

# The Impact of Residual Syntax Score as a Predictor of Major Cardiovascular Events During Treatment and 3 Months After Limited Percutaneous Coronary Intervention on Lesions Causing ST-Segment Elevation Myocardial Infarction

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## ABSTRACT

**Background:** Acute myocardial infarction with ST-segment elevation (STEMI) is one of the leading causes of morbidity and mortality due to cardiovascular disease. In STEMI patients with multivessel disease, percutaneous coronary intervention (PCI) strategies are often limited to culprit-only PCI, leaving residual lesions that may increase the risk of major cardiovascular events (MCEs). The residual SYNTAX Score (rSS) is a quantitative tool for assessing the anatomical burden of residual coronary artery disease after intervention and is thought to have predictive value for MCE. **Objective:** This study aims to evaluate the role of the residual SYNTAX score as a predictor of major cardiovascular events during hospitalisation and within 3 months after limited percutaneous coronary intervention on the causative lesion in STEMI patients, as well as to determine the optimal rSS cut-off value in predicting these events. **Methods:** This study is an analytical observational study with a retrospective cohort design conducted at Ngoerah Hospital from January to September 2025. A total of 166 STEMI patients who underwent PCI limited to the causative lesion and met the inclusion criteria were analysed. The residual SYNTAX score was calculated based on post-PCI angiography and categorised using Receiver Operating Characteristic (ROC) analysis. Major cardiovascular events during hospitalisation and 3 months after PCI were recorded. Analyses were performed using the Chi-square test, ROC curve, and Cox regression to determine independent predictors. **Results:** Of the 166 patients, 64 patients (38.6%) had high rSS ( $\geq 8.5$ ), and 102 patients (61.4%) had low rSS ( $< 8.5$ ). The incidence of KKM during hospitalisation was significantly higher in the high rSS group compared to the low rSS group (57.8% vs 10.8%;  $p < 0.001$ ). Similarly, KKM within 3 months after IKP was higher in the high rSS group (56.2% vs 13.7%;  $p < 0.001$ ). ROC analysis showed an rSS cut-off value of 8.5 with an AUC of 0.806 ( $p < 0.001$ ), sensitivity of 77.1%, and specificity of 77.1%. In multivariate analysis, high rSS was an independent predictor of KKM during hospitalisation with an HR of 4.65 (95% CI 2.26–9.58;  $p < 0.001$ ). **Conclusion:** A high residual SYNTAX score ( $\geq 8.5$ ) is an independent predictor of major cardiovascular events during treatment and 3 months after limited percutaneous coronary intervention on the causative lesion in STEMI patients. A cut-off value of 8.5 can be used for risk stratification to identify patients with a higher risk of major cardiovascular events.

**Keywords:** Residual SYNTAX score; STEMI; percutaneous coronary intervention; culprit-only PCI; major cardiovascular events, risk stratification

## INTRODUCTION

Cardiovascular diseases (CVD) remain the leading cause of death globally and pose a significant public health challenge in the 21st century. According to recent reports, approximately 17.9 million deaths occur annually due to CVD, with over 80% attributed to myocardial infarction and stroke [1]. Alarmingly, one-third of these deaths affect individuals under 70 years old, highlighting a substantial disease burden on the productive age group [2,3]. Although global

CVD mortality has declined by 34.9% from 1990 to 2022, the absolute number of cases and disease burden remain high [3]. This decline does not offset population growth and aging, which cumulatively increase absolute case numbers and strain national health systems, particularly in low- and middle-income countries [3]. In Indonesia, epidemiological data indicate CVD mortality rates ranging from 356.05 to 412.46 per 100,000 population, with incidence exceeding 15,000 per 100,000 [4,5].

Acute myocardial infarction (AMI) is one of the most acute and deadly forms of CVD, resulting from severe and prolonged myocardial ischemia characterized by necrosis of heart muscle tissue due to coronary blood flow disruption. AMI is classified into two main types based on electrocardiographic findings: ST-elevation (STE) and non-ST-elevation myocardial infarction (NSTEMI). ST-elevation represents transmural ischemia from total coronary artery occlusion and is the leading cause of death in acute coronary syndrome globally [6,7]. In STE management, primary percutaneous coronary intervention (PCI) is the preferred reperfusion therapy, aimed at rapidly restoring myocardial perfusion by opening the occluded artery using balloon angioplasty and stent implantation [8]. Success hinges on timing, with international guidelines recommending a first medical contact to device time of  $\leq 90$  minutes as a key indicator of effective STE care systems [8].

However, in clinical practice, 40% to 65% of STE patients have multivessel disease [3]. For this population, culprit-only PCI is a common strategy, limiting intervention to the culprit lesion to minimize procedure duration and maintain hemodynamic stability, while ignoring other significant lesions. Though practical, this approach is linked to higher risks of major adverse cardiovascular events (MACE) in both short- and long-term follow-up [9–11]. Large trials like PRAMI, CULPRIT, and COMPLETE demonstrate that culprit-only PCI increases MACE risk, including cardiovascular mortality, recurrent infarction, and repeat revascularization. In the COMPLETE trial, patients receiving only culprit PCI had a 10.5% cardiovascular event rate over 3 years, compared to 7.8% in those with complete revascularization [11]. This underscores the need to assess residual coronary disease burden post-intervention.

One quantitative tool for evaluating residual coronary artery disease is the Residual SYNTAX Score (rSS), calculated by scoring untreated lesions after primary PCI to reflect the complexity and extent of unmanaged disease [12]. Farooq et al. (2013) [13] categorization, rSS is classified as complete revascularization (rSS = 0), mild incomplete (rSS  $\leq 8$ ), or significant incomplete (rSS  $> 8$ ). Patients with rSS  $> 8$  consistently show higher mortality and MACE rates [13,14]. Most studies evaluate overall MACE without distinguishing events from intervened versus non-culprit lesions, a critical gap in culprit-only PCI, where residual lesions may cause reinfarction or reintervention. The subacute phase, up to three months post-PCI, is particularly vulnerable due to heightened risks of stent thrombosis, restenosis, and non-culprit lesion progression amid post-STEMI pro-inflammatory and pro-thrombotic states [15,16].

Given these factors, there is an urgent need for predictive tools assessing MACE risk during hospitalization and the first three months after culprit-only PCI. While clinical parameters (e.g., advanced age, low LVEF, diabetes, CKD) and

biomarkers (e.g., troponin, BNP, inflammatory markers) have been studied as MACE predictors [17,18], few objectively quantify residual anatomical disease burden. rSS emerges as a promising score, capturing revascularization incompleteness and potentially predicting MACE tied directly to intervened lesions. Thus, this study aims to evaluate the impact of the Residual SYNTAX Score as a predictor of major cardiovascular events during treatment and three months post-culprit-only PCI in ST-elevation patients with multivessel disease at Ngoerah Hospital in Denpasar. The findings are expected to inform individualized treatment strategies and optimal decision-making in multivessel STE management.

## METHOD

This study employs an analytical observational design with a retrospective cohort approach. Patients diagnosed with ST-elevation myocardial infarction (STEMI) who underwent percutaneous coronary intervention (PCI) at RSUP Prof. Dr. I.G.N.G. Ngoerah Denpasar, identified from medical records upon first hospital admission, serve as research subjects. All patients meeting inclusion and exclusion criteria are included, with the Residual SYNTAX Score (rSS) calculated post-PCI to assess residual coronary artery damage. Subjects are followed for 3 months post-procedure to record major adverse cardiovascular events (MACE), captured via medical records and follow-up visits. Patients experiencing MACE during this period are categorized as events, while those surviving without MACE are classified as non-events.

The study was conducted at RSUP Prof. Ngoerah, the primary referral hospital for Bali and Nusa Tenggara regions, from January to September 2025. The target population comprises all patients aged  $\geq 18$  years diagnosed with STEMI and treated with PCI. The accessible population includes those treated at the study hospital within the specified timeframe. Samples are selected non-randomly (purposive sampling) from the accessible population based on complete medical data availability and follow-up feasibility, yielding a minimum of 75 per group (total 166, adjusted +10% for dropout), calculated using the formula for comparing two proportions ( $Z_{1-\alpha/2}=1.96$ ,  $Z_{1-\beta}=0.84$ ,  $P_1=36\%$  high rSS MACE,  $P_2=16\%$  low rSS MACE per Génèreux et al., 2012).

Inclusion criteria are patients aged  $\geq 18$  years with confirmed STEMI undergoing PCI. Exclusion criteria encompass incomplete medical records preventing rSS calculation or 3-month follow-up; patient refusal or uncontactability; Killip IV STEMI; single-vessel CAD with complete revascularization; congenital heart disease or non-atherosclerotic vascular anomalies; immunodeficiency affecting treatment/follow-up; other malignancies influencing cardiovascular outcomes; or non-cardiovascular deaths (e.g., accidents). Independent variable is rSS (ordinal, low/high per ROC, calculated via standardized angiography software assessing residual lesion location, length, and complexity post-PCI).

Dependent variable is 3-month post-PCI MACE (nominal: yes/no), including cardiovascular death, cardiogenic shock, recurrent infarction, heart failure, arrhythmia, and repeat revascularization, confirmed via biomarkers, ECG, echocardiography, and records. Control variables include age, sex, hypertension, smoking history, CKD (eGFR<60 mL/min/1.73m<sup>2</sup>), ejection fraction, TIMI flow (0-3/4 grades), Killip class (I-IV), door-to-balloon time, infarct location, TIMI risk score (low/intermediate/high), diabetes, and symptom onset.

Study materials comprise secondary data: coronary angiography results from the cardiac catheterization lab detailing lesions and post-PCI rSS; patient records with clinical characteristics (age, sex, comorbidities, blood pressure, smoking, etc.); and MACE recording forms for events like recurrent infarction or revascularization. Instruments include angiography data sheets interpreted by interventional cardiologists; clinical data worksheets; MACE documentation forms; and SPSS software for analysis on computers.

Research procedures begin with proposal approval, ethical clearance from the Udayana University Medical Faculty Ethics Committee, and hospital permission. Eligible STEMI-PCI patients (January-September 2025) are recruited retrospectively, with clinical data (demographics, comorbidities, lesion details) extracted from records. Post-PCI rSS is computed and categorized. Three-month follow-up tracks MACE via records, clinic visits, and phone interviews, confirmed by diagnostics (e.g., troponin for infarction, angiography for revascularization). Data are processed in SPSS for analysis, with results organized into tables/graphs for thesis reporting and potential journal publication.

## RESULT

Table 1 presents the baseline characteristics of 166 patients undergoing PCI, stratified by Residual SYNTAX Score (rSS): high ( $\geq 8.5$ , n=64) versus low ( $< 8.5$ , n=102). Significant differences emerged in Killip class, chronic kidney disease, and MACE outcomes, while demographics and most risk factors were comparable.

**TABLE 1:** Characteristics of the sample residual SYNTAX.

Characteristic	High rSS ( $\geq 8.5$ ) n=64	Low rSS ( $< 8.5$ ) n=102	p-value
<b>Age (n, %)</b>			
≥60 years	30 (46.9%)	36 (35.3%)	0.138
<60 years	34 (53.1%)	66 (64.7%)	
<b>Sex (n, %)</b>			
Male	58 (90.6%)	90 (88.2%)	0.630
Female	6 (9.4%)	12 (11.8%)	
<b>Killip class (n, %)</b>			
I	41 (64.1%)	76 (74.5%)	0.001*
II	10 (15.6%)	23 (22.5%)	
III	13 (20.3%)	3 (2.9%)	
<b>Infarct area (n, %)</b>			
Anterior	33 (51.6%)	55 (53.9%)	0.767
Non-anterior	31 (48.4%)	47 (46.1%)	
<b>TIMI score (n, %)</b>			
High	6 (9.4%)	7 (6.9%)	0.801
Intermediate	21 (32.8%)	32 (31.4%)	
Low	37 (57.8%)	63 (61.8%)	
<b>Hypertension (n, %)</b>			
Yes	16 (25.0%)	24 (23.5%)	0.829
No	48 (75.0%)	78 (76.5%)	
<b>Door-to-balloon (n, %)</b>			
≥90 minutes	40 (62.5%)	59 (57.8%)	0.552
<90 minutes	24 (37.5%)	43 (42.2%)	
<b>TIMI flow (n, %)</b>			
Non-TIMI 3 flow	45 (70.3%)	81 (79.4%)	0.182
TIMI 3 flow	19 (29.7%)	21 (20.6%)	
<b>Chronic kidney disease (eGFR &lt;60 mL/min) (n, %)</b>			
Yes	21 (32.8%)	13 (12.7%)	0.002*
No	43 (67.2%)	89 (87.3%)	

Characteristic	High rSS ( $\geq 8.5$ ) n=64	Low rSS ( $< 8.5$ ) n=102	p-value
<b>Ejection fraction (n, %)</b>			
Reduced $< 55\%$	58 (90.6%)	92 (90.2%)	0.927
Normal $\geq 55\%$	6 (9.4%)	10 (9.8%)	
<b>Smoking (n, %)</b>			
Yes	51 (79.7%)	87 (85.3%)	0.348
No	13 (20.3%)	15 (14.7%)	
<b>Diabetes (n, %)</b>			
Yes	22 (34.4%)	27 (26.5%)	0.277
No	42 (65.6%)	75 (73.5%)	
<b>In-hospital MACE (n, %)</b>			
Yes	37 (57.8%)	11 (10.8%)	$< 0.001^*$
No	27 (42.2%)	91 (89.2%)	
<b>3-month MACE (n, %)</b>			
Yes	36 (56.2%)	14 (13.7%)	$< 0.001^*$
No	28 (43.8%)	88 (86.3%)	

\*Significant ( $p < 0.05$ ).

Receiver Operating Characteristic (ROC) analysis evaluated the ability of the Residual SYNTAX Score (rSS) to predict major adverse cardiovascular events (MACE). The ROC curve is shown in Figure 2, while the area under the curve (AUC), sensitivity, specificity, and optimal cutoff values are presented in Table 2 below.

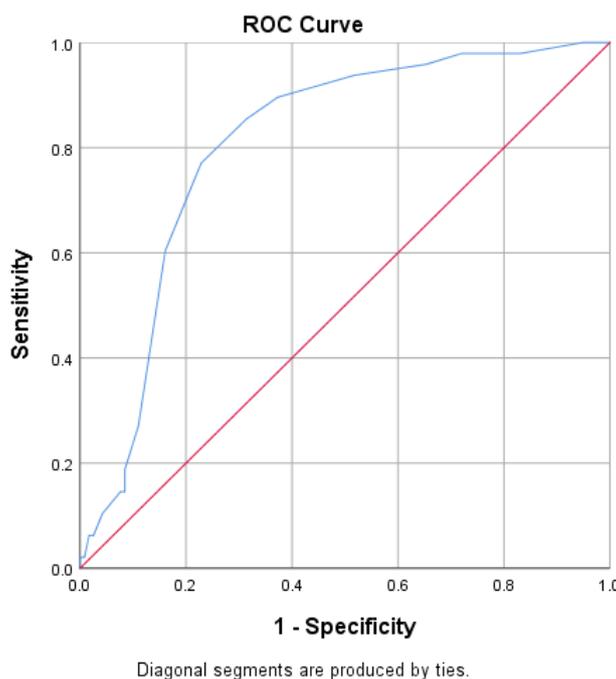
The analysis revealed an AUC of 0.806 for rSS, indicating good discriminatory power in distinguishing patients with and without MACE

( $p < 0.001$ ). This value suggests strong predictive performance, where AUC  $> 0.8$  is conventionally considered excellent for clinical risk stratification.

The optimal rSS cutoff was 8.5, balancing sensitivity (77.1%) and specificity (77.1%). This threshold effectively identifies high-risk patients (rSS  $\geq 8.5$ ) for closer monitoring or complete revascularization, supporting its utility in STEMI management post-culprit-only PCI.

**TABLE 2:** Cut-off sensitivity and specificity of the Residual SYNTAX.

AUC	Sensitivity	Specificity	Cutoff	p-value
0.806	77.1%	77.1%	8.5	$< 0.001$



**FIGURE 2:** Receiver Operating Characteristic (ROC) analysis evaluated the ability of the Residual SYNTAX.

Table 3 outlines major adverse cardiovascular events (MACE) and other clinical outcomes stratified by Residual SYNTAX Score (rSS): high ( $\geq 8.5$ , n=64) vs. low ( $< 8.5$ , n=102). High rSS patients exhibited significantly higher in-hospital MACE (57.8% [37 patients] vs. 10.8% [11 patients];  $p < 0.001$ ), reflecting greater residual disease burden. Acute heart failure (31.3% vs. 2.9%;  $p < 0.001$ ), malignant

arrhythmia (17.2% vs. 2.9%;  $p < 0.001$ ), and cardiogenic shock (28.1% vs. 2.9%;  $p < 0.001$ ) were markedly more frequent in high rSS during hospitalization. At 3 months, MACE remained elevated (56.2% vs. 13.7%;  $p < 0.001$ ), driven by chronic heart failure (35.9% vs. 13.7%;  $p = 0.001$ ); recurrent ACS ( $p = 0.236$ ) and mortality ( $p = 0.528$ ) showed no differences.

**TABLE 3:** Major adverse cardiovascular events (MACE) and other clinical outcomes stratified by Residual SYNTAX.

Characteristic	High rSS ( $\geq 8.5$ ) n=64	Low rSS ( $< 8.5$ ) n=102	p-value
<b>In-hospital MACE</b>			
Yes	37 (57.8%)	11 (10.8%)	$< 0.001^*$
No	27 (42.2%)	91 (89.2%)	
<b>Acute heart failure</b>			
Yes	20 (31.3%)	3 (2.9%)	$< 0.001^*$
No	44 (68.8%)	99 (97.1%)	
<b>Malignant arrhythmia</b>			
Yes	11 (17.2%)	3 (2.9%)	$< 0.001^*$
No	53 (82.8%)	99 (97.1%)	
<b>Cardiogenic shock</b>			
Yes	18 (28.1%)	3 (2.9%)	$< 0.001^*$
No	46 (71.9%)	99 (97.1%)	
<b>3-month MACE</b>			
Yes	36 (56.2%)	14 (13.7%)	$< 0.001^*$
No	28 (43.8%)	88 (86.3%)	
<b>Chronic heart failure</b>			
Yes	23 (35.9%)	14 (13.7%)	0.001*
No	41 (64.1%)	88 (86.3%)	
<b>Recurrent ACS</b>			
Yes	11 (17.2%)	11 (10.8%)	0.236
No	53 (82.8%)	91 (89.2%)	
<b>Mortality</b>			
Yes	5 (7.8%)	11 (10.8%)	0.528
No	59 (92.2%)	91 (89.2%)	

\*Significant ( $p < 0.05$ ).

Bivariate analysis assessed factors associated with in-hospital major adverse cardiovascular events (MACE) in 166 STEMI-PCI patients, comparing

MACE-positive (n=48) and MACE-negative (n=118) groups in Table 4.

**TABLE 4:** Bivariate analysis assessed factors associated with in-hospital major adverse cardiovascular events (MACE).

Characteristic	MACE+ (n=48)	MACE- (n=118)	HR	95% CI	p-value
<b>Residual SYNTAX</b>					
High ( $\geq 8.5$ )	37 (57.8%)	27 (42.2%)	5.36	2.95-9.73	$< 0.001^*$
Low ( $< 8.5$ )	11 (10.8%)	91 (89.2%)			
<b>Age</b>					
$\geq 60$ years	24 (36.4%)	42 (63.6%)	1.51	0.94-2.43	0.086
$< 60$ years	24 (24.0%)	76 (76.0%)			
<b>Sex</b>					
Male	42 (28.4%)	106 (71.6%)	0.85	0.42-1.71	0.662
Female	6 (33.3%)	12 (66.7%)			

Characteristic	MACE+ (n=48)	MACE- (n=118)	HR	95% CI	p-value
<b>Killip class</b>					
I	29 (24.8%)	88 (75.2%)	0.36	0.18-0.72	0.004*
II	8 (24.2%)	25 (75.8%)	0.35	0.14-0.87	0.025*
III	11 (68.8%)	5 (31.2%)			
<b>Infarct area</b>					
Anterior	31 (35.2%)	57 (64.8%)	1.61	0.97-2.68	0.057
Non-anterior	17 (21.8%)	61 (78.2%)			
<b>TIMI score</b>					
High	7 (53.8%)	6 (46.2%)	2.44	1.04-5.72	0.039*
Intermediate	19 (35.8%)	34 (64.2%)	1.63	0.88-3.01	0.119
Low	22 (22.0%)	78 (78.0%)	Ref		
<b>Hypertension</b>					
Yes	13 (32.5%)	27 (67.5%)	1.17	0.69-1.98	0.566
No	35 (27.8%)	91 (72.2%)			
<b>Door-to-balloon</b>					
≥90 min	32 (32.3%)	67 (67.7%)	1.35	0.81-2.26	0.239
<90 min	16 (23.9%)	51 (76.1%)			
<b>TIMI flow</b>					
Non-TIMI 3	36 (28.6%)	90 (71.4%)	0.95	0.55-1.64	0.862
TIMI 3	12 (30.0%)	28 (70.0%)			
<b>CKD (eGFR&lt;60)</b>					
Yes	19 (55.9%)	15 (44.1%)	2.54	1.64-3.94	<0.001*
No	29 (22.0%)	103 (78.0%)			
<b>Ejection fraction</b>					
Reduced <55%	47 (31.3%)	103 (68.7%)	5.01	0.74-33.93	0.070
Normal ≥55%	1 (6.3%)	15 (93.7%)			
<b>Smoking</b>					
Yes	39 (28.3%)	99 (71.7%)	0.87	0.48-1.60	0.680
No	9 (32.1%)	19 (67.9%)			
<b>Diabetes</b>					
Yes	15 (30.6%)	34 (69.4%)	1.08	0.65-1.80	0.755
No	33 (28.2%)	84 (71.8%)			

\*Significant (p<0.05). HR = Hazard Ratio; CI = Confidence Interval; Ref = Reference.

Multivariate Cox regression analysis identified independent predictors of in-hospital major adverse cardiovascular events (MACE) among 166 STEMI-PCI patients in Table 5. Variables with clinical relevance and/or bivariate p<0.25 were entered into the model. High residual SYNTAX score (≥8.5) emerged as the sole independent predictor, with patients facing 4.65 times higher MACE risk

compared to low rSS (HR 4.65, 95% CI 2.26-9.58, p<0.001). All other factors lost significance after adjustment, including age ≥60 years (HR 1.19, p=0.585), CKD (HR 1.31, p=0.433), reduced EF (HR 3.58, p=0.217), Killip class, TIMI score, hypertension, procedural delays, TIMI flow, smoking, and diabetes.

**TABLE 5:** Multivariate Cox regression analysis identified independent predictors of in-hospital major adverse cardiovascular events (MACE).

Variable	HR	95% CI	p-value
High rSS (≥8.5)	4.65	2.26-9.58	<0.001*
Male sex	0.80	0.23-2.73	0.725
Age ≥60 years	1.19	0.62-2.28	0.585
<b>Killip Class</b>			
I (vs III)	0.77	0.34-1.74	0.772
II (vs III)	0.72	0.25-2.02	0.722

<b>TIMI Score</b>			
High (vs Low)	1.49	0.53-4.23	0.447
Intermediate (vs Low)	1.16	0.56-2.37	0.680
Hypertension	1.15	0.58-2.29	0.683
Door-to-balloon >90 min	1.09	0.57-2.09	0.781
Non-TIMI 3 flow	1.13	0.57-2.25	0.718
CKD (eGFR<60 mL/min)	1.31	0.66-2.57	0.433
EF reduced <55%	3.58	0.47-27.16	0.217
Smoking	0.92	0.47-1.85	0.815
Diabetes	0.92	0.47-1.81	0.820

\*Significant (p<0.05). HR = Hazard Ratio; CI = Confidence Interval. This confirms rSS as the dominant prognostic factor post-culprit-only PCI.

Bivariate analysis evaluated factors associated with 3-month major adverse cardiovascular events (MACE) in 166 STEMI-PCI patients, comparing

MACE-positive (n=50) and MACE-negative (n=116) groups in Table 6.

**TABLE 6:** Bivariate analysis evaluated factors associated with 3-month major adverse cardiovascular events (MACE).

Characteristic	MACE+ (n=50)	MACE- (n=116)	HR	95% CI	p-value
<b>Residual SYNTAX</b>					
High (≥8.5)	36 (56.3%)	28 (43.8%)	4.09	2.40-6.97	<0.001*
Low (<8.5)	14 (13.7%)	88 (86.3%)			
<b>Age</b>					
≥60 years	18 (27.3%)	48 (72.7%)	0.85	0.52-1.38	0.516
<60 years	32 (32.0%)	68 (68.0%)			
<b>Sex</b>					
Male	45 (30.4%)	103 (69.6%)	1.09	0.50-2.39	0.819
Female	5 (27.8%)	13 (72.2%)			
<b>Killip class</b>					
I	29 (24.8%)	88 (75.2%)	0.39	0.19-0.81	0.012*
II	11 (33.3%)	22 (66.7%)			
III	10 (62.5%)	6 (37.5%)			
<b>Infarct area</b>					
Anterior	32 (36.4%)	56 (63.6%)	1.57	0.96-2.57	0.063
Non-anterior	18 (23.1%)	60 (76.9%)			
<b>TIMI score</b>					
High	4 (30.8%)	9 (69.2%)	1.18	0.41-3.39	0.754
Intermediate	20 (37.7%)	33 (62.3%)			
Low	26 (26.0%)	74 (74.0%)			
<b>Hypertension</b>					
Yes	16 (40.0%)	24 (60.0%)	0.82	0.62-1.08	0.118
No	34 (27.0%)	92 (73.0%)			
<b>Door-to-balloon</b>					
≥90 min	33 (33.3%)	66 (66.7%)	1.47	0.73-2.93	0.273
<90 min	17 (25.4%)	50 (74.6%)			
<b>TIMI flow</b>					
Non-TIMI 3	33 (26.2%)	93 (73.8%)	0.61	0.38-1.98	0.052
TIMI 3	17 (42.5%)	23 (57.5%)			
<b>CKD (eGFR&lt;60)</b>					
Yes	15 (44.1%)	19 (55.9%)	1.66	1.03-2.67	0.046*
No	35 (26.5%)	97 (73.5%)			

Characteristic	MACE+ (n=50)	MACE-(n=116)	HR	95% CI	p-value
<b>Ejection fraction</b>					
Reduced <55%	47 (31.3%)	103 (68.7%)	1.67	0.58-4.76	0.297
Normal ≥55%	3 (18.8%)	13 (81.2%)			
<b>Smoking</b>					
Yes	39 (28.3%)	99 (71.7%)	1.18	0.86-1.62	0.246
No	11 (39.3%)	17 (60.7%)			
<b>Diabetes</b>					
Yes	18 (36.7%)	31 (63.3%)	1.34	0.83-2.15	0.229
No	32 (27.4%)	85 (72.6%)			

\*Significant (p<0.05). HR = Hazard Ratio; CI = Confidence Interval; Ref = Reference. High rSS remained the strongest predictor at 3 months.

Multivariate Cox regression analysis determined independent predictors of 3-month major adverse cardiovascular events (MACE) in 166 STEMI-PCI patients. Clinically relevant variables and those with a bivariate p<0.05 were included in Table 7. High residual SYNTAX score (≥8.5) was the only independent predictor, increasing MACE risk 3.81-

fold versus low rSS (HR 3.81, 95% CI 1.97-7.38, p<0.001). Bivariate associations (e.g., Killip I HR 0.39, p=0.012, CKD HR 1.66, p=0.046) attenuated after adjustment. Demographics, risk factors, Killip class, TIMI score, procedural variables, EF, smoking, and diabetes showed no independent effects.

**TABLE 7:** Multivariate Cox regression analysis determined independent predictors of 3-month major adverse cardiovascular events (MACE).

Variable	HR	95% CI	p-value
High rSS (≥8.5)	3.81	1.97-7.38	<0.001*
Male sex	1.35	0.41-4.42	0.611
Age ≥60 years	0.16	0.83-2.92	0.729
<b>Killip Class</b>			
I (vs III)	0.89	0.37-2.10	0.795
II (vs III)	1.18	0.43-3.20	0.743
<b>TIMI Score</b>			
High (vs Low)	1.05	0.31-3.54	0.938
Intermediate (vs Low)	1.25	0.62-2.53	0.522
Hypertension	1.20	0.63-2.26	0.570
Door-to-balloon >90 min	1.04	0.55-1.95	0.889
Non-TIMI 3 flow	0.73	0.39-1.37	0.333
CKD (eGFR<60 mL/min)	1.07	0.53-2.18	0.835
EF reduced <55%	1.30	0.38-4.44	0.671
Smoking	0.64	0.27-1.49	0.304
Diabetes	1.06	0.54-2.07	0.848

\*Significant (p<0.05). HR = Hazard Ratio; CI = Confidence Interval. rSS dominance aligns with studies showing its prognostic value in STEMI post-PCI.

## DISCUSSION

ST-elevation myocardial infarction (STEMI) remains one of the leading causes of cardiovascular morbidity and mortality worldwide, despite significant advances in reperfusion strategies and adjunctive therapies. Percutaneous coronary intervention (PCI) has proven effective in reducing mortality and improving clinical outcomes in STEMI patients. However, residual untreated lesions can lead to high mortality and morbidity rates. Residual lesions refer to the remaining burden or impact of heart disease after treatments such as angioplasty or stent placement. Although medical interventions have rapidly evolved, including drug-eluting stents,

most patients still face long-term risks from coronary artery disease (CAD), particularly if uncontrolled risk factors like diabetes, hypertension, or smoking persist.

Studies demonstrate that while modern treatments improve coronary blood flow and alleviate symptoms, the long-term risk from residual lesions remains substantial, especially in patients with prior myocardial infarction or heavy disease burden. Residual coronary artery disease often progresses to severe cardiac conditions such as congestive heart failure or arrhythmias.

This retrospective cohort study was conducted at RSUP Prof. Dr. I.G.N.G. Ngoerah, Denpasar, from January to September 2025, with a 3-month follow-up post-PCI. The research aimed to evaluate the role of the residual SYNTAX score as a predictor of major adverse cardiovascular events (MACE) during hospitalization and at 3-month follow-up in acute coronary syndrome (ACS) patients undergoing PCI. Analysis results showed that a residual SYNTAX score cutoff of  $\geq 8.5$  demonstrated good discriminatory ability in predicting MACE, both in-hospital and at 3 months.

This study included 166 patients meeting the inclusion criteria, selected via consecutive sampling from the study population. Most baseline characteristics, including age, sex, hypertension, diabetes mellitus, smoking status, TIMI score, door-to-balloon time, and post-procedure TIMI flow, showed no significant differences between high ( $\geq 8.5$ ) and low ( $< 8.5$ ) residual SYNTAX score groups. This indicates comparable initial clinical profiles and reperfusion quality between groups, suggesting that observed MACE differences primarily reflect residual coronary disease burden rather than baseline clinical factors or procedural success. These findings align with prior research by Généreux et al. (2012) and Farooq et al. (2013) [13,19], which established residual SYNTAX score as a representation of anatomical complexity and incomplete revascularization with independent prognostic impact post-PCI, independent of baseline patient characteristics and initial reperfusion parameters.

However, certain variables were significantly associated with high residual SYNTAX score, namely Killip class and chronic kidney disease. The study subjects were predominantly male, reflecting STEMI epidemiology, where acute myocardial infarction occurs more frequently in men than women. Higher acute myocardial infarction incidence in males with more typical clinical presentations, leading to earlier identification and reperfusion therapy [6].

Higher Killip class reflects greater acute heart failure severity and extent of ischemic myocardium. Taguchi Eiji et al. (2017) studied 2,062 patients at Saiseikai Kumamoto Hospital, Japan, finding Killip class IV (severe heart failure or cardiogenic shock) carried a 16-fold higher mortality risk compared to lower classes [20]. Despite advanced technology and mechanical support, in-hospital mortality remained unchanged across periods (2005–2009 vs. 2010–2014). High Killip class correlates with coronary disease complexity and worse ACS outcomes, consistent with this study [6,21].

In this research, kidney function was represented by chronic kidney disease (CKD) as a baseline characteristic. No variables explicitly defined post-procedure kidney function deterioration, such as acute kidney injury or contrast-associated AKI. CKD is a slowly progressive condition where the kidneys lose function over time, often influenced by heart disease, particularly multivessel CAD. CKD involves reduced nitric oxide bioavailability, elevated pro-

inflammatory cytokines (CRP, IL-6, TNF- $\alpha$ ), and oxidative stress activation, accelerating diffuse and complex atherosclerotic plaque formation that hinders complete revascularization, resulting in high residual SYNTAX scores [3]. Additionally, calcium-phosphate metabolism disorders and elevated FGF-23 in CKD cause medial and intimal coronary calcification. Heavily calcified lesions increase anatomical complexity and reduce complete revascularization success, elevating residual SYNTAX scores [14]. This aligns with Malkin (2013), showing CKD independently associates with coronary artery calcification progression beyond traditional risk factors, explaining high residual SYNTAX scores due to revascularization challenges in impaired kidney function patients [12].

Left ventricular ejection fraction showed no significant difference between high and low residual SYNTAX score groups and did not emerge as an independent MACE predictor. This stems from EF measurement during the acute infarction phase, where myocardial stunning affects accuracy. LVEF indicates left ventricular systolic function but does not specifically reflect residual coronary burden or post-revascularization plaque distribution/myocardial perfusion. Residual SYNTAX score quantifies post-PCI lesion complexity and residual stenosis, relating to long-term ischemic risk like MACE, but not directly influencing initial pre-PCI LVEF. Thus, high and low rSS groups may have similar baseline LVEF due to multifactorial influences beyond pure coronary anatomy. Some severe CAD patients exhibit ventricular remodelling or compensation, maintaining relatively preserved LVEF despite residual disease. This matches Ösken et al. (2018) prospective study, where rSS was linked to long-term MACE, but LVEF was non-significant in simple multivariate models [14]. Martinez et al. (2022) in 175 STEMI patients developed a functional residual SYNTAX score combining rSS and clinical parameters, outperforming LVEF alone in outcome prediction [22].

This study demonstrates the residual SYNTAX score's meaningful discriminatory ability in predicting MACE during hospitalization and 3-month follow-up. The obtained AUC indicates rSS as a reliable risk stratification tool in revascularized CAD patients. Clinically, these findings confirm that post-PCI residual coronary disease significantly impacts patient outcomes. Despite target lesion revascularization, significant anatomical residual stenosis potentially sustains myocardial ischemic burden, vascular inflammation, and subsequent thrombotic events. The study's rSS cutoff optimally balances sensitivity and specificity, applicable for early high-risk patient identification.

These results align with the SYNTAX Trial sub-analysis showing residual disease burden (rSS) as an independent MACE predictor after incomplete revascularization. High rSS patients exhibited higher death, myocardial infarction, and repeat revascularization incidence versus more complete revascularization.

Farooq et al. (2013) reported that each rSS increase significantly raises MACE risk, even after adjusting for age, diabetes, and LVEF, reinforcing rSS as both descriptive and prognostic anatomical parameter [13].

Généreux et al. (2012) found rSS predicts post-PCI outcomes better than baseline SYNTAX score, particularly in multivessel high-complexity anatomy patients [19]. Their AUC values, comparable to those in this study, indicate cross-population consistency. Residual coronary disease contributes to short-term heart failure and cardiovascular death in ACS patients with incomplete revascularization, relevant to this study's in-hospital MACE prediction by rSS [3]. Differences in this study's rSS cutoff versus prior literature remain rational, influenced by the STEMI population, culprit-only PCI strategy leaving non-culprit lesions, and short-term outcomes assessment, where lower residual burden already yields meaningful clinical impact.

High residual SYNTAX score ( $\geq 8.5$ ) is significantly associated with increased in-hospital MACE. High rSS patients experienced 57.8% in-hospital MACE versus 10.8% in the low rSS group ( $p < 0.001$ ), highlighting the post-PCI residual coronary burden's role in acute STEMI phase clinical stability. Specifically, high rSS was linked to acute heart failure (31.3% vs. 2.9%;  $p < 0.001$ ), malignant arrhythmia (17.2% vs. 2.9%;  $p < 0.001$ ), and cardiogenic shock (28.1% vs. 2.9%;  $p < 0.001$ ). This reflects ongoing myocardial ischemia from incomplete revascularization, causing left ventricular dysfunction, hemodynamic instability, and myocardial electrical disturbances. Findings align with Généreux et al., establishing rSS as a strong predictor of MACE and mortality post-PCI, especially in multivessel CAD patients with significant residual atherosclerosis burden, increasing in-hospital complications.

Farooq et al.'s SYNTAX trial post-hoc analysis reported revascularization completeness degree (rSS) strongly correlates with short- and long-term outcomes, including heart failure and cardiogenic shock. At 3-month follow-up, high rSS remained significantly associated with MACE (56.2% vs. 13.7%;  $p < 0.001$ ), confirming residual coronary impact extends beyond acute into subacute/early chronic post-STEMI phases. Dominant 3-month MACE component in high rSS was chronic heart failure (35.9% vs. 13.7%;  $p = 0.001$ ), supporting residual ischemia and atherosclerosis contributing to post-infarct adverse ventricular remodelling leading to chronic heart failure.

Conversely, recurrent ACS (17.2% vs. 10.8%;  $p = 0.236$ ) and 3-month mortality (7.8% vs. 10.8%;  $p = 0.528$ ) showed no statistical differences, likely due to few events and limited follow-up duration, reducing statistical power for hard endpoints like mortality. Yamaji et al. in multivessel STEMI patients showed high rSS associates with increased heart failure and rehospitalization in medium-term

follow-up, though early mortality differences are often non-significant.

This study shows that higher residual SYNTAX score (rSS) patients had greater MACE incidence in-hospital and up to 3 months post-PCI, affirming rSS reflects post-revascularization residual coronary anatomical complexity and serves as an early clinical risk stratification tool in STEMI. rSS quantifies residual coronary burden, potentially causing sustained myocardial ischemia. Incomplete revascularization leaves the myocardium hypoperfused, rapidly contributing to hemodynamic instability, malignant arrhythmias, worsening acute heart failure, and cardiovascular death in acute STEMI. Thus, high rSS clinically identifies limited myocardial perfusion reserve and higher in-hospital complication risk patients. High rSS typically reflects multivessel involvement and complex lesion characteristics like proximal location, bifurcation, and heavy calcification technically challenging for optimal acute revascularization. This strengthens rSS as an early risk indicator requiring intensive monitoring and potential additional interventions during hospitalization.

Findings consistent with Généreux et al. (2012), establishing rSS as an independent in-hospital MACE predictor in ACS-PCI patients. High rSS patients had significantly higher mortality and in-hospital complications versus low rSS, confirming rSS's role in early treatment phase risk prediction [19]. Recent evidence supports residual coronary disease as the primary short/medium-term outcome determinant post-STEMI. COMPLETE and CvLPRIT sub-analyses show untreated non-culprit lesions associate with early post-PCI recurrent ischemia, conceptually aligning with higher rSS [10,11]. This affirms the residual coronary burden's meaningful short-term clinical implications, matching this study's observation period.

Other clinical variables like EF, Killip, and CKD reflect hemodynamic status or comorbidities at presentation. EF is influenced by ventricular remodeling, myocardial compensation, or post-PCI medical therapy. Killip indicates the degree of acute heart failure, not residual anatomical burden. CKD ( $GFR < 60$ ) reflects general clinical state and comorbidity, but outcome effects are often masked by stronger variables like rSS. Post-multivariate adjustment, their independent MACE contributions became non-significant. This matches Zhai (2025) in 831 low-GFR ACS-PCI patients, where rSS remained a strong cardiac death/MACE predictor while GFR was non-independent multivariately [18]. CKD's prognostic effect is mainly mediated via incomplete revascularization, reflected by high rSS. Contemporary studies like Jae (2025) show TIMI flow/door-to-balloon primarily affect very early outcomes but limited medium-term MACE prediction in the modern PCI era with optimized reperfusion times [23]. Thus, this study reinforces residual anatomical parameter (rSS) having a stronger prognostic value than initial clinical risk

scores, epicardial flow parameters, or metabolic comorbidities.

rSS serves as a clinically applicable early prognostic parameter not only depicting anatomical revascularization results but aiding clinicians in early risk stratification, monitoring intensity determination, and therapy planning during hospitalization and the early post-PCI period.

This study has limitations warranting consideration in result interpretation. First, the observational design yields associative rather than causal relationships between residual SYNTAX score and MACE. Despite multivariate adjustment for confounders, residual confounding cannot be fully eliminated. Second, single-center conduct limits generalizability; study population characteristics may not represent broader populations with differing clinical profiles or healthcare systems. Third, rSS assessment relied on coronary angiography (anatomical), not reflecting lesion functional significance. Lack of physiological evaluation, like FFR/iFR, may overestimate/underestimate true myocardial ischemic burden. Fourth, short follow-up (in-hospital to 3 months) precludes long-term impact assessment on outcomes like long-term mortality or recurrent cardiovascular events. Fifth, no specific evaluation of the staged PCI strategy or medication changes during follow-up, potentially influencing MACE. Guideline-directed medical therapy adherence variations have not been analyzed deeply. Sixth, sample size is adequate for main analyses but limits subgroup power, e.g., severe CKD or very high anatomical complexity CAD patients.

Despite limitations, findings retain strong clinical relevance, reflecting real-world STEMI management with a culprit-only PCI strategy, positioning rSS as a simple, applicable early risk stratification tool meaningfully predicting early post-intervention MACE.translate.

## CONCLUSION

This retrospective cohort study at RSUP Prof. Dr. I.G.N.G. Ngoerah (January-September 2025) demonstrated that Residual SYNTAX Score (rSS)  $\geq 8.5$  significantly predicts major adverse cardiovascular events (MACE) during hospitalization and 3-month post-PCI follow-up among 166 STEMI patients, with optimal discriminatory ability (AUC 0.806). Bivariate and multivariate analyses confirmed high rSS as an independent predictor of in-hospital MACE (HR 4.65,  $p < 0.001$ ) and 3-month MACE (HR 3.81,  $p < 0.001$ ), outperforming other clinical factors such as Killip class, CKD, or LVEF, establishing rSS's strong prognostic value for risk stratification following culprit-only PCI in real-world STEMI management.

## CONFLICT OF INTEREST

The author declares that there is no conflict of interest related to the publication of this research article.

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## Ethics in Research

This research received approval from the research ethics committee of Ngoerah Hospital/Faculty of Medicine, Udayana University.

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