

# Incidence and Outcome Predictors in the Treatment of In-Stent Restenosis with Drug-Eluting Ballons

AFTAB AHMED SOLANGI<sup>1</sup>, NASRULLAH<sup>1</sup>, AMIR JAMIL<sup>1</sup>, MUHAMMAD TAHIR<sup>2</sup>, JALALUDIN<sup>3</sup>, KHURSHID ALI<sup>4</sup>

<sup>1</sup>Medical Officer (FCPS Cardiology), Punjab Institute of Cardiology, Lahore

<sup>2</sup>Medical Officer/ Resident (FCPS Cardiology), Punjab Institute of Cardiology, Lahore

<sup>3</sup>Post Graduate Resident (FCPS Cardiology), Punjab Institute of Cardiology, Lahore

<sup>4</sup>Medical Officer (FCPS Cardiology), District Headquarter Hospital, Batkhela

Corresponding author: Nasrullah, Email: [nasrullah\\_jan80@yahoo.com](mailto:nasrullah_jan80@yahoo.com)

## ABSTRACT

**Background and Aim:** In-stent restenosis (ISR) in coronary artery disease patients can be effectively treated with drug-eluting ballons (DEB). Yet, the prevalence and binary restenosis related factors have not been assessed in the past. The present study intended to determine the incidence and outcome predictors in drug-eluting ballons treatment of in-stent restenosis.

**Methods:** This retrospective study was carried out on 152 coronary artery disease patients in Punjab Institute of Cardiology, Lahore from January 2021 to July 2022. Prior to study conduction, the research and ethical committees approved the procedure. Patient's demographic details, clinical characteristics, laboratory tests, and lesion features were recorded. Data analysis was done in SPSS version 26.

**Results:** Of the total CAD patients, 110 (72.4%) were male and 42 (27.6%) were females. The overall mean age was  $56.82 \pm 4.56$  years. The prevalence of different risk factors for cardiovascular disease such as diabetes, hypertension, smoking, LDL  $>1.40$  mmol/l, and family history was 82 (53.9%), 94 (61.8%), 92 (60.5%), 64 (42.1%), and 16 (10.5%) respectively. Other comorbidities such as chronic kidney disease and heart failure were present in 58 (38.2%) and 12 (7.9%) respectively. High-dose statin therapy was given to 40 (26.3%) patients. The occurrence of MACEs, myocardial infarction, targeted vessel revascularization (TVR), and target lesion revascularization (TLR) during follow-up was 56 (36.8%), 40 (26.3%), 10 (6.6%), and 33 (21.7%) respectively. The mortality rate was 13 (8.6%). Multivariate logistic regression were used to identify the independent factors such as diffuse ISR [OR=2.21; CI 95%, (1.2-1.76), stents  $\geq 2$  per lesion [OR=1.78; 95% CI (1.12-2.19)], proximal left anterior descending artery [OR=1.31; 95% CI (1.2-1.76)], and triple vessel disease [OR=2.87, 95% CI (1.1-6.3),  $p=0.005$ ].

**Conclusion:** The present study concluded that In-stent restenosis is a coronary angioplasty serious complication with adverse outcomes. For in-stent restenosis, drug-eluting ballons are an effective alternative to stenting. MACE was shown to be prevalent in our data. MACE is a measure of all-cause mortality in a high-risk group and demonstrates that DEB provides both short-term and long-term advantages in ISR.

**Keywords:** In-stent restenosis, Drug-eluting ballons, Predictor outcomes.

## INTRODUCTION

The slow re-narrowing coronary artery stented lesion due to arterial injury with successive neointimal tissue growth is referred to in-stent restenosis [1]. The introduction of drug-coated ballons has reduced the prevalence of coronary artery in-stenosis restenosis [2]. It is, however, still seen in percutaneous coronary procedures from 5% to 15% [3]. In-stent restenosis (ISR) in coronary artery disease patients can be effectively treated with drug-eluting ballons (DEB) [4]. Stenosed coronary arteries percutaneous intervention was made possible by drug-coated ballons. However, their effectiveness is limited by flow-limiting dissections and elastic rebound. Drug-eluting stents (DES) were developed to treat restenosis by mixing a BMS support scaffold with an ant proliferative drug [5]. Despite being a significant improvement over BMS, a DES is not a perfect therapy for every CAD patient [6]. For coronary heart disease, the percutaneous coronary intervention (PCI) frequent complication was in-stent restenosis defined as lumen diameter  $\geq 50\%$  as a stenosis or stent edge up to 5 mm [7].

Drug-eluting stent implantation has been confirmed as an effective procedure employing drug-eluting stents (DES). Several investigations found that ballons cutting and simple ballons angioplasty has lower effect than re-implantation in DES [8]. The restenosis lower rate was significantly contributed by second-generation DES usage. The target lesion revascularization (TLR) rate increased from 10% to 20 in a span of 5 years [9, 10]. Coronary artery lesions can be effectively treated by combination of medicine with drug-eluting ballons as a revolutionary device [11]. A previous meta-analysis conducted on 4800 patients reported that DES and DCB outdone ISR related interventional therapy [12]. However, binary restenosis was found in many drug-coated therapy and limited studies had been done on ISR treatment with re-occurrence of post-DCB re-restenosis. Therefore, the presented study intended to determine the incidence and

predictor's outcome in the treatment of in-stent restenosis with drug-eluting ballons.

## METHODOLOGY

This retrospective study was carried out on 152 coronary artery disease patients in Punjab Institute of Cardiology, Lahore from January 2021 to July 2022. Research and ethical committee approved the study protocol before study conduction. Patient's demographic details, clinical characteristics, laboratory tests, and lesion features were recorded. Patients with ISR confirmed angiographic diagnosis were enrolled. Previously treated ISR or stent thrombosis patients were excluded. Prior to study conduction, the research and ethical committees approved the procedure. Patient's baseline characteristics were gender, age, different risk factors for cardiovascular disease such as hypertension, smoking, diabetes, family history, LDL, and other comorbidities such as heart failure and chronic kidney disease. High dose statins therapy was referred to 80 mg atorvastatin daily or 20 mg rosuvastatin daily. Frequency, stents types, and diameter were initial procedural aspects collected. Procedural complications such as residual stenosis and coronary artery dissection (iatrogenic) and procedural complications were recorded.

Data analysis was carried out in SPSS version 26. Quantitative variables were expressed as mean and standard deviation. Qualitative variables were described as frequency and percentages. Categorical variables were compared using Chi-square test whereas different of continuous data were evaluated with Student t-test. Univariate analysis was done for MACEs occurrence during follow-up associated with procedural factors and clinical angiography. Multivariate logistic regression was used for identification of independent factors. All the descriptive statistics was carried out by calculating odds ratio taking 95% confidence interval and 5% level of significance.

**RESULTS**

Of the total CAD patients, 110 (72.4%) were male and 42 (27.6%) were females. The overall mean age was 56.82±4.56 years. The prevalence of different risk factors for cardiovascular disease such as diabetes, hypertension, smoking, LDL >1.40 mmol/l, and family history was 82 (53.9%), 94 (61.8%), 92 (60.5%), 64 (42.1%), and 16 (10.5%) respectively. Other comorbidities such as chronic kidney disease and heart failure was present in 58 (38.2%) and 12 (7.9%) respectively. High-dose statin therapy was given to 40 (26.3%) patients. The prevalence of MACEs, myocardial infarction, targeted vessel revascularization (TVR), and target lesion revascularization (TLR) during follow-up was 56 (36.8%), 40 (26.3%), 10 (6.6%), and 33 (21.7%) respectively. The mortality rate was 13 (8.6%). Multivariate logistic regression were used to identify the independent factors such as diffuse ISR [OR=2.21: CI 95%, (1.2-1.76), stents ≥2 per lesion [OR=1.78; 95% CI (1.12-2.19)], proximal left anterior descending artery [OR=1.31; 95% CI (1.2-1.76)], and triple vessel disease [OR=2.87, 95% CI (1.1-6.3), p=0.005]. Gender's distribution is illustrated in Figure-1. The prevalence of various cardiovascular risk factors is shown in Figure-2. Different comorbidities found in in-stent restenosis is shown in Figure-3. During follow-up, major adverse cardiac events are depicted in Figure-4. Multivariate logistics regression carried out for in-stent restenosis is represented in Table-1.

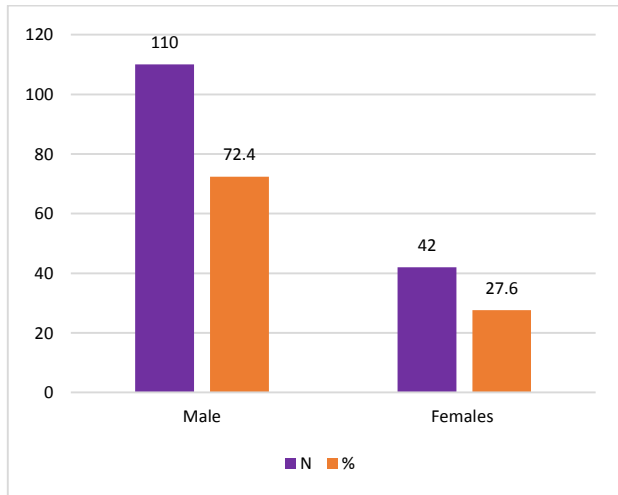


Figure-1: Gender's distribution

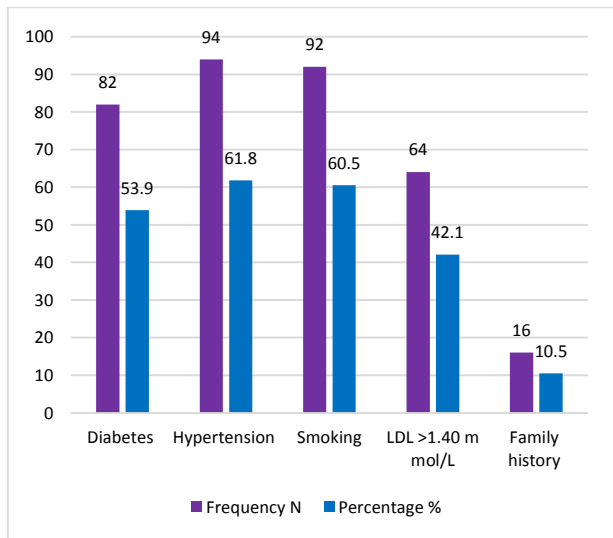


Figure-2: prevalence of various cardiovascular risk factors

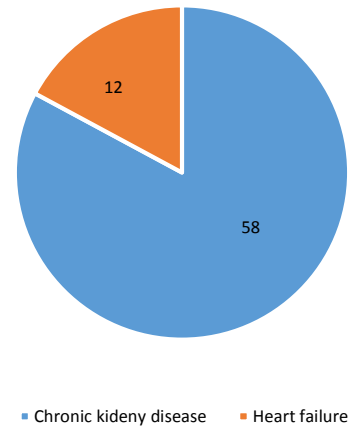


Figure-3: in-stent restenosis comorbidities

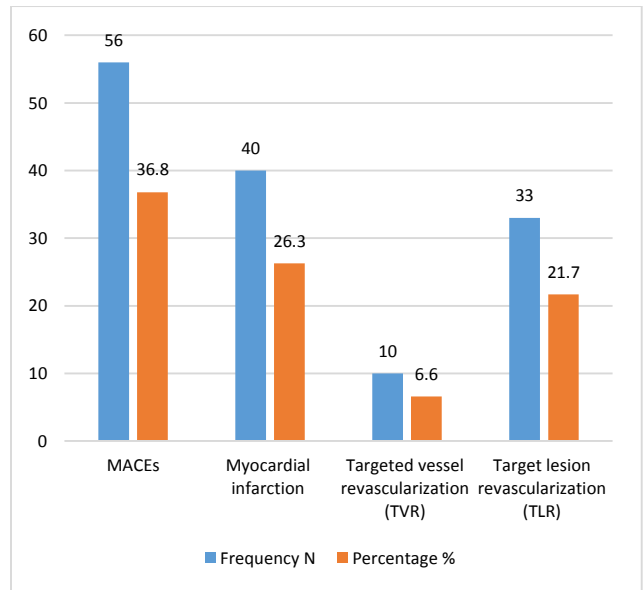


Figure-4: Incidence of major adverse cardiac events

Table-1: Multivariate logistics regression carried out for in-stent restenosis

Variables	Odd Ratio (OR), 95% CI	P-value
Diffuse ISR	2.21 (1.2-1.76)	0.005
Stent ≥2 per lesion	1.78 (1.12-2.19)	0.005
Proximal left anterior descending artery	1.31 (1.2-1.76)	0.005
Triple vessel disease	2.87 (1.1-6.3)	0.005

**DISCUSSION**

The present study mainly investigated the incidence and predictor's outcome in in-stent restenosis using stent-eluting ballons and found that In-stent restenosis is a coronary angioplasty significant complication with negative consequences. Drug-eluting ballons are an effective alternative to stenting for in-stent restenosis. MACE was shown to be common in our data. MACE is a measure of all-cause mortality in a high-risk cohort that shows that DEB gives both short-term and long-term benefits in ISR. CAD is a significant cardiovascular disease that affects people all around the world. PCI is a successful therapy for CAD, and interventional cardiology, various devices, including as different generations of drug-eluting stents and drug-coated ballons, are now in clinical use [13].

The DCB was initially offered as a unique interventional technique to DES lower the restenosis rate. It can provide interventional therapy without removing the implant, lowering the unusual implantation-related problems, eliminating numerous stents, and lowering the thrombosis incidence. Additionally, after DCB treatment, the dual antiplatelet medication duration is significantly shortened [14]. DCB is increasingly being employed in coronary intervention, particularly in the treatment of ISR. Due to a paucity of validated randomised controlled studies without intrinsic bias, the usefulness and protection of DCB for DES ISR versus DES continue to be determined [15].

A previous study conducted on recurrent restenosis predictors after treatment with sirolimus-eluting stents reported that 66 patients with 78 lesions had recurrent restenosis among 1393 patients and 1965 lesions [16]. Another study by Cheng et al [17] found that increased intimal thickness, strong inflammatory reaction, and severe vascular injury is significantly associated with longer stents. These findings had close resemblance with our study results. Restenosis occurs when the lesion length is increased, the intima lesion area is increased, the inflammatory response is worsened, and blood flow resistance is increased. As a result, this data when treating a patient with lengthy lesions is critical to thoroughly analyze the lesion and pick the proper equipment. Meanwhile, tiny vascular lesions are a risk factor for ISR. The restenosis rate was higher 30% treating small vessel lesion with DES causing late lumen loss [18] and coronary arteries like small channel disease were poorly treated with DES and BMS [19].

The endothelial cells shape and function can be damaged by stent implantation besides increasing new atherosclerosis and impairing vascular endothelium healing [20]. It has been found that patients with two targeted lesions had a higher risk of acquiring ISR. Other lesions related parameters were lesion calcification and targeted vascular types [21]. Diabetes, smoking history, LDL, and hypertension have been identified as ISR and atherosclerosis related potential risk factors [22, 23]. Numerous studies reported that a significant elevated atherosclerosis was caused by diabetes, CAD causing risk factors, and hypertension that increases CAD with 2 to 4-fold higher in general population [24, 25]. The increased risk of CAD is significantly associated with hypertension [26]. CAD has the most serious consequences. After correcting for other potential risk variables such as blood lipids, all-cause, blood pressure, cardiovascular, and age-related mortality in diabetic patients was considerably greater than in non-diabetic patients [27].

## CONCLUSION

The present study concluded that In-stent restenosis is a coronary angioplasty serious complication with adverse outcomes. For in-stent restenosis, drug-eluting balloons are an effective alternative to stenting. MACE was shown to be prevalent in our data. MACE is a measure of all-cause mortality in a high-risk group and demonstrating that DEB provides both short-term and long-term advantages in ISR.

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