ORIGINAL ARTICLE

QUANTIFICATION OF THROMBUS BURDEN AS AN INDEPENDENT PREDICTOR OF INTRA-PROCEDURAL NO-REFLOW IN PATIENTS WITH ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION UNDERGOING PRIMARY PERCUTANEOUS CORONARY REVASCULARIZATION

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Background: Aim of this study was to perform quantitative evaluation of high thrombus burden (Grade ≥4) as an independent predictor of slow/no reflow phenomenon during primary percutaneous coronary interventions (PCI) of patients with ST-segment elevation myocardial infarction (STEMI). **Methods**: In this analytical cross-sectional study we included consecutive patients who have undergone primary PCI for STEMI at a tertiary care cardiac center of the Pakistan. High thrombus burden was defined as angiographic thrombus grade ≥4. The thrombolysis in myocardial infarction (TIMI) flow rate < III was defined as slow/no reflow phenomenon. Results of multivariate logistic regression analysis for slow/no reflow phenomenon were reported as odds ratio (OR). **Results**: This analysis included 747 patients, 78.2% (584) patients were male and mean age was 55.82±11.54 years. High thrombus burden was observed in 68.1% (509) of the patients. Slow/no reflow phenomenon was observed in 33.6% (251) which was more common among patients in high thrombus burden group, 39.7% (202/509) vs. 20.6% (49/238); p<0.001. Adjusted OR of thrombus Grade ≥ 4 was 2.33 [1.6 -3.39]; p<0.001. Other significant variables were female gender (1.51 [1.01 -2.27]; p=0.045), left ventricular end-diastolic pressure (LVEDP) ≥20 mmHg (2.34 [1.69 -3.26]; p<0.001), total lesion length ≥20 cm (1.54 [1.09-2.16]; p=0.014), and neutrophil count ≥8.8 cells/μL (1.72 [1.22 -2.43]; p=0.002). **Conclusion:** High thrombus burden (Grade ≥4) is a significant and an independent predictor of the slow/no reflow phenomenon. While predicting slow/no reflow phenomenon, thrombus burden should be given due importance along with other significant factors such as gender, LVEDP, lesion length, and neutrophil counts.

Keywords: ST elevation myocardial infarction (STEMI); Primary percutaneous coronary interventions; Slow/no-reflow; thrombus burden; predictors

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INTRODUCTION

ST-segment elevation myocardial infarction (STEMI) remains the most lethal manifestation of ischemic heart diseases (IHD). According to current clinical practice guidelines, primary percutaneous coronary intervention (PCI) remains the first line management option, with superior outcomes as compared to other available pharmacological or surgical management options, for such patients.[1,2] Evidences from clinical practice around the world in recent year's unveiled a significant improvement in short- and log-term outcomes of primary PCI owing to the technological and pharmacological advancement.[3,4] Among various other complications, inadequate myocardial perfusion due to microvascular obstruction in infarct related artery, known as slow/no reflow phenomenon, remains a major concern of modern day interventional cardiology. Not only has it questioned the effectiveness of primary PCI as treatment option for STEMI patients but also found associated with poor short- and long-term prognosis. Its reported incidence rate is at least 4% which goes as high as 44% in some cases.[5–8]

There is no lack of conscience in scientific literature regarding causative mechanisms for this phenomenon. Pathophysiology is considered to be complex and multifactorial, various postulates have been made which included distal micro-

embolization of thrombus fragments, endothelial swelling due to ischemic injury or reperfusion, and microvascular spasm.[9–11]

Nevertheless, extensive research work is needed not only regarding the management of this complication but also regarding increased understanding of underlying mechanisms as well as associated factors in order to optimize the effectiveness of primary PCI for these patients. Research efforts to date have narrowed down various factors associated with increased risk of incidence of slow/no reflow phenomenon, these associated factors consisted of system as well as patient related factors.[8,11–14] It is vital to evaluate the scientific merit and clinical integrity of these factors so that evidence based a comprehensive risk stratification schema can be formulated for slow/no reflow phenomenon. Among various other factors, the high thrombus burden is one such factor observed to be stand out as an independent factor for slow/no reflow phenomenon,[12,14–17] therefore, it is important to assess the legitimacy of this factor among various other independent predictors so that future attempts towards development of any risk stratification schema can place due importance to this factor.

Therefore, aim of this study was to perform quantitative evaluation of high thrombus burden (Grade ≥4) as an independent predictor of slow/no reflow phenomenon during primary percutaneous coronary interventions (PCI) of patients with ST-segment elevation myocardial infarction (STEMI).

MATERIAL AND METHODS

In the analytical cross-sectional study, we included consecutive patient's undergone primary percutaneous coronary intervention (PCI) of native vessel for ST-segment elevation myocardial infarction (STEMI) at cardiac catheterization laboratory of the largest public sector cardiac center and training center of the Pakistan between September 2020 and February 2021. Study was approved by the ethical review committee of the Institute. Verbal consent for participation in the study was obtained by the investigators from all the patients and written informed consent was taken from their attendants. Patients who developed peri-procedure coronary artery dissection and those who were undergoing PCI of graft vessel and patient with vessels not suitable for PCI with stenting were not included in this study.

Diagnosis and management of the patients were done as per the clinical practice guidelines and institutional protocols. All the patients were managed by the experienced cardiologists and there was uniformity in the pre-, peri- and post procedure management protocols for all the patients, especially pre-procedural antiplatelet and anticoagulation regimen. Uncoated chewable Aspirin of 300 mg, clopidogrel 600mg per oral and unfractionated Heparin intravenously of 70–100 IU/Kg was given to all patients on confirmation of STEMI diagnosis. The thrombolysis in myocardial infarction (TIMI) flow rate of less than III even after mechanical opening of the infarct-related artery was noted as slow/no reflow phenomenon. Clinical, demographic and angiographic characteristics were recorded for all the patients including thrombus burden as angiographic thrombus grade categorized as "Grade 0: no thrombus, Grade 1: Possible thrombus, Grade 2: the thrombus' greatest dimension is <1/2 vessel diameter, Grade 3: Greatest dimension >1/2 to <2 vessel diameters, Grade 4: Greatest dimension >2 vessel diameters, Grade 5: total vessel occlusion due to thrombus".[18] Angiogram of all the procedures were assessed and interpreted by three independent interventional cardiologists blinded to assessment of one another to avoid biasness in the interpretation.

Patients were stratified into two groups based on thrombus grade as low thrombus burden group (Grade <4) and high thrombus burden groups (Grade ≥4). IBM SPSS version 21 was used for the analysis of collected data. Clinical, demographic, and angiographic characteristics between low and high thrombus burden groups were compared by applying appropriate independent sample t-test or Chi-square test. Multivariate logistic regression analysis with backward variable selection method was utilized.

Dependent variable was dichotomous variable of presence or absence of slow/no reflow phenomenon and candidate predictors were shortlisted based on literature search,[8,11–14] which included female gender, age ≥65 years, total ischemic time (TIT) of more than 7 hours, Killip class (III or IV), presence of arrhythmias at presentation, cardiac arrest state, CPR status, previous PCI, risk factors (hypertension, smoking, diabetes mellitus, family history of ischemic heart disease, history of stroke (CVA/TIA), chronic kidney disease (CKD), congestive heart failure (CHF), LVEDP ≥20 mmHg, LVEF ≤35%, temporary pacemaker (TPM) implant, use of IABP, high thrombus burden (Grade ≥4), mean vessel diameter ≥3.0, total lesion length ≥20 cm, multi-vessel disease, random blood sugar (RBS) >200 mg/dL, hemoglobin (HB) <13 mg/dL, neutrophil count ≥ 8.8 cells/μL, and platelet count > 250

cells/µL. Odds ratios (OR) [95% CI] were reported and $p \leq 0.05$ was considered statistically significant.

RESULTS

Total 747 patients were included in the study, 78.2% (584) patients were male and mean age was 55.82±11.54 years. Most common pre-existing co-morbid condition was hypertension (55.7%), followed by diabetes (38.2%), 28.5% were smokers. Forty (5.4%) patients were in cardiac arrest, arrhythmias at presentation were present in 11.9%. High thrombus burden was observed in 68.1% (509) of the patients. Comparison of clinical and demographic characteristics between low and high thrombus burden group was done which revealed no significant differences on most of the parameters except history of CHF, presence of arrhythmias at presentation and neutrophil counts which were here in high thrombus burden group. Clinical and demographic characteristics stratified by the thrombus burden are presented in Table-1.

Angiographic and procedural characteristics stratified by the thrombus burden are presented in Table 2. Mean LVEDP was significantly higher among high thrombus burden groups, 19.8±7 vs. 18.4±6.2 mmHg; p=0.006, while, mean LVEF was higher among low thrombus burden groups, 41.4±9.3 vs. 38.6±9.2%; p<0.001. TPM implantation and use of IABP was more common for high thrombus burden group with mean rates of 9% (46) vs. 2.9% (7); p=0.002 and 6.1% (31) vs. 2.1% (5); p=0.018 respectively. High thrombus burden was also observed to be associated with poor pre- as well as post-procedure TIMI flow grade. Slow/no reflow phenomenon was more common among patients in high thrombus burden group as compared to low thrombus burden, which was observed in 39.7% (202) vs. 20.6% (49); p<0.001 respectively. Similarly, in-hospital mortality was also relatively higher for high as compared to low thrombus burden group with mortality rate of 4.5% (23) vs. 2.1% (5); p=0.105 respectively (Figure-1).

In-hospital mortality rate was significantly higher among patients who developed slow/no reflow phenomenon during primary PCI with mortality rate of 6.0% (15/251) vs. 2.6% (13/496); p=0.023 for patients with and without slow/no reflow respectively. Results of initial and final solution of multivariate logistic regression analysis for slow/no reflow phenomenon during primary PCI are presented in Table-3. Independent predictors of slow/no reflow phenomenon were found to be female gender (OR = 1.51 [1.01 -2.27]; p= 0.045), CHF (OR=3.91 [0.97 -15.75]; p= 0.055), LVEDP ≥20 mmHg (OR= 2.34 [1.69 - 3.26]; p<0.001), thrombus Grade ≥ 4 (OR = 2.33 [1.6 -3.39]; p<0.001), total lesion length ≥20 cm (OR= 1.54 [1.09 -2.16]; p=0.014), and neutrophil count ≥8.8 cells/µL (OR= 1.72 [1.22 -2.43]; p= 0.002).

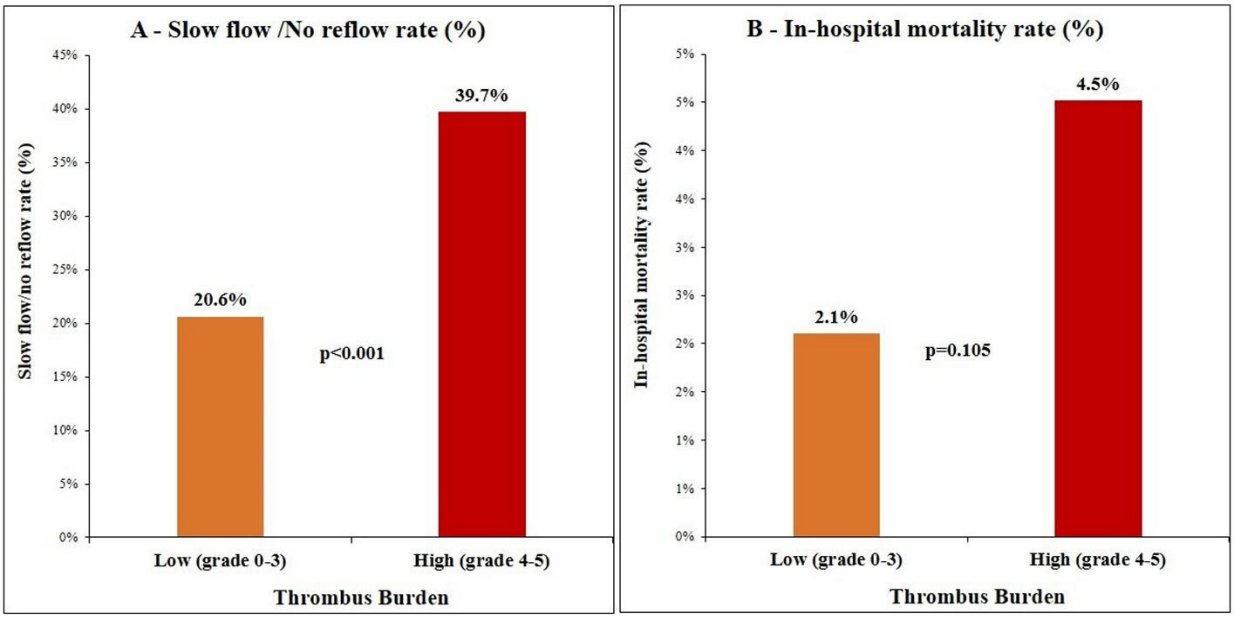

Figure-1: Slow/no reflow phenomenon (A) and in-hospital mortality (B) stratified by thrombus burden

Table-1: Clinical and demographic characteristics stratified by the thrombus burden

Characteristics	Total	Thrombus Burden		*p*-value
		Low	High	
Total (N)	**747**	**238 (31.9%)**	**509 (68.1%)**	-
Gender				
Male	78.2% (584)	79.8% (190)	77.4% (394)	0.455
Female	21.8% (163)	20.2% (48)	22.6% (115)	
Age (years)	55.82 ± 11.54	55.35 ± 11.43	56.04 ± 11.59	0.45
Young (≤ 45 years)	21.2% (158)	21% (50)	21.2% (108)	0.767
Middle (46 to 65 years)	62.8% (469)	64.3% (153)	62.1% (316)	
Old (> 65 years)	16.1% (120)	14.7% (35)	16.7% (85)	
Body mass index (kg/m2)	26.52 ± 3.49	26.62 ± 3.47	26.48 ± 3.5	0.606
Under weight	0.8% (6)	0.8% (2)	0.8% (4)	0.621
Normal weight	34.8% (260)	31.9% (76)	36.1% (184)	
Over weight	53.4% (399)	54.6% (130)	52.8% (269)	
Obese	11% (82)	12.6% (30)	10.2% (52)	
Systolic blood pressure (mmHg)	130.5 ± 25.4	131.5 ± 23.6	130 ± 26.3	0.426
Heart Rate (bpm)	84.6 ± 19.9	84.5 ± 15.8	84.6 ± 21.5	0.971
Symptom to hospital arrival time (hours)	4.4 ± 3.1	4.2 ± 2.7	4.5 ± 3.3	0.213
Door to balloon time (hours)	1.8 ± 1.1	1.8 ± 1	1.8 ± 1.1	0.649
Total Ischemic Time (hours)	6.2 ± 3.6	6 ± 3.2	6.3 ± 3.7	0.22
1st quartile (≤ 3.83 hours)	23.6% (176)	25.2% (60)	22.8% (116)	0.885
2nd quartile (3.83 to 5.5 hours)	27.4% (205)	27.3% (65)	27.5% (140)	
3rd quartile (5.5 to 7.42 hours)	24% (179)	22.7% (54)	24.6% (125)	
4th quartile (>7.42 hours)	25% (187)	24.8% (59)	25.1% (128)	
Killip Class				
I	74.8% (559)	79% (188)	72.9% (371)	0.076
II	12% (90)	12.6% (30)	11.8% (60)	
III	9.5% (71)	6.3% (15)	11% (56)	
IV	3.6% (27)	2.1% (5)	4.3% (22)	
Co-morbid conditions				
Hypertension	55.7% (416)	55% (131)	56% (285)	0.808
DM- non insulin dependent	35.5% (265)	35.7% (85)	35.4% (180)	0.926
DM - insulin dependent	2.7% (20)	1.7% (4)	3.1% (16)	0.249
Smoking	28.5% (213)	31.9% (76)	26.9% (137)	0.157
Family history of IHD	2.5% (19)	2.9% (7)	2.4% (12)	0.637
Chronic kidney disease	1.1% (8)	2.1% (5)	0.6% (3)	0.061
History of PCI	8.3% (62)	6.7% (16)	9% (46)	0.850
History of CVA/TIA	2.1% (16)	2.5% (6)	2% (10)	0.625
History of CHF	1.5% (11)	0% (0)	2.2% (11)	0.022*
Type of myocardial infarction (MI)				
Anterior	56.4% (421)	58.8% (140)	55.2% (281)	0.648
Inferior	40.6% (303)	38.7% (92)	41.5% (211)	
Lateral	1.6% (12)	1.7% (4)	1.6% (8)	
Posterior	1.5% (11)	0.8% (2)	1.8% (9)	
Rhythm at presentation				
Normal sinus rhythm	98.4% (735)	98.7% (235)	98.2% (500)	0.607
Atrial fibrillation (Afib)	1.6% (12)	1.3% (3)	1.8% (9)	
Arrhythmias at presentation				
None	88.1% (658)	93.7% (223)	85.5% (435)	0.017*
Bradycardia	7.1% (53)	3.4% (8)	8.8% (45)	
Ventricular fibrillation (V-fib)	1.6% (12)	1.3% (3)	1.8% (9)	
Ventricular tachycardia (V-Tach)	2.9% (22)	1.3% (3)	3.7% (19)	
Premature ventricular contractions	0.3% (2)	0.4% (1)	0.2% (1)	
Cardiac arrest	5.4% (40)	3.8% (9)	6.1% (31)	0.192
Cardiopulmonary resuscitation (CPR)	4.7% (35)	2.9% (7)	5.5% (28)	0.123
Intubated				
Not Intubated	84.2% (629)	90.3% (215)	81.3% (414)	0.005*
Before Procedure	12.4% (93)	8.4% (20)	14.3% (73)	
During or After Procedure	3.3% (25)	1.3% (3)	4.3% (22)	
Random glucose level (mg/dL)	180.13 ± 79.93	176 ± 72.41	182.06 ± 83.22	0.335
≤ 200 mg/dL	71.5% (534)	70.2% (167)	72.1% (367)	0.585
> 200 mg/dL	28.5% (213)	29.8% (71)	27.9% (142)	
Hemoglobin level (mg/dL)	13.99 ± 2.03	13.89 ± 2.03	14.04 ± 2.03	0.368
< 13 mg/dL	27.6% (206)	27.3% (65)	27.7% (141)	0.911
≥ 13 mg/dL	72.4% (541)	72.7% (173)	72.3% (368)	
Neutrophil count (cells/µL)	10.15 ± 4.12	9.53 ± 3.75	10.44 ± 4.26	0.003*
< 8.8 cells/µL	42.8% (320)	46.2% (110)	41.3% (210)	0.202
≥ 8.8 cells/µL	57.2% (427)	53.8% (128)	58.7% (299)	
Platelet count (cells/µL)	248.63 ± 82.87	252.16 ± 90.55	246.98 ± 79.07	0.427
≤ 450 cells/µL	98.1% (733)	97.9% (233)	98.2% (500)	0.755
> 450 cells/µL	1.9% (14)	2.1% (5)	1.8% (9)	

DM=diabetes mellitus, IHD=ischemic heart disease, PCI=percutaneous coronary intervention, CVA= cerebrovascular accident, TIA= transient ischemic attack, CHF=congestive heart failure *Significant at 5%

Table-2: Angiographic and procedural characteristics stratified by the thrombus burden

Characteristics	Total	Thrombus Burden		*p*-value
		Low	High	
Total (N)	**747**	**238**	**509**	**-**
Access for procedure				
Radial	66.1% (494)	71.4% (170)	63.7% (324)	0.191
Femoral	32.4% (242)	27.3% (65)	34.8% (177)	
Switchover	1.3% (10)	1.3% (3)	1.4% (7)	
Ulnar	0.1% (1)	0% (0)	0.2% (1)	
LVEDP (mmHg)	19.4 ± 6.8	18.4 ± 6.2	19.8 ± 7	0.006*
LVEF (%)	39.5 ± 9.3	41.4 ± 9.3	38.6 ± 9.2	<0.001*
TPM implanted	7.1% (53)	2.9% (7)	9% (46)	0.002*
IABP used	4.8% (36)	2.1% (5)	6.1% (31)	0.018*
Fluoroscopy time (minutes)	16.1 ± 9.2	15.9 ± 9.5	16.2 ± 9.1	0.697
Contrast volume (ml)	124.6 ± 38.5	125.5 ± 40.2	124.1 ± 37.7	0.639
Number of vessels involved				
None	0.3% (2)	0% (0)	0.4% (2)	0.424
Single vessel disease	35.7% (267)	35.3% (84)	36% (183)	
Two vessel disease	34.1% (255)	37.4% (89)	32.6% (166)	
Three vessel disease	29.9% (223)	27.3% (65)	31% (158)	
Recanalised vessel	3.3% (25)	9.2% (22)	0.6% (3)	<0.001*
Culprit coronary artery				
Left anterior descending artery	56.1% (419)	58.8% (140)	54.8% (279)	0.836
Right coronary artery	31.2% (233)	29% (69)	32.2% (164)	
Left circumflex	10.8% (81)	10.9% (26)	10.8% (55)	
Diagonal	0.9% (7)	0.4% (1)	1.2% (6)	
Ramus	0.5% (4)	0.4% (1)	0.6% (3)	
Left main	0.4% (3)	0.4% (1)	0.4% (2)	
Pre-procedure TIMI flow				
0	60.9% (455)	0% (0)	89.4% (455)	<0.001*
I	10.7% (80)	10.9% (26)	10.6% (54)	
II	18.7% (140)	58.8% (140)	0% (0)	
III	9.6% (72)	30.3% (72)	0% (0)	
Stent deployed	91.8% (686)	95% (226)	90.4% (460)	0.001*
Mean stent diameter	3.3 ± 0.3	3.3 ± 0.3	3.3 ± 0.3	0.458
Total stent length	27.4 ± 13.1	28 ± 13.1	27.1 ± 13.1	0.410
Slow flow/No reflow	33.6% (251)	20.6% (49)	39.7% (202)	<0.001*
Post-procedure TIMI flow				
0	0.4% (3)	0% (0)	0.6% (3)	<0.001*
I	2.4% (18)	0.4% (1)	3.3% (17)	
II	10.3% (77)	3.8% (9)	13.4% (68)	
III	86.9% (649)	95.8% (228)	82.7% (421)	
In-hospital mortality	3.7% (28)	2.1% (5)	4.5% (23)	0.105

LVEDP= left ventricular end-diastolic pressure, LVEF= left ventricular ejection fraction, TPM=temporary pacemaker, IABP= intra-aortic balloon pump, TIMI= thrombolysis in myocardial infarction *Significant at 5%

Table-3: Multivariate logistic regression analysis for slow/no reflow phenomenon

Factors	Initial Solution		Final Solution	
	OR [95% CI]	*p*-value	OR [95% CI]	*p*-value
Female	1.64 [1.03 -2.61]	0.036*	1.51 [1.01 -2.27]	0.045*
Age ≥65 years	1.22 [0.78 -1.91]	0.391	-	-
TIT >7 hours	1.08 [0.76 -1.53]	0.674	-	-
Killip class (III or IV)	1.08 [0.61 -1.93]	0.795	-	-
Arrhythmia	0.61 [0.32 -1.15]	0.128	-	-
Cardiac Arrest	0.93 [0.09 -9.57]	0.951	-	-
Cardiopulmonary resuscitation	1.15 [0.1 -13.32]	0.909	-	-
Previous PCI	0.97 [0.51 -1.84]	0.924	-	-
Hypertension	0.69 [0.48 -0.99]	0.045*	0.73 [0.52 -1.02]	0.066
Smoking	0.61 [0.4 -0.93]	0.022*	0.6 [0.4 -0.91]	0.015*
DM Non- Insulin Dependent	1.19 [0.77 -1.85]	0.440	-	-
DM Insulin Dependent	0.82 [0.28 -2.4]	0.721	-	-
Family history of IHD	0.36 [0.09 -1.41]	0.145	-	-
CVA/TIA	0.91 [0.28 -3.01]	0.882	-	-
CKD	1.73 [0.34 -8.67]	0.507	-	-
CHF	4.05 [0.93 -17.67]	0.063	3.91 [0.97 -15.75]	0.055
LVEDP ≥20 mmHg	2.06 [1.4 -3.04]	<0.001*	2.34 [1.69 -3.26]	<0.001*
LVEF ≤35%	1.2 [0.82 -1.77]	0.350	-	-
TPM Implanted	1.83 [0.88 -3.81]	0.106	-	-
IABP Used	1.3 [0.56 -3.01]	0.537	-	-
Thrombus Grade ≥ 4	2.35 [1.59 -3.46]	<0.001*	2.33 [1.6 -3.39]	<0.001*
Mean stent diameter ≥ 3.0	1.22 [0.86 -1.72]	0.261	-	-
Total lesion length ≥ 20 cm	1.5 [1.05 -2.13]	0.025*	1.54 [1.09 -2.16]	0.014*
Multi-vessel disease	1.11 [0.77 -1.59]	0.584	-	-
RBS > 200 mg/dL	0.75 [0.48 -1.18]	0.220	-	-
HB < 13 mg/dL	0.98 [0.64 -1.5]	0.912	-	-
Neutrophil count ≥ 8.8 cells/µL	1.65 [1.15 -2.37]	0.006*	1.72 [1.22 -2.43]	0.002*
Platelet count > 250 cells/µL	0.62 [0.44 -0.88]	0.007*	0.63 [0.45 -0.88]	0.007*

OR=odds ratio, CI= confidence interval, TIT= total ischemic time, PCI=percutaneous coronary intervention, DM=diabetes mellitus, IHD=ischemic heart disease, CVA= cerebrovascular accident, TIA= transient ischemic attack, CHF=congestive heart failure, LVEDP= left ventricular end-diastolic pressure, LVEF= left ventricular ejection fraction, TPM=temporary pacemaker, IABP= intra-aortic balloon pump, TIMI= thrombolysis in myocardial infarction *Significant at 5%

DISCUSSION

Aim of this analysis was a quantitative evaluation of high thrombus burden as an independent predictor of slow/no-reflow phenomenon and results of this study revealed that high thrombus burden is a significant and independent predictor of the phenomenon and patients with angiographic thrombus Grade of four or higher are more likely to develop slow/no-reflow during primary PCI procedure with adjusted odds ratio of 2.33 [1.6 -3.39]; p<0.001. Rate of development of slow/no reflow phenomenon was observed to be 39.7% (202/509) vs. 20.6% (49/238); p<0.001 for patients with high and low thrombus burden respectively. Analysis results also showed that other patient related characteristics, such as female gender (OR= 1.51; 95% CI: 1.01 -2.27), LVEDP ≥20 mmHg (OR= 2.34; 95% CI: 1.69 -3.26), total lesion length ≥ 20 cm (OR= 1.54; 95% CI: 1.09 -2.16), and neutrophil count ≥ 8.8 cells/μL (OR= 1.72; 95% CI: 1.22 -2.43), have good predictive value for slow/no-reflow phenomenon. Any future attempt of formulation of risk stratification risk score should give due importance to these factors. However, negative association of no-reflow with smoking and platelet count was observed with adjusted OR of 0.6 [0.4 -0.91] and 0.63 [0.45 -0.88] respectively, these associations need further exploration for plausible clinical and biological explanation.

Our observation regarding state of an independent predictor of high thrombus burden in the context of slow/no-reflow phenomenon is alike various other research studies which have also endorsed these findings.[12,14–17] In a study of 181 patients Sabin P *et al.*[12] reported OR of 11.04 [5.12–23.8] against high thrombus burden for predicting slow/no-reflow phenomenon on univariate logistic regression analysis. However, thrombus burden was insignificant on multivariate analysis, significant independent predictors reported in this study were old age (>60 years), total ischemic time of more than six hours, longer lesion length, and poor pre-procedure TIMI flow. Abdi S *et al.*[14] in their study of 438 patients reported thrombus grade as a strong in predictor of no-reflow along with other patient and system related factors such as white blood cell (WBC) count, maximal ST-change, high sensitivity C-reactive protein (hs-CRP), duration of chest pain, LV function, coronary anatomy, eccentricity, and bifurcation. Fajar JK *et al.*[16] in their meta-analysis investigated predictors of no-reflow phenomenon and reported high thrombus burden (OR=3.69 [2.39–5.68]) and initial TIMI flow ≤1 (OR=3.83 [2.77–5.29]) as most impacted no-reflow phenomenon risk factors. Zhou H *et al.*[17] in their study have highlighted various clinical, procedural, and angiographic features as predictor no-reflow phenomenon, these include high thrombus burden with and adjusted OR of 1.60 [1.47–2.76]. Other features were age >65 years, total ischemic time >6 hours, low systolic blood pressure (SBP) on admission <100 mmHg, IABP use before PCI, low (≤1) pre-procedure TIMI flow grade, and long target lesion.

Prognostic role of slow/no-reflow phenomenon is well documented in past studies,[8,12,14,15] similarly in this study, in-hospital mortality rate was significantly higher among patients who developed slow/no reflow phenomenon during primary PCI with mortality rate of 6.0% (15/251) vs. 2.6% (13/496); p=0.023 for patients with and without slow/no reflow respectively.

Considering the prognostic role of slow/no-reflow phenomenon during primary PCI, more extensive research efforts are required to formulate evidence based approached to predict, prevent, and manage this phenomenon in order to optimize the benefit of procedure. In this regard, deeper understand of underlying mechanism and identification of potential predictors, such as high thrombus burden, are important so that early suspicion about risk of developing slow/no-reflow could be made. Beforehand alert about potential risk will be very helpful to the interventional cardiologists to prepare and plan logistics, preventive measures, and management strategy of the slow/no-reflow phenomenon during primary PCI.

To the best of our knowledge this is the largest study of its type from this region, in spite of it there are certain limitations such as single center experience, additionally, slow/no-reflow was defined based on available angiographic findings instead of myocardial blush grading (MBG).

CONCLUSION

High thrombus burden (Grade ≥ 4) is a significant and an independent predictor of the slow/no reflow phenomenon during primary PCI for STEMI. Patients with angiographic thrombus Grade of four or higher are more than twice times more likely to develop slow/no-reflow. Among other features female gender, LVEDP ≥20 mmHg, total lesion length ≥20 cm, and neutrophil count ≥8.8 cells/μL have good predictive value for slow/no-reflow phenomenon. Hence, any future attempt of formulation of risk stratification risk score should give due importance to these factors.

AUTHORS' CONTRIBUTION

RK, KAK, JS, AA, JAS, and MK contributed to the concept and design of study, RK, JS, AA, DK, SKh, SKa, and MM contributed to the collection, analysis

and interpretation of data, RK, JS, AA, DK, SKh, SKa and MK contributed to the drafting of the manuscript, and JAS and KAK critically analyzed for content. All authors have read and approved the manuscript.

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