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Thrombolysis in Myocardial Infarction (TIMI) Flow and Myocardial Blush (MB) as Predictors of Left Ventricular Ejection Fraction Improvement in Patients with Acute Myocardial Infarction with ST Segment Elevation Undergoing Primary Percutaneous Coronary Intervention

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ABSTRACT

Background: Reperfusion success in ST-elevation myocardial infarction (STEMI) is often measured by macrovascular TIMI flow. However, myocardial tissue perfusion, assessed via Myocardial Blush (MB), may provide a more accurate prognosis. This study evaluates TIMI flow and MB as predictors of Left Ventricular Ejection Fraction (LVEF) improvement in STEMI patients post-Primary Percutaneous Coronary Intervention (PCI). ***Methods:*** This prospective cohort study included STEMI patients undergoing PCI. TIMI flow and MB (using QuBE software) were measured post-procedure. LVEF was evaluated at baseline and 2-month follow-up. Data were analyzed using Chi-square for Relative Risk (RR) and Cox regression for Adjusted RR. ***Results:*** High MB (QuBE ≥9 AU) was a significant independent predictor of LVEF improvement. Patients with high MB had a 1.6 times greater chance of functional recovery compared to those with low MB (RR 1.60; 95% CI 1.21–2.11; $p<0.001$). Conversely, TIMI flow grade, clinical risk factors (age, diabetes, hypertension), and total ischemic time showed no significant association with LVEF improvement ($p>0.05$). Multivariate analysis confirmed high MB as the sole independent predictor of LVEF recovery (Adjusted RR 1.57; 95% CI 1.04–2.63; $p=0.045$). ***Conclusion:*** Microvascular perfusion (MB), rather than macrovascular flow (TIMI), is the primary determinant of left ventricular functional recovery post-PCI. Achieving successful reperfusion at the myocardial tissue level is critical for long-term cardiac improvement.

Keywords: acute myocardial infarction; myocardial blush; TIMI flow; LVEF

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death worldwide, with a mortality rate of 126 per 100.000 people, particularly in low- and middle-income countries [1, 2]. In 2019, 18.6 million deaths were caused by CVD, with 58% occurring in Asia.[3] Based on data from the Indonesian Ministry of Health (Kemenkes) in 2021, the prevalence of heart disease in Indonesia was found to be 2 million cases [4]. Acute coronary syndrome (ACS) is often the first clinical manifestation of CVD [3, 5]. ACS is caused by damage, rupture, or erosion of unstable atherosclerotic plaques in the coronary arteries, leading to thrombosis and/or partial or total microembolism, which reduces blood flow to the myocardium and causes myocardial ischemia.

ACS is divided into three categories based on severity: unstable angina pectoris (UAP), acute myocardial infarction without ST-segment elevation (STEMI), and acute myocardial infarction with ST-segment elevation (STEMI). In STEMI, coronary plaque rupture causes total blockage and can lead to ischemia and transmural myocardial infarction [6].

In STEMI, revascularization is necessary to restore blood flow and myocardial reperfusion as quickly as possible, which can be done medically using fibrinolytic agents or mechanically with primary percutaneous coronary intervention (PCI) [5]. In patients with STEMI, PCI is the preferred therapy [7, 8].

Decreased left ventricular ejection fraction (LVEF) caused by infarction remains an important predictor of morbidity and mortality in STEMI patients [9, 10]. Factors associated with improved LVEF after PCI include shorter reperfusion time, as evaluated by door-to-wire time, which is related to infarct size and thrombolysis in myocardial infarction flow (TIMI flow), which reflects the quality of macrovascular reperfusion [11–14]. Additionally, microvascular perfusion quality through Myocardial Blush (MB) may also influence LVEF after PCI [15]. Other factors that may also influence LVEF improvement include gender, age, smoking history, hypertension, diabetes mellitus, hyperlipidaemia, prior history of coronary artery disease, and the location of the primary lesion causing arterial blockage [8, 10].

The success of reperfusion can be assessed based on TIMI flow after PCI, with TIMI flow grade 3, which means reperfusion has been achieved in the epicardial artery that experienced infarction. However, patients with TIMI flow grade 3 do not always achieve adequate myocardial perfusion, especially if there is a long delay between symptom onset and restoration of epicardial flow.[16] Myocardial perfusion can be evaluated through MB, which has a good prognostic role for patients with STEMI after PCI. In a study of 43 STEMI patients who underwent PCI with a TIMI flow grade of 3, nearly one-third of patients had MBG 0 or 1, indicating poor perfusion of the myocardial tissue [17].

Most previous studies have emphasized the success of PCI based on TIMI flow as the main parameter. However, there is increasing evidence that TIMI flow alone is not sufficient to predict LVEF improvement. Myocardial blush (MB) has emerged as an additional indicator in assessing the success of reperfusion at the microvascular level [17]. Therefore, this study aims to evaluate TIMI flow and MB as predictors of LVEF improvement in STEMI patients undergoing PCI.

METHODS

Study Design

This study is an observational analytic study with a prospective cohort design. This study evaluates TIMI flow and myocardial blush in patients diagnosed with STEMI at the completion of Primary Percutaneous Coronary Intervention (PCI) who were admitted between June and August 2025 at Prof. Dr. I.G.N.G. Ngoerah Denpasar Central General Hospital, in order to categorize TIMI flow and MB conditions. Each category was followed up for 2 months after PCI to evaluate the occurrence of LVEF improvement. Evaluation of LVEF was performed before and after PCI.

Study Setting and Period

Samples were selected according to inclusion criteria when patients arrived at the emergency unit of Prof. Dr. I.G.N.G. Ngoerah Denpasar Central General Hospital. Echocardiography will be performed in the emergency unit and in the echocardiography room of the Integrated Heart Facility at Prof. Dr. I.G.N.G. Ngoerah Denpasar Central General Hospital. TIMI flow and myocardial blush measurements will be performed in the Cath Lab room of the Integrated Heart Facility at Prof. Dr. I.G.N.G. Ngoerah Denpasar Central General Hospital. The study will be conducted from May 2025 to November 2025.

Study Population and Sample

The target population is all patients diagnosed with STEMI aged over 18 years with onset < 12 hours. The accessible population is patients with a diagnosis of STEMI aged over 18 years with onset < 12 hours who will undergo PCI in the Cath Lab room at the Integrated Heart Facility Building at Prof. Dr. I.G.N.G. Ngoerah Denpasar Central General Hospital from June to August 2025. The research sample was obtained from the accessible population using consecutive sampling, meaning that all subjects who met the sample criteria would be included in the study until the required number was reached.

Eligibility Criteria

Eligible patients are those aged ≥18 years with chest pain onset <12 hours who are diagnosed with STEMI and have successfully undergone PCI and hospitalization at Prof. Dr. I.G.N.G. Ngoerah Denpasar Central General Hospital. Patients are excluded if they have STEMI with failed pharmacotherapy reperfusion therapy, patients with STEMI who only underwent coronary angiography without stent placement, patients with severe aortic and/or mitral stenosis or regurgitation, patients with life-threatening arrhythmias such as ventricular tachycardia or ventricular fibrillation without a pulse and cardiac arrest, patients who refused to participate after informed consent, and patients who died after PCI or were lost to follow-up.

Sample Size Calculation

The minimum sample size was calculated using the cohort study formula proposed by Lwanga and Lemeshow. With a type I error of 5% and a statistical power of 80%, the assumed proportion of left ventricular ejection fraction improvement was 22% in the high TIMI flow group and 2.4% in the low TIMI flow group, based on previous literature. The calculated minimum sample size was 41 participants per group. To account for potential dropouts, an additional 10% was added, resulting in 45 participants per group and a total sample size of 90 patients.

Study Variables

The independent variables in this study were TIMI flow and myocardial blush. TIMI flow assesses antegrade radiocontrast flow in arteries affected by infarction, which is evaluated during angiography at the end of the PCI procedure, whereby the degree of TIMI flow is a categorical variable. Myocardial blush is a quantitative assessment of cardiac perfusion by evaluating the contrast reaching the myocardial tissue and the speed of its clearance by the epicardial coronary arteries. MB is evaluated during angiography at the end of the PCI procedure using the Quantitative Myocardial Blush (QuBE) program.

MB is a categorical variable. Meanwhile, LVEF is a dependent variable. LVEF is a parameter for measuring left ventricular systolic function, measured using 2-dimensional transthoracic echocardiography with the biplane Simpson's method using a GE Vivid device when the patient is admitted to the hospital before PCI and 2 months after PCI. Improvement in LVEF is a categorical variable. Finally, the control variables consisted of age, gender, infarct location, and culprit lesion, total ischemic time (onset to door and door to wire time), hypertension, diabetes mellitus, smoking, and adherence to anti-remodelling medication (ACE-I/ARB, beta blocker, statin), all of which were considered in the multivariate analysis.

Data Collection Procedures

Data collection began with rigorous screening of STEMI patients undergoing PCI at Prof. dr. I.G. N. G. Ngoerah Central General Hospital based on inclusion and exclusion criteria, as well as the signing of informed consent forms. Baseline data were collected through a complete medical history, physical examination, and laboratory tests. After the stent placement procedure in the cath lab, two types of post-procedure perfusion assessments were performed: macrovascular evaluation through TIMI flow assessment reviewed by a panel of interventional experts (senior fellows and consultants), and microvascular evaluation through Myocardial Blush analysis using the QuBE program with DICOM data format.

Outcome Assessment

The primary outcome in this study was changes in cardiac function assessed through follow-up for two months after PCI. The evaluation was performed using transthoracic echocardiography to measure Left Ventricular Ejection Fraction (LVEF). To maintain objectivity, echocardiography data collection was performed blindly by trained cardiology residents without knowing the initial LVEF data, which was then confirmed by a consultant echocardiography specialist. Clinical improvement in LVEF was defined as an absolute increase in LVEF of ≥ 5% compared to the initial LVEF value before the procedure.

Statistical Analysis

All statistical analyses were performed using SPSS software. Descriptive analysis aims to describe the characteristics of the research subjects and variables based on the TIMI flow and MB categories. Numerical data variables will be presented as means and standard deviations. Categorical data variables will be presented as relative frequencies. A chi-square comparison test (for categorical variables) was performed to compare LVEF improvement based on TIMI flow and MB categories. This analysis was performed by creating a cross-tabulation. The measure of association calculated was relative risk. Furthermore, a Cox regression analysis was performed to assess TIMI flow and MB as predictors of LVEF improvement after controlling for confounding variables in the analysis. The measure of association used was the adjusted hazard ratio. Conclusions were drawn based on the 95% confidence interval of the hazard ratio and the P-value at an alpha level of 0.05.

RESULT

The basic characteristics of the research subjects, including sociodemographic data, cardiovascular risk factors, and clinical and angiographic parameters, were summarized based on the categories of high MB (QuBE ≥9 AU) and low MB (QuBE <9 AU). The results of the analysis show that both groups have comparable distributions across all variables, including age, gender, smoking status, history of comorbidities (hypertension and diabetes), and technical characteristics such as ischemia time and post-intervention TIMI flow ($p > 0.05$). This comparability of baseline characteristics ensured that there were no significant confounding factors, making the two groups suitable for further comparison to analyze differences in left ventricular ejection fraction improvement outcomes. The baseline characteristics of the study subjects are presented in Table 1.

TABLE 1: Subject Characteristics Based on Myocardial Blush Category.

Characteristics	High Myocardial Blush (QuBE ≥9 AU) (n=43)	Low Myocardial Blush (QuBE <9 AU) (n=49)	p-value
Age			
<60 years	28 (65.1%)	39 (79.5%)	0.119
≥60 years	15 (34.9%)	10 (20.5%)	
Gender			
Male	39 (90.6%)	45 (91.8%)	0.847
Female	4 (9.4%)	4 (8.2%)	
Hypertension			
Yes	18 (41.8%)	23 (46.9%)	0.625
No	25 (58.2%)	26 (53.1%)	
Type 2 DM			
Yes	9 (20.9%)	8 (16.3%)	0.570
No	34 (79.1%)	41 (83.7%)	
Smoking			
Yes	28 (65.1%)	36 (73.4%)	0.385
No	15 (34.9%)	13 (26.6%)	

Characteristics	High Myocardial Blush (QuBE ≥9 AU) (n=43)	Low Myocardial Blush (QuBE <9 AU) (n=49)	p-value
Medication Adherence			
Yes	43 (100%)	49 (100%)	-
Cardiac Rehabilitation			
Yes	4 (9.3%)	5 (10.2%)	0.885
No	39 (90.7%)	44 (89.8%)	
Ischemia Time (minutes)			
<300 minutes	7 (16.2%)	6 (12.2%)	0.579
≥300 minutes	36 (83.8%)	43 (87.8%)	
Coronary Involvement			
CAD 1VD	11 (25.5%)	18 (36.7%)	0.199
CAD 2 VD	20 (46.5%)	14 (28.5%)	
CAD 3 VD	12 (28%)	17 (34.8%)	
TIMI flow			
TIMI 3 *flow*	40 (93%)	45 (91.8%)	0.830
TIMI 2 *flow*	3 (7%)	4 (8.2%)	
Culprit Coronary Artery			
LAD	22 (51.1%)	28 (57.1%)	0.778
RCA	17 (39.5%)	18 (36.7%)	
LCx	4 (9.4%)	3 (6.2%)	

*Significant at $p < 0.05$. Abbreviations: DM: Diabetes Mellitus; CAD: Coronary Artery Disease; VD: Vessel Disease (Vascular Disease); TIMI: Thrombolysis In Myocardial Infarction; LAD: Left Anterior Descending Artery; RCA: Right Coronary Artery; LCx: Left Circumflex Artery; QuBE: Quantitative Blush Evaluator; AU: Arbitrary Units.

Analysis of the basic characteristics of subjects grouped based on epicardial coronary flow showed a homogeneous distribution between the TIMI 3 flow group (n=85) and the TIMI 2 flow group (n=7). Sociodemographic profiles, cardiovascular risk factors, and clinical variables, including age, gender, hypertension, diabetes mellitus, and smoking status, did not show statistically significant differences between the two groups (p > 0.05). In addition, angiographic parameters such as total ischemia time, coronary artery involvement, and culprit artery location were also found to be comparable. The consistency of these baseline data confirms that the two groups had relatively equivalent risk profiles prior to analysis of the clinical outcome of left ventricular ejection fraction improvement.

TABLE 2: Subject Characteristics Based on TIMI Flow Category.

Characteristics	TIMI 3 flow (n=85)	TIMI 2 flow (n=7)	p-value
Age			
<60 years	63 (74.1%)	4 (57.1%)	0.332
≥60 years	22 (25.9%)	3 (42.9%)	
Gender			
Male	78 (91.7%)	6 (85.7%)	0.585
Female	7 (8.3%)	1 (14.3%)	
Hypertension			
Yes	38 (44.7%)	3 (42.9%)	0.925
No	47 (55.3%)	4 (57.1%)	
Type 2 DM			
Yes	16 (18.8%)	1 (14.3%)	0.766
No	69 (81.2%)	6 (85.7%)	
Smoking			
Yes	58 (68%)	6 (85.7%)	0.334
No	27 (32%)	1 (14.3%)	
Medication Adherence			
Yes	85 (100%)	7 (100%)	-
Cardiac Rehabilitation			
Yes	8 (9.4%)	1 (14.3%)	0.667
No	77 (90.6%)	6 (85.7%)	

Characteristics	TIMI 3 flow (n=85)	TIMI 2 flow (n=7)	p-value
Ischemia Time (Minutes)			
<300 minutes	12 (14.1%)	1 (14.3%)	0.990
≥300 minutes	73 (85.9%)	6 (85.7%)	
Coronary Involvement			
CAD 1VD	27 (31.7%)	2 (28.6%)	0.789
CAD 2 VD	32 (37.6%)	2 (28.6%)	
CAD 3 VD	26 (30.7%)	3 (42.8%)	
Myocardial blush			
High Myocardial Blush (QuBE ≥9 AU)	40 (47%)	3 (42.9%)	0.830
Low Myocardial Blush (QuBE <9 AU)	45 (53%)	4 (57.1%)	
Culprit Coronary Artery			
LAD	44 (51.7%)	6 (85.7%)	0.215
RCA	34 (40%)	1 (14.3%)	
LCx	7 (8.3%)	0 (0%)	

*Significant at $p < 0.05$. Abbreviations: DM: diabetes mellitus; CAD: coronary artery disease; VD: vessel disease; TIMI: thrombolysis in myocardial infarction; LAD: left anterior descending artery; RCA: right coronary artery; LCx: left circumflex artery; QuBE: quantitative blush evaluator; AU: arbitrary units.

Analysis of the success of macrovascular reperfusion showed that the majority of subjects achieved TIMI 3 flow after PCI. However, the evaluation results showed that the incidence of LVEF improvement between the TIMI 3 flow and TIMI 2 flow groups was almost similar, at 70.6% and 71.4%, respectively. Statistical tests found no significant difference between the two groups in terms of clinical outcomes (RR = 0.98; 95% CI: 0.60–1.61; p = 0.963). These findings indicate that achieving epicardial coronary flow based on TIMI flow assessment alone is not sufficient to predict improvement in left ventricular ejection fraction in patients with STEMI after intervention.

TABLE 3: Comparison of LVEF Improvement Based on TIMI Flow.

Characteristics	Improved Ejection Fraction (Δ ≥5%) (n=65)	Constant Ejection Fraction (Δ <5%) (n=27)	RR	95% CI	p-value
TIMI flow					
TIMI 3 flow	60 (70.6%)	25 (29.4%)	0.98	0.60-1.61	0.963
TIMI 2 flow	5 (71.4%)	2 (28.6%)			

*Significant at $p < 0.05$. Abbreviations: LVEF: left ventricular ejection fraction; TIMI: thrombolysis in myocardial infarction; RR: relative risk; CI: confidence interval.

Analysis of microvascular perfusion quality showed significant differences in LVEF improvement between the two groups. Subjects in the high MB category (QuBE ≥ 9 AU) showed a much higher incidence of LVEF improvement, namely 88.4%, compared to the low MB group (QuBE < 9 AU), which was only 55.1%. Statistical testing confirmed a significant association with an RR value of 1.60 (95% CI: 1.21–2.11; p < 0.001), meaning that patients with good microvascular perfusion quality had a 1.6 times higher chance of experiencing recovery of cardiac systolic function. These findings confirm that high MB values are a strong clinical predictor of LVEF improvement in STEMI patients after PCI.

TABLE 4: Comparison of LVEF Improvement Based on Myocardial Blush.

Characteristics	Improved Ejection Fraction (Δ ≥5%) (n=65)	Constant Ejection Fraction (Δ <5%) (n=27)	RR	95% CI	p-value
Myocardial Blush					
High Myocardial Blush (QuBE ≥9 AU)	38 (88.4%)	5 (11.6%)	1.60	1.21-2.11	<0.001*
Low Myocardial Blush (QuBE <9 AU)	27 (55.1%)	22 (44.9%)			

*Significant at $p < 0.05$. Abbreviations: RR: relative risk; CI: confidence interval; QuBE: quantitative blush evaluator; AU: arbitrary units; LVEF: left ventricular ejection fraction.

The analysis was conducted to evaluate whether sociodemographic factors and clinical characteristics affected improvement in heart pump function (ΔLVEF ≥ 5%). The comparison results showed that variables such as age, gender, and cardiovascular risk factors, such as hypertension, type 2 diabetes mellitus, and smoking status, were not significantly associated with LVEF improvement ($p > 0.05$). In addition, clinical variables, including treatment adherence, cardiac rehabilitation participation, total ischemia time, degree of coronary artery involvement, and culprit artery location, also showed relatively similar distributions of LVEF improvement between groups. Statistically, no demographic or clinical variables were found to act as predictors of changes in left ventricular ejection fraction in this study, suggesting that these factors are not the main determinants of systolic function recovery after PCI compared to tissue perfusion quality.

TABLE 5: Comparison of LVEF Improvement Based on Sociodemographic and Clinical Characteristics.

Characteristics	Improved Ejection Fraction (Δ ≥5%) (n=65)	Constant Ejection Fraction (Δ <5%) (n=27)	RR	95% CI	p-value
Age					
<60 years	47 (70.1%)	20 (29.9%)	0.97	0.72-1.30	0.862
≥60 years	18 (72%)	7 (28%)			
Gender					
Male	60 (71.4%)	24 (28.6%)	1.14	0.65-1.98	0.569
Female	5 (62.5%)	3 (37.5%)			
Hypertension					
Yes	28 (68.3%)	13 (31.7%)	0.94	0.72-1.23	0.656
No	37 (72.5%)	14 (27.5%)			
Type 2 DM					
Yes	11 (64.7%)	6 (35.3%)	0.89	0.61-1.31	0.551
No	54 (72%)	21 (28%)			
Smoking					
Yes	45 (70.3%)	19 (29.7%)	0.98	0.74-1.30	0.914
No	20 (71.4%)	8 (28.6%)			
Medication Adherence					
Yes	65 (70.7%)	27 (29.3%)	-	-	-
Cardiac Rehabilitation					
Yes	6 (66.7%)	3 (33.3%)	1.06	0.65-1.72	0.782
No	59 (71.1%)	24 (28.9%)			
Ischemia Time (minutes)					
<300 minutes	10 (76.9%)	3 (23.1%)	1.10	0.79-1.53	0.592
≥300 minutes	55 (69.9%)	24 (30.4%)			
Coronary Involvement					
CAD 1VD	18 (62.1%)	11 (37.9%)	1.00	0.25-1.92	1.000
CAD 2 VD	29 (85.3%)	5 (14.7%)	1.37	0.76-2.47	0.289
CAD 3 VD	18 (62.1%)	11 (37.9%)	Reff		
Culprit Coronary Artery					
LAD	38 (76%)	12 (24%)	1.33	0.47-3.72	0.587
RCA	23 (65.7%)	12 (34.3%)	1.15	0.39-3.32	0.796
LCx	4 (57.1%)	3 (42.9%)	Reff		

*Significant at $p < 0.05$. Abbreviations: DM: diabetes mellitus; CAD: coronary artery disease; VD: vessel disease; TIMI: thrombolysis in myocardial infarction; LAD: left anterior descending artery; RCA: right coronary artery; LCx: left circumflex artery; QuBE: quantitative blush evaluator; AU: arbitrary units.

Cox proportional hazards regression analysis was performed to identify variables that act as independent predictors of left ventricular ejection fraction improvement (ΔLVEF ≥ 5%). This analysis model involved various potential variables, including demographic factors, cardiovascular risk, clinical characteristics, ischemia time, and angiographic parameters such as TIMI flow and Myocardial Blush (MB). Multivariate analysis results showed that only the high MB variable (QuBE ≥9 AU) was statistically significantly associated with LVEF improvement. Subjects with high MB were 1.57 times more likely to experience cardiac function recovery compared to subjects with low MB (Adjusted RR 1.57; 95%CI 1.04–2.63; p = 0.045). Conversely, other variables such as age, gender,

culprit artery location, ischemia time, and even TIMI 3 flow did not show a significant association after adjustment in the multivariate model ($p > 0.05$). These findings confirm that microcirculatory perfusion quality is the most dominant determinant of left ventricular function recovery after STEMI compared to other clinical or epicardial parameters.

TABLE 6: Cox Regression Analysis of Predictors for LVEF Improvement.

Variable	B	S.E	Adjusted RR	95% CI	P-value
Age <60 years	0.064	0.297	1.06	0.59-1.90	0.829
Gender (Male)	-0.067	0.559	0.93	0.28-3.02	0.911
Culprit Coronary Artery					
LAD	0.539	0.562	1.71	0.57-5.15	0.337
RCA	0.324	0.564	1.38	0.45-4.17	0.566
LCx	Reff				
Coronary Artery Involvement					
CAD 1 VD	-0.087	0.376	0.91	0.43-1.91	0.817
CAD 2 VD	0.277	0.313	1.31	0.71-2.43	0.377
CAD 3 VD	Reff				
TIMI 3 *flow*	0.041	0.500	1.04	0.39-2.77	0.935
Total Ischemic Time < 300 minutes	-0.12	0.361	0.98	0.48 – 2.00	0.974
Hypertension	0.012	0.269	1.01	0.59-1.71	0.963
Type 2 DM	-0.173	0.373	0.84	0.40-1.74	0.643
Smoking	0.057	0.333	1.05	0.55-2.03	0.865
High MB (QuBE ≥9 AU)	0.457	0.261	1.57	1.04-2.63	0.045*

*Significant at $p < 0.05$. Abbreviations: DM: diabetes mellitus; CAD: coronary artery disease; VD: vessel disease; TIMI: thrombolysis in myocardial infarction; LAD: left anterior descending artery; RCA: right coronary artery; LCx: left circumflex artery; QuBE: quantitative blush evaluator; AU: arbitrary units; RR: relative risk.

DISCUSSION

The main findings of this study emphasize that recovery of left ventricular systolic function after PCI is determined more by microcirculatory integrity than by epicardial coronary artery patency alone. Although PCI successfully opened macrovascular occlusions (as indicated by TIMI 3 flow), this success does not always guarantee LVEF recovery. This reinforces the theory of the no-reflow phenomenon, in which, even though the main pathway has been opened, damage at the capillary level due to inflammation and intracellular edema prevents adequate oxygenation of myocardial tissue.

In this study, Myocardial Blush (MB) was found to be a strong independent predictor, with QuBE values < 9 AU significantly associated with persistent (non-improving) LVEF. MB reflects the quality of perfusion at the tissue level, which is an absolute requirement for myocardial salvage. Conversely, the absence of a meaningful relationship between TIMI flow and LVEF improvement in these two-month observations suggests that macrovascular assessment alone has limitations in predicting long-term myocardial viability. These results support a paradigm shift that the evaluation of reperfusion success in STEMI patients should include a more in-depth microvascular assessment to provide a more accurate prognostic picture.

This study involved a total of 92 STEMI patients undergoing PCI with baseline characteristics distributed homogeneously between the high and low Myocardial Blush (MB) groups. There were no significant differences in age, gender, cardiovascular risk factors (hypertension, diabetes mellitus, and smoking status), ischemia time, and initial angiographic profiles, indicating that the two groups were relatively comparable clinically and angiographically. This condition ensures that the differences in cardiac pump function improvement found are most likely related to myocardial perfusion quality, not confounding factors. However, it should be noted that there was a clear dominance of the TIMI 3 flow group, which limited the ability of this parameter to describe clinical outcomes in a varied manner.

An important finding in this study shows that TIMI flow is not significantly associated with improvement in LVEF, either in bivariate or multivariate analysis. Although the majority of patients achieved TIMI 3 flow after PCI, not all patients showed recovery of left ventricular function. This reflects the limitations of TIMI flow as a parameter of microvascular reperfusion, where optimal epicardial patency does not always guarantee adequate myocardial reperfusion [18].

Pathophysiologically, the opening of the main coronary artery is not always followed by effective cellular perfusion. Phenomena such as no-reflow, distal embolization, myocardial edema, endothelial dysfunction, and microvascular obstruction (MVO) can still occur even though epicardial flow appears optimal, resulting in suboptimal myocardial function recovery.

This explains why TIMI flow does not fully reflect the success of myocardial salvage. Previous studies by van't Hof (2010) and Annibali et al. (2022) also showed a discrepancy between epicardial artery patency and actual myocardial tissue perfusion.[18, 19] Therefore, indicators that assess microvascular perfusion, such as myocardial blush, are theoretically more relevant in predicting left ventricular function improvement after PCI.

The results of this study confirm that myocardial microcirculatory perfusion quality is the main determinant of left ventricular function recovery after STEMI. Bivariately, patients with high MB (QuBE ≥9 AU) were 1.60 times more likely to experience LVEF improvement ($p<0.001$). This significance is reinforced by Cox regression analysis, where after controlling for various confounding variables such as age, gender, risk factors, and even TIMI flow, high MB remains the only independent predictor of LVEF improvement (adjusted RR 1.57; $p=0.045$). These findings are consistent with the study by Nabrdalik et al. (2023), which found an association between low MB values and poorer LVEF function [20]. Additionally, Gu et al. (2011) support the use of QuBE measurements post-catheterization to assess left ventricular functional recovery more quickly and accurately than enzymatic parameters [21].

The significant role of microvasculature in reperfusion success is often hampered by the no-reflow phenomenon, which has been reported to occur in approximately 25% of patients after PCI despite angiographic success [22]. This study demonstrates that QuBE biologically reflects the actual degree of myocardial perfusion and is time-dependent. Porto et al. (2011) demonstrated a linear relationship between QuBE values, necrosis markers, and total ischemic time; the longer the ischemia time, the more severe the degree of Microvascular Obstruction (MVO) reflected in low QuBE values. This distinguishes QuBE from TIMI flow, which only assesses epicardial patency without considering myocardial microcirculation conditions [23].

Assessment with QuBE also has clinical value in evaluating the effectiveness of adjuvant therapy. An increase in QuBE values after administration of vasoactive drugs or GPIIb/IIIa inhibitors may indicate better clinical outcomes [24]. No-reflow management itself includes pharmacological approaches such as the administration of calcium channel blockers, adenosine, and statins, which have pleiotropic effects. Conversely, non-pharmacological approaches such as thrombus aspiration are now class III recommendations according to ESC guidelines because they have not been shown to reduce 30-day mortality [18]. Overall, these findings reinforce the concept that the success of reperfusion in STEMI should be defined based on the success of myocardial tissue perfusion, not merely the patency of the epicardial coronary artery.

The results of this study indicate that sociodemographic variables and clinical characteristics such as age, gender, hypertension, diabetes mellitus, smoking status, Total Ischemic Time, vessel involvement, and culprit artery location have no significant relationship with LVEF improvement. These findings indicate that in the early post-infarction phase, myocardial reperfusion quality (microcirculation) is a more dominant factor in determining left ventricular function recovery than chronic risk factors or patient clinical profiles.

The study subjects were predominantly male, reflecting the global epidemiology of AMI-EST. In line with the report by Čulić et al. (2002), men not only have a higher incidence but also tend to show more typical clinical presentations, making them easier to identify for reperfusion therapy. On the other hand, the most common risk factors were smoking, followed by hypertension and diabetes mellitus. Čulić et al. (2002) also noted that diabetes and advanced age are often associated with atypical symptoms, which risk causing delays in treatment and prolonging the duration of myocardial ischemia [25].

These findings are supported by a study by Wu et al. (2020), which also found no significant differences in age, gender, or traditional risk factors for LVEF improvement after covariate adjustment. Wu et al. (2020) emphasized that recovery of ejection fraction is a very strong prognostic determinant of long-term mortality, regardless of age or comorbidities. Patients without LVEF improvement have a significantly higher risk of cardiovascular death, confirming that failure to recover systolic function reflects severe and irreversible myocardial damage rather than merely the influence of chronic risk factors [13].

The results of Cox regression analysis show that the majority of clinical and angiographic variables, including age, gender, hypertension, diabetes mellitus, smoking status, and TIMI flow, have no significant relationship with LVEF improvement. These findings indicate that traditional risk factors, although they play a role in coronary pathogenesis, do not directly determine systolic function recovery in the early post-reperfusion phase. This confirms that clinical success should be defined as a combination of TIMI 3 flow and adequate myocardial perfusion [19].

This study is consistent with previous studies showing that tissue perfusion-based parameters, such as MB grade or QuBE, have a stronger correlation with myocardial viability and LVEF improvement than epicardial assessment alone. Ndrepepa et al. confirmed that patients with poor myocardial perfusion had smaller myocardial salvage and larger infarct size, even though optimal epicardial reperfusion had been achieved. In line with this, Porto et al. (2011) suggested the use of QuBE during PCI to quantitatively assess risk, where low QuBE values could serve as a basis for further imaging studies such as CMR [23].

Vogelzang et al. (2009) emphasized that mortality rates remain high if the myocardium does not receive adequate blood flow despite achieving TIMI 3 flow, which ultimately leads to heart failure [26]. This finding is reinforced by Tomasik et al. (2019), who reported that myocardial perfusion impairment (low QuBE) is an independent predictor of long-term heart failure and poor left ventricular remodelling [24]. Overall, microcirculation evaluation via MB provides crucial additional information for risk stratification and clinical follow-up planning in STEMI patients, as it accurately reflects the actual degree of myocardial reperfusion compared to conventional visual assessment [19, 24].

This study has several limitations, including a single-center design in a tertiary referral hospital with a limited sample size, which may affect the generalization of results to a wider population. In addition, there was an imbalance in the distribution of subjects between the TIMI 3 flow and TIMI 2 flow groups, which could potentially limit the statistical power to detect differences in outcomes between these groups. The LVEF evaluation, which was only performed once in the second month after PCI, was also unable to describe the dynamics of long-term changes in heart function. Finally, although multivariate analysis was performed, this study did not evaluate all other potential biological factors, and there was still operator variability in the semi-quantitative angiographic assessment. Based on these considerations, future multicenter studies with longer and continuous follow-up periods are needed to provide a more comprehensive clinical picture.

CONCLUSION

This study concluded that high myocardial microcirculatory perfusion quality assessed by Myocardial Blush (MB) (QuBE ≥9) is a significant independent predictor of LVEF improvement in STEMI patients after PCI, while TIMI flow was not found to have similar predictive value. These findings confirm the superiority of MB over epicardial flow alone in predicting left ventricular function recovery and performing clinical risk stratification. Therefore, it is recommended that clinicians integrate QuBE assessment as a routine post-PCI evaluation to identify high-risk patients early and optimize preventive therapy for cardiac remodeling. Additionally, future multicenter studies with longer longitudinal follow-up periods are needed, supported by intensive patient family education regarding treatment adherence and lifestyle modifications to ensure successful long-term recovery.

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