ORIGINAL RESEARCH

Peri-Procedural Blood Pressure Changes and Their Relationship with MACE in Patients Undergoing Percutaneous Coronary Intervention: A Cross-Sectional Study

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Background: Peri-procedural blood-pressure (BP) changes were investigated and correlated to Major adverse cardiovascular events (MACE) as predictor of outcome for patients undergoing percutaneous coronary intervention (PCI); whether acute coronary syndrome (Unstable angina, or MI; STEMI or NSTEMI) or scheduled for elective PCI.

Methods: Resting BP in the 204 recruited patients undergoing PCI throughout 2018 was measured thrice – in the ward before transferring to the cardiac catheterization lab (cath lab), in the cath lab, and after transfer to the recovery room. Patients were categorized based on their systolic and diastolic BP peri-procedural difference as systolic (SBP): with a large difference (>20 mmHg, n=47), with a small difference (\leq 20 mmHg, n=157) (shock patients excluded); diastolic (DBP): with a large difference (>10 mmHg, n=65), and with a small difference (\leq 10 mmHg, n=139). The primary end-points were MACE including all-cause mortality, non-fatal myocardial infarction, and stroke during the hospital stay. The Mann–Whitney U and Chi-square tests were used to analyze the data accordingly (p<0.005).

Results: Within the category of MACE, cardiac mortality was the only adverse cardiac event encountered in the study sample. Cardiac mortality was significantly higher in both the large SBP-difference group versus the other group (10.6% vs 0.6%, p=0.003) and the large DBP-difference group versus the small-difference group (7.7% vs 0.7%, p=0.013).

Conclusion: Peri-procedural systolic and diastolic BP differences, greater than 20 mmHg and 10 mmHg, respectively, correlated with MACE in all patients undergoing PCI.

Keywords: percutaneous coronary intervention, major adverse cardiovascular events, periprocedural BP changes

Introduction

Coronary heart disease (CHD) is a major cause of death and disability in developed countries. Although CHD mortality rates worldwide have decreased over the past four decades, CHD remains responsible for one-third or more of all deaths in individuals over age of 35. Also CHD is a leading cause of disease burden in developing countries as well.^{1–3} In 2001, there were 7.3 million deaths and 58 million disability-adjusted life years (DALYs) lost due to CHD worldwide. Three-fourths of these global deaths and 82% of the total DALYs occurred in the low- and middle-income countries.⁴

In our study, we aimed to use simple parameters as arterial blood pressure as predictors of outcome in patients undergoing PCI on emergency and elective bases.

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Coronary heart disease occurs due to complex pathological process named as atherosclerosis. Several factors promote atherosclerosis including genetic predisposition, cholesterol level, diabetes, hypertension, smoking, obesity, sedentary lifestyle, advancing age, gender, psychological status, and other risk factors (as homocysteine).⁵

Major adverse cardiovascular events (MACE) are the most commonly used composite end-point in cardiovascular research. By definition, MACE as well as other composite end-points includes numerous clinical events of varying degrees of relatedness. MACE is an important cause of morbidity and mortality in CAD patients undergoing percutaneous coronary interventions (PCI). The detection and treatment of the risk factors for MACE is critical to improve health and longevity.^{6–8}

This study aimed to evaluate a simple parameter, arterial blood pressure, as a predictor of outcome in patients undergoing PCI both on emergency and elective bases. A correlation, if any, between the change in BP during the procedure and any MACE reported was evaluated. The cardiac adverse events used as end-points for this study were in-hospital mortality, non-fatal myocardial infarction, target vessel revascularization, and stroke. The follow-up period was limited to the in-hospital stay. Secondarily, various baseline characteristics, risk factors, and procedural parameters were also evaluated for association with MACE.

Materials and Methods

Study Population and Study Design

It is a prospective study conducted using an observational study design. 204 patients, admitted from January 2018 to July 2018 to the Kasr Alainy university hospital with diagnosis of an acute coronary syndrome (ACS); (unstable angina/myocardial infarction), including patients who have undergone or are scheduled for a PCI (both emergency and elective), were recruited for the study. Ethical approval was obtained from the Ethical Committee, Cairo University Hospital Faculty of Medicine, Egypt. The Declaration of Helsinki and its subsequent modifications were strictly followed during the conduct of the study. Written informed consent and a verbal oration to ensure clear comprehension of the procedure were obtained from all patients who agreed to participate. The confidentiality of the data for each recruited patient was cautiously and strictly maintained.

All patients going to PCI with a sinus rhythm were included in the study. The patients were excluded based on these criteria - non-sinus rhythm (e.g., atrial and ventricular arrhythmias, and paced rhythm), cardiogenic shock patients, patients in whom BP in the upper limb could not be measured and patients' refusing enrollment in the study.

Procedure

All patients underwent a full history taking and clinical examination before the intervention. A thorough account of related comorbidities including a family history of CAD, atherosclerotic-related comorbidities as hypertension, dyslipidemia, diabetes mellitus, and possible risk factors like smoking were taken. Hypertensive patients continued their medications till the time of admission to the cath lab. Pre- and post-procedural ECGs were done, besides the regular lab investigations-renal function tests, liver function tests, cardiac enzymes (CK, CK-MB), Troponin T, lipid profile. The recent echocardiograms were obtained from the central database or done during inhospital stay. The resting BP in the right arm in supine lying was measured thrice - first; in the ward before transfer to the cath lab, second after the patient was laid down on the cath lab table before the PCI after the arterial puncture, and lastly post-procedure in the recovery room or the CCU. The differences in systolic and diastolic BP between CCU or ward pre-procedural, during cath lab intra-procedural, and post-procedural in CCU or recovery room were assessed. The indirect method, which involves collapsing the artery with an external cuff, was applied by a physician using an auscultatory sphygmomanometer. It provides an inexpensive and reproducible way to measure blood pressure.

A key component in measuring BP manually is Korotkoff's phases. The Korotkoff's phases have been classified as 5 phases with Phase I, IV, and V integral for obtaining an accurate BP measurement.^{9–12} Two measurements, which were later averaged out, at each location with at least a 1-minute interval between recordings were taken. Patients were divided according to the differences in systolic (SBP) and diastolic (DBP) into – systolic: group I with SBP difference > 20mmHg and group II with SBP difference \leq 20 mmHg; diastolic: group I with DBP difference > 10 mmHg and group II with DBP difference \leq 10 mmHg.

Procedure for PCI

All patients received a loading dose of 300 mg Aspirin, 600 mg Clopidogrel, or 180 mg Ticagrelor according to the presence or absence of contraindications and risk factors. All medications were given before catheterization and an I.V. dose of unfractionated heparin (100 IU/kg) was given after the arterial puncture. Stents were implanted using standard techniques. A successful PCI was defined as the achievement of <30% residual stenosis diameter of all treated lesions as assessed by visual inspection or quantitative coronary angiography.¹⁵ Post PCI, unless contraindicated patients were continued on Aspirin indefinitely, and on Clopidogrel or Ticagrelor for at least 12 months.

Study Definitions and Endpoints

The primary endpoints were cardiac death, non-fatal MI, and stroke. Secondary outcomes were target vessel revascularization (TVR) and target lesion revascularization (TLR). Cardiac death was defined as death resulting from an evident cardiac cause, any death related to PCI, unwitnessed death, or death from an unknown cause after non-cardiac deaths were excluded. Non-fatal MI was defined using the fourth universal definition of myocardial infarction.¹² Stroke is classically characterized as a neurological deficit attributed to an acute focal injury of the central nervous system (CNS) by a vascular cause, including cerebral infarction, intracerebral hemorrhage (ICH), and subarachnoid hemorrhage (SAH), and is a major cause of disability and death worldwide.¹³ TVR was defined as any clinically driven repeat PCI or surgical bypass of any segment within the entire epicardial coronary artery containing the target lesion.¹⁴ TLR was defined as any clinically driven repeat revascularization caused by 50% stenosis within the stent or within a 5-mm border proximal or distal to the stent.¹⁴

Statistical Analysis

Data were statistically described in terms of mean \pm standard deviation (SD), median and range, or frequencies (number of cases) and percentages as appropriate. A comparison of numerical variables between the study groups was done using the Mann–Whitney *U*-test for independent samples. For comparing categorical data (baseline characters, risk factors, and procedural parameters) the Chi-square (χ^2) test was performed. Fisher's exact test was used instead when the expected frequency was less than 5. p < 0.05 was considered statistically significant. All statistical calculations were done using the IBM SPSS Statistics v. 22.

Results

Of the 204 patients included in the study, there were 172 males and 32 females with a mean age of 58 ± 10.66 years, ranging from 28 to 84 years. All patients undergoing PCI were included apart from our exclusion criteria, including patients for emergency and elective PCI. Our sample size involved 115 were elective cases, while the rest 90 had emergency PCI (36 STEMI, 33 NSTEMI, and 21 unstable angina patients). Table 1 shows the baseline characteristics of our sample size.

Echo reports were present for 115 out of 204 patients (our sample size).BP difference was used as predictor of outcome for PCI patients, outcome was measured as MACE, study revealed that large systolic difference group (systolic difference >20 mmHg) was significantly related to MACE with P value 0.006. In patients with MACE systolic maximum difference mean was (27.33 mmHg) while patients with smooth outcome systolic maximum difference mean was 15.82 mmHg) as shown in Figure 1.

The large DBP difference group was significantly related to MACE (p=0.016). In patients with a major adverse cardiovascular event, the mean diastolic maximum difference was (15.33 mmHg) while the patients with smooth outcome mean diastolic maximum difference was (10 mmHg) as shown in Figure 2.

Enrolled in our study were 198 with smooth outcome and 6 with MACE in form of cardiac mortality only, no patients had non-fatal MI or target vessel revascularization or stroke. Screening of MACE was done all through intrahospital stay of patients which average was 1 day stay to 2 weeks.

Also, pre-procedural SBP (range- 80-170 mmHg, mean value 121 mmHg) demonstrated a statistically significant relation with MACE (p=0.001); the mean pre-procedural SBP in patients with MACE was 93.33 mmHg while in patients without MACE was 121.07 mmHg. The correlation between intra-procedural systolic BP (range-80-170mmHg mean value 117.2 mmHg) and MACE was statistically significant (p=0.004), with the mean intra-procedural SBP in patients with MACE of 92.33 mmHg and patients without MACE was 117.22. Similarly, the association of post-procedural SBP (range-85-180mmHg, mean value 123.64) with MACE was statistically significant with p=0.018, with a mean post-procedural SBP in

Table I Baseline Characteristics or	Table I Baseline Characteristics of the Sample Size				
Baseline Characteristics		Mean ± SD			
Age	(in yrs.)	58.44 +10.662			
Sex					
Male	n(%)	172 (84.31%)			
Female	n(%)	32 (15.69%)			
Diabetes	n(%)	105 (51.7%)			
Hypertension	n(%)	113 (55.4%)			
Smoker n(%)					
Non-smoker	n(%)	94 (46.08%)			
Smoker	n(%)	89 (43.63%)			
Ex-smoker	n(%)	21 (10.29%)			
Dyslipidemia	n(%)	71 (34.8%)			
Family history	n(%)	26 (12.8%)			
Elevated cardiac biomarkers	n(%)	68 (34%)			
ECG					
Normal	n(%)	37 (18.782%)			
ST elevation	n(%)	36 (18.274%)			
ST depression	n(%)	124 (62.944%)			
Indication of procedure:					
Elective patients	n(%)	115 (56.372%)			
Emergency patients					
Unstable angina	n(%)	21 (10.294%)			
NSTEMI	n(%)	33 (16.176%)			
STEMI	n(%)	36 (17.647%)			
LV EF <50%	n(%)	54 (47%)a			
Procedure time	(in mins)	49.115 + 28.996			
Dissection	n(%)	I (0.5%)			
No reflow	n(%)	2 (1%)			
Side branch compromise	n(%)	5 (2.5%)			
Number of diseased vessels	n(%)	1.71 + 0.777			
Number of stents deployed	n(%)	1.74 + 0.935			
Blood pressure (systolic in mmHg)					
Pre-procedural		120.25 + 16.332			
Intra-procedural		116.49 + 15.574			
Post-procedural		123.04 + 17.789			
Blood pressure (diastolic in mmHg)					
Pre-procedural		74.39 + 9.311			
Intra-procedural		74.54 + 9.337			
Post-procedural		76.61 + 10.215			

Table I Baseline Characteristics of the Sample Size

patients with MACE of 93.75 mmHg and 123.64 mmHg in patients without MACE. These results are presented in Table 2.

The pre-procedural DBP (range-55-100mmHg, mean-74.72 mmHg) demonstrated a statistically significant relation with MACE (P value p=0.007), with a mean pre-procedural DBP of 63.33 mmHg in patients with MACE,

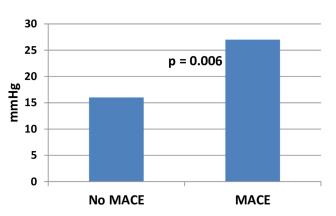


Figure I The mean of the maximum change reached in systolic blood pressure (in mmHg) according to the occurrence of MACE.

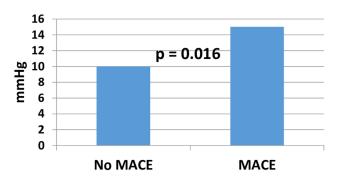


Figure 2 The mean of the maximum change reached in diastolic blood pressure (mmHg) according to the occurrence of MACE.

and 74.72 mmHg in patients without MACE. Following this pattern, the intra-procedural DBP (range- 50-111 mmHg, mean- 75.02 mmHg) was significantly related to MACE with (p=0.002), with a mean intra-procedural DBP of 58.67 mmHg in patients with MACE and 75.02 mmHg in patients without MACE. However, the relation between post-procedural DBP (range- 55-120 mmHg, mean- 76.87 mmHg) and MACE was statistically non-significant

Table 2 MACE Relation with Systolic Blood Pressure MaximumDifference, Pre-Procedural, Intra-Procedural and Post-Procedural Systolic Blood Pressure

MACE		SBP Pre	SBP Intra	SBP Post	SBP Max Diff
No	Mean	121.07	7.22	123.64	15.82
	N	198	98	198	198
	Standard deviation	15.574	4.900	17.237	11.859
Yes	Mean	93.33	92.33	93.75	27.33
	N	6	6	4	6
	Standard deviation	19.408	19.470	22.867	7.941
P-value		0.001	0.004	0.018	0.006

Table 3 MACE Relation with Diastolic Blood Pressure MaximumDifference, Pre-Procedural, Intra-Procedural, and Post-Procedural Diastolic Blood Pressure

MACE		DBP Pre	DBP Intra	DBP Post	DBP Max Diff
No	Mean	74.72	75.02	76.87	10.08
	N	198	198	198	198
	Standard deviation	9.141	8.909	10.024	7.053
Yes	Mean	63.33	58.67	63.75	15.33
	N	6	6	4	6
	Standard deviation	8.756	10.033	12.920	3.615
P-value		0.007	0.002	0.052	0.016

(p=0.052). The mean post-procedural DBP in patients with MACE was 63.75 mmHg, while it was 76.87 mmHg in patients without MACE (Table 3).

One hundred and ninety-eight of the recruited sample had a smooth outcome, with only six faced a MACE in the form of cardiac mortality. No other major cardiac adverse event (nonfatal MI or target vessel revascularization or stroke) was reported. Screening of MACE was done throughout the patients' intra-hospital stay, which was a 1-day to 2 weeks stay on average. Cardiac mortality was significantly higher in the large SBP difference group compared to the small difference group (10.6% vs 0.6%, p=0.003) (Table 4). Likewise, it was higher in the large DBP difference group compared to the small difference group (7.7% vs 0.7%, p=0.013) (Table 5).

We had six patients with MACE, which was confined to cardiac mortality. Cardiac mortality was significantly higher in the large systolic BP difference group compared to the small difference group (10.6% vs 0.6%) with P-value 0.003. Also it was higher in the large diastolic difference group compared to small difference group (7.7% vs 0.7%) with P-value 0.013.

All patient characteristics including the co-morbidities (age, sex, diabetes mellitus, hypertension, dyslipidemia, family history, and smoking) were evaluated for a correlation with MACE. Of the 204 recruited patients, 105 patients had Diabetes Mellitus, 113 were hypertensive, 71 were known cases of dyslipidemia, 26 had a family history of coronary heart disease, and in terms of smoking habit 94 were non-smokers, 89 smokers and 21 were exsmokers, characteristics of the MACE population is shown in Table 6. It was found that age and sex were not correlated with MACE, with P values 0.469 and p=1.000, respectively. In the same way, diabetes, hypertension, family history, dyslipidemia, and smoking were not statistically significant to show a correlation with MACE (p=0.213, 0.694, 0.565, 0.186, and 0.508, respectively).

The electrocardiogram of 37 patients was normal, while 124 patients had significant ST changes (apart from ST-elevation) and 36 patients had an ST-segment elevation. The ECG changes were statistically significant to demonstrate a correlation with MACE (p=0.001). Fifty-four of the recruited patients (with available recent echo-cardiography reports or indication of performing Echo during their hospital stay) had impaired left ventricular systolic function (when the EF was less than 50%), which significantly correlated with MACE (p=0.009). Sixty-eight patients had elevated cardiac enzymes (out of the valid labs for 200 patients). Elevated cardiac enzymes indicating a myocardial infarction, whether STEMI or NSTEMI, correlated well with MACE when statistical significance was evaluated (p=0.018).

Regarding the PCI procedure, the correlation between the procedure time and MACE was not statistically significant (p=0.102). The "number of vessels affected" statistics

			MACE		Total
			No Yes		
SBP max diff group	20 or less	Count % within SBP max diff group % within MACE	156 99.4% 78.8%	I 0.6% I6.7%	157 100.0% 77.0%
	> 20	Count % within SBP max diff group % within MACE	42 89.4% 21.2%	5 10.6% 83.3%	47 100.0% 23.0%
Total		Count % within SBP max diff group % within MACE	198 97.1% 100.0%	6 2.9% 100.0%	204 100.0% 100.0%

			MACE		Total
			No	Yes	
DBP max diff group	10 or less	Count % within DBP max diff group % within MACE	138 99.3% 69.7%	 0.7% 6.7%	139 100.0% 68.1%
	>10	Count % within DBP max diff group % within MACE	60 92.3% 30.3%	5 7.7% 83.3%	65 100.0% 31.9%
Total	·	Count % within DBP max diff group % within MACE	198 97.1% 100.0%	6 2.9% 100.0%	204 100.0% 100.0%

Table 5 Correlation of the Diastolic Blood Pressure Maximum Difference Groups with MACE

showed that 94 patients had a single vessel disease, while 69 patients had a two-vessel disease, and 39 patients had three-vessel disease. When this factor was evaluated for correlation with MACE, the results were not statistically significant (p=0.666). The number of stents deployed during the procedure (maximum stents deployed=5) was not statistically significant enough to correlate with MACE (p=0.988).

During the study, there were some procedural complications related to PCI - 1 patient had vessel dissection, 5 patients had vessel side-branch compromise, and 2 patients had no-

Table 6	Characteristics	of MACE	Population
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MACE	6 Patients
Hypertensive	5 patients
Diabetic	5 patients
LV EF <50%	5 patients
Elevated Cardiac biomarkers	5 patients
Indication of PCI STEMI	4 patients
N-STEMI	l patient
Unstable angina	l patient
Smoker	2 patients
Family history of CAD	l patient
Systolic BP (in mmHg)	
Pre-procedural	93.33
Intra-procedural	92.33
Post-procedural	93.75
Diastolic BP (in mmHg)	
Pre-procedural	63.33
Intra-procedural	58.67
Post-procedural	63.75

reflow. All these complications were not statistically significant when correlated with MACE (p=1.000, 1.000, and 1.000).

Discussion

This study observed the relationship between peri-procedural BP changes and the outcome of PCI in patients during the inhospital stay, where the outcome was measured in terms of MACE which included all-cause mortality, cardiac mortality, non-fatal myocardial infarction, target vessel revascularization, and finally stroke. The results of the study demonstrate that peri-procedural BP changes were significantly related to MACE for patients undergoing PCI, with a cut-off value for systolic blood pressure maximum difference of >20 mmHg, and >10 mmHg for diastolic blood pressure maximum difference. The pre, intra, and post-procedural readings for systolic BP, and pre and intra-procedural diastolic BP readings were significantly related to the MACE during the hospital stay. Several baseline characteristics like ECG ischemic changes, including the ST-elevation and ST changes (T wave ischemic changes and ST depression), and left ventricular function (EF < 50%) were significantly related to MACE.

Ae-Young Her et al discussed the association of blood pressure to outcome in patients undergoing PCI. The study examined the relationship between BP differences and longterm clinical outcomes in patients subjected to PCI with drugeluting stents (DES), showing that the differences in BP from ward-to-cath lab can adversely affect their long-term clinical outcomes. The present study investigated the peri-procedural BP (systolic and diastolic) changes at two other instances besides the pre-procedural measurement in the ward, as a second reading in the cath lab after the arterial puncture, and third after the procedure in the recovery room or CCU. However, unlike Ae-Young Her et al, only the short-term outcome (in-hospital stay MACE) and not the long-term 1-year outcome was researched. Also, the present study recruited all patients undergoing PCI (both elective and emergency, including ACS-NSTEMI and STEMI), concluding that the systolic and diastolic BP significantly related to MACE during the in-hospital stay.

Lingman et al studied the impact of hypertension and diabetes on the long-term outcome in patients undergoing PCI in a sample of 44,268 patients. Hypertension per se was not associated with increased mortality, but increased the risk for MI, stroke, and congestive heart failure, and probably related to widespread coronary artery disease.¹⁶ Hypertension, as a disease, was correlated to the outcome of coronary intervention in the study by Lingman et al. In this study, acute peri-procedural systolic and diastolic maximum blood pressure changes were correlated with MACE, while some of our patients with systolic and diastolic maximum changes greater than the set cut-off values were not even known hypertensive. Consequently, hypertension per se was not statistically related to MACE during the hospital stay (short-term outcome) in the present study.

During our investigation of in-hospital MACEs cardiac death was the only reported MACE, with no account of any non-fatal MI, target vessel revascularization, or stroke. In 2014, Spyridopolous et al studied the shock index as a novel predictor of long-term outcomes, in terms of mortality and other parameters, following a primary PCI (PPCI).¹⁷ The aim of study was to evaluate the shock index (ratio of heart rate/systolic blood pressure on admission) as a predictor of mortality post PPCI in addition to other parameters.¹⁸ Invasively measured shock index before PPCI is the strongest independent predictor of long-term outcome in elderly patients.

We also measured blood pressure pre, intra, and postprocedural, also in hospital MACE (short-term outcome) was our evaluated outcome, while in the other study, shortand long-term outcome were evaluated. In our study, the pre-procedural systolic blood pressure was significantly related to the in-hospital MACE in our sample which included both elective and emergency patients (ACS-NSTEMI and STEMI). A series of studies have shown that the prognosis of acute myocardial infarction is better in patients who have a higher BP at admission.^{19–22} SBP is included in several acute coronary syndrome prognosis scores.^{23–30} A retrospective study by Mornos et al suggested that vital signs, HR and SBP, reported on the admission of STEMI patients can provide valuable information about the risk of in-hospital death after a primary PCI. HR \ge 80 bpm and SBP \le 105 mmHg correlated well with an increased risk of death in this retrospective study.¹⁸

Regarding BP, peri-procedural systolic and diastolic BP changes with cut off values >20 mmHg and >10 mmHg for systolic BP changes and diastolic changes, respectively, were significantly related to in hospital MACE also Pre-procedural, intra-procedural, and postprocedural systolic blood pressure were significantly related to MACE with mean values 93.33, 92.33, and 93.75 mmHg, respectively. Also pre-procedural and intraprocedural diastolic BP were significantly related to Inhospital MACE with mean values 63.33 and 58.67 mmHg, respectively.

Limitations of the Study

The sample size of 204 was small when considering the prevalence of CHD requiring PCI. Also, the method of blood pressure variability (wherein the 24 hours ambulatory BP monitoring is done) for detecting changes in BP was not employed. However, the three peri-procedural readings (pre-procedural, intra-procedural, and post-procedural) are representative of a more feasible method used in the routine clinical practice. Although fortunate, the limited adverse events that happened (six patients reporting cardiac death, and a small number of procedural complications in the form of dissection, no-reflow, and side branch compromise) limit the generalization of the study results. Lastly, the major adverse events were monitoring), and no long-term outcomes were investigated.

Abbreviations

ACS, Acute Coronary Syndrome; BP, Blood Pressure; CAD, Coronary Artery Disease; CCU, Coronary Care Unit; CK, Creatine Kinase; CK-MB, Creatine Kinase Myocardial Band; CHD, Coronary Heart Disease; DALYs, Disability Adjusted Life Years; DBP, Diastolic Blood Pressure; EF Ejection Fraction; HR, Heart Rate; IU, International Unit; MACE, Major Adverse Cardiovascular Events; N-STEMI, Non-ST Elevated Myocardial Infarction; PCI, Percutaneous Coronary Intervention; SBP, Systolic Blood Pressure; STEMI, ST-Elevated Myocardial Infarction; SD, Standard Deviation; TLR, Target Lesion Revascularization; TVR, Target Lesion Revascularization.

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Disclosure

The authors report no conflicts of interest for this work.

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