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Original Article

The Predictors of Spontaneous Coronary Reperfusion in Patients with ST-Segment Elevation Myocardial Infarction at the West Nusa Tenggara General Hospital

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ABSTRACT

Background: In ST-segment elevation myocardial infarction (STEMI) management, some patients undergo spontaneous coronary reperfusion (SCR) with a better prognosis than those without SCR, but predictors for SCR remain unclear.
Objective: To investigate several potential predictors of SCR, including smoking status, BMI, DAPT loading time, hemoglobin levels, platelet count, random blood sugar levels, uric acid levels, creatinine clearance, and the Syntax score.
Material and Methods: This case-control study was conducted at the West Nusa Tenggara General Hospital in Indonesia from December 2022 to September 2023. Data collection encompassed various patient demographics and clinical parameters, including name, medical record number, age, gender, smoking status, BMI, DAPT loading time, hemoglobin levels, platelet count, random blood sugar, uric acid, creatinine clearance, the Syntax score, and the occurrence of SCR. Statistical analysis for this study involved multivariate logistic regression analysis.
Result: A total of thirty-two patients were included, evenly divided into 16 subjects allocated to the SCR group and 16 to the non-SCR group. The analysis indicated that only BMI demonstrated a statistically significant association with SCR occurrence. However, the study did not yield conclusive evidence regarding the influence of smoking status, DAPT loading time, hemoglobin levels, platelet count, random blood sugar levels, uric acid levels, creatinine clearance, and the Syntax score on the likelihood of SCR.
Conclusion: A normal BMI is identified as a robust predictor for the incidence of SCR in patients diagnosed with STEMI.

1. Introduction

Acute myocardial infarction continues to represent a prominent contributor to worldwide morbidity and mortality rates. The cornerstone of treatment for ST-segment elevation myocardial infarction (STEMI) involves reperfusion therapy, aimed at promptly reopening coronary artery occlusions to mitigate further myocardial damage.[1] Intravenous fibrinolysis and percutaneous coronary intervention (PCI) have significantly advanced patient outcomes in this regard.[2] However, despite concerted efforts to improve patient care, disparities persist between guideline recommendations and clinical practice.[3] A notable phenomenon observed in STEMI management is the occurrence of spontaneous coronary reperfusion (SCR), wherein some patients exhibit resolution of ST-segment elevation[4] and absence of total coronary occlusion upon coronary angiography (CAG).[1] SCR, characterized by Thrombolysis in Myocardial Infarction (TIMI) flow grade 3, is observed in approximately 30% of STEMI patients undergoing primary PCI.[4] This subset of patients, referred to as the SCR group, demonstrates a smaller infarct area and a more favorable prognosis compared to the non-SCR group.[4] Furthermore, the SCR group exhibits lower short-term mortality rates and reduced risk of heart failure.[1] However, the precise clinical factors influencing SCR incidence in STEMI patients remain unclear, necessitating further study to identify predictors of SCR occurrence.

Various studies have identified several potential clinical conditions associated with the incidence of SCR.[1,5] However, there was a critical need for practical, simple, and easily applicable predictors in diverse clinical settings, particularly in rural areas. Among these predictors were clinical factors such as smoking status, body mass index (BMI), and dual antiplatelet therapy (DAPT) loading time, along with laboratory parameters including hemoglobin levels, platelet count, random blood sugar levels, uric acid levels, and creatinine clearance. Additionally, predictors from angiography, like the Syntax score, were considered. While some publications consistently associated smoking, platelet count, uric acid levels, and blood sugar levels with SCR, results varied.[1,5] There were even reports suggesting that diabetic patients with STEMI had a lower likelihood of developing SCR and a worse prognosis.[6] Conversely, evidence supporting the influence of BMI, hemoglobin levels, and creatinine clearance on SCR incidence was lacking, despite frequent examination in similar studies. The prompt administration of DAPT was crucial, as recommended by STEMI guidelines, significantly reducing mortality and improving prognosis.[7] The impact of the Syntax score on SCR remained uncertain due to the lack of supporting data. Nevertheless, some angiography studies suggested a close relationship between lesions in distal coronary arteries and SCR events, warranting further investigation into coronary anatomical severity using the Syntax score.[1] Therefore, this study aimed to identify whether smoking status, BMI, DAPT loading time, hemoglobin levels, platelet count, random

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blood sugar levels, uric acid levels, creatinine clearance, and the Syntax score had implications for SCR occurrence in STEMI patients.

2. Material and Methods

Study Design

This study utilized a case-control design conducted at the West Nusa Tenggara General Hospital in Indonesia, spanning from December 2022 to September 2023. The subjects of our study were consecutively categorized into SCR and non-SCR groups, each with equal sample sizes. The SCR group consisted of patients with TIMI flow grade 3 who had not received prior reperfusion therapy, such as intravenous fibrinolysis or PCI. In contrast, the non-SCR group included patients with TIMI flow grade 0-2. To achieve our objective, data extraction from patient medical records was performed to identify potential contributing factors to SCR incidents. Adherence to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist for case-control studies[8] and the principles outlined in the Helsinki Declaration[9] was maintained throughout this investigation. The study protocol underwent review and approval by the local ethical committee (No: 070/18/0292/RSUDP/2022).

Participants & Eligibility Criteria

The sample size for this study was determined considering the reported prevalence of SCR in patients with STEMI, which is generally estimated to range between 15% and 30%.[4] Based on an estimated effect size of 1, an α error of 0.05, and a desired statistical power of 95%, the minimum sample size required was computed to be 16 patients allocated to both the SCR group and the non-SCR group. Sample size calculations were carried out using G*power software version 3.1 (Universität Düsseldorf, Düsseldorf, Germany, RRID:SCR_013726). Inclusion criteria comprised STEMI patients who underwent primary PCI and provided informed consent for participation, as well as those with STEMI onset occurring within < 12 hours. Exclusion criteria encompassed patients who had received routine antiplatelet-anticoagulant therapy and intravenous fibrinolysis therapy prior to hospital admission, individuals with a history of prior STEMI, patients diagnosed with atrial fibrillation, and those presenting with any bundle branch block. Prior to primary PCI, each patient received the same DAPT-anticoagulant regimen consisting of 320 mg aspirin, 600 mg clopidogrel, and 100 IU/kg intravenous heparin.

Data Collection

Data collection was performed from medical records using a pilot form designed to meet standardized criteria. Information collected for each patient included: name, medical record number, age, gender, smoking status, BMI, DAPT loading time, hemoglobin levels, platelet count, random blood sugar, uric acid, creatinine clearance, the Syntax score, and the occurrence of SCR. A thorough evaluation of angiographic features was also performed, including right/left coronary dominance, number of lesions, segments impacted per lesion, total occlusion, trifurcation/bifurcation lesions, aorto-osteal lesions, severe tortuosity, length of lesions exceeding 20 mm, severe calcification, thrombus, and diffuse disease. The results of these features are represented by the Syntax score.

Study Covariates

The outcome covariate in this study was SCR among patients diagnosed with STEMI. The SCR group consisted of individuals with TIMI flow grade 3 who had not undergone prior reperfusion therapy, such as intravenous fibrinolysis or PCI. Conversely, the non-SCR group was defined as patients with TIMI flow grade 0-2. The predictor covariates investigated in this study included smoking status, BMI, DAPT loading time, hemoglobin levels, platelet count, random blood sugar levels, uric acid levels, creatinine clearance, and the Syntax score.

Statistical Analysis

Numerical data following a normal distribution were reported as mean ± SD, whereas those deviating from normality were represented as median (IQR). Categorical data were exhibited as frequencies expressed as a percentage of the total. Comparative analysis of numerical data involved the utilization of either an unpaired T-test or Mann-Whitney test, the choice depending on the distributional characteristics of the dataset. Similarly, categorical data underwent analysis using either a Chi-square test or Fisher's exact test, with the selection contingent upon the nature of the data. Statistical significance was established at a significance level of $p<0.05$. Variables exhibiting p-values <0.25 in univariate analysis were incorporated into a multivariate logistic regression analysis. The data were analyzed using the Statistical Package for the Social Sciences (SPSS) software version 29.0 (IBM Corp., USA).

3. Results

Baseline Characteristics of Patients

A total of thirty-two patients were enrolled, with 16 assigned to the SCR group and 16 to the non-SCR group. The mean age of the subjects was 55.6 ± 12.5 years, with males representing the majority at 84.4%. Among the participants, 75.0% were identified as smokers. The majority of STEMI patients were referred from other hospitals (87.5%), while 12.5% were admitted directly to the PCI center. Most STEMI patients did not exhibit arrhythmias (53.1%), with AV block (25.5%), PVC (12.5%), VT (6.3%), and SA block (3.1%) being less common. Lesions were most frequently observed in the LAD artery (50%), followed by the RCA (46.9%) and LCx artery (3.1%). Detailed baseline characteristics of the patients are outlined in Table 1.

Table 1. Clinical characteristics of the subjects

Subject characteristics	n (%), mean ± sd, N=32
Age (years)	55.7 ± 12.5
Sex	
Male	27 (84.4)
Female	5 (15.6)
Smoking	
Smoker	24 (75.0)
Non-smoker	8 (25.0)
Admission	
From another hospital	28 (87.5)
Straight to PCI center	4 (12.5)
Culprit's vessel	
LAD	16 (50.0)
LCx	1 (3.1)
RCA	15 (46.9)

Note, AV block, atrioventricular block; LAD, left anterior descending artery; LCx, left circumflex artery, PCI, percutaneous coronary intervention; PVC, premature ventricular contraction; RCA, right coronary artery; SA Block, sinoatrial block; VT, ventricular tachycardia.

Table 2. The impact of various factors on the occurrence of spontaneous coronary reperfusion in patients diagnosed with STEMI.

Parameters	n(%), mean±sd, median(IQR)			Adjusted	
	SCR (n=16)	Non-SCR (n=16)	p	OR (95% CI)	p
Smoking					
Smoker	11 (45.8)	13 (54.2)	0.685"		
Non-smoker	5 (62.5)	3 (37.6)			
BMI	23.5 ± 2.3	26.7 ± 2.8	0.001'	0.558 (0.344-0.904)	0.018#
DAPT loading time (hour)	6.1 ± 3.3	5.1 ± 3.4	0.406'		
Hb (g/dL)	13.8 (12.3-15.2)	14.5 (13.6-15.3)	0.497*		
Platelet (u/L)	236,362 ± 62,854	246,194 ± 66,106	0.669'		
RBS (mg/dL)	131 (32-229)	172 (105-240)	0.318*		
UA (mg/dL)	6.6 ± 1.8	7.1 ± 1.9	0.483'		
Clearance creatinin (mL/mnt)	70.1 ± 28.2	81.9 ± 24.8	0.221'	0.997 (0.964-1.031)	0.841#
Syntax score	17.8 ± 10.2	21.1 ± 10.0	0.356'		

Note, BMI, body mass index; DAPT, dual antiplatelet therapy; Hb, hemoglobin; IQR, interquartile range; RBS, random blood sugar; SCR, spontaneous coronary reperfusion; UA, uric acid.
'Unpaired T-test, *Mann-Whitney test, "Fisher test, #Binary logistic test

Factors related to the occurrence of SCR in STEMI patients

In bivariate analysis, our findings indicated that BMI was the sole predictor associated with the development of SCR, with a statistically significant difference observed between the two groups (23.5 ± 2.3 vs. 26.7 ± 2.8, p<0.001). Subsequently, in multivariate analysis, among all the predictors evaluated, only two variables, BMI and creatinine clearance, were included. The results of multivariate analysis demonstrated that only BMI exhibited a significant association with SCR (adjusted OR: 0.558, 95% CI: 0.344-0.904, p=0.018). Detailed results of our study are presented in Table 2.

4. Discussion

In this study, only BMI significantly affected SCR, with the SCR group exhibiting a normal BMI and the non-SCR group having an overweight BMI. This observation is logically consistent, considering that overweight and obesity are well-documented risk factors for coronary heart disease. A study by Wen et al. demonstrated an elevated risk of cardiovascular mortality among overweight and obese individuals compared to those with normal weight.[10] While no previous publications have highlighted the significant effect of BMI on SCR, this discovery presents a novel insight. The concepts of coronary flow and metabolic syndrome offer a starting point for understanding how BMI influences SCR. Obese individuals and those with metabolic syndrome often exhibit impaired neurovascular control over blood flow during both exercise and rest. Increased sympathetically-mediated vasoconstriction, coupled with elevated inflammation and/or oxidative stress levels, profoundly impacts blood flow regulation in these populations.[11] Moreover, anomalies in the coronary microvasculature, a critical regulator of coronary blood flow, are associated with obesity. Coronary microvascular disease, linked to higher BMI, is pathophysiologically associated with endothelial dysfunction and potentially small vessel remodeling.[12] Reduced coronary microvascular density, also correlated with obesity and its associated elevation in left ventricular filling pressure, may explain the diminished maximal myocardial blood flow and compromised myocardial metabolism observed in obese individuals.[13]

We were unable to elucidate the influence of DAPT loading time on SCR (6.1 ± 3.3 vs. 5.1 ± 3.4, p=0.406). To date, no literature has explored the association between DAPT loading time and SCR. The closest study is a meta-analysis by Luca et al., which investigated the effects of early versus delayed intravenous administration of antiplatelet glycoprotein IIb–IIIa inhibitors. This meta-analysis, involving 1,662 subjects from 11 studies, concluded that early administration of antiplatelets is associated with an increased incidence of SCR and improved ST-segment resolution on ECG. However, no significant difference was observed in mortality rates.[14] The discrepancy in findings between our study and the meta-analysis may be attributed to the type of antiplatelet agent administered, with intravenous agents potentially exhibiting superior efficacy and platelet inhibition potential.

This study observed no significant impact of platelet count, random blood sugar, and uric acid levels on the risk of SCR. These findings contrast with previous studies. Li et al. demonstrated that various variables, including lower platelet levels, lower RBS levels, and lower UA levels, significantly influenced SCR.[1] Platelets play a crucial role in coronary flow dynamics. Sharif et al. noted that patients with lower platelet counts upon admission had a higher likelihood of achieving TIMI flow grade 3 before primary PCI.[15] Earlier studies have also suggested an increased risk of adverse outcomes, particularly re-infarction and mortality, in STEMI patients with elevated platelet counts upon admission.[16-18] Theoretically, elevated UA levels may hinder thrombus autolysis by inhibiting natural anticoagulants and promoting mural thrombosis through platelet or inflammatory pathways.[19,20] Hyperglycemia could heighten platelet activation, impair endothelium-dependent vasodilation, and trigger augmented inflammatory responses, potentially impacting blood coagulation, platelet function, and fibrinolysis, leading to the formation of recalcitrant thrombi.[21]

This study also revealed no significant impact of hemoglobin, creatinine clearance, and the Syntax score as predictors of SCR. These findings presented a complex scenario to interpret, but several factors might offer insights into our results. The relationship between Hb and SCR is intricate due to Hb's reverse J-shaped association with major adverse cardiovascular events. Sabatine et al. observed that among patients with non-ST-elevation acute coronary syndrome, the risk of cardiovascular death, myocardial infarction, or recurrent ischemia escalated as hemoglobin levels declined below 11 g/dL for every one g/dL decrease in hemoglobin concentration. Furthermore, patients with hemoglobin levels exceeding 16 g/dL demonstrated an elevated incidence of death or ischemic events.[22] While creatinine clearance serves as a significant independent predictor of severe bleeding and hospital death in acute coronary syndrome patients, its relationship with SCR remains uncertain due to limited supporting data.[23] The Syntax score, employed as an angiographic measure to evaluate the complexity of coronary artery lesions, has been correlated with an increased likelihood of major adverse cardiovascular events.[24] However, it cannot be utilized as a determinant of SCR since SCR is a localized event within the culprit vessel, whereas the Syntax score describes the overall severity of the lesion.

The study presented several potential limitations. First, our study encountered a small sample size issue, with only 16 subjects included in the SCR group despite data collection spanning nearly a year. This challenge arose partly due to the rural location of the hospital, as well as the exclusion of numerous potential subjects because primary PCI procedures exceeded the optimal 12-hour window. Consequently, many STEMI patients were ineligible for the study due to the prohibitive costs of primary PCI and insufficient insurance coverage. Second, the subjects of our study were derived from a homogeneous population within a single center, which limits the generalizability of the findings to a broader population. Third, the presence of numerous uncontrolled confounding variables, such as comorbidities or pre-admission medications, may have introduced bias into the study outcomes.

5. Conclusion

In summary, BMI stands out as the singular predictor significantly impacting SCR in patients with STEMI. Given its modifiable nature as a cardiovascular risk factor, optimizing BMI management holds potential for improving SCR outcomes. However, additional study employing larger sample sizes and encompassing more heterogeneous populations across multiple centers is imperative to validate these findings.

6. Declaration

6.1 Ethics Approval and Consent to participate
The study protocol underwent review and approval by the local ethical committee (No: 070/18/0292/RSUDP/2022).

6.2. Consent for publication
Not applicable.

6.3 Availibility of data and materials
Data used in our study were presented in the main text.

6.4 Competing interests
Not applicable.

6.5 Funding Source
Not applicable.

6.6 Authors contributions
Idea/concept: RE. Design: RE. Control/supervision: RE, YP, DPS, YI, KA. Data collection/processing: RE, YP, DPS, YI, KA. Analysis/interpretation: RE. Literature review: RE, YP, DPS, YI, KA. Writing the article: RE. Critical review: RE, YP, DPS, YI, KA. All authors have critically reviewed and approved the final draft and are possible for the content and similarity index of the manuscript.

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