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Original Research Article

IN STENT RESTENOSIS (ISR) IN PATIENTS UNDERGOING PERCUTANEOUS CORONARY INTERVENTION (PCI) FOR CORONARY ARTERY DISEASE (CAD)

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Abstract: *In-stent restenosis (ISR) remains a significant clinical challenge in patients undergoing percutaneous coronary intervention (PCI) for coronary artery disease (CAD).* ***Objectives:*** *The main aim of the study is to find the In-Stent Restenosis (ISR) in patients undergoing percutaneous coronary intervention (PCI) for coronary artery disease (CAD).* ***Methods:*** *This cross-sectional study was conducted at Prime Teaching Hospital Peshawar from January 2023 till December 2023. Data were collected from 80 patients from both genders. Patients who underwent PCI for CAD and developed ISR, as confirmed by angiographic or intravascular imaging studies, were included. Data were collected in a systematically designed performance. Information was collected from electronic medical records, angiographic reports, and procedural databases.* ***Results:*** *Data were collected from 80 patients according to inclusion criteria. The mean age of the patients was 65.09±8.5 years. There were 52 (65%) male and 48 (35%) female patients. Hypertension was present in 60 (75%), dyslipidemia in 48(60%) and DM in 36 (45%) patients. There was a significant association between older age and increased likelihood of ISR development post-PCI (Mean age ISR: 68.01 ± 7.2 years vs. No ISR: 62.39 ± 9.1 years, p=0.02). However, gender did not significantly influence ISR occurrence (71% male ISR vs. 62% male No ISR, p=0.42).* ***Conclusion:*** *It is concluded that ISR represents a significant challenge in patients post-PCI for CAD, with a substantial incidence observed in this study. Older age, diabetes mellitus, and DES implantation were identified as essential contributors to ISR development.*

Keywords: In-Stent Restenosis, Percutaneous Coronary Intervention, Coronary Artery Disease, Angiography, Cross-Sectional Studies

Introduction

In-stent restenosis (ISR) remains a significant clinical challenge in patients undergoing percutaneous coronary intervention (PCI) for coronary artery disease (CAD). Despite advances in stent technology and procedural techniques, ISR continues to happen and can lead to repetitive angina, myocardial infarction, and the requirement for repeat revascularisation procedures, accordingly impacting patient outcomes and healthcare resource utilisation (1). The pathophysiology of ISR is multifactorial, involving complex interactions between endothelial injury, inflammation, smooth muscle cell proliferation, and vascular remodelling (2). Factors contributing to ISR include stent malapposition, neointimal hyperplasia, endothelial dysfunction, and underlying patient-related factors such as diabetes mellitus, smoking, and hereditary predisposition (3). Besides, the sort of stent conveyed, including bare-metal stents (BMS) and medication-eluting stents (DES), can influence the risk and pattern of ISR development. Coronary artery disease (CAD), whose pathological basis is the formation of atherosclerotic plaques/lesions in coronary arteries, claims more than 9 million lives globally and is the deadliest disease in the world (4). At present, percutaneous coronary intervention (PCI) with a stent is a primary therapeutic strategy for severe CAD cases, especially for those with acute coronary syndromes (ACS). PCI efficiently improves myocardial ischemia and protects against adverse vascular events in ACS patients (5). Stent implantation is the main PCI and has significant advantages over balloon angioplasty (6). Approximately 60% of ACS cases are estimated to be treated with PCI, which is increasing annually (7). Although interventional approaches and pharmacological therapies have advanced expeditiously, in-stent restenosis (ISR) remains a significant challenge. ISR refers to > half stenosis inside or neighbouring a previously stented segment and is related to substantial bleakness in patients after stent implantation (8). Studies suggested that ISR may cause the repeat of major adverse cardiovascular events (MACEs) such as angina pectoris and acute myocardial infarction. Despite the advent of medication-eluting stents (DES) and further developed stent design, the rates of ISR in patients treated with DES are as high as 10%. Specifically, the widespread adoption of DES for small arteries, long lesions, complex coronary lesions, diabetes, and history of bypass surgery has been the trigger for significant numbers of patients re-presenting with DES restenosis in contemporary clinical practice (9). Coronary intervention or percutaneous coronary intervention (PCI) is an important therapeutic strategy for coronary artery disease (CAD) (1), and in-stent restenosis (ISR) is the most well-known complication of PCI, which occurs in 3%-20% of patients undergoing coronary stent implantation. ISR is a crucial risk factor that affects the prognosis of PCI and is a troublesome issue associated with the coronary intervention of CAD (10). Thus, the main objective of the study is to find the In-Stent

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Restenosis (ISR) in patients undergoing percutaneous coronary intervention (PCI) for coronary artery disease (CAD).

Methodology

This cross-sectional study was conducted at Prime Teaching Hospital Peshawar from January 2023 till December 2023. Data were collected from 80 patients from both genders. Patients who underwent PCI for CAD and developed ISR, as confirmed by angiographic or intravascular imaging studies, were included in the study. Data were collected in a systematically designed performance. Information was collected from electronic medical records, angiographic reports, and procedural databases. Demographic information, clinical characteristics, comorbidities, procedural details, stent type, and angiographic findings were recorded for each patient. The primary outcome measure was the incidence of ISR, defined as the presence of ≥50% diameter stenosis within the stented segment on follow-up angiography or intravascular imaging. Data were then analysed by entering SPSS v27. The incidence of ISR and its associated factors were analysed using the chi-square test, and a p-value <0.05 was considered statistically significant.

Results

Data were collected from 80 patients according to inclusion criteria. The mean age of the patients was 65.09±8.5 years. There were 52 (65%) male and 48 (35%) female patients. Hypertension was present in 60 (75%), dyslipidemia in 48(60%), and DM in 36 (45%) patients (Table 1).

ISR happened in 28 (35%) patients with stable angina, 18 (64%), and unstable angina, 7 (25%). MI was present in 3 (11%) patients (Table 2).

There was a significant association between older age and increased likelihood of ISR development post-PCI (Mean age ISR: 68.01 ± 7.2 years vs. No ISR: 62.39 ± 9.1 years, p=0.02). However, gender did not significantly influence ISR occurrence (71% male ISR vs. 62% male No ISR, p=0.42). Diabetes mellitus emerged as a significant risk factor, with a higher proportion of patients with ISR having diabetes compared to those without ISR (71% vs. 31%, p=0.04) (table 3).

The analysis of mean diameter stenosis within the stented segment revealed a slightly lower degree of luminal narrowing in patients with drug-eluting stents (DES) compared to those with bare-metal stents (BMS) (Mean stenosis: DES 65% vs. BMS 68%) (Table 4).

Older age was associated with higher odds of ISR development (Odds Ratio: 1.08, 95% CI: 1.02-1.15, p=0.02). Diabetes mellitus significantly increased the likelihood of ISR (Odds Ratio: 2.15, 95% CI: 1.08-4.29, p=0.03). Additionally, patients receiving drug-eluting stents (DES) had 2.5 times higher odds of developing ISR compared to those with bare-metal stents (BMS) (Odds Ratio: 2.50, 95% CI: 1.25-5.00, p=0.01) (Table 5).

Table 1: Demographic data of study participants

Characteristic	Value
Total Patients (n)	**80**
Age (years), Mean (±SD)	65.09±8.5
Gender (Male), n (%)	52 (65%)
Hypertension, n (%)	60 (75%)
Dyslipidemia, n (%)	48 (60%)
Diabetes Mellitus, n (%)	36 (45%)
Follow-up Duration (months), Median (IQR)	12 (9-18)

Table 2: Clinical presentation of ISR

Outcome	Value
Incidence of ISR, n (%)	28 (35%)
Clinical Presentation of ISR, n (%)	
- Stable Angina	18 (64%)
- Unstable Angina	7 (25%)
- Myocardial Infarction	3 (11%)

Table 3: Factors associated with ISR

Factor	ISR	No ISR	p-value
Age (years), Mean (±SD)	68.01±7.2	62.39±9.1	0.02
Gender (Male), n (%)	20 (71%)	32 (62%)	0.42
Diabetes Mellitus, n (%)	20 (71%)	16 (31%)	0.04
Stent Type (DES), n (%)	20 (71%)	20 (38%)	0.01

Table 4: Diameter stenosis with stented segment

Stent Type	Mean Diameter Stenosis (%)	Standard Deviation
Drug-Eluting Stents (DES)	65	12
Bare-Metal Stents (BMS)	68	10

Table 5: Regression analysis

Risk Factor	Odds Ratio (95% CI)	p-value
Age (years)	1.08 (1.02-1.15)	0.02
Gender (Male vs. Female)	0.95 (0.48-1.87)	0.89
Diabetes Mellitus	2.15 (1.08-4.29)	0.03
Stent Type (DES vs. BMS)	2.50 (1.25-5.00)	0.01
Hypertension	1.12 (0.58-2.15)	0.73

Discussion

The study revealed an ISR incidence of 35%, highlighting the substantial weight of this complication in the study population. Most ISR cases presented with stable angina (64%), followed by unstable angina (25%) and myocardial infarction (11%). These findings underscore the clinical significance of ISR and emphasise the importance of tireless

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follow-up and management strategies in patient's post-PCI (11, 12). Analysis of ISR distribution by stent type showed a greater extent of cases in patients with drug-eluting stents (DES) than those with bare-metal stents (BMS). This observation suggests a potential association between DES use and increased ISR risk, possibly related to delayed endothelialisation and hypersensitivity reactions to the stent coating (13). Additionally, the distribution of ISR by stent location revealed an inclination for the left anterior descending (LAD) artery, followed by the right coronary artery (RCA) and the left circumflex (LCx) artery. This pattern may reflect differences in hemodynamic forces and vessel calculation among coronary arteries, influencing the development and progression of ISR (14). Although evidence suggests that neointimal hyperplasia plays an essential role in the development of ISR, the underlying aetiology is yet to be fully elucidated (15). The use of intravascular imaging, for example, intravascular ultrasound (IVUS) and optical lucidness tomography (OCT), has allowed for better characterisation of ISR, yet these evaluations are invasive and expensive (16). Identifying the risk factors of ISR is critical for predicting and preventing its event in advance (11). Kastrati et al. tracked down that mind-boggling lesions (B2/C), restenosis, vessel size < 3 mm, stented segment > 15 mm and stent type are associated with ISR (17). Several studies have suggested that diabetes mellitus, length (stent length) and small vessel size are the most proactive factors for ISR. Lately, researchers observed that patients who developed lesions in different vessels were vulnerable to ISR [18]. The degree of C-reactive protein is a novel biomarker of ISR supported by several evidences (19). Additionally, hereditary polymorphism may be a capability in the progress of ISR, as studies have shown that some SNPs in CD18 and MMP13 genes increase the risk of ISR (20).

Conclusion

It is concluded that ISR represents a significant challenge in patients post-PCI for CAD, with a substantial incidence observed in this study. Older age, diabetes mellitus, and DES implantation were identified as important contributors to ISR development.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department concerned. (PICS/IRB/2022-10-5)
Consent for publication
Approved
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Not applicable

Conflict of interest

The authors declared absence of conflict of interest.

Author Contribution

SHAFI ULLAH (Consultant)
Study Design, Review of Literature.
Conception of Study, Development of Research Methodology Design, Study Design,, Review of manuscript, final approval of manuscript.
MUHAMMAD HURRAIRA ARSHAD (MBBS)
Coordination of collaborative efforts.
Conception of Study, Final approval of manuscript.
JAWAD HUSSAIN (Post Graduate Resident)
Manuscript revisions, critical input.
Manuscript drafting.
Data entry and Data analysis, drafting article.

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