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Original Article

Association Between Diabetes Mellitus and In-Stent Restenosis at a Military Hospital in Jakarta

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Abstract

Background: In-Stent Restenosis (ISR) refers to the recurrence of luminal narrowing within the stented segment after Percutaneous Coronary Intervention (PCI) and continues to pose a clinical challenge, especially in individuals with Diabetes Mellitus (DM). Elevated blood glucose levels lead to endothelial injury, persistent inflammation, and excessive neointimal tissue growth, all of which increase the likelihood of ISR.

Methods: This research employed an analytical observational approach with a cross-sectional design and was conducted at a military hospital in Jakarta. Data were collected from the medical records of patients diagnosed with Coronary Artery Disease (CAD) who underwent PCI between January 2021 and December 2023. A total sampling method was applied to all patients who underwent PCI and had a clinically indicated follow-up coronary angiography during the study period, yielding 66 eligible patients. Bivariate analysis was performed using the Chi-square test, followed by multivariable logistic regression to adjust for relevant clinical covariates.

Results: Of the 66 patients included in this study, 44 (66.7%) were diagnosed with DM, and 44 (66.7%) had ISR. Bivariate analysis showed that DM was significantly associated with ISR (OR 4.08; 95% CI: 1.36–12.21; p = 0.0097). Multivariate analysis showed that poor glycemic control remained independently associated with ISR (OR 5.39; 95% CI: 1.04–27.84; p = 0.044), while diabetes status alone was no longer independently associated.

Conclusions: DM is associated with higher ISR after PCI, with poor glycemic control independently associated, underscoring the importance of optimized glycemic management.

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Introduction

Coronary Artery Disease (CAD) represents a major contributor to global morbidity and mortality, posing a substantial health burden across developing regions.[1-2] The disease results from atherosclerotic narrowing of the coronary arteries, leading to myocardial ischemia, infarction, and heart failure.[3] Advances in interventional cardiology, particularly the development of Percutaneous Coronary Intervention (PCI) with stent implantation, have significantly improved survival and reduced ischemic complications in CAD patients.[4-5] However, the long-term success of PCI is limited by the occurrence of In-Stent Restenosis (ISR), a complication that continues to challenge clinicians despite advances in stent design and pharmacotherapy.[6-8]

ISR is characterized by a reduction in the luminal diameter of the stented coronary segment, primarily driven by proliferative neointimal formation and remodeling processes within the vessel.[9-10] ISR can lead to recurrent angina, Myocardial Infarction (MI), and the need for repeat revascularization.[6,12] The pathological process is initiated by endothelial disruption during stent implantation, inducing a cascade of smooth muscle cell hyperproliferation, matrix deposition, and sustained inflammatory response.[8,13]

Among the various risk factors associated with ISR, DM plays a dominant role.[14-15] Diabetes Mellitus (DM) is characterized by chronic hyperglycemia that triggers endothelial dysfunction, oxidative stress, and inflammation, leading to accelerated atherosclerosis.[3,16] High glucose levels stimulate smooth muscle cell proliferation and impair endothelial regeneration, resulting in increased neointimal growth.[14,17] Poor glycemic control, long duration of diabetes, and coexisting metabolic abnormalities such as dyslipidemia and hypertension further increase the risk of restenosis.[19-20]

Globally, the prevalence of DM is increasing and is projected to reach 643 million cases by 2030, with the highest growth in developing nations such as Indonesia.[16,21] The *Riset Kesehatan Dasar* (Riskesdas, Basic Health Survey) 2023 reported that the proportion of individuals with diabetes in Indonesia reached 3.7%, and cardiovascular disease is consistently listed as a major cause of mortality nationwide.[21] The dual burden of CAD and DM poses a major challenge to cardiovascular health, particularly in high-risk populations such as the military community, which is exposed to lifestyle and stress-related risk factors that predispose to metabolic syndrome and atherosclerosis. Understanding this association is essential for improving post-PCI outcomes and guiding secondary prevention strategies. Therefore, this research was conducted to assess the association between DM, a metabolic risk factor, and the incidence of ISR among CAD patients who underwent PCI at a military hospital in Jakarta.

Methods

This study employed a cross-sectional observational design and was conducted at a military hospital in Jakarta. The study population comprised patients diagnosed with CAD who underwent PCI with stent placement between January 2021 and December 2023. All consecutive PCI patients who underwent follow-up coronary angiography during the study period were included using a total sampling approach, yielding 66 patients. Follow-up coronary angiography was performed based on clinical indications, such as recurrent symptoms or objective evidence of ischemia, and was not routinely conducted in all post-PCI patients. Data were extracted from hospital medical records, covering demographic information, clinical characteristics, and angiographic results.

The inclusion criteria consisted of adult patients (18–56 years) and older adult patients (>56 years) diagnosed with CAD, verified through coronary angiography with the result of significant coronary artery stenosis requiring PCI, as determined by the treating interventional cardiologist, who also had clinically indicated follow-up angiographic evaluation after their PCI procedure. All patients included in this study were military personnel (active or retired) treated at a military hospital. Patients were excluded if they had incomplete medical records, a prior history of Coronary Artery Bypass Graft (CABG), or documented chronic inflammatory disorders.[6,9-10]

DM was identified according to the diagnostic standards of the American Diabetes Association (ADA), which include fasting plasma glucose ≥126 mg/dL, random plasma glucose ≥200 mg/dL, or a known diagnosis requiring ongoing treatment. Glycemic control is classified as well-controlled or poorly controlled DM. Poorly-controlled DM was defined as Hemoglobin A1c (HbA1c) ≥7% and documented during follow-up.[16,18] Dyslipidemia was defined based on lipid profile abnormalities, including low-density lipoprotein cholesterol (LDL-C) ≥130 mg/dL, triglycerides ≥150 mg/dL, and/or high-density lipoprotein cholesterol

(HDL-C) <40 mg/dL in men or <50 mg/dL in women.[19] Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg on repeated measurements, or a documented history of hypertension requiring antihypertensive treatment.[22] ISR was defined as a reduction of ≥50% in the lumen diameter within the stent or up to 5 mm from its margins during clinically indicated follow-up angiography.[7-8,10]

The association between DM and ISR was assessed using the Chi-square statistical test. Multivariable logistic regression analysis was performed to evaluate the association between DM and ISR after adjustment for available clinical covariates. Results were reported as adjusted odds ratios with 95% confidence intervals. A p-value of less than 0.05 was considered statistically significant. Data processing was performed using IBM SPSS Statistics version 26.0. Ethical approval for the study was obtained from the Health Research Ethics Committee of the Faculty of Military Medicine, Universitas Pertahanan Republik Indonesia, and patient data were treated confidentially throughout the research.

Results

This study included 66 patients with CAD who underwent PCI. Among them, 44 patients (66.7%) had DM, while 22 patients (33.3%) were non-diabetic. The mean age of the study population was 62.7 ± 8.8 years (range 41–89 years). Most participants were male (52 patients; 78.8%), with females accounting for 14 patients (21.2%).

Hypertension was present in 42 patients (63.6%), and dyslipidemia was identified in 41 patients (62.1%). Regarding glycemic status, 24 patients (36.4%) had poorly controlled diabetes (HbA1c ≥7%), while 42 patients (63.6%) had well-controlled glycemic status. ISR was observed in 44 patients (66.7%), whereas 22 patients (33.3%) did not experience ISR. Baseline characteristics of the study population are summarized in Table 1.

Bivariate analysis showed that ISR occurred more frequently in patients with DM than in non-diabetic patients (77.3% vs 45.5%). DM was significantly associated with ISR (OR 4.08; 95% CI: 1.36–12.21; p = 0.0097). The distribution of ISR according to diabetes status is shown in Table 2.

Table 1. Characteristics of research subjects.

Characteristics	N (%)
Gender	
Male	52(78.8%)
Female	14(21.2%)
Age	
18-56	14(21.2%)
> 56	52(78.8%)
DM Status	
DM	44(66.7%)
Non-DM	22(33.3%)
ISR Incidence	
ISR	44(66.7%)
Non-ISR	22(33.3%)
Hypertension	
HT	42(63.6%)
Non-HT	24(36.4%)
Dyslipidemia	
Dyslipidemia	41(62.1%)
Non-Dyslipidemia	25(37.9%)
Glycemic Control	
Poorly-controlled	24(36.4%)
Well-controlled	42(63.6%)

DM: Diabetes Mellitus; HT: Hypertension; ISR: In-Stent Restenosis.

Table 2. Relationship of DM and ISR.

DM Status	ISR Incidence		Total	P-Value	OR (95% CI)
	ISR	Non-ISR			
DM	34(77.3%)	10(22.7%)	44(66.7%)	0.00974	4.08 (1.36–12.21)
Non-DM	10(45.5%)	12(54.5%)	22(33.3%)		

DM: Diabetes Mellitus; ISR: In-Stent Restenosis; OR: Odds Ratio.

Table 3. Multivariable analysis of factors associated with in-stent restenosis.

Characteristics	P-Value	OR (95% CI)
Gender		
Male	0.15137	3.02 (0.67-13.69)
Female		1.00
Age		
18-56	0.51123	0.60 (0.14-2.67)
> 56		1.00
DM Status		
DM	0.31265	1.95 (0.53-7.12)
Non-DM		1.00
Hypertension		
HT	0.85239	0.88 (0.22-3.49)
Non-HT		1.00
Dyslipidemia		
Dyslipidemia	0.46622	1.68 (0.41-6.82)
Non-Dyslipidemia		1.00
Glycemic Control		
Poorly-controlled	0.04441	5.39 (1.04-27.84)
Well-controlled		1.00

DM: Diabetes Mellitus; HT: Hypertension; ISR: In-Stent Restenosis; OR: Odds Ratio.

Multivariable logistic regression analysis was performed to evaluate factors independently associated with ISR. After adjustment for age, sex, hypertension, dyslipidemia, and diabetes status, poor glycemic control remained independently associated with ISR (OR 5.39; 95% CI: 1.04–27.84; p = 0.044). DM status alone, as well as age, sex, hypertension, and dyslipidemia, were not independently associated with ISR in the multivariable model. The results of the multivariable analysis are presented in Table 3.

Discussion

This study demonstrates a significant association between DM and the occurrence of ISR among patients with CAD undergoing PCI. The bivariate analysis showed that patients with diabetes had approximately fourfold higher odds of developing ISR compared with non-diabetic patients. This finding is consistent with previous studies identifying DM as a major risk factor for restenosis after PCI.[6,8,14-15]

The underlying mechanisms linking DM and ISR are multifactorial. Chronic hyperglycemia induces endothelial dysfunction through oxidative stress, increased production of reactive oxygen species, and persistent inflammatory activation.[3,14] These processes stimulate vascular smooth muscle cell proliferation and extracellular matrix deposition, leading to excessive neointimal hyperplasia within the stented segment.[8,14-15] Additionally, insulin resistance, platelet hyperreactivity, and impaired fibrinolysis in diabetic patients further contribute to luminal re-narrowing after PCI.[12,15]

In the present study, multivariable analysis demonstrated that poor glycemic control (HbA1c ≥7%) remained independently associated with ISR, while diabetes status alone was no longer significant after adjustment. This suggests that the degree of metabolic control plays a more critical role in the development of restenosis than the presence of DM itself. Similar findings were reported by Marfella et al., who showed that elevated HbA1c levels were significantly associated with recurrent restenosis after PCI in patients with type 2 diabetes.[17] Poor glycemic control is known to perpetuate endothelial injury, impair vascular healing, and maintain a pro-inflammatory and pro-proliferative vascular environment, even in patients treated with drug-eluting stents.[8,14,17]

The overall ISR incidence in this study (66.7%) was higher than that reported in many international studies, which generally range between 10–20%.[7-8,11] This discrepancy may be explained by clinically driven follow-up angiography, the relatively small sample size, and the high prevalence of cardiometabolic risk factors in the study population. The exclusive inclusion of military personnel may also contribute, as occupational stress and lifestyle factors in this population have been associated with increased cardiovascular and metabolic risk.[21]

Several limitations should be acknowledged. Important confounders such as smoking status, body mass index, duration of diabetes, medication use (including statins and antidiabetic agents), and stent-related characteristics were not consistently available. Additionally, follow-up angiography was performed based on clinical indications, which may have introduced selection bias and overestimation of ISR incidence. Despite these limitations, the findings reinforce the importance of optimal glycemic control as a key strategy to reduce ISR in patients with diabetes undergoing PCI.

Conclusion

This study demonstrates that DM is significantly associated with the occurrence of ISR among patients with CAD who underwent PCI at a military hospital in Jakarta. Bivariate analysis showed that patients with diabetes had higher odds of ISR compared with non-diabetic patients. However, after multivariable adjustment, poor glycemic control (HbA1c ≥7%), rather than diabetes status alone, remained independently associated with ISR. These findings indicate that the degree of glycemic control plays a more critical role in the development of ISR than the mere presence of DM.

Optimized glycemic control should be emphasized in patients with DM undergoing PCI, as poor glycemic status is independently associated with ISR. Further studies are needed to address limitations related to small sample size, smoking status, Body Mass Index (BMI), and the unavailability of data on stent characteristics, medication use, and the timing of ISR.

List of Abbreviations

ADA	American Diabetes Association
BMI	Body Mass Index
CABG	Coronary Artery Bypass Graft
CAD	Coronary Artery Disease
DM	Diabetes Mellitus
HbA1c	Hemoglobin A1c
HDL-C	High-Density Lipoprotein Cholesterol
ISR	In-Stent Restenosis
LDL-C	Low-Density Lipoprotein Cholesterol
MI	Myocardial Infarction
OR	Odds Ratio
PCI	Percutaneous Coronary Intervention
Riskesdas	Basic Health Survey

Ethical Clearance

Ethical approval for the study was obtained from the Health Research Ethics Committee of the Faculty of Military Medicine, Universitas Pertahanan Republik Indonesia, and patient data were treated confidentially throughout the research.

Publication Approval

All authors consent to the publication of this manuscript.

Authors' Contributions

AFHH did the conception and design of the study, acquisition of data, statistical analysis, interpretation of the data, drafting the manuscript, and revising the manuscript critically for important intellectual content. TH and AHP did the conception and design of the study, interpretation of the data, and revised the manuscript critically for important intellectual content.

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Conflict of Interest

None.

Availability of Data and Materials

Not applicable.

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Generative AI and AI-Assisted Technologies in the Writing Process

The authors acknowledge that ChatGPT Plus was used solely to assist with language editing, grammar correction, and improving the clarity of the manuscript. The AI tool was not used to generate or modify the scientific content, study design, data collection, data analysis, interpretation of the findings, or conclusions. All scientific content was reviewed, verified, and approved by the authors, who take full responsibility for the final manuscript.

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