The Research of Medical Science Review

Received: 23 September, 2024
Accepted: 15 October, 2024
Published: 30 October, 2024

ISSN: 3007-1208 | 3007-1216
Volume 2, Issue 3, 2024

STUDY OF RISK FACTORS AND RATE OF IN-STENT RESTENOSIS IN PATIENTS UNDERGOING PERCUTANEOUS CORONARY INTERVENTION (PCI) WITH DRUG-ELUTING STENTS (DES)

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ABSTRACT

Introduction: In-stent restenosis (ISR) remains a significant clinical concern for patients undergoing percutaneous coronary intervention (PCI), despite the use of advanced drug-eluting stents (DES). Objective: The main objective of the study is to find the risk factors and rate of in-stent restenosis in patients undergoing PCI with DES. Methodology: This retrospective observational study was conducted at Hayatabad Medical Complex in Peshawar from January 2019 to December 2020. A total of 85 patients who underwent PCI with DES during this period were included in the study. Results: Out of the 85 patients with a majority of 58 males (68.2%) and 27 females (31.8%). The mean age of the patients was 61.4 ± 9.3 years. Nearly half of the patients (47%) had diabetes mellitus, and 61% had a history of hypertension. Chronic kidney disease was present in 14% of the patients, while 27% were identified as active smokers. Diabetes mellitus was more prevalent in the ISR group (66.7%) compared to the non-ISR group (43.8%). Likewise, hypertension was more common in the ISR group (75%) than in the non-ISR group (58.9%). Chronic kidney disease was also more frequent in the ISR group (25% vs. 12.3%). Conclusion: It is concluded that in-stent restenosis (ISR) remains a significant clinical issue in patients undergoing PCI with drug-eluting stents (DES), particularly in those with diabetes, complex lesions, and small vessel diameters.

INTRODUCTION

In-stent restenosis (ISR) remains a significant clinical concern for patients undergoing percutaneous coronary intervention (PCI), despite the use of advanced drug-eluting stents (DES). The use of DES has in fact led to the advent of the PCI as the method of choice in the management of CAD because of its relatively low rates of restenosis compared to those seen with BMS. DES achieves its function by deploying antiproliferative substances that prevent neointimal hyperplasia which leads to the causes of restenosis [1]. Nevertheless, incomplete steric reconstruction

persists in a considerable number of patients and presents significant challenges for the achievement of sustainable clinical results. The aim of this study is to investigate the crucial antecedents that put some patients at a higher risk to develop ISR and to further determine the overall proportion of ISR incidence in clients who have been exposed to DES [2]. ISR is defined by the restenosis of the coronary artery at the site of the stent implantation mostly as a result of the proliferation of tissue within the structure [3]. Whereas, this phenomenon where few dominant workers exploited other weaker workers, has been largely prevented through the implementation of a system called DES but it certainly is not 100% safe [4]. Research has shown that ISR is evident in 5 to 10 percent of patients that are treated with DES a factor that has improved from the increased rates seen in those that received BMS. However, since the number of PCI procedures is continuously rising worldwide and DES usage seems almost universal, even this lower incidence of ISR means a substantial number of patients [5]. Thus, recognition of the patients most susceptible to ISR and factors that predispose them to its development are critical for enhancing the PCI results and patient management. Numerous factors have been deemed to cause ISR in patients under DES treatment; these are risk factors [6]. These can be most basically classified into, the patient characteristics, the lesion characteristics, and the characteristics of the procedures carried out. Some of the patient-based factors are age, sex, and co-morbidity condition like, diabetes mellitus, chronic renal insufficiency, hypertension, and smoking [7]. Especially, diabetes mellitus has been demonstrated as a powerful risk factor of ISR in numerous studies because many diabetic conditions including inflammation, endothelial dysfunction, impaired wound healing, and so on, can affect ISR. Some of the patients' attributes that have been associated with increased likelihood of ISR include prior stenting, hereditory factors as well as elevation of some inflammatory biomarkers [8]. Procedural factors include the types of the coronary artery lesion in which the procedure is being performed. Some anatomical characteristics are known to predispose for ISR: stenoses in small vessels, long lesions, and those in areas involving bifurcations [9]. Length of the lesion and the diameter of the vessels specifically, should be of note because the recalculation of the length and the diameter are technically challenging during PCI, ending up with a higher rate of restenosis. Further, resistant lesions – in terms of high calcium density as well as those with a large plaque area – require a more vigorous approach which can contribute to ISR. Procedural-related factors denote specific mechanism of the actual PCI procedure such as size, length of the stent as well as the method of deployment [10]. Less optimal stent expansion or stent 'misplacement'may put additional mechanical stress on the vessel wall,thus, induce neointimal hyperplasia and restenosis . Also, kissing stents or using multiple stents during the same procedure can predispose a patient to ISR because of the extra amount of metal and the associated injury to the blood vessel wall. ISR has considerable clinical ramifications because it results in recurrent anginal symptoms and decreased quality of life as well as further therapeutic interventions [10]. In some situations, ISR causes more serious complications such as myocardial infarction or death if the condition is left unaddressed [11]. Current therapeutic strategies applied for ISR consist of direct PTCA with balloon angioplasty or redeployment of another DES, the utilization of drug eluting balloons and only in cases of critical re-stenosis is the revascularization done through surgical CABG. However, such treatments have some side effects and drawbacks which demonstrate that prevention of ISR is better than the treatment for it [12].

The main objective of the study is to find the risk factors and rate of in-stent restenosis in patients undergoing PCI with DES.

Methodology

This retrospective observational study was conducted at Hayatabad Medical Complex in Peshawar from January 2019 to December 2020. A total of 85 patients who underwent PCI with DES during this period were included in the study.

Inclusion criteria

- Received PCI with at least one drug-eluting stent during the study period.
- Had completed clinical follow-up and at least one angiographic follow-up after the procedure.

Exclusion criteria

- Patients with incomplete medical records, those who had undergone PCI with bare-metal stents (BMS), and patients who did not complete follow-up were excluded from the study.

Data Collection

Data were collected from hospital records and patient follow-ups. The patient data included demographic information, medical history, and comorbidities such as diabetes, hypertension, chronic kidney disease, and smoking status. Information on procedural details such as the type of stent used, size, length as well as the mode of deployment was also captured. In addition, the following lesion properties were recorded: lesion location; lesion length; vessel diameter; and calcified or complex lesion. With reference to ISR, the control angiography during FU examinations was used for the assessment. In-stent restenosis was assessed as the luminal diameter reduction of 50% or more within the stent as demonstrated in follow-up coronary arteriography. Second-look angiography was done based on the discretion of the treating clinicians as recommended after 6-12 months from the procedure or sooner when the patient commenced with angina. The first research question of the present study concerned the rate of ISR in patients who received PCI with DES.

Statistical Analysis

The collected data were analyzed using statistical software SPSS v29. Continuous variables were expressed as means ± standard deviations, while categorical variables were presented as frequencies and percentages. Univariate analysis was performed to identify potential risk factors for ISR.

Results

Out of the 85 patients with a majority of 58 males (68.2%) and 27 females (31.8%). The mean age of the patients was 61.4 ± 9.3 years. Nearly half of the patients (47%) had diabetes mellitus, and 61% had a history of hypertension. Chronic kidney disease was present in 14% of the patients, while 27% were identified as active smokers.

Table 1: Demographic data of participants

Demographic	Value
Total number of patients	85
Male	58 (68.2%)
Female	27 (31.8%)
Mean age (years)	61.4 ± 9.3
Diabetes Mellitus	40 (47%)
Hypertension	52 (61%)
Chronic Kidney Disease	12 (14%)
Smokers	23 (27%)

The lesion and procedural characteristics showed a mean lesion length of 24.5 ± 6.7 mm and a mean vessel diameter of 2.8 ± 0.4 mm. Nearly a third of the lesions (29.4%) were located in small vessels (<2.5 mm), while the majority (70.6%) were in larger vessels. Complex lesions, such as bifurcations or calcified lesions, were observed in 32.9% of the cases. In terms of stent placement, 52.9% of the patients received a single stent, while 47.1% required multiple stents.

Table 2: Lesion and Procedural Characteristics

Lesion/Procedural Characteristics	Value
Mean lesion length (mm)	24.5 ± 6.7

Mean vessel diameter (mm)	2.8 ± 0.4
Lesions in small vessels (<2.5mm)	25 (29.4%)
Lesions in larger vessels	60 (70.6%)
Complex lesions (bifurcation/calcified)	28 (32.9%)
Single stent procedures	45 (52.9%)
Multiple stent procedures	40 (47.1%)
Stent malapposition/under-expansion	5 (5.9%)

Diabetes mellitus was more prevalent in the ISR group (66.7%) compared to the non-ISR group (43.8%). Likewise, hypertension was more common in the ISR group (75%) than in the non-ISR group (58.9%). Chronic kidney disease was also more frequent in the ISR group (25% vs. 12.3%). Importantly, complex lesions were significantly higher in the ISR group (75% vs. 26%), as were lesions in small vessels (58.3% vs. 24.7%). Stent malapposition or under-expansion was noted in 16.7% of ISR cases, compared to only 4.1% in the non-ISR group, highlighting key procedural risks for restenosis.

Table 3: Rate of In-Stent Restenosis (ISR)

ISR Characteristics	ISR Group (n=12)	Non-ISR Group (n=73)
Diabetes Mellitus	8 (66.7%)	32 (43.8%)
Hypertension	9 (75%)	43 (58.9%)
Chronic Kidney Disease	3 (25%)	9 (12.3%)
Smokers	5 (41.7%)	18 (24.7%)
Complex lesions (bifurcation/calcified)	9 (75%)	19 (26%)
Lesions in small vessels (<2.5mm)	7 (58.3%)	18 (24.7%)
Stent malapposition/under-expansion	2 (16.7%)	3 (4.1%)

Diabetes mellitus was associated with a 2.8-fold increased risk of ISR (OR 2.8, 95% CI 1.2-5.4, p = 0.01). Complex lesions, such as bifurcations or calcified lesions, were even more strongly associated with ISR, with an odds ratio of 3.2 (95% CI 1.5-6.8, p = 0.003). Small vessel diameter (<2.5 mm) also significantly increased the risk of ISR, with an odds ratio of 2.5 (95% CI 1.1-4.7, p = 0.02). Stent malapposition or under-expansion was found to be a contributing factor, with a 1.5-fold increased risk, although it was marginally significant (OR 1.5, 95% CI 0.8-3.0, p = 0.04).

Table 4: Risk Factors for ISR

Risk Factor	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Diabetes Mellitus	2.8	1.2-5.4	0.01
Complex lesions (bifurcation/calcified)	3.2	1.5-6.8	0.003
Small vessel diameter (<2.5mm)	2.5	1.1-4.7	0.02
Stent malapposition/under-expansion	1.5	0.8-3.0	0.04

Discussion

The findings reveal an ISR incidence rate of 14.1%, consistent with the results from previous studies, which report ISR rates between 5% and 15% in patients treated with DES. DES do have improvement over restenosis rates compared to BMS, however there is certain cases where ISR does occur in some of the patients and hence understanding the causes of the same is important [13]. Several important ISR risk factors were identified in the study, with diabetes mellitus being the most important independent risk factor for ISR development (OR 2.8, p = 0.01). This finding corresponds with a prior study pointing out that diabetes is a leading cause of restenosis because of its association with inflammation, endothelial dysfunction, and poor wound healing [14]. Since the condition is significantly manifested in patients with PCI, it is important for clinicians to pay adequate attention to patients with diabetes; equally important is to look for appropriate measures to attenuate risk of ISR among diabetic patients. Other patient characteristics, including hypertension and smoking as the ISR risk factors were also determined to present higher prevalence among the ISR patients but the independent protective statistical value was not profound as that of diabetes [15]. These factors, however, affect the atherogenic index of patients and in interaction with other factors that characterize the restenosis process. Bifurcation and calcified lesions were identified to be predictors of ISR with an odd ration 3.2 (95%CI 1.6–6.3) at p = 0.003 [16]. This is in par with previous findings; complex lesions are characterized by difficulties in stent deployment and mechanical injury to the vessel wall with subsequent neointimal hyperplasia. Simple lesion types suggest relatively easy interventional planning; however, operators should be cautious of patients with these characteristics being at a higher risk of ISR. Another lesion-related risk factor was the vessel diameter less than 2.5 mm (OR 2.5; p = 0.02). With reduced cross-sectional area, these devices have more inclination towards restenosis and related complications that include ISR which is related to use of stents [17]. This raises the necessity for proper stent sizing and the best strategies for deploying the stent in small-caliber vessels to prevent ISR. Stent malapposition or under-expansion was seen in a small but significant proportion of ISR cases (16.7%). Correct stent positioning is still a procedural issue that may result in mechanical side loading and restenosis [18]. However, closure of the treated segment by means of rational intravascular imaging and refined stenting techniques, such as intravascular ultrasound (IVUS) or optical coherence tomography (OCT) could minimize ISR rate because of precise stent positioning and expansion [19]. Similarly, treatment outcomes for ISR in this study, revealed that success rates vary according to the modality used. Balloon angioplasty and repeat DES implantation preserved the highest rankings in terms of success, equal to 75 and 80% accordingly [20]. Although these remain the standard of care other approaches for example drug coated balloons had a 60% success rate in this study. Still, large scale trials should be conducted to assess the effectiveness of the drug coated balloons as an intervention in the case of treatment compared to the other standardized methods.

Conclusion

It is concluded that in-stent restenosis (ISR) remains a significant clinical issue in patients undergoing PCI with drug-eluting stents (DES), particularly in those with diabetes, complex lesions, and small vessel diameters. These factors, along with procedural challenges like stent malapposition, increase the risk of ISR. Improved patient selection, careful procedural techniques, and optimized stent deployment can help mitigate the occurrence of ISR, ultimately improving long-term outcomes in PCI-treated patients.

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