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Original Research Article

EFFICACY AND SAFETY OF DRUG-ELUTING BALLOON VS DRUG-ELUTING STENTS IN THE TREATMENT OF IN-STENT RESTENOSIS

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Abstract: *The in-stent restenosis (ISR) treatment remains related to the higher recurrence rate. This comparative study aimed to compare the effectiveness and safety of drug-eluting balloon (DEB) vs drug-eluting stents (DES) in the in-stent restenosis treatment. Sixty-four patients who underwent PCI for ISR in the Department of Cardiology, Peshawar Institute of Cardiology, Peshawar, from October 2022 to March 2023 were enrolled. Patients were distributed as Group-I patients treated with drug-eluting balloons (n=28, 43.8%) and Group-II patients treated with drug-eluting stents (n=36, 56.2%). Clinical outcomes were recorded. Target lesion revascularization (TLR), myocardial infarction, and cardiac death were different endpoints of major adverse cardiac events (MACE). The overall mean age was 64.12±4.65 years. The incidence of MACEs in groups I and II was 14.3% (n=4) and 16.7% (n=6) respectively. Group I and II had insignificant associations regarding baseline characteristics except for MI's prior history. TLR was more frequent in the DEB group (7.1%, n=2) than in the DES group (2.8%, n=1). The incidence of diabetes, hypertension, current smokers, and previous myocardial infarction in Group I vs. Group II was 42.9% vs. 38.9%, 64.3% vs. 47.2%, 14.3% vs. 22.2%, and 17.9% vs. 47.2%, respectively. Drug-eluting balloons showed effective results for PCI, a viable alternative to placing drug-eluting stents for the coronary in-stent restenosis treatment.*

Keywords: In-Stent Restenosis, Drug-Eluting Balloon, Drug-Eluting Stents, Efficacy

Introduction

Percutaneous coronary intervention (PCI) has become a widely used procedure for treating coronary artery disease. However, a significant challenge associated with PCI is the occurrence of in-stent restenosis (ISR), where the previously treated artery becomes narrowed again. ISR is particularly common in cases where bare-metal stents (BMS) were used, accounting for approximately 20% to 40% of all PCI cases (Oh et al., 2016).

Drug-eluting stents (DES) were introduced to address this issue, significantly reducing the rates of ISR compared to BMS. However, despite the advantages of DES, there is still a considerable risk of ISR in complex coronary lesions and high-risk patients, with recurrence rates ranging from 3% to 20% (Giacoppo et al., 2020b; Pilgrim et al., 2018).

Interestingly, the increased use of DES has also led to higher restenosis rates in certain challenging cases and complicated patient populations. While several treatment options are available for managing ISR, such as balloon angioplasty, additional stent placement, and intracoronary brachytherapy, determining the most suitable alternative strategy has proven to be a complex task (Cassese et al., 2015; Kufner et al., 2019).

In recent years, drug-eluting balloons (DEB), which deliver anti-proliferative medications directly to the affected area, have emerged as a promising option for ISR treatment. Although prior clinical studies have suggested that DEB can effectively address ISR, their precise role and significance in ISR management remain firmly established (Alfonso et al., 2014a; Buchanan et al., 2018; Richardt et al., 2013).

Given this context, the current study aims to comprehensively compare drug-eluting balloons (DEB) efficacy and safety with traditional drug-eluting stents (DES) to treat in-stent restenosis. This research shows whether DEB could represent a superior or equally effective alternative in managing this challenging condition.

Methodology

This study is a retrospective analysis of 64 patients who underwent percutaneous coronary interventions (PCIs) for in-stent restenosis (ISR) at the Department of Cardiology, Peshawar Institute of Cardiology, Peshawar. The study was conducted between October 2022 and March 2023.

Patients who had a reference value of lesion length < 30 mm and vessel diameter between 2.5 and 3.5 mm were included in the study. Patients with significant calcification of the target lesion, total coronary artery occlusion, thrombus within the target vessel, and contraindications to dual antiplatelet therapy were excluded. The interventional cardiologist chose the therapy technique for ISR. The size of the restenosis stent was used to predilate all uncoated balloon catheter ISR lesions. A paclitaxel-eluting balloon was employed in the DEB group, and the DEB and pre-dilatation balloon had similar diameters. Heparin was administrated in each individual until the active clotting time was 200-250 seconds. For at least 6 months, clopidogrel 75 mg, acetylsalicylic acid 100 mg, and dual antiplatelet medication were administrated. Medical records were evaluated for angiographic data, demographic details,

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procedural data, clinical findings, and follow-up results. Stent thrombosis was defined as 'probable' when inexplicable mortality arose within acute MI intervention 30 days.

For properly distributed data, all the quantitative parameters are reported as mean and standard deviations. Absolute and relative (percentage) frequencies are used to characterize categorical variables. The three groups were compared using the Pearson Chi-square test for continuous variables. Data analysis was done using SPSS version 27 by considering the 5% significance level.

Results

The overall mean age was 64.12±4.65 years. The incidence of MACEs in groups I and II was 14.3% (n=4) and 16.7% (n=6) respectively. Besides previous MI history, there was no significant variation in the baseline characteristics of both groups. Target lesion revascularization was more frequent in the DEB group (7.1%, n=2) than in the DES group (2.8%, n=1). The prevalence of diabetes, hypertension, current smokers, and previous myocardial infarction in Group I vs. Group II was 42.9% vs. 38.9%, 64.3% vs. 47.2%, 14.3% vs. 22.2%, and 17.9% vs. 47.2%, respectively. Demographic and baseline characteristics are shown in Table I.

Table 2 provides a comparative overview of two groups, Group-I (DEB - Drug-Eluting Balloon) and Group-II (DES - Drug-Eluting Stent), regarding the treatment of in-stent restenosis (ISR). Group I treated 34 lesions, while Group II treated 38 lesions, with varying distributions across coronary arteries. The table details the previously implanted stents, including mean diameters and lengths. Moreover, it categorizes the ISR lesions into four patterns: focal, diffuse, proliferative, and occlusive, with the number and percentage of lesions in each pattern for both groups, offering a comprehensive view of the study's comparative analysis of ISR treatments.

Table 3 presents a comparison between two groups, Group-I (DEB - Drug-Eluting Balloon) with 28 participants and Group-II (DES - Drug-Eluting Stent) with 36 participants, in terms of follow-up duration and major adverse cardiac events (MACE). The follow-up duration for both groups is provided as mean ± standard deviation, with Group I have a mean follow-up duration of 16.8 ± 9.4 months and Group II having a mean of 15.9 ± 12.6 months, with no statistically significant difference (p-value = 0.988). The table also displays the occurrence of MACE and its components, including cardiac death, myocardial infarction, target lesion revascularization (TLR), and stent thrombosis. There were no significant differences in the occurrence of these events between the two groups, as indicated by the p-values provided.

Discussion

The present study mainly focused on the efficacy and safety of drug-eluting balloons versus drug-eluting stents in the treatment of in-stent restenosis and found that drug-eluting balloons for PCI might be a viable alternative to the placement of drug-eluting stents for the treatment of coronary in-stent restenosis. Angiographic outcome study revealed that DEB or DES had a considerably reduced probability of binary restenosis during follow-up (3-6 months).

Table I Demographic and baseline characteristics

Parameters	Group-I (DEB) N=28	Group-II (DES) N=36
Age (years)	64.2 ± 6.24	64.04±3.06
Gender N (%)		
Male	17 (60.7)	27 (75)
Females	11 (39.3)	9 (25)
Risk Factors N (%)		
Diabetes	12 (42.9)	14 (38.9)
Hypertension	18 (64.3)	17 (47.2)
Current smokers	4 (14.3)	8 (22.2)
Previous Myocardial infarction	5 (17.9)	17 (47.2)
ISR Clinical presentation	22 (78.6)	26 (72.2)
Stable angina	4 (14.3)	7 (19.4)
Unstable angina	2 (7.1)	3 (8.3)
Acute myocardial infarction		

Table II Different characteristics of lesions

Parameters	Group-I (DEB)	Group II (DES)
No of Lesions	34	38
Target Vessel		
Left Main	2 (5.9)	0 (0)
Left Anterior Descending	16 (47.1)	19 (50)
Left Circumflex	5 (14.7)	5 (13.2)
Right Coronary Artery	11 (32.4)	14 (36.8)
Previous stent		
Diameters (mm)	2.9 ± 0.5	3.1± 0.5
Length (mm)	21.6 ± 5.8	20.8 ± 5.4
The pattern of in-stent restenosis	20 (58.8)	23 (60.5)
Focal (I)	11 (32.4)	4 (10.5)
Diffuse (II)	0 (0)	3 (7.9)
Proliferative (III)	3 (8.8)	8 (21.1)
Occlusive (IV)		

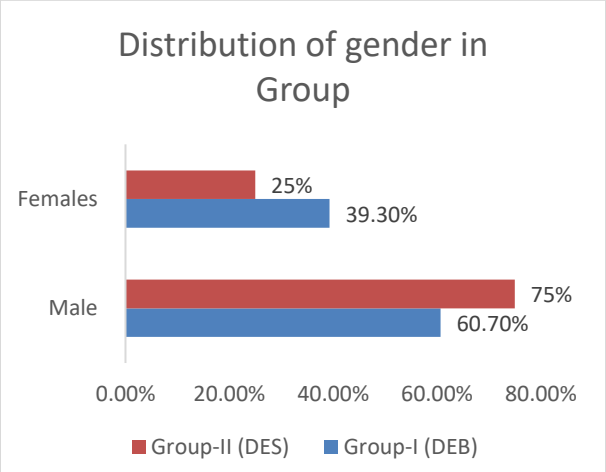

Figure 1: Distribution of gender in both Groups

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Table-III clinical outcome during follow-up

Parameters	Group-I DEB (N=28)	Group-II DES (N=36)	P-value
Follow-up duration (months)	16.8 ± 9.4	15.9 ± 12.6	0.988
Major adverse cardiac event (MACE)	4 (14.3)	6 (16.7)	1.000
Cardiac death	1 (3.6)	2 (5.6)	0.610
Myocardial infarction	0 (0)	2 (5.6)	0.229
TLR	2 (7.1)	1 (2.8).	0.372
Stent thrombosis	0 (0)	2 (5.6)	0.229

The current study examined DES and DEB; the effectiveness was equivalent, but DEB demonstrated a non-statistically significant tendency of MI reduced risk than DES in terms of safety. DEB was the most likely to be selected as the initial treatment choice for ISR, with the lowest risk of TLR, MI, all-cause mortality, and MACE. Regardless of whether the preceding treatment was with BMS or DES, the DEB favorable benefits lowered the TLR risk and were comparable to those detected in multiple investigations. Regarding TLR, all-cause mortality, and MACE, DES had the highest likelihood of being classified as the second treatment choice for ISR (Unverdorben et al., 2009).

The best therapy for ISR has yet to be established. The ISR higher recurrent restenosis rates of conventional BA were 39% to 45% (Byrne et al., 2013a; Xu et al., 2014), whereas comparable outcomes were produced by implantation done in BMS to ISR treatment by conventional BA (Alfonso et al., 2014b). The DES additional implantation in ISR lesions, such as a paclitaxel-eluting stent, resulted in restenosis rates ranging from 14% to 22% (Adriaenssens et al., 2014; Alfonso et al., 2015). Yet, a major concern in stent-in-stent approaches includes the stent layer's long-term implications in the native coronary artery wall, including a) late stent thrombosis increasing the risk for non-resorbable polymer's chronic inflammation, b) insufficient stent expansion, and c) recurrent restenosis limited treatment alternative.

DEB is a viable therapy option for ISR and has various advantages to second stent insertion, including the following: a) homogeneous anti-proliferative medication delivery; b) highly concentrated medication temporary release can lead to healing improvement, c) the stent's multiple layer's absence, and d) dual antiplatelet treatment significant reduction (Baan et al., 2018; Pleva et al., 2016).

The important question, however, was the DEB's relative efficacy and safety compared to the DES, which is the standard of therapy in lesions with ISR. In the PEPCAD II study, the Se-Quent Please paclitaxel-eluting balloon was compared to a paclitaxel-eluting stent in lesions with ISR. The experiment found that the DEB group had decreased binary restenosis rates and late lumen loss (Wong et al., 2018). Thus, in patients with ISR, the DEB was at least as safe and effective as the DES.

ISR in DES is generally documented to be more difficult to treat, with DES in this condition having greater MACE and revascularization rates (Giacoppo et al., 2020a; Jensen et al., 2018). Steinberg et al.'s latest study reveals their experience with Se-Quent. Please use DEB in the treatment of bifurcating lesions with DES-ISR (Steinberg et al., 2009). Previously, two meta-analyses compared the effectiveness and safety of DEB to plain old balloon angioplasty (POBA) or DES (Alfonso et al., 2017; Byrne et al., 2013b). The two analyses indicated that DEB had better efficacy based on 4 or 5 RCTs than a control group. However, they combined two fundamentally unrelated therapies into a single control group. Therefore, the higher efficacy of DEBs was driven by POBA group comparison. The persistent increase in DES's efficacy in ISR treatment compared to POBA and DEB was the major challenge in clinical practice (Nakano et al., 2013; Song et al., 2017).

There are various drawbacks to this study. The first important constraint was the small number of patients. Second, due to the small number of patients, ISR lesions were not divided based on risk factors such as diabetes in the previous stent type.

Conclusion

Drug-eluting balloons for PCI might be a viable alternative to the placement of drug-eluting stents for treating coronary in-stent restenosis.

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.
Consent for publication
Approved
Funding
Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

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