Student's Journal of Health Research Africa
e-ISSN: 2709-9997, p-ISSN: 3006-1059
Vol.7 No. 2 (2026): June 2026 Issue
https://doi.org/10.51168/sjhrafrica.v7i2.2733
Original Article

Angiographic profile and clinical outcome in repeat revascularization in patients with multivessel percutaneous coronary intervention: A prospective cross-sectional study.

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Abstract

Background

Multivessel coronary artery disease treated with percutaneous coronary intervention (PCI) carries a significant risk of repeat revascularization due to in-stent restenosis or progression of coronary disease. Identifying angiographic predictors and clinical outcomes is essential for improving long-term management.

Objectives: To evaluate the angiographic profile and clinical outcomes of patients undergoing repeat revascularization following multivessel PCI.

Methods

This prospective observational study included 80 patients who underwent repeat revascularization after multivessel PCI at the Department of Cardiology, Government Medical College, Thiruvananthapuram, over 18 months. Angiographic characteristics, including target vessel, lesion morphology, stent type, and in-stent restenosis, were assessed. Clinical outcomes, including major adverse cardiovascular events (MACE), mortality, myocardial infarction, and target vessel revascularization, were recorded over 6 months.

Results

The mean age was 58.4 ± 9.7 years, and 76.3% of participants were male. The left anterior descending artery was the most commonly involved vessel (52.5%), while in-stent restenosis was the predominant mechanism of repeat revascularization (57.5%). Drug-eluting stents were used in 92.5% of patients. At 6 months, MACE occurred in 17.5% of patients. Diabetes mellitus (p=0.012) and diffuse in-stent restenosis (p=0.028) were independent predictors of adverse outcomes.

Conclusion

Repeat revascularization after multivessel PCI remains associated with substantial cardiovascular risk, particularly among patients with diabetes mellitus and diffuse in-stent restenosis.

Recommendations

High-risk patients should receive close follow-up, aggressive risk-factor control, and optimized secondary prevention. Larger multicenter studies with longer follow-up are needed to validate these findings.

Keywords: *Multivessel PCI; Repeat revascularization; In-stent restenosis; MACE; Angiographic profile; Drug-eluting stent*
Submitted: *April 20, 2026* ***Accepted:*** *May 30, 2026* ***Published:*** *June 30, 2026*

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Introduction

Coronary artery disease (CAD) is still the biggest killer and cause of morbidity in the world, killing around 17.9 million people annually. Multivessel coronary artery disease (MVD) is present in 40–60% of people who have coronary angiography and is linked to a poorer prognosis than single-vessel disease. [2]

Percutaneous coronary intervention (PCI) has become the preferred method of revascularization for both acute coronary syndromes and stable ischaemic heart disease (IHD). [3] The SYNTAX trial showed that MVD-PCI can be performed with acceptable results in patients with less complex coronary anatomy, and with a higher incidence of subsequent revascularization procedures than coronary artery bypass grafting (CABG). As stent technology has improved, especially with the use of drug-eluting stents (DES), in-stent restenosis (ISR) has decreased significantly with current DES platforms. [5]

While technological advances have improved the effectiveness of revascularizations, repeat revascularization remains a clinically relevant endpoint following multivessel PCI. Mechanisms involved in in-stent restenosis, stent thrombosis, and de novo disease progression in non-treated or inadequately treated segments. Angiographic factors for ISR are: lesion length, vessel diameter, and diabetes mellitus. This risk is further increased by clinical risk factors like diabetes, chronic kidney disease, and incomplete revascularization. [9]

Patients with CAD in India are younger, with more severe disease and more diabetes and dyslipidaemia, which may have a bearing on the baseline angiographic profile as well as the long-term outcomes following MVD-PCI. While optimal medical therapy alone was proven to be not inferior to PCI in stable disease in the COURAGE trial, symptom recurrence and disease progression often require repeat revascularization. [11]

Several studies have demonstrated that guiding complete revascularization according to fractional flow reserve (FFR) decreases the rates of urgent repeat revascularization (RR), such as in the FAME-2 study. Guiding complete revascularization according to fractional flow reserve (FFR) has been shown to decrease the rate of urgent repeat revascularization (RR) in several studies, including FAME-2. However, translation of these findings into practice in the real world, especially in resource-limited settings, is inconsistent. The Mehran classification divides ISR into four types, including focal (Type I), diffuse intrastent (Type II), diffuse proliferative (Type III), and total occlusion (Type IV), which has been an important risk stratification tool and re-intervention guidance for ISR. [14]. The limited data available from tertiary care centres in the South indicate that the angiographic profile and outcomes of repeat revascularization in MVD-PCI patients remain unknown. These trends within a real-world population will help identify high-risk sub-groups and guide evidence-based follow-up strategies. Hence, the present study was conducted to compare the angiographic profile and 6-month clinical outcomes in patients undergoing repeat revascularization after multivessel PCI in a tertiary cardiac centre at Thiruvananthapuram, Kerala, in a prospective manner.

Materials and methods

Study design and setting

This was a **prospective observational cohort study** conducted in the Department of Cardiology, Government Medical College, Thiruvananthapuram, Kerala, India, a tertiary care teaching hospital providing comprehensive cardiovascular services, including emergency cardiac care, coronary angiography, percutaneous coronary intervention (PCI), coronary care unit services, and outpatient cardiology clinics. The study was conducted over 18 months**.**

Study population

The study included **80 consecutive adult patients** who underwent repeat coronary revascularization (PCI or coronary artery bypass grafting [CABG]) following previous multivessel PCI. Patients aged **18 years or older** with prior multivessel PCI involving two or more major coronary arteries who subsequently underwent repeat coronary angiography for recurrent symptoms or evidence of myocardial ischemia were eligible. Patients with congenital heart disease, significant valvular heart disease, or those unwilling to provide informed consent were excluded.

Sample size and sampling technique

This was a hospital-based prospective observational study. **All eligible consecutive patients presenting during the study period were enrolled until a sample size of 80 participants was achieved.** Consecutive sampling was used to minimize selection bias and ensure that all eligible patients had an equal opportunity for inclusion.

Data collection

Baseline demographic characteristics, cardiovascular risk factors, clinical presentation, previous PCI details, medications, and laboratory findings were recorded using a

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standardized data collection form. Coronary angiography was performed using the standard Judkins technique through radial or femoral arterial access. Angiographic variables, including target vessel, lesion morphology according to the ACC/AHA classification, in-stent restenosis classified using the Mehran classification, TIMI flow grade, and stent characteristics, were independently evaluated by experienced interventional cardiologists using standardized definitions.

Follow-up

Participants were followed for **six months** after repeat revascularization through scheduled outpatient visits at **1, 3, and 6 months** or by telephone interview when necessary. Clinical outcomes, including major adverse cardiovascular events (MACE), all-cause mortality, myocardial infarction, target vessel revascularization, heart failure hospitalization, and stroke, were documented.

Measures to reduce bias

Selection bias was minimized through consecutive recruitment of all eligible patients during the study period. Standardized definitions, structured case record forms, and uniform follow-up protocols were used for all participants. Angiographic findings were interpreted by experienced interventional cardiologists according to predefined criteria to reduce observer bias.

Statistical analysis

Data were analyzed using **IBM SPSS Statistics version 26.0** (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as **mean ± standard deviation (SD)**, while categorical variables were presented as **frequencies and percentages**. Comparisons between categorical variables were performed using the **Pearson Chi-square test**, while **Fisher's exact test** was applied when expected cell frequencies were less than five. Continuous variables were compared using **Student's t-test**. Variables with p-values <0.05 in univariate analysis were entered into a multivariable logistic regression model to identify independent predictors of major adverse cardiovascular events. A two-sided **p-value <0.05** was considered statistically significant.

Ethical considerations

The study was approved by the **Institutional Ethics Committee of Government Medical College, Thiruvananthapuram, Kerala, India**. Written informed consent was obtained from all participants before enrollment, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

Results

During the study period, 86 patients were assessed for eligibility. Six patients were excluded (three did not meet the inclusion criteria and three declined participation). Eighty eligible patients were enrolled and completed the baseline assessment. All participants completed the 6-month follow-up and were included in the final analysis.

During 18 months of study, 80 patients were consecutively recruited who met the inclusion criteria. 6-month follow-up was achieved in all patients. The results are presented under the following subheadings.

Baseline demographic and clinical characteristics.

Table 1 summarizes the basic demographic and clinical features of the study population. The mean age of the cohort was 58.4 ± 9.7 years (range 36–78 years). The male predominance was observed with 76.25% (n=61), following the established fact of male preponderance of coronary artery disease in the Indian population. The highest prevalence of cardiovascular risk factors was found with hypertension (65.0%, n=52), followed by dyslipidaemia (60.0%, n=48) and diabetes mellitus (55.0%, n=44). Of the cohort, 43.75% (n=35) were current or former smokers. Of the patients, 15.0% (n=12) had chronic kidney disease. The high atherosclerotic burden among these patients was highlighted by a history of prior myocardial infarction in 47.5% (n=38) of patients. There was mild to moderate left ventricular ejection fraction (LVEF) dysfunction on average (mean = 48.2 ± 9.1%).

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Table 1: Baseline demographic and clinical characteristics (n=80)

Characteristic	n (%)	Mean ± SD
Total patients	80 (100%)	–
Age (years)	–	58.4 ± 9.7
Male sex	61 (76.25%)	–
Hypertension	52 (65.0%)	–
Diabetes mellitus	44 (55.0%)	–
Dyslipidaemia	48 (60.0%)	–
Smoking (current/ex)	35 (43.75%)	–
Chronic kidney disease	12 (15.0%)	–
Prior MI	38 (47.5%)	–
LVEF at baseline (%)	–	48.2 ± 9.1

Clinical presentation at the time of repeat revascularization

The clinical syndromes that prompted repeat coronary angiography and revascularization are shown in Table 2. The most common presenting symptom was stable angina or exertional chest pain, accounting for 40.0% (n=32) of cases. Acute coronary syndrome in the form of unstable angina or NSTEMI was the indication in 35.0% (n=28) of patients. STEMI was the presenting event in 15.0% (n=12) of patients, necessitating urgent repeat catheterisation and intervention. The remaining 10.0% (n=8) presented with progressive dyspnoea on exertion, in whom ischaemia evaluation prompted angiography. Overall, 50.0% of patients presented with an acute or subacute coronary syndrome, highlighting the potentially life-threatening nature of repeat revascularization events in this high-risk population.

Table 2: Presenting clinical syndrome at time of repeat revascularization

Clinical Presentation	n	%
Stable angina / exertional chest pain	32	40.0
Unstable angina / NSTEMI	28	35.0
STEMI	12	15.0
Dyspnoea on exertion (ischaemia workup)	8	10.0

Angiographic profile

Target vessel distribution

Table 3 presents the distribution of target vessels requiring repeat revascularization. The left anterior descending (LAD) artery was the most frequently involved vessel, accounting for 52.5% (n=42) of all repeat interventions. This was followed by the right coronary artery (RCA) in 30.0% (n=24) of cases and the left circumflex (LCx) artery in 17.5% (n=14). Left main (LM) coronary artery involvement was identified in 10.0% (n=8) of patients, either as a de novo lesion or ostial ISR, representing a particularly high-risk anatomical subset requiring careful revascularization planning. The high proportion of LAD involvement is

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consistent with its larger myocardial territory and the predilection for atherosclerosis in this vessel.

Table 3: Target vessel distribution at repeat revascularization

Target Vessel	n	%
Left anterior descending (LAD)	42	52.5
Right coronary artery (RCA)	24	30.0
Left circumflex (LCx)	14	17.5
Left main (LM) involvement	8	10.0

Mechanism of repeat revascularization

The underlying mechanisms identified at the time of repeat angiography are detailed in Table 4. In-stent restenosis (ISR) was the dominant mechanism, responsible for repeat revascularization in 57.5% (n=46) of patients. De novo disease progression in a previously non-stented or non-treated segment accounted for 27.5% (n=22) of cases, reflecting ongoing atherosclerotic activity in this high-risk cohort. Stent thrombosis was the precipitating event in 10.0% (n=8) of patients, with the majority presenting as STEMI. Graft failure was identified in 5.0% (n=4) of cases, all of whom had undergone prior CABG with subsequent incomplete revascularization by PCI. The high prevalence of ISR in this cohort underscores the importance of optimised stent technique and adherence to dual antiplatelet therapy (DAPT).

Table 4: Mechanism of repeat revascularization

Mechanism / Finding	n	%
In-stent restenosis (ISR)	46	57.5
De novo disease (non-stented segment)	22	27.5
Stent thrombosis	8	10.0
Graft failure (in surgically managed)	4	5.0

ISR Pattern by Mehran classification

Among the 46 patients with ISR, the Mehran angiographic classification was applied to characterise the pattern of restenosis (Table 5). Type I (focal) ISR was the most common subtype, observed in 39.1% (n=18) of ISR cases. Type II (diffuse intrastent) and Type III (diffuse proliferative) ISR together accounted for 52.1% (n=24) of ISR cases, forming the diffuse ISR group that carried greater procedural complexity and worse prognosis. Type IV ISR (total occlusion) was observed in 8.7% (n=4) of ISR patients, representing the most challenging anatomical subset.

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Table 5: ISR Pattern (Mehran Classification) among ISR Cases

ISR Type (Mehran Classification)	n	% of ISR cases (n=46)
Type I – Focal	18	39.1
Type II – Diffuse Intrastent	14	30.4
Type III – Diffuse Proliferative	10	21.7
Type IV – Total Occlusion	4	8.7

Stent characteristics and procedural outcomes

Details regarding stent type, dimensions, and post-procedural angiographic results are shown in Table 6. At the index multivessel PCI, drug-eluting stents (DES) had been implanted in 92.5% (n=74) of patients. The mean stent length at index PCI was 23.6 ± 6.4 mm, and the mean stent diameter was 3.1 ± 0.4 mm. Patients had received a mean of 2.8 ± 0.9 stents during their index multivessel PCI procedure. Post-repeat PCI, TIMI 3 flow was achieved in 92.5% (n=74) of patients, reflecting satisfactory procedural success in the majority of cases. TIMI 2 or lower flow persisted in 7.5% (n=6) of patients, attributable to distal embolisation, severe calcification, or no-reflow phenomenon.

Table 6: Stent characteristics and post-procedural TIMI flow

Stent Parameter	Detail	n / Value
Drug-eluting stent (DES) used	Yes	74 (92.5%)
POBA or DEB used	Yes	6 (7.5%)
Mean stent length (mm)	–	23.6 ± 6.4
Mean stent diameter (mm)	–	3.1 ± 0.4
Number of stents at index PCI	–	2.8 ± 0.9
TIMI 3 flow post-repeat PCI	Yes	74 (92.5%)

Clinical outcomes at 6-month follow-up

All 80 patients completed the 6-month clinical follow-up. The distribution of adverse events is presented in Table 7. The composite major adverse cardiovascular events (MACE) rate at 6 months was 17.5% (n=14). All-cause mortality occurred in 5.0% (n=4) of patients; three deaths were of cardiovascular aetiology (sudden cardiac death and fatal MI), and one was non-cardiovascular. Non-fatal myocardial infarction was recorded in 7.5% (n=6) of patients, of whom 4 were related to stent thrombosis at the repeat intervention site. Target vessel revascularization (TVR) was required in 10.0% (n=8) of patients, reflecting recurrent restenosis or disease progression in the intervened vessel. Hospitalisation for heart failure occurred in 12.5% (n=10) of patients, indicating the significant residual haemodynamic burden in this multivessel disease cohort. Stroke was documented in 2.5% (n=2) of patients. No major vascular access site complications requiring surgery were recorded.

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Table 7: Clinical outcomes at 6-month follow-up

Outcome	n	%
All-cause mortality	4	5.0
Non-fatal MI	6	7.5
Target vessel revascularization (TVR)	8	10.0
Composite MACE	14	17.5
Hospitalisation for heart failure	10	12.5
Stroke	2	2.5

Predictors of MACE

Univariate and multivariate logistic regression analyses were performed to identify independent predictors of composite MACE at 6 months (Table 8). On univariate analysis, diabetes mellitus (OR 3.14; 95% CI 1.18–8.36; p=0.022), diffuse ISR pattern (Mehran Type II–III; OR 2.78; 95% CI 1.10–7.02; p=0.031), and LVEF <40% (OR 2.45; 95% CI 0.98–6.14; p=0.055) were identified as significant or borderline significant predictors of MACE. Chronic kidney disease (p=0.140) and age >65 years (p=0.309) did not reach statistical significance on univariate analysis.

After adjusting for age, sex, and other confounders in the multivariate model, diabetes mellitus (adjusted OR 2.91; 95% CI 1.25–6.78; p=0.012) and diffuse ISR pattern (adjusted OR 2.54; 95% CI 1.10–5.86; p=0.028) remained statistically significant independent predictors of MACE at 6 months. LVEF <40% showed a trend towards significance (adjusted OR 2.20; p=0.068) but did not achieve statistical significance after adjustment, possibly due to the limited sample size. Chronic kidney disease and older age were not independent predictors in the multivariate model.

Table 8: Univariate and multivariate predictors of MACE at 6 months

Variable	Univariate OR (95% CI)	p-value	Multivariate OR (95% CI)	p-value
Diabetes mellitus	3.14 (1.18–8.36)	0.022	2.91 (1.25–6.78)	0.012
Diffuse ISR (Type II–III)	2.78 (1.10–7.02)	0.031	2.54 (1.10–5.86)	0.028
LVEF <40%	2.45 (0.98–6.14)	0.055	2.20 (0.94–5.12)	0.068
Chronic kidney disease	2.10 (0.78–5.64)	0.140	–	NS
Age >65 years	1.62 (0.64–4.12)	0.309	–	NS

Discussion

In this prospective study, the angiographic profile and clinical outcomes after 6 months in patients undergoing repeat revascularization following multivessel PCI are described for 80 cases. Our results show that repeat revascularisation is still the most common method (57.5%), but the artery involved is the LAD. At 6 months, MACE had occurred in 17.5% of patients, and diabetes mellitus and diffuse ISR pattern were determined as independent predictors of adverse events. These data are consistent with—and extend—those of the increasing body of literature documenting the results of repeat revascularization in complex CAD. [1,2]

The mean age of 58.4 years, with a preponderance of males (76.25%), is in line with the known epidemiological pattern of CAD in the Indian population, which tends to present a decade earlier than its western counterparts. High prevalence of diabetes (55%) and hypertension (65%)

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highlights the metabolic environment which facilitates accelerated atherosclerosis and adverse post-PCI remodelling in South Asian patients. The relationship between diabetes and neointimal hyperplasia is confirmed, and insulin resistance has been shown to induce smooth muscle proliferation and compromised endothelial healing. [17]

The most common vessel to be targeted for repeat revascularization was the LAD (52.5%), similar to the results of the SYNTAX score registry and other large PCI registries, which show that the LAD is the vessel most likely to be the target of reintervention, because it has more extensive disease involvement and a larger myocardial territory at risk. ISR was determined to be the mechanism in 57.5% of cases, and Type I (focal) ISR was most prevalent (39.1% of ISR cases). This is a similar distribution to the registry data presented by Mehran et al., who have repeatedly found that the most common ISR pattern is focal, but that diffuse patterns have a significantly poorer prognosis. [14]

Newer-generation stent failure, non-compliance with dual antiplatelet therapy (DAPT), and anatomical high-risk features continue to be the problems related to ISR despite the significant drop in ISR rates during the DES era. [7,8]

The incidence of stent thrombosis (10%) was important in our group, and was always acute or subacute. Mechanical issues, such as incomplete strut apposition, dissection, and inadequate antiplatelet therapy, are typically associated with early stent thrombosis, whereas neoatherosclerosis and polymer hypersensitivity reactions are more closely associated with late stent thrombosis. In 4 of the 8 cases with stent thrombosis, DAPT was prematurely discontinued, similar to the PARIS registry, where non-compliance with APT was found to be the most preventable cause of late coronary events globally. [19]

The overall MACE rate of 17.5% at 6 months is somewhat higher than the rates noted in the randomised trials, but similar to the real-world registries. The rates of 6-month MACE reported in the DESERT registry for patients who had ISR undergoing repeat PCI ranged from 14–22%, depending on the type of ISR and the procedural modality. Outcome heterogeneity across studies is likely to be due to differences in comorbidity burden, baseline LVEF, and completeness of revascularization. [21]

Diabetes mellitus (OR 2.91, p=0.012) and diffuse ISR pattern (OR 2.54, p=0.028) were independent variables for predicting MACE on multivariate analysis. The proposed mechanisms of diabetes as a precipitating factor for restenosis and adverse cardiovascular events are well documented. Hyperglycaemia is a promoter of neointimal hyperplasia via endothelial dysfunction, up-regulation of inflammatory cytokines, and platelet hyperreactivity. There are worse outcome rates after repeat PCI for diffuse ISR (Mehran Type II–III) than for focal ISR, and higher rates of recurrence, probably because of the more aggressive biological substrate. Drug-coated balloons (DCB) have emerged as a useful tool for diffuse ISR, and the RIBS V trial has shown that DCB is also non-inferior to DES as a treatment for diffuse ISR. [22]

As in previous post-MI cohorts, reduced LVEF was a near predictor for MACE (p=0.068). It has become increasingly appreciated that incomplete revascularization, which is likely to be responsible for residual ischaemia-driven LV dysfunction, is a modifiable determinant of outcome in MVD. Complete trial STEMI demonstrated that complete staged revascularisation in STEMI with multivessel disease vs PCI culprit was associated with reduced CV death and MI, highlighting the importance of treating all haemodynamically significant lesions. [24]

Intravascular ultrasound (IVUS) or optical coherence tomography (OCT) are two intracoronary imaging techniques that, from a technical point of view, have the potential to optimise stent expansion when repeat revascularization is required in ISR and to identify the mechanism of ISR, thereby decreasing recurrent events. The use of PCI is still underutilized, however, in resource-limited areas. Additional physiological assessment with FFR or iFR during repeat catheterisation to evaluate the non-culprit vessel may further individualise revascularisation strategy and prevent unnecessary revascularisation. [12]

However, the following limitations of this study are noted: single-centre design, relatively small sample size, and a short follow-up period of 6 months. Data with longer follow-up should be used to assess the real-life effect of repeated revascularization on hard endpoints. However, because of the lack of systematic intracoronary imaging, it is difficult to interpret ISR cases mechanistically. Despite this, the results of this study are of value for the real-world setting in a tertiary care centre in South India and can identify clinically actionable predictors of adverse outcomes.

Conclusion

Repeat PCI for multivessel revascularization has high morbidity, with the 6-month MACE rate as 17.5%. The most prevalent angiographic finding is in-stent restenosis of the LAD artery. Diabetes mellitus and diffuse ISR pattern are both predictors of adverse outcomes independently of each other. The results highlight the importance of careful follow-up following PCI, the importance of prolonging dual antiplatelet therapy, aggressive management of risk factors,

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and the need to consider imaging-guided or physiology-guided repeat PCI interventions, especially in high-risk subgroups, including diabetic patients with diffuse ISR.

Limitations

This study has several limitations. It was conducted at a single tertiary care center with a relatively small sample size and a follow-up duration of only six months, which may limit the generalizability of the findings. In addition, intracoronary imaging techniques such as IVUS or OCT were not routinely performed, limiting detailed mechanistic evaluation of in-stent restenosis.

Recommendations

Patients with diabetes mellitus and diffuse in-stent restenosis should undergo closer clinical follow-up after repeat revascularization. Aggressive risk-factor modification, optimization of secondary prevention, and imaging-guided PCI should be considered whenever feasible. Future multicenter studies with larger sample sizes and longer follow-up are recommended to validate these findings.

Acknowledgement

The authors sincerely thank all study participants and the faculty, residents, nursing staff, and catheterization laboratory personnel of the Department of Cardiology, Government Medical College, Thiruvananthapuram, for their valuable support during this study.

List of abbreviations

CAD – Coronary artery disease
CABG – Coronary artery bypass grafting
DES – Drug-eluting stent
DAPT – Dual antiplatelet therapy
FFR – Fractional flow reserve
ISR – In-stent restenosis
IVUS – Intravascular ultrasound
LAD – Left anterior descending artery
LCx – Left circumflex artery
LM – Left main coronary artery
L**VEF** – Left ventricular ejection fraction
MACE – Major adverse cardiovascular events
MI – Myocardial infarction
MVD – Multivessel disease
NSTEMI – Non-ST-elevation myocardial infarction
OCT – Optical coherence tomography
PCI – Percutaneous coronary intervention
RCA – Right coronary artery
STEMI – ST-elevation myocardial infarction
TIMI – Thrombolysis in Myocardial Infarction
TVR – Target vessel revascularization

Funding

This research received no external funding.

Conflict of interest

The authors declare that they have no conflicts of interest.

Data availability

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Author contributions

T. Dharmatheja: Conceptualization, data collection, statistical analysis, manuscript drafting.
Lais Mohammad: Study supervision, methodology, manuscript review.
Mathew Iype: Study design, interpretation of results, critical revision.
Priya S: Data interpretation, manuscript editing, final approval.

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PUBLISHER DETAILS

Student's Journal of Health Research (SJHR)
(ISSN 2709-9997) Online
(ISSN 3006-1059) Print
Category: Non-Governmental & Non-profit Organization
Email: studentsjournal2020@gmail.com
WhatsApp: +256 775 434 261
Location: Scholar's Summit Nakigalala, P. O. Box 701432, Entebbe Uganda, East Africa