroke (Table 1). The distribution of events in patients with and without CS is presented in Fig. 2. Survival analysis showed lower rates of event-free survival in the CS group for MACE, HF, cardiovascular (CV) death and all-cause mortality (Fig. 3).

Among the subgroup of patients who developed CS, 108 (51.9 %) died at 2 years. Apart from being significantly older (63.7 ± 12.5 vs 58.4 ± 12.1 years, p = 0.002), patients who died at 2 years had a higher prevalence of chronic kidney disease (19.4 % vs 9.0 %, p = 0.032) compared to those who were alive. There was also a significantly lower coronary stenting rate (71.3 % vs 87.0 %, p = 0.006), post-procedure TIMI 3 flow (79.6 % vs 92.0 %, p = 0.011), and LVEF (16.8 ± 18.7 vs 41.1 ± 12.6, p < 0.001) compared to those who were alive (Supplementary Table 3). Prevalence of Killip III/IV acute pulmonary edema (47.2 % vs 31.0 %, p = 0.017), ventricular arrhythmias (VT/VF) (54.6 % vs 36.0 %, p = 0.007) were higher among patients with CS who died at 2 years. Information on ventilatory, inotropic and mechanical circulatory support are described in Supplementary Table 4.

Table 1
In-hospital and follow-up outcomes.

Variable	Total (n = 1791)	Cardiogenic shock (n = 208)	No cardiogenic shock (n = 1583)	p-value
2-year follow up				
All-cause mortality	**183 (10.2)**	**108 (59.9)**	**75 (4.7)**	**<0.001**
Cardiac mortality	**126 (7.0)**	**91 (43.8)**	**35 (2.2)**	**<0.001**
MACE*	**345 (19.3)**	**85 (59.1)**	**222 (14.0)**	**<0.001**
Unplanned revascularization	64 (3.6)	3 (1.4)	61 (3.9)	0.078
MI	61 (3.4)	6 (2.9)	55 (3.5)	0.659
Heart Failure	**94 (5.2)**	**18 (8.7)**	**76 (4.8)**	**0.019**
Stroke	23 (1.3)	2 (1.0)	21 (1.3)	1.000
Bleeding	63 (3.5)	4 (1.9)	59 (3.7)	0.184
In-hospital events and short-term follow-up				
Killip III/IV Acute Pulmonary Edema	**189 (10.6)**	**82 (39.4)**	**107 (6.8)**	**<0.001**
Sepsis	**91 (5.1)**	**55 (26.4)**	**36 (2.3)**	**<0.001**
Atrial Fibrillation	**115 (6.4)**	**33 (15.9)**	**82 (5.2)**	**<0.001**
Bleeding	**171 (9.5)**	**50 (24.0)**	**121 (7.6)**	**<0.001**
VT/VF	**180 (10.1)**	**95 (45.7)**	**85 (5.4)**	**<0.001**
AKI	**207 (11.6)**	**86 (41.3)**	**121 (7.6)**	**<0.001**
30-day All-cause mortality	**118 (6.6)**	**90 (43.3)**	**28 (1.8)**	**<0.001**

AKI, acute kidney injury; CV, cardiovascular; MACE, major adverse cardiovascular events; MACE, major adverse cardiovascular events; MI, myocardial infarction; VT, ventricular tachycardia; VF, ventricular fibrillation
*MACE includes subsequent all-cause mortality, MI, repeat unplanned revascularization, heart failure, stroke.

3.4. Predictors of development of cardiogenic shock and adverse events

Compared to patients without CS, patients who developed CS had a lower LVEF along with less favorable baseline and PPCI procedural characteristics. Multivariable analysis identified background diabetes mellitus as an independent predictor for development of CS, while a higher LVEF and establishment of TIMI 3 flow following primary PCI were factors independently associated with lower risk of CS (Table 2).

On Cox regression analysis, a higher LVEF was independently associated with lower MACE, while older age, diabetes mellitus, and CS during index admission were independent predictors of higher MACE during follow-up (Table 3).

Regression analysis was also performed among the subgroup of patients with CS to identify predictors of mortality. Again, a higher LVEF was an independently associated with lower mortality, while a higher serum lactate concentration and lower arterial pH at onset of shock were independent predictors of mortality (Supplementary Table 5). Finally, a higher serum lactate concentration was the only factor independently associated with mechanical circulatory support (MCS) use (Table 4).

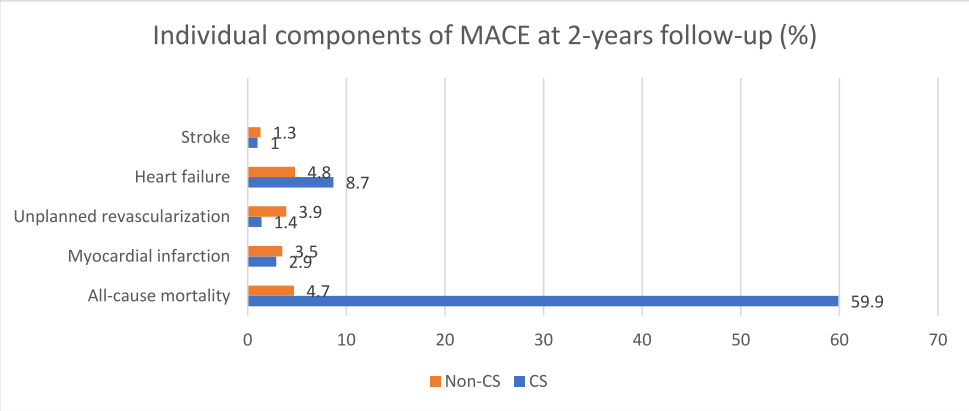

Fig. 2. Distribution of individual major adverse cardiovascular events (MACE) in patients with and without cardiogenic shock (CS) at 2-year follow-up.

4. Discussion

Our study demonstrated that (1) 11.6 % of patients with STEMI developed CS during index admission; (2) Patients who developed CS were significantly older, had a higher prevalence of DM, CKD, previous diagnosis of HF, longer DTBT and lower LVEF; (3) Successful PPCI with coronary stent deployment and post-PCI TIMI 3 flow rates were significantly lower in CS patients compared to non-CS patients; (4) Higher serum lactate concentration and lower arterial pH at onset of shock were independent predictors of mortality; and (5) Development of CS was also independently associated with in-hospital adverse events and increased risk of MACE during long-term follow-up.

The development of CS complicating STEMI in our contemporary real-world cohort of Asian patients treated with PPCI remains high and is consistent with prevalence of 5 % to 10 % reported elsewhere [1,11]. Continued efforts to improve the management of these patients is vital as CS is associated with high immediate and long-term morbidities and mortality. CS results from a primary insult to myocardial performance leading to reduced cardiac output, hypotension, systemic vasoconstriction, and cardiac ischemia. The clinical hallmark of CS is peripheral vasoconstriction and hypoperfusion of vital end-organs, leading to multi-organ failure, which arises from ineffective stroke volume and inadequate circulatory compensation. This culminates in diminished perfusion of peripheral tissues, and eventually, the heart [1,12]. In our study, CS was more likely to occur in patients with pre-existing comorbidities such as diabetes mellitus, heart failure and chronic kidney disease. We did not find any association between culprit vessel territory and development of CS in our patients, suggesting that the area of ischemic risk alone may not be an independent predictor of STEMI-related CS. It is plausible that patients who developed CS in our cohort had more advanced or extensive coronary artery disease as evidenced from lower rate of successful PCI with implantation of coronary stents or establishment of TIMI III flow when compared to those without CS.

Our study found a higher 30-day mortality rate compared to a recent study by Wada et al[13], which may be explained by differences in patient population. Our study cohort consisted of a STEMI population compared to an undifferentiated AMI population reported by Wada et al, with STEMI consisting of 69 % of the total study population. Previous literature [14] have reported an increased risk of short-term events among patients with STEMI. Furthermore, mortality was reported to be higher in CS attributed to STEMI compared to NSTEMI [15], which is consistent with results from our study, with significantly raised in all-cause mortality at 2 years among CS patients (59.9 % vs 4.7 %, $p < 0.001$).

In contrast to a report by Aissaoui et al[15] which described increased risk of death up to one year following among patients with AMI complicated by CS, following which mortality is similar to patients without CS. We observe a consistently higher prevalence of all-cause mortality on long-term follow up among CS compared to non-CS patients who were discharged alive from the index hospitalization (Fig. 2e). A potential explanation for the difference in findings could include a significantly lower LVEF in our CS population compared to theirs (28 % vs 42 %), suggesting more infarct with downstream myocardial ischemia, consequent neurohormonal abnormalities and end-organ injury[12].

Apart from inpatient care, multiple society guidelines [16,17] have emphasized the importance of GDMT for optimal long-term patient outcomes. Our results showed a significant discrepancy in LVEF between patients with CS compared to those without (28.5 % vs 48.8 %, $p < 0.001$), further emphasizing the need to institute appropriate GDMT for this subgroup of patients. However, physicians are often cautioned when initiating medications with proven prognostic benefit in the post-MI setting, such as angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB), beta-blockers, or mineralocorticoid receptor antagonists (MRA) to patients with AKI or impaired renal function. This may have potential downstream effects on post-STEMI adverse cardiac remodelling, LVEF, and long-term prognosis [18,19]. Consistent with this, our study demonstrated LVEF as the only independent factor that is protective against long-term mortality (Supplementary Table 5).

Our study highlights that establishment of TIMI III flow with PPCI was an independent factor associated with lower likelihood of development of CS complicating STEMI and reduced the risk of CS by at least 2 folds. Normal TIMI flow could be a surrogate marker for successful revascularization or favorable outcome following PPCI, reflecting not only the severity of the culprit lesion, but also overall integrity of the coronary microvasculature and myocardial viability of the territory supplied by the culprit artery. Poor TIMI flow following PPCI could be partly related to with microvascular dysfunction which is known to be associated with a suboptimal long-term outcomes [20]. In tandem with our findings, among patients assigned to revascularization in the SHOCK trial, a lower 30-day mortality was reported among patients who had successful compared to unsuccessful angioplasty (38 % vs 79 %, $p = 0.003$).

Despite inclusion of exclusively STEMI patients with more advanced CS state as evidenced by higher serum lactate concentration, the 30-day mortality rate among our patients was similar to that observed in the other studies investigating treatment undifferentiated AMI-related CS such as the (Intra-arterial balloon pump) IABP SHOCK II[21]. A possible explanation for such relatively similar outcome between two group of patients with different risk profile might be partly explained by the variances in clinical practice. Patients randomized to receiving adjunctive IABP treatment in IABP SHOCK II trial underwent IABP insertion within 24 h from randomization, which is not in tandem with the current approach that advocates early use of mechanical circulatory support

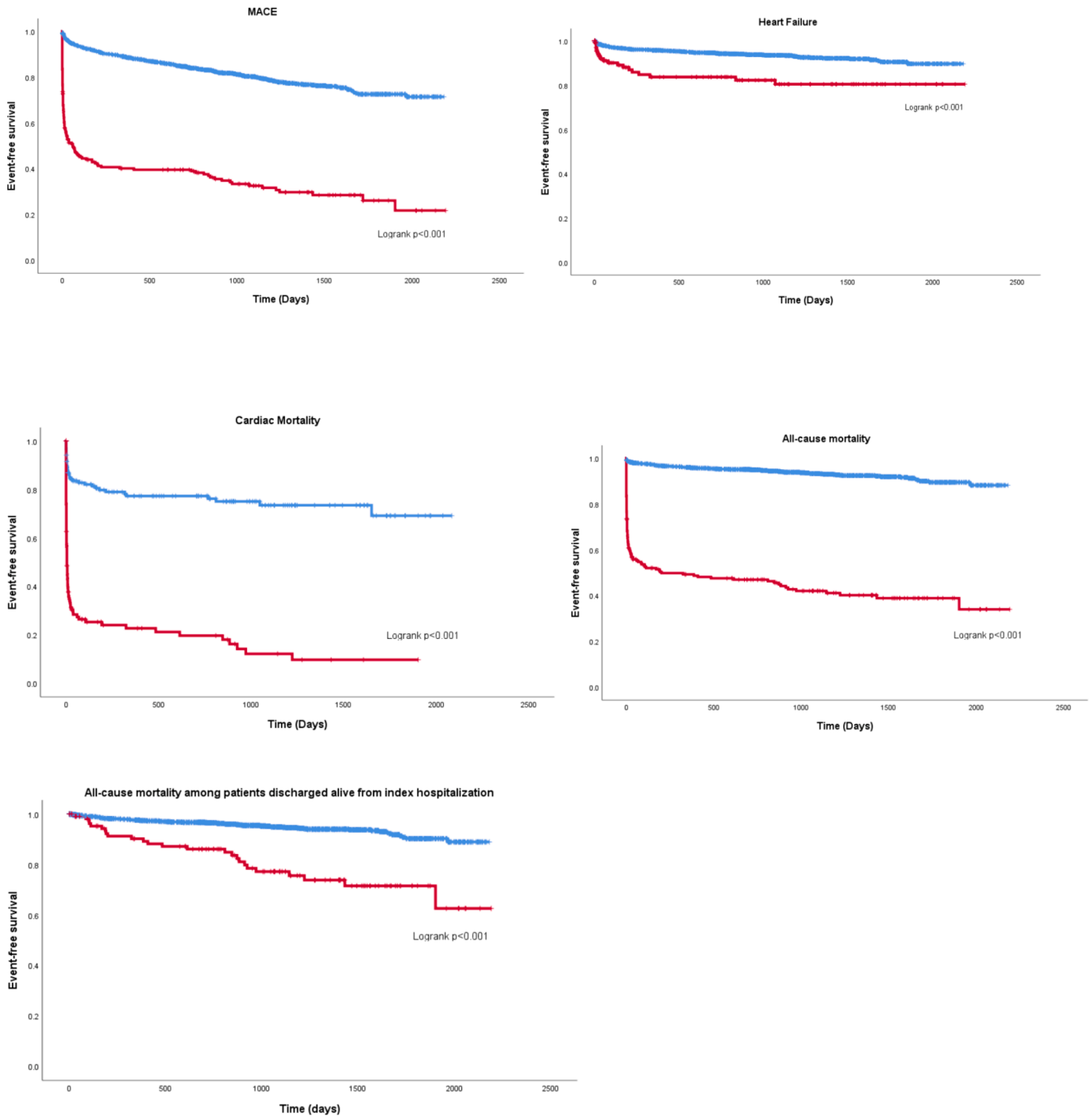

Fig. 3. Kaplan-Meier curves of event-free survival for of a) major adverse cardiac events (MACE); b) heart failure (HF); c) cardiovascular death; d) all-cause mortality; and e) all-cause mortality among patients discharged alive between cardiogenic shock (red) and non-cardiogenic shock (blue) groups. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

(MCS). It is also in contrast with our institutional practice of early initiation of MCS among CS patients once clinically indicated. Nevertheless, at the time of study conduct, IABP was the most utilized MCS among our patients with STEMI-related CS, with select few initiated on VA-ECMO. More robust MCS devices such as Impella and ECMO might be able to alter the disease course and prognosis of patients with AMI-related CS.

It has been increasingly recognized that early administration of MCS device therapy is vitally important to improve the outcome of patients with AMI complicated by CS. The Detroit Cardiogenic Shock Initiative Pilot Study[22] reported a 76 % survival rate at discharge with standardized protocols involving early percutaneous left ventricular assist device (pVAD) insertion prior to PCI. This compares favorably against the SHOCK[23], IABP SHOCK II[21] and IMPRESS in Severe Shock[24] studies that reported approximately 50 % mortality over 6 to 12 months despite the use of MCS devices. Importantly, the timing of initiation of MCS (IABP/Impella) was at the discretion of the treating physician in both IABP SHOCK II and IMPRESS. Finally, data from a multicenter registry reported improved survival rates with initiation of MCS prior to, rather than following PCI [25]. These studies highlight the benefits of

Table 2
Univariate and Multivariate logistic regression analysis of predictors of cardiogenic shock.

Variable	Univariate			Multivariate		
	OR	95 % CI	p-value	aOR	95 % CI	p-value
Age	**1.022**	**1.010–1.034**	**<0.001**	1.005	0.992–1.019	0.458
Male Sex	0.981	0.638–1.508	0.929			
Diabetes Mellitus	**1.669**	**1.241–2.245**	**0.001**	**1.574**	**1.111–2.231**	**0.011**
Previous HF	**3.411**	**1.386–8.391**	**0.008**	0.793	0.265–2.375	0.679
LVEF (per % increase)	**0.922**	**0.912–0.932**	**<0.001**	**0.924**	**0.914–0.934**	**<0.001**
Door-to-balloon time (per min increase)	**1.001**	**1.000–1.003**	**0.007**	1.001	1.000–1.002	0.138
Culprit LM/LAD	1.125	0.815–1.555	0.473			
LMTVD	1.105	0.682–1.790	0.684			
Coronary Stenting	**0.579**	**0.403–0.833**	**0.003**	1.118	0.708–1.764	0.633
Post-procedure TIMI 3	**0.250**	**0.158–0.396**	**<0.001**	**0.500**	**0.280–0.893**	**0.019**

HF, heart failure; LAD, left anterior descending; LM, left main; LMTVD, left main triple vessel disease; LVEF, left ventricular ejection fraction; TIMI; thrombolysis in myocardial infarction

Table 3
Univariate and Multivariate Cox regression analysis of predictors of subsequent MACE* at 2 years.

Variable	Univariate			Multivariate		
	HR	95 % CI	p-value	aHR	95 % CI	p-value
Age	**1.035**	**1.027–1.044**	**<0.001**	**1.020**	**1.011–1.029**	**<0.001**
Male Sex	0.650	0.494–0.855	0.002	0.807	0.601–1.084	0.154
Diabetes Mellitus	**2.168**	**1.755–2.678**	**<0.001**	**1.708**	**1.368–2.132**	**<0.001**
LVEF (per % increase)	**0.923**	**0.917–0.929**	**<0.001**	**0.934**	**0.926–0.941**	**<0.001**
Door-to-balloon time (per min increase)	**1.001**	**1.000–1.002**	**0.005**	0.999	0.998–1.000	0.241
Culprit LM/LAD	1.087	0.875–1.349	0.452			
Coronary Stenting	0.527	0.409–0.679	<0.001	0.882	0.677–1.151	0.356
TIMI 3	0.466	0.325–0.666	<0.001	0.885	0.610–1.284	0.521
New-onset AF	2.079	1.484–2.912	<0.001	0.983	0.691–1.399	0.925
VT/VF (In- hospital stay)	3.350	2.596–4.323	<0.001	1.202	0.888–1.629	0.234
Cardiogenic shock	**6.920**	**5.542–8.639**	**<0.001**	**2.370**	**1.767–3.178**	**<0.001**

AF, atrial fibrillation; LAD, left anterior descending; LM, left main; LVEF, left ventricular ejection fraction; TIMI, thrombolysis in myocardial infarction; VF, ventricular fibrillation; VT, ventricular tachycardia.
*MACE includes subsequent all-cause mortality, MI, repeat unplanned revascularization, heart failure, stroke.

Table 4
Univariate and Multivariate logistic regression analysis of predictors of mechanical circulatory support use.

Variable	Univariate			Multivariate		
	OR	95 % CI	p-value	aOR	95 % CI	p-value
Age	0.996	0.973–1.019	0.712			
Male sex	1.654	0.728–3.757	0.229			
Diabetes	0.945	0.528–1.690	0.848			
ASCVD	0.929	0.523–1.648	0.800			
Chronic kidney disease	0.878	0.393–1.964	0.752			
Heart failure	0.682	0.148–3.133	0.622			
LVEF (per % increase)	0.992	0.978–1.007	0.284			
Door-to-balloon time (per min increase)	1.003	0.998–1.007	0.230			
Culprit LM/LAD	0.847	0.465–1.543	0.587			
LMTVD	1.041	0.400–2.708	0.935			
TIMI 3	1.857	0.849–4.066	0.121	0.855	0.237–3.085	0.811
VT/VF (on presentation)	0.842	0.459–1.543	0.577			
VT/VF (in-hospital stay)	1.131	0.635–2.014	0.675			
AKI	1.777	0.975–3.237	0.060	1.199	0.509–2.823	0.678
RRT	1.594	0.418–6.083	0.495			
Maximum lactate (per mmol/L increase)	**1.116**	**1.025–1.215**	**0.011**	**1.101**	**1.008–1.203**	**0.032**
Arterial pH at onset of shock (per unit increase)	1.174	0.916–1.504	0.205	1.146	0.865–1.519	0.342

AKI, acute kidney injury; ASCVD, atherosclerotic cardiovascular disease; LAD, left anterior descending; LM, left main; LMTVD, left main triple vessel disease; LVEF, left ventricular ejection fraction; RRT, renal replacement therapy; TIA, transient ischaemic attack; TIMI, thrombolysis in myocardial infarction; VT, ventricular tachycardia; VF, ventricular fibrillation.

timely MCS initiation to reverse or minimize further metabolic derangements and end-organ damage that contributes to poor outcome in AMI-related CS.

Receiver operating characteristic (ROC) curve for serum lactate concentration to predict all-cause mortality at 2 years is shown in Fig. 4, with an area under curve (AUC) of 0.75 (95 % CI 0.66–0.83). Based on our data, a serum lactate concentration of 7.85 mmol/L has a sensitivity of 0.566 and specificity of 0.136 for the prediction of all-cause mortality at 2 years. With reference to prior studies, patients recruited in the IMPRESS[24] trial had an average serum lactate concentration of >7

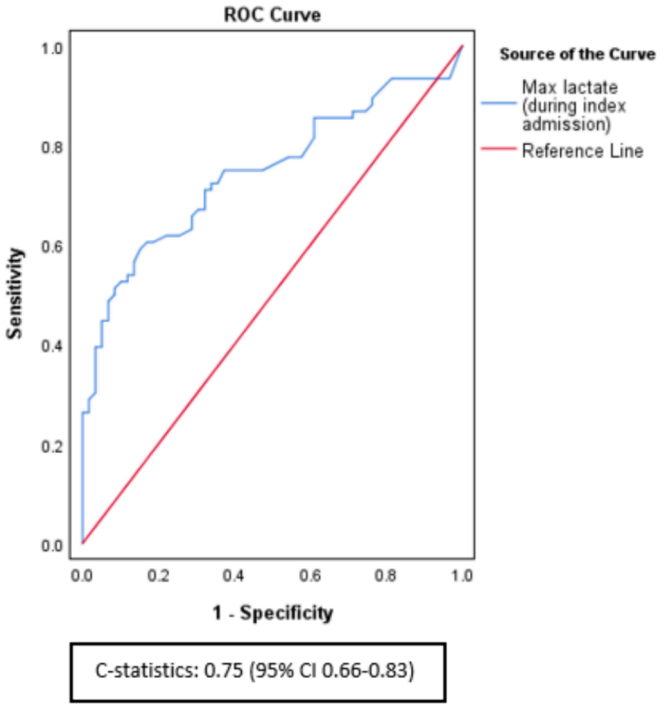

Fig. 4. Receiver Operating Characteristic (ROC) curve of serum lactate concentration and all-cause mortality at 2 years.

mmol/L, with an overall survival of approximately 50 %. Though the Detroit Cardiogenic Shock Initiative Pilot Study [22] did not specify a specific serum lactate concentration for the initiation of MCS, patients enrolled in the study had an average serum lactate concentration of 4.7 mmol/L, and 65.9 % of patients had Impella insertion pre-PCI, with an average door-to-support time of 83 ± 58 min and a 71 % reduction in patients having a reduction in pharmacological hemodynamic support within 24-hours of their index procedure, ultimately with a 76 % survival to discharge rate. Hence, these results suggest for earlier MCS initiation to maximize survival in AMI-related CS, especially in the presence of supporting laboratory evidence of end-organ hypoperfusion and tissue hypoxia.

5. Strengths and limitations

Our study's strength lies in the inclusion of consecutive patients with STEMI undergoing PPCI in a real-world population within a single academic center, thus eliminating potential source of confounders including selection bias and heterogenous practice. However, several limitations need to be acknowledged. First, the study population consisted of only STEMI patients, hence the findings of this study might not be generally applicable to all AMI patients. Second, information on complexity of coronary anatomy (SYNTAX score) and periprocedural complications (slow-flow, no-reflow phenomenon) was not available. Third, Impella was not available in our center during the period of this study and most of our patients received IABP when MCS was needed. Although there was a selection criterion for VA-ECMO in our center, the timing and type of MCS device was left to the discretion of the principal physicians or interventional cardiologists. Fourth, the etiology of CS in our patients was pump failure as mechanical complications precipitating CS was rare. Hence, our findings might not be generalizable to other etiologies of CS.

6. Conclusion

Cardiogenic shock complicating STEMI is not uncommon and associated with extremely poor outcomes especially when ventilatory, inotropic and mechanical circulatory support is needed in addition to emergency revascularization and guideline-directed medical therapy. Higher LVEF on index admission is associated with better immediate and long-term outcomes, while lactic acidosis could predict the need for MCS and mortality. Cardioprotective strategies that help to preserve ventricular function and prevent or reverse metabolic perturbance are urgently needed and might alter the short- and long-term outcomes in patients with STEMI and CS.

We adhere to the statement of ethical publishing as appears in the International Journal of Cardiology (citable as: Shewan LG, Rosano GMC, Henein MY, Coats AJS. A statement on ethical standards in publishing scientific articles in the International Journal of Cardiology family of journals. Int. J. Cardiol. 170 (2014) 253–254 https://doi.org/10.1016/j.ijcard.2013.11).

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CRediT authorship contribution statement

Andie Hartanto Djohan: Conceptualization, Data curation, Formal analysis, Investigation, Writing – original draft, Writing – review & editing. **Lauren Kay Mance Evangelista:** Data curation, Investigation. **Koo-Hui Chan:** Supervision. **Weiqin Lin:** Supervision. **Anand Ambhore Adinath:** Supervision. **Jie Li Kua:** Supervision. **Hui Wen Sim:** Supervision. **Mark Y. Chan:** Supervision. **Gavin Ng:** Supervision. **Robin Cherian:** Supervision. **Raymond C.C. Wong:** . **Chi-Hang Lee:** . **Huay-Cheem Tan:** Supervision. **Tiong-Cheng Yeo:** Supervision. **James Yip:** Supervision. **Adrian F Low:** Supervision. **Ching-Hui Sia:** Conceptualization, Data curation, Formal analysis, Supervision. **Poay Huan Loh:** Methodology, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.

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