INPLASY PROTOCOL

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None declared.

Coronary In-Stent Restenosis Predictors following Drug-Eluting Stent Implantation: A Meta-analysis Study

Rohman, MS[1]; Waranugraha, Y[2]; Masbuchin, AN[3]; Baskoro, SS[4]; Sishartami, LW[5]; Pratiwi, BB[6].

Review question / Objective: **What is the predictors of In-Stent Restenosis in patients after six month DES implantation?**
Condition being studied: **Restenosis is described as a narrowing of the lumen diameter after a successful percutaneous coronary intervention (PCI) procedure with or without stent insertion. In-stent restenosis (ISR) is still defined as stenosis of more than 50% of the artery lumen diameter as assessed by coronary angiography within the stented segment or its edge (5-mm segments next to the stent). The use of a drug-eluting stent (DES) for any PCI is now recommended by the latest European Society of Cardiology/ European Association of Cardiothoracic Society guideline. Despite the fact that the prevalence of restenosis in DES was significantly reduced, ISR remained a challenge for post-PCI management. According to a large cohort study, DES-ISR affects approximately 10% of the population.**
Factors that play the essential role in the development of ISR can be classified into four main groups: (1) biological; (2) arterial; (3) stent; and (4) implantation factors. The last three factors can be modified.5 Currently, numerous studies have investigated predictors of restenosis in first-generation DES, but only a few have investigated second-generation DES.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 May 2023 and was last updated on 24 May 2023 (registration number INPLASY202350092).

INTRODUCTION

Review question / Objective: **What is the predictors of In-Stent Restenosis in patients after six month DES implantation?**

Rationale: **Despite prevalence of restenosis in DES was significantly reduced, In-Stent Restenosis (ISR) remains challenge for post-PCI management. The predictors are**

inconsistent. Therefore we conduct this meta-analysis to systematically find the predictors of ISR among DES-implanted patients.

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Factors that play the essential role in the development of ISR can be classified into four main groups: (1) biological; (2) arterial; (3) stent; and (4) implantation factors. The last three factors can be modified.5 Currently, numerous studies have investigated predictors of restenosis in first-generation DES, but only a few have investigated second-generation DES.

METHODS

Search strategy: We conducted an article search from electronic scientific databases (Embase, ProQuest, PubMed, ClinicalTrials.gov, and CENTRAL) regarding coronary ISR following a successful DES implantation procedure using these following keywords: "coronary artery disease" OR "CAD," AND "In-stent restenosis" OR "stent restenosis" OR "ISR," AND "drug-eluting stent" OR "DES," AND "risk factor" OR "predicting factor" OR "predictor." Duplicate results were also eliminated. Three investigators conducted the literature search, which was completed on February 15th, 2021.

Participant or population: Patients who underwent second generation of Drug Eluting Stent implantation in coronary artery after at least six months.

Intervention: Second generation of Drug-Eluting stent implantation.

Comparator: (not applicable) There was no intervention comparation. We compare the outcomes which are ISR vs non-ISR events.

Study designs to be included: The included studies were randomized controlled trial and/or cohort studies.

Eligibility criteria: The inclusion criteria of included studies were: (1) randomized controlled trial (RCT) or cohort study and (2) included CAD patients undergoing PCI with DES implantation followed by assessment of restenosis for a minimum of 6 months. We excluded the articles with the following criteria: (1) duplications; (2) non-original research article; (3) written in non-English language; (4) non-coronary ISR; (5) non-DES implantation; (6) unclear ISR definition; (7) unreported follow-up duration; and (8) low quality study. The study selection process was completed by three investigators.

Information sources: We conducted an article search from electronic scientific databases (Embase, ProQuest, PubMed, ClinicalTrials.gov, and CENTRAL) regarding coronary ISR following a successful DES implantation procedure using these following keywords: "coronary artery disease" OR "CAD," AND "In-stent restenosis" OR "stent restenosis" OR "ISR," AND "drug-eluting stent" OR "DES," AND "risk factor" OR "predicting factor" OR "predictor." Duplicate results were also eliminated. Three investigators conducted the literature search, which was completed on February 15th, 2021.

Main outcome(s): We have 17 outcomes (Alcohol consumption, bifurcation lesion, complex lesion, diabetes mellitus, dyslipidemia, familiy history, hypertension, male gender, multivessel diseases, smoking, stent type (limus-eluting stent),

target vessel (LAD), age, BMI, stent diameter, stent length) to be evaluated as predictors of ISR in population receiving DES.

Quality assessment / Risk of bias analysis: We asses the quality of primary studies using JADAD score for RCT studies and New castel-Ottawa scores for cohort studies.

Strategy of data synthesis: We performed statistical analysis using Comprehensive Meta-Analysis version 3.0 and Review Manager version 5.4. The p-value of heterogeneity (pHet) of <0.1 indicated the presence of heterogeneity. The fixed-effects model was used in the absence of heterogeneity. On the other hand, the random-effect model was used in the absence of heterogeneity.11 The Egger's test was performed to assess the small-study effect bias.12 The pooled odds ratio (OR) and 95% confidence interval (CI) for categorical data were calculated using the Mantel–Haenszel statistical method. The pooled mean difference (MD) and 95% CI for continuous data were determined using the inverse variance statistical method. The statistical analysis process was completed by three investigators.

Subgroup analysis: If the study found to be statistically significant in the heterogeneity, we would perform subgroup analysis.

Sensitivity analysis: If possible, the sensitivity analsysis is performed to measure the analysis robustness.

Language restriction: English-only literature.

Country(ies) involved: Indonesia.

Keywords: in-stent restenosis, drug eluting stent, predictors, coronary artery disease.

Contributions of each author:

Author 1 - Mohammad Saifur Rohman: Conceptualization, study quality assessment, data interpretation, writing-review and editing, and supervising.

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Author 5 - Lintang Widya Sishartami: literature search, data extraction, and writing-original draft.

Author 6 - Bunga Bella Pratiwi: literature search, data extraction, and writing-original draft.