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Original Article

Predictive accuracy of systolic blood pressure to left ventricular end-diastolic pressure ratio versus TIMI score for short-term mortality after primary percutaneous coronary intervention

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Abstract

Introduction: Aim of this study was to evaluate the predictive performance of systolic blood pressure (SBP) to left ventricular end-diastolic pressure (LVEDP) ratio for the prediction of in-hospital and short-term mortality in a contemporary cohort of patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI) at a tertiary care cardiac center.

Methods: This study included a consecutive series of patients diagnosed with STEMI who underwent primary PCI. The SBP/LVEDP ratio and TIMI (Thrombolysis in Myocardial Infarction) score were calculated, and their ability to predict in-hospital and short-term mortality was evaluated by analyzing the area under the curve (AUC) on the receiver operating characteristics (ROC) curve.

Results: This study involved 977 patients, with 780 (79.8%) being male and a mean age of 55.6 ± 11.5 years. Among them, 191 (19.5%) had an SBP/LVEDP ≤ 5.4. The in-hospital mortality rate was 4.3% (42), and the short-term all-cause mortality rate after a mean follow-up of 5.9 ± 2.4 months was 15% (140). Patients with SBP/LVEDP ≤ 5.4 had higher in-hospital mortality rates (14.1% vs. 1.9%; $P < 0.001$) and short-term mortality rates (35.1% vs. 9.8%; $P < 0.001$) compared to those with SBP/LVEDP > 5.4. The AUCs of SBP/LVEDP and TIMI for predicting in-hospital mortality were 0.766 [0.681-0.851] and 0.787 [0.713-0.861], respectively. For short-term mortality, the AUCs of SBP/LVEDP and TIMI were 0.731 [0.682-0.780] and 0.736 [0.690-0.782], respectively.

Conclusion: In conclusion, SBP/LVEDP showed sufficiently high predictive power comparable to the TIMI risk score. SBP/LVEDP is a readily available ratio that can rapidly provide valuable prognostic information during primary PCI.

Keywords: STEMI, Primary PCI, Systolic blood pressure, Left ventricular end-diastolic pressure, Prognosis

Introduction

Ischemic heart disease (IHD) stands as a predominant global health concern, accounting for a significant portion of morbidity and mortality worldwide. Among its manifestations, "ST-segment elevation myocardial infarction" (STEMI) emerges as a particularly critical and life-threatening subtype.[1] Fortunately, advancements in medical interventions, notably "primary percutaneous coronary intervention" (PCI) alongside evidence-based pharmacological strategies and procedural techniques, have notably enhanced outcomes for STEMI patients.[1] However, despite these advancements, a notable proportion of individuals continue to face adverse outcomes, ranging from 2.5% to 10% within 30 days post-procedure.[2-4] Such outcomes encompass a spectrum of complications, including cardiogenic shock, heart failure, arrhythmias, ventricular remodeling, recurrent infarction, thromboembolic events, valvular dysfunction, and sudden cardiac death,[5] with variabilities influenced by factors such as infarction extent, comorbidities, and timely medical intervention.[6,7]

Identifying patients at heightened risk of adverse events is paramount in clinical practice,[8] enabling proactive measures to mitigate post-procedural complications.[9] Several clinical indices and scoring systems have been devised for risk stratification in STEMI patients, including widely recognized ones like the TIMI, PAMI, GRACE, and CADILLAC scores.[10-13] However, their complex calculations, often necessitating online calculators, limit their practical utility, particularly in high-volume PCI centers.[14] Consequently, simpler bedside and invasive indices have garnered attention, leveraging parameters such as heart rate (HR), systolic blood pressure (SBP), "left ventricular ejection fraction" (LVEF), and "left ventricular end-diastolic pressure" (LVEDP).[8,9,15-17] Invasive hemodynamic measurements during the procedure offer theoretical advantages, providing a more precise assessment of left ventricular loading conditions and afterload, thus potentially offering superior predictive power for adverse outcomes.[14] Notably, recent literature underscores the significance of a low SBP to LVEDP ratio as an indicator of short-term mortality following primary PCI,[14] yet comprehensive data on its predictive performance remain scarce.

Therefore, this study aims to assess the predictive efficacy of the SBP to LVEDP ratio for in-hospital and short-term mortality in a contemporary cohort of STEMI patients undergoing primary PCI at a tertiary care cardiac center in a developing country.

Materials and Methods

Study Population

This study included a consecutive series of patients who were diagnosed with STEMI and underwent primary PCI at the National Institute of Cardiovascular Diseases (NICVD) from August 2020 to July 2021. The study protocol was approved by the ethical review board of the institution in accordance with the Declaration of Helsinki. All participants provided their consent to participate in the study after receiving a comprehensive explanation of the study's objectives and procedures.

Inclusion and exclusion criteria

The study primarily included adult patients (aged ≥ 18 years), of any gender, who met the diagnosis criteria for STEMI as defined below. These patients were promptly transferred to a catheterization laboratory for primary PCI within 12 hours of symptom onset, except for patients in cardiogenic shock who underwent primary PCI regardless of symptom duration. Patients who did not provide consent and those requiring multi-vessel intervention during the initial procedure were excluded from the study. Diagnostic criteria for STEMI were; "history of typical chest pain for at least 20 minutes" and presenting ECG finding of "ST elevation in at least two contiguous leads > 2mm in men or > 1mm in women in leads V2 to V3 and/or > 1mm in other contiguous chest leads or limb leads"

Data collection

We collected data on various aspects of the routine workup for STEMI at presentation, including demographic details, patient risk profile, and 12-lead electrocardiography (ECG) results. The information obtained included the patient's age (in years), gender, total ischemic time (in minutes), vital signs at presentation (blood pressure in mmHg and heart rate in bpm), routine lab investigations such as random plasma glucose level (in mg/dL) and serum creatinine level (in mg/dL). Additionally, we recorded the patient's Killip class, presence of arrhythmias, cardiac arrest, intubation status, and type of myocardial infarction.

All primary PCI procedures followed the standard management protocol for STEMI patients. We also gathered data on procedure characteristics and angiographic findings, such as thrombus burden, infarct-related artery, and the number of involved vessels. Furthermore, we obtained information on hemodynamic parameters, specifically LVEDP and LVEF. The SBP to LVEDP ratio (SBP/LVEDP) was obtained. SBP and LVEDP were measured invasively at the start of procedure with the help of a 6F multipurpose catheter placed in aorta and left ventricle, respectively. The zero reference line was taken at the level of right atrium and calibrated as per standard protocol before each patient was studied.

Additionally, the standard TIMI (Thrombolysis in Myocardial Infarction) score was also obtained as per the standard calculation criteria as comparator to the SBP/LVEDP.[18] All the patients were followed up to six months and occurrence of major adverse cardiovascular events (MACE) were recorded which included all-cause mortality, recurrent myocardial infarction needing revascularization, unplanned hospitalization due to heart failure, and thromboembolic events such as stroke or cerebrovascular events (CVA). The last known status of patients was considered to mark the short-term MACE status of patients.

Data analysis

Data collected for analysis were entered into IBM SPSS 21 software and analyzed accordingly. Receiver operating characteristic (ROC) curve analysis was conducted to evaluate the predictive performance of SBP/LVEDP and the TIMI score for in-hospital mortality. The optimal cutoff value was determined using maximum Youden's J statistic. Based on this optimal cutoff value, patients were divided into two groups. Clinical and procedural characteristics, as well as in-hospital and short-term outcomes, were compared between these two groups using appropriate statistical tests.

For variables that followed an approximately normal distribution, the independent sample t-test was used. If the variables were not normally distributed, the Mann-Whitney U test was employed. Categorical response variables were compared using the Chi-square test, and in cases where the expected cell frequency was low, Fisher's Exact Test or Likelihood ratio test was applied as appropriate.

The analysis provided the area under the curve (AUC), sensitivity (proportion of actual positives that are correctly identified), specificity (proportion of actual negatives that are correctly identified), accuracy (proportion of correct predictions among all predictions made), positive predictive value (proportion of actual positives among the samples that were predicted as positive), and negative predictive value (proportion of actual negatives among the samples that were predicted as negative), along with their corresponding 95% confidence intervals (CI). All statistical analyses were performed with a significance criterion of p-value < 0.05.

Results

Baseline and clinical characteristics

A total of 977 patients were included in this study, of whom 780 (79.8%) were male. The mean age of the patients was 55.6 ± 11.5 years, with 149 (15.3%) being under the age of 45. During presentation, 101 (11.4%) patients were classified as Killip class III/IV, 121 (12.4%) exhibited arrhythmias, 59 (6%) experienced cardiac arrest, and 130 (13.3%) required intubation. A ratio of SBP to LVEDP ≤ 5.4 was observed in 191 (19.5%) patients.

Patients with SBP/LVEDP ≤ 5.4 were found to have longer ischemic time (median, 390 [290-540] vs. 330 [230-470]; P = 0.001), higher heart rate (mean, 91 ± 29.3 vs. 82.8 ± 16.7; P < 0.001), a higher incidence of anterior wall myocardial infarction (72.3% vs. 47.7%), a higher prevalence of Killip class III/IV (28.8% vs. 1.9% and 20.4% vs. 0.3%), a higher occurrence of arrhythmias and cardiac arrest at the time of presentation (32.5% vs. 7.5%; P < 0.001 and 20.9% vs. 2.4%; P < 0.001), and a higher prevalence of diabetes (49.2% vs. 36%; P = 0.001) compared to those with SBP/LVEDP > 5.4 (Table 1).

Angiographic and procedural characteristics

Patients with SBP/LVED P ≤ 5.4 were found to have higher need of IABP placement (19.9% vs. 0.9%; P < 0.001), three vessel involvement (41.4% vs. 28.4%), pre-procedure TIMI 0 flow (71.7% vs. 52.3%), high thrombus grade (G5, 70.7% vs. 51.4%), and low post-procedure TIMI III flow (76.4% vs. 92.6%) compared to those with SBP/LVEDP > 5.4 (Table 2).

Post-procedure outcomes

The in-hospital mortality rate was 4.3% (42) and after a mean follow-up of 5.9 ± 2.4 months, short-term all-cause mortality rate was 15% (140). Both in-hospital (14.1% vs. 1.9%; P < 0.001) and short-term mortality rate (35.1% vs. 9.8%; P < 0.001) was found to be significantly higher for patients with SBP/LVED P ≤ 5.4 compared to those with SBP/LVEDP > 5.4 (Table 2).

Receiver operating characteristics curve analysis

The sensitivity and specificity analysis of SBP/LVEDP and TIMI score for the prediction of in-hospital mortality are

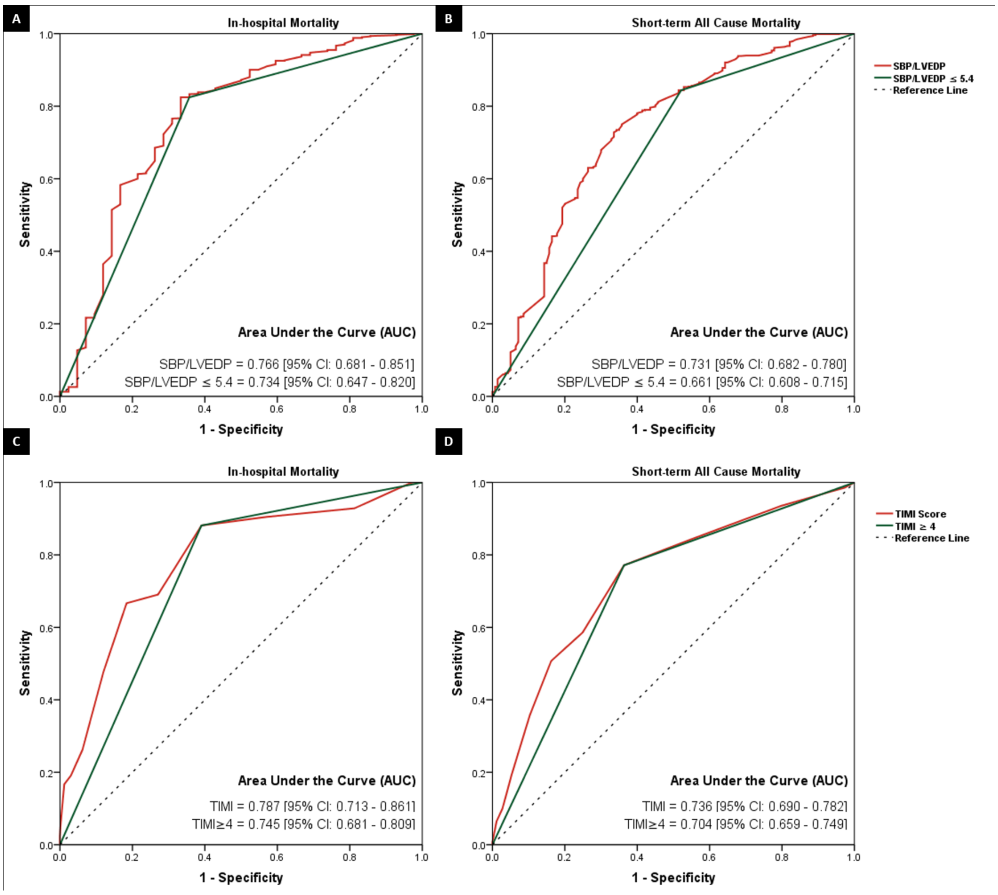

Figure 1. The receiver operating characteristics curve analysis of SBP to LVEDP ration and TIMI score for the prediction of in-hospital and short-term mortality after primary PCI
SBP = systolic blood pressure, LVEDP = left ventricular end-diastolic pressure, TIMI = thrombolysis in myocardial infarction, CI = confidence interval

Table 1. Comparative distribution of clinical and demographic characteristics between the two study groups based on SBP to LVEDP ratio

Characteristics	Total	SBP/LVEDP ≤5.4	SBP/LVEDP >5.4	*P*-value
Total (N)	**977**	**191 (19.5%)**	**786 (80.5%)**	**-**
Gender				
Female	20.2% (197)	20.4% (39)	20.1% (158)	0.922
Male	79.8% (780)	79.6% (152)	79.9% (628)	
Age (years)	55.6 ± 11.5	57.2 ± 12.6	55.2 ± 11.1	0.048
< 45 years	15.3% (149)	14.1% (27)	15.5% (122)	0.042
45 to 64 years	59.9% (585)	53.9% (103)	61.3% (482)	
≥ 65 years	24.9% (243)	31.9% (61)	23.2% (182)	
Total ischemic time (hours)	348 [240-480]	390 [290-540]	330 [230-470]	0.001
Heart rate (bpm)	84.4 ± 20	91 ± 29.3	82.8 ± 16.7	< 0.001
Systolic blood pressure (mmHg)	130.9 ± 24.9	110.6 ± 23.2	135.8 ± 22.8	< 0.001
Serum creatinine (mg/dL) on arrival	1.0 ± 0.5	1.1 ± 0.4	1.0 ± 0.5	0.102
Random glucose level (mg/dL)	156 [130-209]	178 [130-238]	155 [129-200]	0.027
Type of myocardial infarction (MI)				
Anterior	52.5% (513)	72.3% (138)	47.7% (375)	< 0.001
Inferior	20.2% (197)	7.3% (14)	23.3% (183)	
Inferior with RV	18.3% (179)	13.6% (26)	19.5% (153)	
Inferio-posterior	5.5% (54)	5.8% (11)	5.5% (43)	
Lateral	1.8% (18)	0% (0)	2.3% (18)	
Posterior	1.6% (16)	1% (2)	1.8% (14)	
Killip Class				
I	77% (752)	34% (65)	87.4% (687)	< 0.001
II	11.7% (114)	16.8% (32)	10.4% (82)	
III	7.2% (70)	28.8% (55)	1.9% (15)	
IV	4.2% (41)	20.4% (39)	0.3% (2)	
Intubated	13.3% (130)	45% (86)	5.6% (44)	< 0.001
Arrhythmias on presentation	12.4% (121)	32.5% (62)	7.5% (59)	< 0.001
Cardiac arrest	6% (59)	20.9% (40)	2.4% (19)	< 0.001
Co-morbid conditions				
Hypertension	57.5% (562)	60.2% (115)	56.9% (447)	0.402
Diabetes mellitus	38.6% (377)	49.2% (94)	36% (283)	0.001
Smoking	30.9% (302)	24.6% (47)	32.4% (255)	0.036
Family history of IHD	1.9% (19)	1.6% (3)	2% (16)	> 0.999
Prior PCI	7.2% (70)	8.9% (17)	6.7% (53)	0.300
History of CVA/TIA	1.9% (19)	2.1% (4)	1.9% (15)	0.776

SBP = systolic blood pressure, LVEDP = left ventricular end-diastolic pressure, IHD = ischemic heart diseases, RV = right ventricular, PCI = percutaneous coronary intervention, TIA = transient ischemic attack, CVA = cerebrovascular accidents

presented in Table 3. The AUCs of SBP/LVEDP for the prediction of in-hospital and short-term mortality were 0.766 [95% CI: 0.681 – 0.851] and 0.731 [95% CI: 0.682 – 0.780], respectively. Similarly, the AUCs of TIMI score for the prediction of in-hospital and short-term mortality were 0.787 [95% CI: 0.713 – 0.861] and 0.736 [95% CI: 0.690 – 0.782], respectively (Figure 1).

Discussion

Given the clinical significance of early risk stratification in STEMI patients, numerous risk stratification models have been formulated and validated over time.[10-13] These models primarily aim to provide early warning signs to attending physicians regarding potential adverse events. Nevertheless, the computational complexity and reliance on non-routine parameters pose challenges to the practical applicability of most of these scoring systems.[14] Therefore, this study aimed to assess the prognostic significance of a simple index based on the ratio of SBP to LVEDP. Our findings revealed that a low SBP/LVEDP ratio (≤ 5.4) is associated with an increased incidence of in-hospital (14.1% vs. 1.9%; $P < 0.001$) and short-term

Table 2. Comparative distribution of angiographic and procedural characteristics and in-hospital mortality between the two study groups based on SBP to LVEDP ratio

Characteristics	Total	SBP/LVEDP		*P*-value
		≤5.4	>5.4	
Total (N)	**977**	**191 (19.5%)**	**786 (80.5%)**	**-**
Left ventricular end-diastolic pressure (mmHg)	40.9±9.1	32.6±8.1	42.9±8.1	<0.001
Left ventricular ejection fraction (%)	18.6±6.7	28.2±6.6	16.3±4.1	<0.001
Intra-aortic balloon pump used	4.6% (45)	19.9% (38)	0.9% (7)	<0.001
Number of vessels involved				
Single vessel disease	36.7% (359)	31.4% (60)	38% (299)	
Two vessel disease	32.3% (316)	27.2% (52)	33.6% (264)	0.002
Three vessel disease	30.9% (302)	41.4% (79)	28.4% (223)	
Culprit coronary artery				
Left main	1.6% (16)	5.8% (11)	0.6% (5)	
LAD: Proximal	34.3% (335)	49.7% (95)	30.5% (240)	
LAD: Non-Proximal	17% (166)	15.7% (30)	17.3% (136)	
Left circumflex	11.6% (113)	8.4% (16)	12.3% (97)	<0.001
Right coronary artery	34.2% (334)	19.9% (38)	37.7% (296)	
Diagonal	1% (10)	0% (0)	1.3% (10)	
Ramus	0.3% (3)	0.5% (1)	0.3% (2)	
Pre-procedure TIMI (Thrombolysis in Myocardial Infarction) flow				
0	56.1% (548)	71.7% (137)	52.3% (411)	
I	18.5% (181)	15.7% (30)	19.2% (151)	<0.001
II	16.3% (159)	11% (21)	17.6% (138)	
III	9.1% (89)	1.6% (3)	10.9% (86)	
Thrombus Grade				
G1	4.1% (40)	0% (0)	5.1% (40)	
G2	5% (49)	1.6% (3)	5.9% (46)	
G3	24.2% (236)	16.2% (31)	26.1% (205)	<0.001
G4	11.6% (113)	11.5% (22)	11.6% (91)	
G5	55.2% (539)	70.7% (135)	51.4% (404)	
Mean vessel diameter (mm)	3.5±0.3	3.5±0.3	3.5±0.3	0.154
Total lesion length (mm)	27.6±11.8	28.4±13.6	27.5±11.3	0.347
Post-procedure TIMI (Thrombolysis in Myocardial Infarction) flow				
0	0.8% (8)	1.6% (3)	0.6% (5)	
I	2.5% (24)	7.3% (14)	1.3% (10)	<0.001
II	7.3% (71)	14.7% (28)	5.5% (43)	
III	89.5% (874)	76.4% (146)	92.6% (728)	
In-hospital mortality	4.3% (42)	14.1% (27)	1.9% (15)	<0.001
Follow-up				
Successful follow-up	95.7% (935)	100% (191)	94.7% (744)	0.001
Follow-up duration (months)	5.9±2.4	5.2±3	6.1±2.1	<0.001
All-cause mortality	15% (140)	35.1% (67)	9.8% (73)	<0.001
Stroke/CVA	0.9% (8)	0% (0)	1.1% (8)	0.371
Hospitalization due to HF	3.5% (33)	7.3% (14)	2.6% (19)	0.001
MI requiring revascularization	6.6% (62)	8.9% (17)	6% (45)	0.158
MACE	20% (187)	39.8% (76)	14.9% (111)	<0.001

SBP=systolic blood pressure, LVEDP=left ventricular end-diastolic pressure, LAD=left anterior descending artery, CVA=cerebrovascular accidents, TIA=transient ischemic attack, HF=heart failure, MI=myocardial infarction

Table 3. Accuracy analysis of SBP to LVEDP ratio and TIMI score for the prediction of in-hospital mortality after primary PCI

	SBP/LVEDP ≤ 5.4	TIMI Score ≥ 4
Sensitivity	64.3% [95% CI; 48.0% to 78.5%]	99.8% [95% CI; 99.6% to 99.9%]
Specificity	82.5% [95% CI; 79.9% to 84.6%]	61.0% [95% CI; 57.5% to 64.1%]
Positive Predictive Value	14.1% [95% CI; 11.2% to 17.7%]	88.2% [95% CI; 87.4% to 89.0%]
Negative Predictive Value	98.1% [95% CI; 97.2% to 98.7%]	99.1% [95% CI; 97.9% to 99.6%]
Accuracy	64.3% [95% CI; 48.0% to 78.5%]	99.8% [95% CI; 99.6% to 99.9%]

SBP = systolic blood pressure, LVEDP = left ventricular end-diastolic pressure, TIMI = thrombolysis in myocardial infarction

mortality (35.1% vs. 9.8%; $P < 0.001$) following primary PCI in a contemporary cohort of STEMI patients. The predictive performance of this simple index was found to be comparable to that of the TIMI risk score. The area under the curve (AUC) was 0.766 (95% CI: 0.681 - 0.851) for the prediction of in-hospital mortality and 0.731 (95% CI: 0.682 - 0.780) for the prediction of short-term all-cause mortality, while the AUC for the TIMI risk score was 0.787 (95% CI: 0.713 - 0.861) and 0.736 (95% CI: 0.690 - 0.782), respectively.

Furthermore, during a mean follow-up period of 5.9 ± 2.4 months, patients with an SBP/LVEDP ratio ≤ 5.4 exhibited a significantly higher rate of major adverse cardiac events (MACE) compared to those with an SBP/LVEDP ratio > 5.4 (39.8% vs. 14.9%; $P < 0.001$). The low SBP to LVEDP ratio was associated with several factors, including longer ischemic time, higher heart rate, a greater incidence of anterior wall myocardial infarction, a higher prevalence of Killip class III/IV, an increased occurrence of arrhythmias and cardiac arrest, a higher prevalence of diabetes, involvement of three vessels, pre-procedure TIMI 0 flow, low post-procedure TIMI III flow, and a greater need for intra-aortic balloon pump (IABP) placement. These factors collectively contribute to the higher incidence of MACE observed in these patients.

The only study thus far regarding the role of SBP to LVEDP ratio is conducted by Sola M et al.[14] This study also reported similar predictive role of SBP/LVEDP for the prediction of in-hospital and 30-day mortality. The likelihood ratio for in-hospital death and IABP usage at SBP/LVEDP ratio of ≤ 4 was 4.7 and 5.8, respectively.[14] Even though, clinical data regarding the prognostic strength of this simple ratio is very limited but prognostic significance of SBP and LVEDP has been extensively studied and reported in numerous clinical investigations.[19] The prognostic role of SBP in patients with STEMI has been extensively established, making it a valuable prognostic indicator for various clinical outcomes.[15-17,19,20] In clinical practice, SBP is commonly utilized in risk stratification models, such as the TIMI risk score, to assess the likelihood of future cardiovascular events and guide appropriate management strategies.[18]

Considering its prognostic significance, several clinical indices have been developed based on SBP. These include the Shock Index (SI), Age-adjusted SI, Modified SI (MSI), TIMI risk index (TRI), and LASH score.[7,15-17,19,20] Each of these indices takes into account SBP and utilizes it as a key component to predict patient outcomes and aid in risk stratification.

Furthermore, left ventricular end-diastolic pressure (LVEDP) is another important invasive measure used to evaluate the hemodynamic status of patients. It has been identified as an independent and combined indicator of poor prognosis, in conjunction with other clinical parameters.[21-24] By assessing LVEDP, healthcare professionals can gather valuable information regarding the patient's cardiac function and prognosis. In summary, the prognostic role of SBP in STEMI patients has been well-established, and it is widely utilized in risk stratification models. Additionally, LVEDP serves as an important indicator of prognosis, both independently and in combination with other clinical parameters. These factors contribute to a comprehensive understanding of patient outcomes and assist in guiding appropriate clinical management decisions. After proper zeroing and calibration of Physiomonitoring system, as per standard protocol, simultaneous single invasive measurement of aortic and LVEDP has lesser measurement biasness as compared to any non-invasive alternative. Secondly, these two measures are routinely performed in our catheterization laboratory. Hence, better accuracy and reliability of these readily available measures makes SBP to LVEDP ratio an attractive choice for risk categorization of these patients. While LVEDP is indeed an invasive marker, its routine measurement during primary PCI and simplicity of the calculation, makes SBP to LVEDP ratio an attractive alternative to complex clinical scoring systems like TIMI, PAMI, GRACE, and CADILLAC scores. Moreover, the invasive nature of LVEDP assessment improves its reliability and positions it as a preferable tool in risk stratification for STEMI patients undergoing intervention.

This observational study utilized prospectively collected data from an adequate number of patients. However, it is important to note that the main limitation of this study is its single-center coverage, which may impact the generalizability of the findings. Additionally, it should be acknowledged that invasive measures such as LVEDP may exhibit inter-operator variability, which could influence the results.

To establish a more robust and comprehensive risk stratification index for patients with STEMI, further large-scale multicenter prospective studies are necessary. These studies would help validate the findings of this study and provide a more reliable and widely applicable risk assessment tool for STEMI patients.

Conclusion

In conclusion, the ratio of SBP to LVEDP (SBP/LVEDP) demonstrated a strong predictive ability, comparable to the TIMI risk score. SBP/LVEDP is a readily available ratio that can rapidly provide valuable prognostic information during primary PCI. With the help of this useful ratio at the time of procedure, it is quite possible to identify a subgroup of patients with a heightened risk of both in-hospital and short-term mortality. This can offer an opportunity to implement more cautious and aggressive management strategies in the Cardiac Catheterization Laboratory, potentially leading to improved outcomes for these high-risk individuals.

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Authors' Contribution

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Competing Interests

The authors declare that they have no conflicts of interest.

Ethical Approval

This study was approval by the ethical review committee of the National Institute of Cardiovascular Diseases (NICVD), Karachi (ERC-30/2020).

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