

Treatment and Outcome of In-Stent Restenosis with Drug-Eluting Balloons; A Real-Life Single-Centre Study

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How to Cite: Ullah R, Ali A, Malik F, Ahmed S, Khubaib S, Siddiqui FA. Treatment and Outcome of In-Stent Restenosis with Drug-Eluting Balloons; A Real-Life Single-Centre Study. APMC 2023;17(1):112-115. DOI: 10.29054/APMC/2023.1287

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Submitted for Publication: 31-01-2023

Accepted for Publication 06-03-2023

ABSTRACT

Background: Potential benefits of drug-eluting balloons (DEBs) in patients suffered from in-stent restenosis was observed in international studies but data is lacking from Pakistan. **Objective:** Treatment and outcome of In-Stent restenosis with drug-eluting balloons: A real-life hospital-based study. **Study Design:** Descriptive cross-sectional. **Settings:** Department of intervention, national institute of cardiovascular diseases, Karachi & other satellite centers, Pakistan. **Duration:** Between the period of June 2022 and November 2022. **Methods:** A hospital-based clinical study in which 109 patients were included through a consecutive sampling technique. The eligibility criteria for patients inclusion was, all adult males and females, age ≥ 18 years, previously treated with a paclitaxel-eluting balloon, and consented to participate. Data were analyzed using SPSS version 26.0 and outcome (MACE, mortality, and TLR) were calculated. **Results:** The mean age of study participants was 53.27 ± 7.91 years. Majority of the patients were males ($n = 72, 66.05\%$), urban dwellers (58.37%), and married (80.73%). Hypertension was the most common comorbid condition (38.53%). The most common indication was ISR-DES ($74.31\%, 81$). Major adverse cardiovascular events and mortality rate were observed 7.33% and 12.84% vs. 2.75% and 6.42% at 3 and 6 months. **Conclusion:** Benefits of DEB in ISR have been observed in our study. MACE and mortality were observed less frequent. Patients should be considered for DEB in ISR.

Keywords: DEB in ISR, Ischemic heart disease, Pakistan.

INTRODUCTION

Coronary artery disease is the leading cause of morbidity and mortality including Pakistan.¹ In a previously published study from Pakistan has observed the prevalence of CAD was 26.9% , and among them women were more prevalent than males, 30% vs. 23.7% , respectively.² Percutaneous coronary intervention is the gold standard treatment in patients with coronary artery occlusion. Since its introduction in medical sciences, dramatic advancement has been observed in the field of interventional cardiology.³ Interventionalist are now following new challenges as the stent technology and new therapies have emerged, including, stent thrombosis and in-stent re-stenosis (ISR).⁴

Considering the aforementioned reasons, Drug-eluting balloons (DEBs) have emerged as a possible solution to the challenge of ISR. On the other hands, some of the interventionalist are still using Plain old balloon angiography (POBA) technique but the results are substandard due to its elastic recoil and flow limiting dissections.⁵ Both DES and DEB have been proven in randomized controlled trials to be effective in BMS and DES-ISR. In a meta-analysis published by Yang *et al*,⁶ it was argued that DEB and DES provided uncertain outcomes for ISR treatment.⁹ While the Restenosis Intra-stent of Drug-eluting Stents: Paclitaxel eluting Balloon vs. Everolimus-eluting Stent (RIBS IV) study demonstrated the superiority of second-generation DES in DES-ISR at one and three years, and its applicability is limited by

differences in trial design between the arms, length of follow-up, and high rate of bailout stenting.⁷

We present the use of DEBs in ISR treatment, with a specific focus on in-hospital outcomes.

METHODS

This study was a hospital-based clinical study in which 109 patients were included through a consecutive sampling technique from the department of intervention, national institute of cardiovascular diseases (NICVD), Karachi & other satellite centers, Pakistan between the period of June 2022 and November 2022. NICVD is the largest center in Pakistan which provides treatment related to cardiovascular diseases including primary coronary intervention to the patients free of cost. The eligibility criteria for patients inclusion was, all adult males and females, age ≥ 18 years, previously treated with a paclitaxel-eluting balloon, and consented to participate.

Ethical approval was taken from hospital's ethical review committee before commencement of the study. Patient's consents were also taken after explaining the purpose and benefits of the study. Information was collected on a pre-designed structured questionnaire and included baseline & characteristics of study participants such as patient demographic history, indication for the procedure, procedural information (such as intervention stage, target vessel, peri and post-procedural therapies), complications, devices used, and procedural outcomes. Angiographic data included pre & post-intervention lesion size, thrombolysis in myocardial infarction (TIMI) flow. ISR was defined as an angiographic luminal narrowing of $> 50\%$ diameter in-stent stenosis or within 5 mm of a stent.

Data were entered and analyzed using statistical package for the social sciences (SPSS) version 26.0. Mean \pm SD was computed for continuous variables while categorical variables were represented as numbers and percentages.

RESULTS

Final analysis was performed on 109 patients. The mean age of study participants was 53.27 ± 7.91 years. Majority of the patients were males ($n = 72$, 66.05%) as compared to females ($n = 37$, 33.4%). Urban dwellers and married patients were predominant, 58.37% vs. 80.73%, respectively. Normal body mass index was observed in 66.05% ($n = 72$) while obese 12.84% ($n = 14$) of the patients were obese. Hypertension was the most common comorbid condition (38.53%) followed by diabetes mellitus (33.02%), dyslipidemia (24.77%), and kidney disease (15.59%). Rest of the detailed description shown in table number 1.

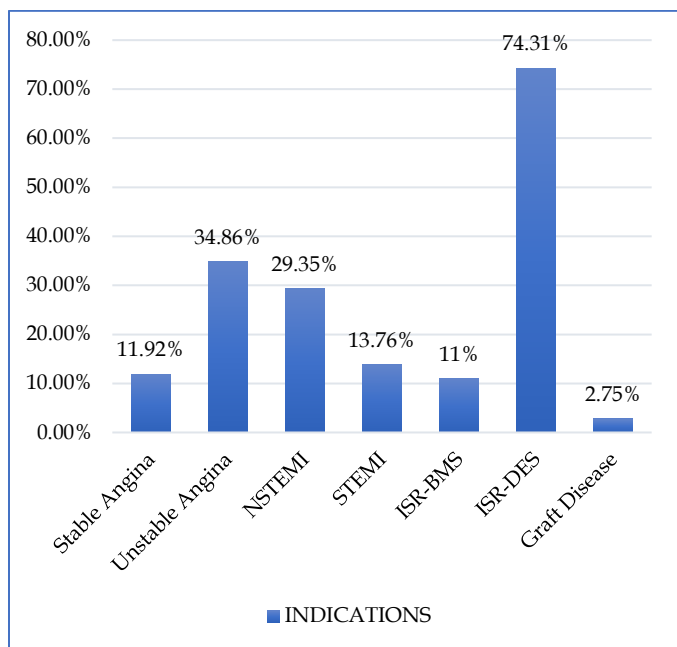
Figure 01 shows indications for procedure in patients with drug-eluting balloons. The most common indication was ISR-DES (74.31%, 81), followed by unstable angina (34.86%, $n = 38$), NSTEMI (29.35%, $n = 32$), and least common was graft disease (2.75%, $n = 3$).

Table 02 shows outcome of patients treated with drug-eluting balloons at 3 months and 6 months. Major adverse cardiovascular events and mortality rate were observed 7.33% and 12.84% vs. 2.75% and 6.42% at 3 and 6 months.

Table 1: Baseline and clinical characteristics of study participants (N = 109)

Baseline & clinical characteristics		Mean \pm SD	
Age - years		53.27 \pm 7.91	
Weight - kg		74.20 \pm 12.87	
Height - cm		167.33 \pm 8.24	
BMI - kg/m ²		23.78 \pm 4.66	
		Number	Percentage
Gender	Male	72	66.05%
	Female	37	33.4%
Area of residence	Urban	64	58.71%
	Rural	45	41.28%
Marital Status	Single	12	11%
	Married	88	80.73%
	Widowed	9	8.25%
BMI Category - kg/m ²	Underweight (<18.5)	5	4.58%
	Normal ($\geq 18.5 - 24.9$)	72	66.05%
	Overweight ($\geq 25 - 29.9$)	18	16.51%
	Obese (≥ 30)	14	12.84%
Comorbids	Hypertension	42	38.53%
	Diabetes Mellitus	36	33.02%
	Dyslipidemia	27	24.77%
	Kidney disease	17	15.59%
Addiction	Smoker	22	20.18%
	Chewable tobacco	48	44.03%
	Prior PCI	108	99.08%
	Prior myocardial infarction	70	64.22%
	Prior CABG	7	6.42%

BMI = body mass index, PCI = percutaneous coronary intervention
CABG = coronary artery bypass grafting

Figure 1: Indications for procedure (N = 109)**Table 2: Outcome of patients treated with drug-eluting balloon (N = 109)**

Outcome	3-months (95%, CI)	6-months (95%, CI)
MACE	7.33% (0.31, 0.64)	12.84 (1.09, 0.18)
Mortality	2.75% (0.48, 0.76)	6.42% (0.88, 0.91)
TLR	5.50% (0.55, 0.43)	18.34% (1.14, 0.63)

MACE=Major Adverse Cardiovascular Events, TLR=Total Lesion Revascularization, CI = Confidence Interval

DISCUSSION

In this study we have observed real-world data of patients had coronary artery disease and treated with drug-eluting balloons after developing in-stent restenosis with a 6 months longer follow-up. The overall outcome with DEB is quite surprising and favorable in terms of MACE and mortality. The overall mortality among patients were 2.75% in 3 months vs, 6.42% in 6 months, respectively. While, MACE was observed less frequent in 3 months vs. 6 months, 7.33% vs. 12.84%, respectively. Almost same increasing pattern was observed in previously published study by Murnaghan K and colleagues⁸ in 2022 in which authors have observed 1-year MACE rate was 11.8% and the five-year MACE rate was 39.8%. Higher MACE rate was observed in that study could be due to duration of their study and possibility of higher prevalence of comorbid conditions such as diabetes mellitus, CABG, and previous history of myocardial infarction.

Restenosis intra-stent of bare metal stents (RIBS IV): Paclitaxel-Eluting Balloon vs. Everolimus-Eluting Stent (RIBS V) trials evaluated the use of DEB and their findings showed lower prevalence of MACE at one-year (1.9%)⁹

but higher prevalence at year 5 (18%).¹⁰ These differences could be due to multiple reasons such as presence of multiple comorbid, severity of disease, younger age groups, or racial differences. In this case, our study's findings are partially in-favorable of RIBS trials. Another study from United Kingdom by Sandeep Basavarajaiah and colleagues evaluated the real-world experience of DEB in the treatment of ISR and de novo coronary artery disease on 275 patients, their study reported mortality rate was 3.8% and MACE was 21.7%, which is slightly higher than ours.¹¹ While, some authors did comparative study in the treatment of DES-ISR with DEB and second-generation DES, and found insignificant differences in clinical outcomes.¹² Hence, use of DEB can be considered in the treatment of ISR with certain advantages.

The mean age of our study participants was 53.27±7.91 years and among them most common were males (66.05%) which is comparable with the previously published study in which authors have observed same proportion of males, diabetes mellitus, and hypertension, but they were older than our study. On the other hands, they have observed higher prevalence of chronic stable angina (78.26%) suffering from ISR.¹³ While in our study unstable angina (38%) was the most common indication for procedure. Also, MACE was observed in 20% of the patients, which is quite higher than our study (12.84%).

A systemic review was conducted in 2018 including 1526 patients (746 DEB, 537 DES, and 243 BA) and found that DEB was associated with lower composite outcome compared to balloon angioplasty alone (19% vs. 47%) and they did not have found any difference in the composite outcome between DEB and DES (20% vs. 17%).¹⁴

CONCLUSION

Benefits of DEB in ISR have been observed in our study. MACE and mortality were observed less frequent. Patients should be considered for DEB in ISR.

LIMITATIONS

There are multiple limitations in this study and most important was smaller number of patients included in this study and only included patients from NICVD. Risk factors of ISR should be included in this study including non-compliance of drugs. Benefits of DEB should also be assessed in patients who had BMS stent.

SUGGESTIONS / RECOMMENDATIONS

A larger scale multi-center study should be conducted to validate the findings of this study.

CONFLICT OF INTEREST / DISCLOSURE

The authors declare that they have no competing interests.

ACKNOWLEDGEMENTS

The authors would like to thank all those who participated in the study.

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