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ORIGINAL ARTICLE

Restenosis Rates in Small-Vessel Disease: Drug-Coated Balloons vs. Drug-Eluting Stents in Diabetic and Non-Diabetic Populations

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ABSTRACT

Objective: This study aimed to assess the effect of diabetes mellitus on the clinical outcome of patients treated for new lesions with drug-eluting stents (DES) or drug-coated balloons (DCBs).

Methods: In this study 260 patients of both genders either with diabetes or not were presented. The specific demographic information of the cases that were enrolled was documented after obtaining written informed consent. 130 patients of group I received drug-coated balloons and group II received drug eluting stunts in 130 cases. Outcomes among both groups were compared with diabetes and non-diabetes cases.

Results: The patients mean age was 62.76±14.58 years with BMI 29.52±6.51 kg/m^2 in group I and mean age of the cases of group II was 65.16±8.51 years with mean BMI 28.41±8.38 kg/m^2. Both groups of non-diabetic subjects did not vary substantially in the rates of major adverse cardiac events (MACE), nonfatal myocardial infarction (MI), or target vessel revascularization (TVR). We found significantly reduction in TVR among patients of DM in group I as compared to group II with p value <0.002.

Conclusion: There is no significant difference in the rates of major adverse cardiac events (MACE) following DCBs and DES for de novo coronary lesions in women and men with diabetes. When DCB was used instead of DES, the necessity for TVR in diabetic people was significantly reduced.

Keywords: Drug-Coated Balloons, Drug-Eluting Stents, diabetic, MACE, DCB, DES, TVR, non-diabetic

INTRODUCTION

Modern drug-eluting stents (DES) and rapid advancements in interventional cardiology have led to a dramatic decline in the occurrence of in-stent restenosis (ISR) in treated vasculature. It is still within the 5-10% range, albeit[1]. There have been significant efforts to discover efficient methods to prevent and manage ISR due to its unexpected clinical effects, which include mortality, acute coronary syndromes (ACS), unscheduled revascularization, and readmissions[2]. The following procedures are currently advocated for use in ISR treatment: optical coherent tomography, intravascular ultrasonography, vascular brachytherapy, intravascular lithotripsy, drug eluting balloons (DEB), and excimer laser coronary atherectomy. When all other methods have been exhausted, coronary artery bypass grafting (CABG) becomes the third choice[3]. Incidence rates of in-stent restenosis and intra-arterial stenoses (ISRs; p = 0.001) after balloon angioplasty were 55% and 20%, respectively, in the general population and diabetic patients.[4]. The prevalence of stent-edge restenosis was also higher in diabetics, according to another study (20.3% vs. 9.2%, p = 0.019).[5]. People with diabetes mellitus (DM) may develop insulin secretory resistance (ISR) due to various possible mechanisms. A number of factors can increase the likelihood of insulin-resistant restenosis (ISR), but the most important ones are hyperinsulinemia, abnormalities in the activity of vascular smooth muscle cells, impaired function of certain glycoproteins (such as plasminogen activator inhibitor-1), and increased platelet aggregation as a result of insulin resistance[6].

When treating coronary artery lesions in small arteries, the drug-eluting stent (DES) remains the treatment of choice due to its ability to diminish both angiographic and clinical restenosis[7]. Because percutaneous coronary intervention (PCI) usually requires the use of more stents with longer lengths and smaller diameters in diabetic patients[9], having diabetes mellitus is a strong predictor of poor outcomes[8]. As a result, the necessity of developing new technologies to substitute DES is being emphasized heavily. Doctors are interested in drug-coated balloons (DCB) as a possible treatment option for de novo lesions and small-vessel coronary artery lesions because they can deliver antiproliferative medications straight into the arterial wall without inserting metallic stents into the artery vessels[10].

When compared to DES, DCB did not exhibit lower therapeutic efficacy or safety in several clinical trials and meta-analyses that looked at its use in treating coronary artery lesions in small vessels. Razzack et al.[11] attempted to determine the efficacy of DCB for diabetic persons using a subgroup analysis, which was the sole method employed in this meta-analysis. It is important to note that this subgroup analysis only included three trials, thus there isn't enough data to decide how DCB and DES vary in treating diabetic persons with small channel coronary artery disease. Also, because to limited sample numbers, most trials couldn't compare DCB and DES in terms of safety and therapeutic efficacy sufficiently[12].

People with diabetes mellitus have a higher risk of major adverse cardiac events (MACE) compared to those without the condition[13]. Compared to individuals who do not have diabetes, patients with the illness are more likely to experience complications such as restenosis, myocardial infarction, and stent thrombosis. In diabetic patients with newly established coronary artery disease, there is an absence of data comparing DCBs to DES. Patients with diabetes mellitus and new lesions in small coronary arteries were the focus of this predefined subgroup analysis that examined the efficacy of DCBs and DES.

MATERIALS AND METHODS

This comparative study was conducted at Lady Reading Hospital, Peshawar February 16, 2022 to December 15, 2022. Total 260 patients were presented in this study. Participation in the trial was contingent upon the patient's meeting the inclusion criteria, which included a need for percutaneous coronary intervention (PCI) due to conditions such as silent ischemia, stable angina pectoris, or acute coronary syndrome, as well as an appropriate angiographical architecture in a small coronary channel with a diameter ranging from 2 to 3 mm. The procedure could only proceed if the lesion had been successfully pre-dilated, meaning there were no higher-degree dissections, reduced blood flow (Thrombolysis In Myocardial Infarction flow grade ≤2), or more than 30% residual stenosis[15]. The diagnosis of diabetes mellitus was based on the patient's medical history or their response to treatment. If a participant had a previous percutaneous coronary intervention (PCI) with lesions 3 mm or larger in the same epicardial coronary artery, was pregnant, took part in another randomized trial, couldn't provide informed consent, had an average lifespan of less than 12 months, or had a previous PCI for in-stent restenosis, they were all removed from the study.

Treatment with DCB or DES was randomly assigned to patients in a 1:1 ratio. Separated into two groups, patients were treated with paclitaxel-coated SeQuent Please balloons and stents that eluted everolimus or paclitaxel, respectively, called Xience and Taxus Element, respectively[4,9]. Both DES have a strut thickness of 81 μm. To compensate for differences in elevation, the DCB had to be two or three millimeters longer than the pre-dilatation balloon on all sides. According to the latest regulations, it had to be inflated to the necessary pressure for 30 seconds[11]. Despite successful lesion preparation, stent implantation was nevertheless performed when flow-limiting dissections persisted following DCB treatment. Treatment with DAPT for patients with acute coronary syndromes lasted twelve months, whereas those with stable conditions received it for four weeks for DCB or six months for DES. Following the operation known as percutaneous coronary intervention (PCI), patients were prescribed DAPT with one of the following doses of acetylsalicylic acid: 100 mg once day, 75 mg once daily, 10 mg once daily, or 90 mg twice daily: ticagrelor.

Current guidelines were followed[12] in patients with oral anticoagulation, regardless of whether they were treated with DCB or DES. Structured clinical questionnaires or phone calls were used for follow-up assessment of medication and clinical events at 12, 24, and 36 months. Median follow-up time for patients was three years.

The intention-to-treat principle was adhered to in all statistical analyses; that is, each patient's data was evaluated based on their assigned treatment. We used R 3.5.0, developed by the R Foundation for Statistical Computing in Vienna, Austria, to perform all of our analyses. We used 2-sided tests and confidence intervals (CIs) without multiple testing correction. With the use of Pearson's chi-square test, we compare the two study arms and display the results as percentages and frequencies for categorical data. A Student's t-test or a Wilcoxon-Mann-Whitney U test is used to examine the difference between the study arms for numerical variables, while the median and interquartile range or mean ± SD are reported as applicable.

RESULTS

The patients mean age was 62.76±14.58 years with BMI 29.52±6.51 kg/m^2 in group I and mean age of the cases of group II was 65.16±8.51 years with mean BMI 28.41±8.38 kg/m^2. Majority of the cases were males in both groups. 78 (60%) cases were smokers in group I and in group II 55 (42.3%) cases were smokers. In group I 75 (57.7%) cases had DM and in group II 83 (63.8%) cases had DM. Other comorbidities were HTN, hypercholesterolemia and COPD.(table 1)

Table-1: Baseline details of the presented cases

Variables	Group I (130)	Group II (130)
Mean age (years)	62.76±14.58	65.16±8.51
Mean BMI	29.52±6.51	28.41±8.38
Gender		
Male	80 (61.5%)	90 (69.2%)
Female	50 (38.5%)	40 (30.8%)
Smokers		
Yes	78 (60%)	55 (42.3%)
No	52 (40%)	75 (57.7%)
Diabetes Mellitus		
Yes	75 (57.7%)	83 (63.8%)
No	55 (42.3%)	47 (36.2%)
Other Comorbidities		
HTN	60 (46.2%)	70 (53.8%)
hypercholesterolemia	40 (30.8%)	45 (34.6%)
COPD	30 (23.1%)	15 (11.5%)

Major adverse cardiac events (MACE), nonfatal myocardial infarction (MI), and target vessel revascularization (TVR) were not statistically different between the two groups of non-diabetic patients..(Table 1)

Table-2: Comparison of outcomes among non-diabetic cases both groups

Variables	Group I (55)	Group II (47)
Patients	Non-DM	Non-DM
Outcomes		
MACE	17 (30.9%)	15 (31.9%)
Nonfatal MI	22 (40%)	17 (36.2%)
TVR	16 (29.1%)	15 (31.9%)

We found significantly reduction in TVR among patients of DM in group I as compared to group II with p value <0.002.(Table 3)

Table-3: Comparison of outcomes among diabetic cases

Variables	Group I (75)	Group II (83)	P Value
Outcomes			
MACE	25 (33.3%)	23 (27.7%)	NA
Nonfatal MI	30 (40%)	30 (36.1%)	NA
TVR	12 (16%)	30 (36.1%)	<0.002

Frequency of sudden death among cases of group II was higher found in 17 cases as compared to group I in 11 cases. Majority of the cases had DM.(table 4)

Table-4: Frequency of sudden death

Variables	Group I (130)	Group II (130)	P Value
Death			
Yes	11 (8.5%)	17 (13.1%)	<0.004
No	119 (91.5%)	113 (96.9%)	-

DISCUSSION

There was an increased incidence of death, nonfatal myocardial infarction (MI), transient ventricular resynchronization (TVR), and major adverse cardiac events (MACE) in individuals with diabetes mellitus compared to nondiabetic patients throughout the three-year follow-up period. Both DCB and DES had comparable rates of mortality, nonfatal MI, and major adverse cardiac events (MACE) in individuals with and without diabetic mellitus. The rate of temporal ventricular resynchronization (TVR) was lower in diabetes patients treated with DCB compared to DES up to three years of follow-up, whereas the numerical greatest rates of nonfatal MI, TVR, or MACE were observed in diabetic patients treated with DES.[14]

Roughly one-third of the survey participants had diabetes. For newly formed lesions in small artery walls (less than 2.8 mm according to ocular assessment), the 182 subjects who participated in the BELLO study were randomly assigned to receive either DES (Taxus Liberté; the city Scientific) or DCB (In-Pact Falcon paclitaxel the DCB; Medtronic)[15]. The Kaplan-Meier analysis showed that after three years of follow-up, DCB had a considerably lower risk of major adverse cardiac events (MACE) compared to DES (14.4% vs 30.4%; P = 0.015). Diabetes mellitus was seen in 38.0% of DES and 43.3% of DCB. The effects of EES and DCB (Elutax SV, Cologne Resonance) were studied in the PICCOLETO II experiment, which involved 122 patients assigned at random to one of the two groups. After one year (P = 0.55) [16], the rates of major adverse cardiac events (MACE) were 7.5% for a DES and 5.6% for DCB.

Diabetic patients constituted over 40% of the total. If a participant's vessel width was less than 2.75 mm, they were randomly assigned to receive either DCB (Cardionovum's RESTORE) or DES (Medtronic's RESOLUTE integrity) in the RESTORE Small Vessel Disorder China trial. There was no discernible difference in the rates of target lesions failure (TLF) and total lesion repair (TLR) between DCB and DES; both were 5.2% (TLF, P = 0.75; TLR, P = 0.50). Diabetes mellitus was present in approximately 50% of DCB patients and DES patients[17]

Considering the high risk that people with diabetes mellitus face over time, it is disturbing that instances involving both diabetes and non-diabetes were tracked for three years. For non-diabetic patients newly diagnosed with coronary artery disease, this follow-up study did not find a difference in outcomes between

DCB and DES. Multiple studies, including the previously mentioned meta-analysis, the BELLO trial, and the SeQuentPlease World Wide Registry, have shown that people with diabetes mellitus have a substantially higher incidence of TVR compared to those without the condition[18]. Neointimal proliferation in tiny vessels is more common in diabetes patients following DES implantation compared to nondiabetic patients, according to the angiographic subgroups evaluation of the BASKET-SMALL 2 study[19], which showed vessel obstructions in the DES group but not in the DCB group.

This may be because DCB has a beneficial influence on the TVR rate in diabetic patients taking DCB medication; there is no long-term risk of stent thrombosis with DCB; DAPT offers the possibility of having a shorter therapy duration; and DCB permits late lumen expansion since it does not leave a metallic cag behind. Additionally, there is no permanent metal structure or polymer to induce inflammation, neoatherosclerosis, as well as neointimal proliferation. The last piece of advice might be crucial for individuals who frequently injure themselves.References[21,22] You increase your risk of thrombotic ischemic events by reducing your antiplatelet medication in response to bleeding.

CONCLUSION

There is no significant difference in the rates of major adverse cardiac events (MACE) following DCBs and DES for de novo coronary lesions in women and men with diabetes. When DCB was used instead of DES, the necessity for TVR in diabetic people was significantly reduced.+

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