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ORIGINAL ARTICLE

Admission Systemic Immune-Inflammation Index and Its Association with High Thrombus Burden and No-Reflow in ST-Segment Elevation Myocardial Infarction: A Retrospective Cohort Study

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ABSTRACT

Background: ST-segment elevation myocardial infarction (STEMI) is a thrombo-inflammatory emergency, and successful epicardial recanalisation during primary percutaneous coronary intervention (PCI) does not always restore myocardial perfusion. The Systemic Immune-Inflammation Index (SII), derived from routine platelet, neutrophil and lymphocyte counts, may reflect thrombo-inflammatory risk.

Objective: This study evaluated the association of admission SII with high thrombus burden and no-reflow in STEMI patients undergoing primary PCI.

Methods: This STROBE-compliant retrospective cohort study consecutively sampled 118 STEMI patients at Prof. dr. I.G.N.G. Ngoerah General Hospital, Denpasar. High thrombus burden was defined as TIMI thrombus grade 4-5 and no-reflow as post-procedural TIMI flow grade =2. The optimal SII cut-off was derived by receiver operating characteristic analysis (Youden index); associations were assessed with chi-square/Fisher tests and modified Poisson regression with robust standard errors.

Results: High thrombus burden occurred in 99 patients (83.9%) and no-reflow in 16 (13.6%). High SII was associated with high thrombus burden (90.8% vs 75.5%; relative risk 1.203, 95% CI 1.013-1.428; p=0.025) and no-reflow (20.0% vs 5.7%; relative risk 3.53, 95% CI 1.062-11.753; p=0.024), persisting after adjustment (adjusted relative risk 1.194 and 3.226, respectively). Discrimination was weak-to-modest (AUC 0.597 and 0.674).

Conclusion: Admission SII was independently associated with high thrombus burden and no-reflow but had insufficient accuracy for standalone prediction, supporting its role as a simple adjunctive marker rather than a definitive predictor.

1. Introduction

Ischaemic heart disease remains the leading cause of death worldwide, and Indonesia has experienced a persistent rise in cardiovascular disease incidence and mortality across three decades of Global Burden of Disease modelling.[1] ST-segment elevation myocardial infarction (STEMI) represents the most time-critical manifestation of coronary atherothrombosis and is most often caused by acute thrombotic occlusion of an epicardial coronary artery.[2,3] Primary percutaneous coronary intervention (PCI) is the preferred reperfusion strategy when it can be delivered promptly, but the restoration of epicardial patency does not guarantee restoration of myocardial tissue perfusion, because microvascular obstruction may persist despite an open culprit artery.[2,4] This disconnect between epicardial and microvascular reperfusion is central to the residual morbidity and mortality that follow otherwise technically successful primary PCI.

Two angiographic phenomena capture this residual risk. High thrombus burden, usually defined as Thrombolysis in Myocardial Infarction (TIMI) thrombus grade 4 or 5, reflects a large intracoronary thrombotic mass and is associated with distal embolisation, slow-flow or no-reflow, procedural complications, larger infarct size and worse clinical outcomes.[5] The no-reflow phenomenon denotes inadequate myocardial perfusion despite opening of the epicardial artery and the absence of significant residual mechanical obstruction; its mechanisms include distal embolisation, microvascular oedema, endothelial dysfunction after reperfusion injury, oxidative stress and microvascular spasm, and clinically it is linked to heart failure, ventricular arrhythmia, larger infarcts and increased mortality.[2,6] Although related, high thrombus burden and no-reflow are not identical: the former is an epicardial, angiographically visible entity, whereas the latter is a downstream, tissue-level failure that may occur through mechanisms beyond visible thrombus.[2,4]

Systemic inflammation is a fundamental driver of atherothrombosis. Neutrophil activation, platelet adhesion and aggregation, endothelial dysfunction and lymphocyte dysregulation converge to amplify thrombotic activity and microvascular injury during acute myocardial infarction.[2,7,8] The Systemic Immune-Inflammation Index (SII), calculated as platelet count × neutrophil count / lymphocyte count, integrates these three haematological limbs into a single composite measure of thrombo-inflammatory status using parameters available from a routine complete blood count.[9-11] Elevated SII has been associated with high thrombus burden, the no-reflow phenomenon and adverse cardiovascular outcomes after PCI in a range of populations, and a meta-analysis of cohort studies reported an independent association between high SII and major adverse cardiovascular events after PCI.[5,7,12,13]

In the Indonesian setting, delays in presentation, inter-hospital transfer, referral coordination and access to catheterisation facilities remain practical barriers to timely reperfusion.[1] Prof. dr. I.G.N.G. Ngoerah General Hospital in Denpasar is a tertiary referral centre that performs primary PCI for a large catchment population in Bali, where prolonged ischaemic times and heterogeneous case-mix make angiographic complications clinically relevant. Local biomarker evidence remains limited: prior studies have reported good diagnostic performance of the SII for high intracoronary thrombus burden, but many did not simultaneously evaluate no-reflow as a reperfusion outcome.[5,13] Because complete blood count testing is inexpensive, universally available and rapidly obtained in acute care, an admission SII could offer a practical adjunctive tool for angiographic risk stratification if its performance were properly characterised in local practice.

This study therefore evaluated the association between the admission SII and two angiographic outcomes—high intracoronary thrombus burden and the no-reflow phenomenon—in patients with STEMI undergoing primary PCI at a tertiary Indonesian centre. The novelty of the work lies in the simultaneous evaluation of both an epicardial and a microvascular endpoint within a single, well-characterised Indonesian cohort, coupled with a deliberate distinction between statistical association and diagnostic discrimination so that the index is neither over-sold nor dismissed. We hypothesised that a higher admission SII would be independently associated with both outcomes, but with discrimination modest enough to position the index as an adjunctive rather than a standalone marker.

Beyond its mechanistic appeal, the SII is attractive from a health-systems perspective in resource-constrained settings. It is calculated from an investigation—the complete blood count—that is already performed in virtually every patient presenting with suspected acute coronary syndrome, so its incremental cost is effectively zero and it introduces no additional phlebotomy, turnaround delay or specialised assay. In a health system where advanced inflammatory biomarkers such as high-sensitivity C-reactive protein, interleukin-6 or myeloperoxidase are not uniformly available at the point of care, a composite index that repurposes routine haematology has obvious pragmatic value—provided that its true discriminatory limits are transparently characterised rather than overstated.[7,10,14] The present analysis was designed with that dual objective: to quantify the association of the admission SII with angiographic complications and, equally, to define the boundaries of its predictive usefulness.

2. Methods

Study design and setting

This analytical observational study used a retrospective cohort design and is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline for cohort studies. Data were obtained from medical records, the laboratory information system, angiography records and catheterisation-laboratory reports of patients with STEMI who underwent primary PCI at Prof. dr. I.G.N.G. Ngoerah General Hospital, Denpasar, Bali, Indonesia—a tertiary referral and cardiac catheterisation centre. Eligible cases were identified from January to December 2025, and data collection and analysis were conducted from April to July 2026.

Participants

Patients were included if they were aged 18 years or older, had a confirmed diagnosis of STEMI according to prevailing universal-definition and ESC criteria, and underwent primary PCI with a complete admission or pre-procedural complete blood count and interpretable angiographic documentation.[2-4] Patients were excluded if clinical, laboratory or angiographic data were incomplete, unavailable or unverifiable, or if they had active infection, chronic inflammatory disease, haematological disease or active malignancy that could independently alter neutrophil, lymphocyte or platelet counts and thereby confound the SII. Eligible patients were enrolled by retrospective consecutive sampling of all cases meeting the criteria within the enrolment window, a strategy chosen to minimise selection bias.

Sample size

The minimum required sample size was estimated using the single-proportion cohort formula $n = Z^2\alpha/2 \times P(1 - P) / d^2$, where $Z\ \alpha/2 = 1.96$ for a two-sided α of 0.05, P is the anticipated proportion of the outcome among exposed patients, and d is the desired absolute precision. Adopting $P = 0.20$ (the anticipated proportion of no-reflow in the high-SII stratum, informed by prior primary-PCI series) and $d = 0.072$ yielded a minimum of approximately 119 patients, consistent with the 118 patients enrolled.[4,12] Post-hoc

power analysis using the observed proportions (no-reflow 20.0% versus 5.7%; high thrombus burden 90.8% versus 75.5%; $\alpha = 0.05$) indicated approximately 61–63% power for both contrasts, a limitation acknowledged particularly for the low-frequency no-reflow endpoint.

Variables and outcome measures

The independent variable was the admission SII, calculated from the admission or pre-procedural complete blood count as SII = (platelet count × neutrophil count) / lymphocyte count, with counts expressed in $\times 10^3/\mu L$. The index was analysed both as a continuous variable and dichotomised into high and low categories; the optimal cut-off separating the categories was determined by receiver operating characteristic (ROC) analysis using the Youden index for high thrombus burden. The dependent variables were high thrombus burden and no-reflow. Thrombus burden was assessed on coronary angiography using the TIMI thrombus grade: grades 0–3 were classified as low thrombus burden and grades 4–5 as high thrombus burden.[4] No-reflow was defined as a post-procedural TIMI flow grade of 2 or less in the absence of significant mechanical epicardial obstruction, whereas grade 3 was classified as normal flow.[4] Pre-specified confounding variables were age, sex, smoking status, hypertension, type 2 diabetes mellitus, symptom-onset-to-intervention time and infarct location.

Data collection

Data were extracted from medical records, laboratory records, angiography documentation and catheterisation-laboratory reports using a structured extraction form. Clinical variables included age, sex, cardiovascular risk factors, symptom-onset-to-intervention time and infarct location. Laboratory variables included neutrophil, platelet and lymphocyte counts. Angiographic variables included TIMI thrombus grade and post-procedural TIMI flow grade. No direct patient examination or additional laboratory testing was performed. To limit misclassification, records with ambiguous or unverifiable angiographic data were excluded rather than imputed; nonetheless, angiographic grades reflected routine clinical documentation rather than independent blinded adjudication, and this is addressed in the limitations.

Statistical analysis

Data were analysed using SPSS version 26.0, with supplementary effect-size and confidence-interval computation. The distribution of continuous variables was assessed with the Shapiro–Wilk test and variance homogeneity with Levene's test; numerical data were summarised as mean ± standard deviation or median with interquartile range, and categorical data as frequencies and percentages with Wilson 95% confidence intervals. ROC analysis was used to determine the discriminatory performance and optimal cut-off of the SII, with the area under the curve (AUC) reported with Hanley–McNeil 95% confidence intervals together with sensitivity, specificity, positive and negative likelihood ratios, and predictive values. Bivariate associations were assessed using the chi-square or Fisher exact test with relative risk, odds ratio and Cramer's V as effect sizes. The primary analysis used modified Poisson regression with robust (sandwich) standard errors to estimate adjusted relative risks, an approach preferred over logistic regression for common outcomes because the odds ratio overstates the relative risk when outcome prevalence is high. Models for both endpoints were adjusted for age, sex, smoking history, hypertension, diabetes mellitus and symptom-onset-to-intervention time. Results are reported as relative risk or adjusted relative risk with 95% confidence intervals and exact p-values to three decimal places; a two-sided p-value below 0.05 was considered statistically significant.

Ethical considerations

This study used secondary data and involved no direct patient intervention. Patient confidentiality was maintained using coded data without personal identifiers. Ethical approval was obtained from the Health Research Ethics Committee of Prof. dr. I.G.N.G. Ngoerah General Hospital, Denpasar, under approval number 1725/UN14.2.2.VII.14/LT/2026, and the committee waived the requirement for individual written informed consent given the retrospective use of de-identified records.

3. Results

Baseline characteristics. A total of 118 patients with STEMI who underwent primary PCI were included. As shown in Table 1, the median age was 54 years (interquartile range, 16) and most patients were male (99 patients, 83.9%; 95% CI 76.2–89.4). A smoking history was present in 74 patients (62.7%; 95% CI 53.7–70.9), hypertension in 34 patients (28.8%; 95% CI 21.4–37.6) and diabetes mellitus in 21 patients (17.8%; 95% CI 11.9–25.7). The median symptom-onset-to-intervention time was 531 minutes (interquartile range, 481.75). The culprit vessel was most commonly the left anterior descending artery (55.1%), followed by the right coronary artery (38.1%) and the left circumflex artery (6.8%).

Using the optimal SII cut-off of 1,506.29, 65 patients (55.1%; 95% CI 46.1–63.8) were categorised as high SII and 53 patients (44.9%) as low SII. Baseline clinical characteristics, cardiovascular risk factors, symptom-onset-to-intervention time and infarct location did not differ significantly between the two groups (all $p > 0.05$; Table 1), indicating reasonable balance of measured covariates across SII strata.

Table 1. Patient demographics and baseline characteristics by SII category (n = 118).

Characteristic	High SII (n=65)	Low SII (n=53)	Total (n=118)	p-value
Age, years, median (IQR)	55 (15.5)	54 (16)	54 (16)	0.922*
Male sex, n (%)	51 (78.5)	48 (90.6)	99 (83.9)	0.075†
Smoking history, n (%)	37 (56.9)	37 (69.8)	74 (62.7)	0.150†
Hypertension, n (%)	22 (33.8)	12 (22.6)	34 (28.8)	0.181†
Diabetes mellitus, n (%)	11 (16.9)	10 (18.9)	21 (17.8)	0.784†
Onset-to-PCI, min, median (IQR)	553 (434)	484 (534)	531 (481.75)	0.723*
Culprit: LAD, n (%)	42 (64.6)	23 (43.4)	65 (55.1)	0.066†
Culprit: LCx, n (%)	3 (4.6)	5 (9.4)	8 (6.8)	—
Culprit: RCA, n (%)	20 (30.8)	25 (47.2)	45 (38.1)	—

*Notes: *Mann–Whitney U test; †Chi-square test. SII, Systemic Immune-Inflammation Index; IQR, interquartile range; PCI, percutaneous coronary intervention; LAD, left anterior descending; LCx, left circumflex; RCA, right coronary artery.*

Laboratory and angiographic findings

The median platelet count was 274 $\times 10^3/\mu L$ (interquartile range, 89.50), the mean neutrophil count was 9.99 ± 3.55 $\times 10^3/\mu L$ and the median lymphocyte count was 1.45 $\times 10^3/\mu L$ (interquartile range, 0.95). The median SII was 1,690 (interquartile range, 1,409). High thrombus burden was observed in 99 patients (83.9%; 95% CI 76.2–89.4), while no-reflow occurred in 16 patients (13.6%; 95% CI 8.5–20.9) (Table 2; Figure 1).

Table 2. Primary outcomes and bivariate association with SII category.

Outcome	High SII n (%)	Low SII n (%)	ARD (%)	RR (95% CI)	OR (95% CI)	Cramer's V	p
High thrombus burden	59 (90.8)	40 (75.5)	15.3	1.203 (1.013–1.428)	3.196 (1.121–9.108)	0.207	0.025
No-reflow	13 (20.0)	3 (5.7)	14.3	3.533 (1.062–11.753)	4.167 (1.120–15.505)	0.208	0.024

Notes: ARD, absolute risk difference; RR, relative risk; OR, odds ratio; CI, confidence interval. p-values from Pearson chi-square test.

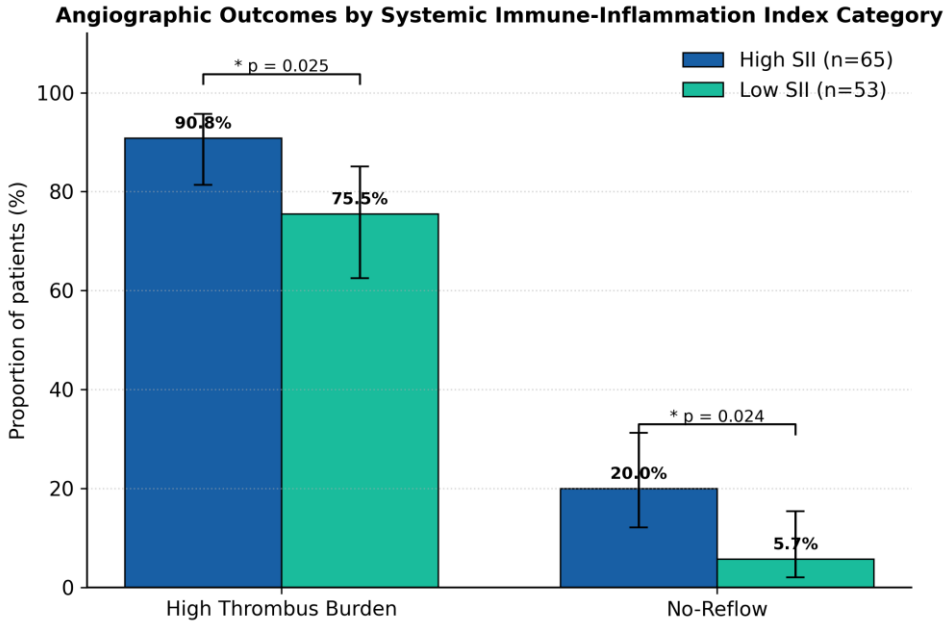

Figure 1. Angiographic outcomes (high thrombus burden and no-reflow) stratified by SII category, with 95% confidence intervals; asterisks denote statistically significant between-group differences.

Receiver operating characteristic analysis. For high thrombus burden, the area under the ROC curve for the SII was 0.597 (95% CI 0.464–0.730; p = 0.152 versus 0.5). The optimal cut-off was 1,506.29, with a sensitivity of 59.6%, a specificity of 68.4% and a Youden index of 0.280; the corresponding positive and negative likelihood ratios were 1.89 and 0.59, and the positive and negative predictive values were 90.8% and 24.5% (Figure 2). For no-reflow, the area under the ROC curve was 0.674 (95% CI 0.521–0.827; p = 0.026

versus 0.5). The optimal cut-off was 1,602.74, with a sensitivity of 81.3% and a specificity of 52.0%; the positive and negative likelihood ratios were 1.69 and 0.36, and the positive and negative predictive values were 21.0% and 94.7% (Figure 2).

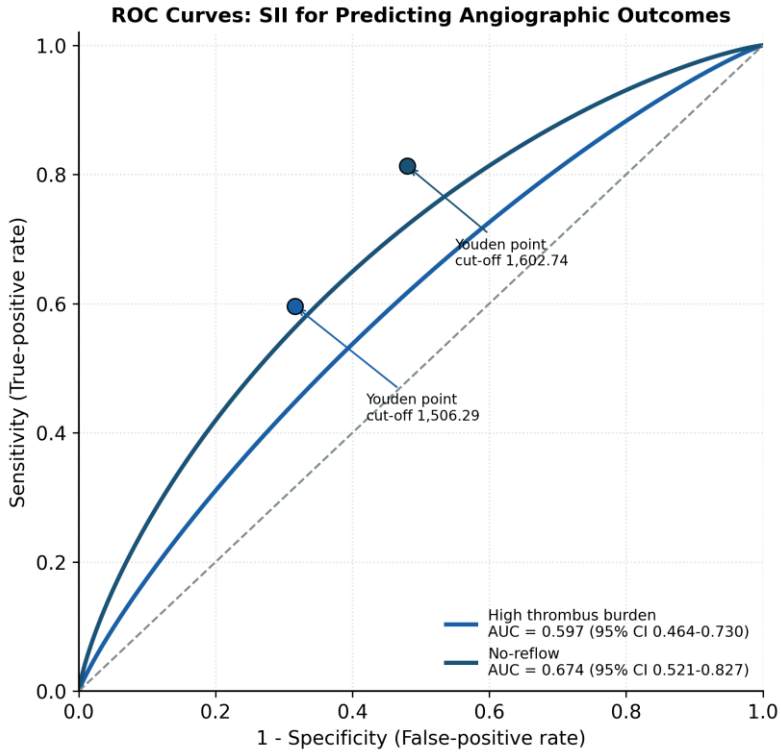

Figure 2. Receiver operating characteristic curves of the SII for predicting high thrombus burden (AUC 0.597; 95% CI 0.464–0.730) and no-reflow (AUC 0.674; 95% CI 0.521–0.827), with Youden-optimal operating points.

Association between SII and angiographic outcomes

High thrombus burden was more frequent in the high-SII group than in the low-SII group (90.8% versus 75.5%). The absolute risk difference was 15.3%, with a relative risk of 1.203 (95% CI 1.013–1.428; p = 0.025); the corresponding odds ratio was 3.196 (95% CI 1.121–9.108) and the effect size was small (Cramer's V = 0.207) (Table 2). No-reflow occurred in 13 patients (20.0%) in the high-SII group and 3 patients (5.7%) in the low-SII group. The absolute risk difference was 14.3%, with a relative risk of 3.533 (95% CI 1.062–11.753; p = 0.024); the odds ratio was 4.167 (95% CI 1.120–15.505) and Cramer's V was 0.208 (Table 2; Figure 1).

Multivariable analysis

After adjustment for age, sex, smoking history, hypertension, diabetes mellitus and symptom-onset-to-intervention time, high SII remained associated with high thrombus burden (adjusted relative risk 1.194; 95% CI 1.004–1.421; p = 0.045). High SII was also independently associated with no-reflow after adjustment for the same covariates (adjusted relative risk 3.226; 95% CI 1.039–10.014; p = 0.043). None of the adjustment covariates reached statistical significance in either model (Table 3; Figure 3). The persistence of both associations after adjustment indicates that the relationships were not fully explained by the measured confounders, although the wide confidence interval for the no-reflow estimate signals limited precision.

Table 3. Multivariable analysis and diagnostic performance of the SII.

Outcome / predictor	Adjusted RR (95% CI)	p	AUC (95% CI)	Youden cut-off	Sn / Sp (%)
High thrombus burden — High SII (adjusted)	1.194 (1.004–1.421)	0.045	0.597 (0.464–0.730)	1,506.29	59.6 / 68.4
No-reflow — High SII (adjusted)	3.226 (1.039–10.014)	0.043	0.674 (0.521–0.827)	1,602.74	81.3 / 52.0

Notes: Adjusted for age, sex, smoking, hypertension, diabetes and onset-to-PCI time (modified Poisson regression, robust SE). AUC 95% CI by Hanley–McNeil. RR, relative risk; AUC, area under the ROC curve; Sn, sensitivity; Sp, specificity.

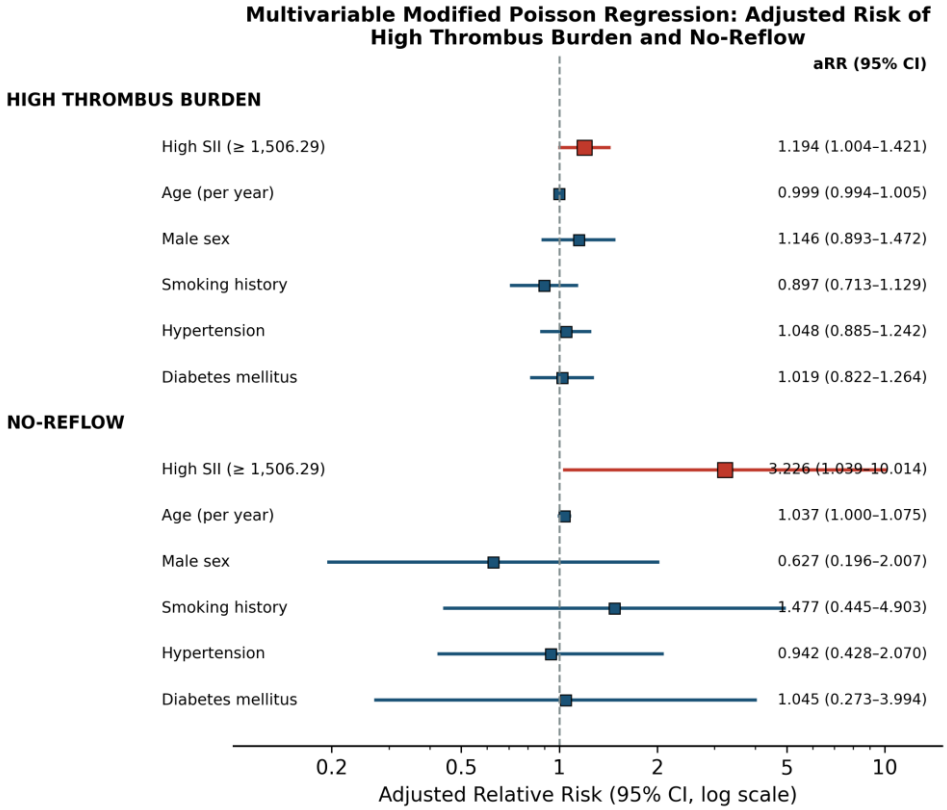

Figure 3. Forest plot of adjusted relative risks (modified Poisson regression) for high thrombus burden and no-reflow, adjusted for age, sex, smoking history, hypertension, diabetes mellitus and symptom-onset-to-intervention time.

4. Discussion

This study evaluated the association between the admission SII and two angiographic outcomes in patients with STEMI undergoing primary PCI: high thrombus burden and no-reflow. The principal finding was that a higher SII was associated with both outcomes, and that these associations persisted after adjustment for age, sex, smoking history, hypertension, diabetes mellitus and symptom-onset-to-intervention time. However, the magnitude and diagnostic performance of the index differed between the two endpoints. The association with high thrombus burden was statistically significant but modest, and ROC analysis showed weak discriminatory performance. For no-reflow, the adjusted association was stronger, but the confidence interval was wide and discrimination remained limited. Taken together, these findings suggest that the SII reflects thrombo-inflammatory activity during acute myocardial infarction but does not, on its own, possess sufficient accuracy to serve as a standalone predictor.

The clinical characteristics of this cohort are relevant to interpretation. Most patients were male and smoking was the most common cardiovascular risk factor, a distribution consistent with prior STEMI primary-PCI populations. Vatan et al. and Şaylık et al. both reported a male predominance among patients with STEMI undergoing primary PCI, and this composition is not merely descriptive: it may shape the inflammatory and thrombotic profile of the cohort.[14,15] Smoking is associated with endothelial dysfunction, platelet activation, plaque instability and inflammatory activation, all of which are directly relevant to acute coronary thrombosis. Özkan et al. similarly reported an association between the SII and coronary thrombus burden in non-ST acute coronary syndrome, supporting a broader relationship between systemic inflammatory activity and thrombotic coronary lesions across the acute coronary syndrome spectrum.[13]

Symptom-onset-to-intervention time is an important contextual feature of this cohort. Many patients had a relatively long interval between symptom onset and primary PCI. Prolonged ischaemic time can worsen myocardial injury, increase endothelial damage, promote microvascular obstruction and raise the probability of no-reflow.[2,6] In the Indonesian setting, delays in presentation, transfer, referral coordination and catheterisation-laboratory access remain practical barriers to timely reperfusion. This system context is consistent with national data showing a rising ischaemic heart disease burden in Indonesia over recent decades.[1] These health-system factors may partly explain why angiographic complications such as high thrombus burden and no-reflow remain clinically salient in local practice.

The high frequency of high thrombus burden in this cohort is clinically meaningful because thrombus burden reflects not only angiographic severity but also procedural complexity and susceptibility to impaired reperfusion.[5] Patients with a large thrombus burden are more likely to experience distal embolisation, impaired epicardial flow, slow-flow, no-reflow and

suboptimal myocardial reperfusion. In the present study, high thrombus burden was present in most patients, which may itself have limited the discriminatory performance of the SII by reducing separation between outcome groups. When the outcome prevalence approaches the ceiling, substantial overlap in index values between patients with and without the outcome is expected. This helps explain why the index remained statistically associated with high thrombus burden yet showed weak ROC performance—biological relevance without sufficient accuracy for individual-level classification.

The association between the SII and high thrombus burden is consistent with Dolu et al., who reported that the index was independently associated with intracoronary thrombus burden in patients with STEMI, and with Özkan et al., who reported that it independently predicted high coronary thrombus burden in acute coronary syndrome.[5,13] However, discrimination in the present study was weaker than in several of these reports, suggesting that a single SII cut-off may not transfer directly across populations without external validation. Variations in patient selection, ischaemic time, baseline inflammatory status, cardiovascular risk profile, procedural practice, timing of blood sampling and outcome prevalence can all influence index performance. Because the SII is derived from neutrophil, platelet and lymphocyte counts, it is a dynamic haematological marker affected not only by coronary thrombus burden but also by systemic stress, acute inflammation, comorbidities and treatment-related factors.[5,7,10]

The modest adjusted relative risk for high thrombus burden warrants careful interpretation. Although the association was statistically significant, the effect size was small. This does not render the finding unimportant, but it does mean that the SII alone contributes limited risk separation for this outcome. The high baseline prevalence of high thrombus burden in both SII strata likely narrowed the relative difference between groups. Clinically, a low SII therefore does not reliably exclude high thrombus burden, particularly in a cohort where most patients already present with severe thrombotic occlusion. For procedural planning, direct angiographic assessment remains essential; the index may help frame thrombo-inflammatory risk before the procedure but cannot replace evaluation of coronary anatomy and thrombus grade.

The association between the SII and no-reflow appeared stronger than its association with high thrombus burden, a plausible pattern because no-reflow is a more complex, integrative endpoint. No-reflow is not determined solely by the amount of thrombus within the culprit artery; it results from a combination of distal embolisation, microvascular obstruction, endothelial dysfunction, interstitial oedema, oxidative stress, vasospasm and reperfusion injury.[2,6] A systemic index that captures neutrophil activation, platelet activity and lymphocyte suppression may therefore be more closely related to microvascular reperfusion failure than to epicardial thrombus grade alone. The present findings are consistent with Esenboğa et al. and Vatan et al., who reported that the SII predicted no-reflow and impaired myocardial perfusion after primary PCI; with Liu et al., who incorporated the index into a validated no-reflow risk nomogram; and with Zorlu et al., who found that combining the SII with the triglyceride–glucose index improved no-reflow prediction.[6,12,14,16]

Despite this consistency, the no-reflow result should be interpreted cautiously. The adjusted relative risk was larger than that for high thrombus burden, but the confidence interval was wide, indicating limited precision that most likely reflects the small number of no-reflow events. A wide confidence interval means that the true magnitude of association could be substantially smaller or larger than the point estimate. The finding supports an association between higher SII and no-reflow but does not provide a stable enough estimate to define a definitive risk threshold; it should be regarded as a signal requiring confirmation in larger cohorts with more events and, preferably, prospective data collection.

The biological mechanism underlying the observed associations is consistent with the thrombo-inflammatory nature of STEMI. By combining neutrophil, platelet and lymphocyte counts, the SII integrates inflammatory, thrombotic and immune-regulatory components into a single haematological marker.[5,7,10] In acute myocardial infarction, neutrophil activation promotes endothelial injury, oxidative stress, release of proteolytic enzymes and formation of neutrophil extracellular traps, which intensify local thrombus formation and contribute to microvascular obstruction.[2,8,17] Platelets participate directly in acute coronary thrombosis through adhesion, activation, aggregation and interaction with leukocytes, and activated platelets contribute to distal embolisation and microvascular plugging relevant to no-reflow.[2,8] Lymphopenia reflects systemic stress and altered immune regulation during acute ischaemic injury. A high SII therefore represents a state in which inflammatory and thrombotic components are activated while adaptive immune balance is relatively suppressed.[5,7]

This mechanism aligns with the pathophysiology of no-reflow described in recent mechanistic reviews: no-reflow is not merely failure to open the epicardial artery but failure to restore adequate tissue-level perfusion despite epicardial recanalisation.[2,6] Distal embolisation of thrombotic and atheromatous material can obstruct small vessels, neutrophil and platelet activation can worsen endothelial swelling and capillary plugging, and reperfusion itself intensifies oxidative stress and endothelial dysfunction. Studies of high-thrombus-burden management have likewise emphasised the relevance of thrombus burden, distal embolisation and microvascular impairment to

procedural outcomes.[5] Together, these mechanisms explain why a high SII may be associated with both high thrombus burden and no-reflow.

The ROC analysis is one of the most important elements of this study because it guards against over-interpretation. For high thrombus burden the AUC was weak; for no-reflow it was higher but still not strong enough to justify independent clinical use. This distinction between association and prediction is critical: a variable can be statistically associated with an outcome yet discriminate poorly. In practical terms, the SII may be higher on average among patients with adverse angiographic outcomes, yet the overlap between groups may be too large for the index to classify individual patients accurately. The safer and more accurate conclusion is therefore that the SII is an adjunctive marker rather than a strong predictor.

The difference between the cut-off values derived here and those reported elsewhere also requires caution. The optimal cut-off for high thrombus burden in this cohort differed from values reported for thrombus burden by Dolu et al. and Özkan et al., and the no-reflow cut-off differed from those reported by Esenboğa et al. and Vatan et al.[5,12-14] Such differences are expected because ROC-derived cut-offs are population-dependent, influenced by outcome prevalence, case-mix, disease severity, laboratory timing and local practice. A cut-off derived in one centre may not retain the same sensitivity and specificity elsewhere. In this study, the high prevalence of high thrombus burden and the small number of no-reflow events likely affected cut-off estimation, so these values should be treated as internal study findings rather than clinical thresholds ready for general use.

A methodological point deserves emphasis because it affects how the effect estimates should be read. We deliberately used modified Poisson regression with robust standard errors rather than logistic regression. When an outcome is common—as high thrombus burden clearly is in this cohort, at 83.9%—the odds ratio diverges substantially from the relative risk and can dramatically exaggerate the apparent strength of association. For example, the crude odds ratio for high thrombus burden in the high-SII group (3.196) is more than two-and-a-half times larger than the corresponding relative risk (1.203), even though both describe the same data. Reporting relative risk therefore provides a more faithful and clinically interpretable measure of association for these endpoints, and it prevents the common error of presenting an inflated odds ratio as though it were a risk ratio. This choice reinforces our central message: the association of the SII with high thrombus burden, while real, is modest in magnitude.[7,15]

It is also worth situating these findings within the wider literature on haematological inflammatory ratios in coronary disease. The neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio and SII have each been evaluated as severity and prognostic markers across the spectrum of coronary artery disease, from stable disease and coronary slow-flow to acute coronary syndromes, infarct size and post-PCI major adverse cardiovascular events.[9,10,11,18] A recurring theme in this body of work, mirrored in our data, is that these indices are consistently associated with adverse phenotypes at the group level yet rarely achieve the discrimination required for confident individual-level classification. Consistent with this, newer composite indices—including the pan-immune-inflammation value, the inflammatory prognostic index and the endothelial activation and stress index—have shown broadly similar or only moderately superior discrimination for no-reflow, and the diagnostic "grey zone" of the SII has been formally quantified.[19,20,21,22] Encouragingly, the inflammatory signal the index captures appears at least partly modifiable, since statin therapy has been shown to lower the SII and related ratios.[23] The SII, by combining three cell lines, may capture a slightly broader thrombo-inflammatory signal than any single ratio, but it does not escape the fundamental limitation that a composite of routine counts is a coarse proxy for complex microvascular biology.

The findings have practical relevance because the SII is derived from complete-blood-count parameters obtained routinely at initial assessment. Unlike specialised inflammatory biomarkers, it requires no additional laboratory testing and can be calculated rapidly, which may be useful in acute settings where quick risk stratification is needed.[7,10,14] In patients undergoing primary PCI, a high index may indicate a more active thrombo-inflammatory state and help identify those warranting closer angiographic and procedural attention. However, these data do not support using the index to determine procedural strategy independently; it should be interpreted alongside symptom duration, haemodynamic status, cardiovascular risk factors, culprit-vessel anatomy, angiographic thrombus burden, baseline coronary flow and operator assessment.[2,3]

The clinical implication is therefore modest but real. A high SII may help identify patients who merit closer angiographic assessment and greater anticipation of reperfusion complications, and its most appropriate role is as part of a broader risk profile rather than a binary decision tool. Patients with delayed presentation, a high inflammatory index, visible thrombus burden and impaired pre-procedural flow would reasonably be considered at higher risk for no-reflow than patients without these features, consistent with the multifactorial nature of impaired reperfusion after primary PCI.[2,3] The index should complement, not override, angiographic findings and clinical judgement, particularly because this study showed significant associations but limited discrimination.

This study also reinforces that thrombus burden and no-reflow, although related, should not be treated as identical outcomes. High thrombus burden reflects angiographically visible thrombotic material in the

epicardial artery, whereas no-reflow reflects failure of microvascular reperfusion after intervention despite restored epicardial patency.[2,4] A patient may have high thrombus burden without no-reflow, and no-reflow may arise through mechanisms beyond visible thrombus, including endothelial injury, oedema, vasospasm, distal embolisation and reperfusion injury.[2,6] By evaluating both endpoints, this study provides a more complete assessment of the relationship between the SII and the angiographic complications of primary PCI, and the stronger association with no-reflow suggests that the index may capture systemic inflammatory and microvascular vulnerability more than visible epicardial thrombus burden alone.[3,5]

Several strengths merit emphasis. The study addressed a clinically relevant question in an Indonesian STEMI population where data remain limited; it evaluated both high thrombus burden and no-reflow, allowing assessment of epicardial and microvascular components; the index was calculated from admission or pre-procedural complete-blood-count values reflecting the timing at which such a marker would realistically be available; and the analysis used adjusted modified Poisson regression rather than relying solely on unadjusted comparisons, correctly estimating relative risk for a common outcome. Finally, the interpretation remained appropriately cautious, recognising that statistical association does not equal strong predictive performance.

Limitations must be acknowledged. First, the retrospective design limited control over the timing of blood sampling; because the SII varies across the acute phase as inflammatory and stress responses evolve, real-world admission values may have contributed to the limited discrimination observed.[5,7] Second, angiographic thrombus burden and post-procedural flow were obtained from catheterisation-laboratory reports rather than independent blinded adjudication, and although established TIMI grades were used, their interpretation can vary between operators, particularly with total occlusion, poor visualisation, overlapping vessels or borderline flow.[4] Third, several procedural and angiographic variables that influence no-reflow—lesion complexity, pre-procedural flow, antithrombotic strategy, aspiration thrombectomy, stent strategy and intraprocedural haemodynamics—were not fully captured, raising the possibility of residual confounding.[2,3,6] Fourth, the single-centre tertiary-referral setting limits external validity, since referral patterns, ischaemic time, catheterisation-laboratory workflow and treatment protocols may differ elsewhere. Fifth, the study focused on angiographic endpoints and did not evaluate infarct size, left ventricular ejection fraction, heart failure, recurrent infarction, major adverse cardiovascular events or mortality, so it cannot determine whether the observed associations translate into worse clinical outcomes; prior work and meta-analysis have linked SII with adverse events after PCI, but that endpoint was not tested here.[7] Finally, the modest achieved power for the low-frequency no-reflow endpoint explains the wide confidence interval and reinforces the need for larger cohorts.

These limitations map directly onto priorities for future research. Studies should validate SII cut-offs in independent cohorts and evaluate whether combining the index with clinical and angiographic variables improves prediction, since a composite model may outperform the index alone for multifactorial outcomes.

Prospective designs would permit standardised timing of blood sampling, clearer documentation of procedural variables and independent, blinded angiographic adjudication, while larger samples would improve precision, particularly for no-reflow. Linking the index and angiographic outcomes to hard clinical endpoints would finally clarify whether the marker carries prognostic value beyond procedural findings.

Interpretation of the covariate structure of our models is instructive. In both the thrombus-burden and no-reflow models, none of the adjustment variables—age, sex, smoking history, hypertension, diabetes mellitus or symptom-onset-to-intervention time—reached statistical significance, and the SII remained the only variable independently associated with each outcome. Two readings are possible. The optimistic reading is that the SII carries independent thrombo-inflammatory information not captured by conventional risk factors. The more cautious reading, which we favour, is that the modest sample size and, in particular, the small number of no-reflow events limited the statistical power to detect the contribution of individual covariates, so the apparent isolation of the SII as the sole significant predictor should not be over-interpreted. The near-significant association of age with no-reflow (adjusted relative risk 1.037 per year; $p = 0.052$) is biologically consistent with the greater microvascular vulnerability of older patients and would plausibly reach significance in a larger series. Infarct location, although not entered into the final adjusted models, showed a non-significant trend toward more anterior (left anterior descending) culprit lesions in the high-SII group, a pattern that merits examination in future work because anterior infarcts are associated with larger myocardial territory at risk and potentially greater microvascular injury.[2,3,6]

A further consideration is how the SII relates to hard downstream outcomes beyond the angiographic endpoints examined here. Although the present study deliberately restricted itself to intraprocedural findings, a growing body of work links the admission SII to infarct size and to major adverse cardiovascular events after primary PCI. Zhu et al., using cardiac magnetic resonance, reported that a high SII was independently associated with larger infarct size and a higher incidence of major adverse cardiovascular events, and a meta-analysis of cohort studies found an approximate doubling of event risk in patients with an

elevated index.[7,10] Prognostic models that embed the SII within established frameworks—such as the TIMI risk score augmented by the SII and lipoprotein(a)—have achieved substantially higher discrimination than the index alone, reinforcing our contention that the SII is most useful as one component of a multivariable model rather than as a standalone classifier.[3] These observations situate our angiographic findings within a coherent biological continuum: a heightened admission thrombo-inflammatory state, indexed by the SII, plausibly links visible epicardial thrombus and microvascular no-reflow to the ultimate clinical consequences of infarct size and adverse events. They also underscore why external validation connecting the index to clinical endpoints—rather than to angiographic surrogates alone—represents the most important next step for this line of research.[14,15]

Finally, the translational trajectory for a marker such as the SII should be explicit. The appropriate next step is not immediate clinical deployment but rigorous external and prospective validation, followed by evaluation within multivariable risk models that combine the index with established clinical and angiographic predictors. Only if such composite models demonstrate incremental discrimination, calibration and, ultimately, an impact on decisions and outcomes would routine reporting of the SII for angiographic risk stratification be justified. Until then, the most scientifically honest position—and the one this study supports—is that the admission SII is a biologically plausible, inexpensive adjunctive marker whose principal value is to heighten clinical vigilance in patients who already carry other markers of thrombo-inflammatory and reperfusion risk.[3,6,7]

5. Conclusion

In conclusion, the admission Systemic Immune-Inflammation Index was independently associated with high thrombus burden (adjusted relative risk 1.194; 95% CI 1.004–1.421) and no-reflow (adjusted relative risk 3.226; 95% CI 1.039–10.014) in patients with STEMI undergoing primary PCI at a tertiary Indonesian centre. These findings support a potential role for this inexpensive, routinely available index as a simple adjunctive marker of thrombo-inflammatory risk during acute reperfusion. However, its weak-to-modest discriminatory performance (AUC 0.597 for thrombus burden and 0.674 for no-reflow), the small effect size for thrombus burden, the limited precision of the no-reflow estimate and the retrospective single-centre design constrain its direct clinical application. The index should therefore complement, rather than replace, clinical assessment and angiographic evaluation, and its cut-off values require external validation in larger, prospective, blinded-adjudication cohorts before general clinical use.

Declarations

Ethics approval

Ethical approval was obtained from the Health Research Ethics Committee of Prof. dr. I.G.N.G. Ngoerah General Hospital, Denpasar (approval number 1725/UN14.2.2.VII.14/LT/2026). Written informed consent was waived given the retrospective use of coded, de-identified secondary data.

Conflict of interest

The authors declare no conflict of interest.

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Author contributions

W.A.P.: conceptualisation, methodology, formal analysis, investigation, and writing of the original draft. H.W.: investigation, data curation, and writing (review and editing). I.K.S.S.D.: methodology, data curation, and writing (review and editing). I.M.J.R.A.: validation, supervision, and writing (review and editing). I.M.P.S.A.: resources, supervision, and writing (review and editing). I.W.G.A.E.P.: formal analysis, software, and writing (review and editing). All authors have read and approved the final version of the manuscript.

Data availability

The datasets generated and analysed during the current study are not publicly available because they contain confidential patient information, but they are available from the corresponding author on reasonable request and with the permission of the institutional ethics committee.

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