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Original Article

Short Term Outcome of Drug Eluting Balloon for Percutaneous Coronary Intervention

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ABSTRACT

Objective: To assess the short-term outcome of Drug Eluting Balloon (DEB) for Percutaneous Coronary Intervention (PCI).

Study Design: Analytical Cross-sectional study

Place and Duration of Study: Armed Forces Institute of Cardiology/National Institute of Heart Diseases, Rawalpindi, from Jan 2022 to July 2022.

Methodology: Patients who underwent DEB-PCI within the past year were chosen via Universal sampling technique. Symptomatic patients were evaluated by conventional coronary angiography, while asymptomatic patients had CT-angiography. Primary outcome was restenosis rate on angiographic follow-up. Patients having <30% visually estimated stenosis in the DEB treated artery were considered to have satisfactory results of DEB. Association of study's variables with DEB outcome was determined by Chi-square test and *p*-value <0.05 was taken as significant.

Results: Majority of patients were males 60(96.8%) and only 2(3.2%) were females. DEB outcome was satisfactory in majority of the study participants 48(77.4%). DEB was used in diagonal branch in majority of the cases 17(26.9%). In small vessels, 33(78.5%) patients showed satisfactory results while in large vessels 15(71.4%) patients had satisfactory outcome. No deaths or other complications related to procedure or device were reported. Out of total 62, 14(22.6%) patients showed unsatisfactory results with significant angiographic stenosis. Among these, 8(13%) patients were further treated with angioplasty and the remaining 6(9.6%) were left on optimal medical therapy. Significant association was found between multi vessel disease and DEB outcome (p=0.02).

Conclusion: Study findings emphasized the safety and effectiveness of DEB as a possible treatment option for atherosclerotic CAD, essentially in small vessels, offering potential benefits in improving patient outcome without metal mesh network in their arteries.

Keywords: Drug Eluting Balloon, Myocardial Infarction, Percutaneous Coronary Intervention.

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INTRODUCTION

Globally the leading cause of morbidity and mortality is Coronary Artery Disease (CAD). In Pakistan the prevalence of CAD is 17.5% in the population of Punjab.[1] Early in 1970s, there was very little understanding of CAD with limited treatment options including Nitroglycerine and Propranolol.[2] First human Percutaneous Trans-Luminal Coronary Angioplasty (PTCA) was done in 1977 by Dr Andreas Gruntzig and now, it is one of the most commonly done medical interventions. [3]

Standard Balloon Angioplasty (BA) and Bare Metal Stents (BMS) are associated with high restenosis rates, repeated need for revascularization and Major Adverse Cardiac Events (MACE).[4] Currently, Drug Eluting Stent (DES) is most widely used mode of PCI for treatment of CAD. DES has overcome some of complications of BMS like In-Stent Restenosis (ISR) and need for repeat Target Lesion Revascularization (TLR). However, there are still some limitations of DES i.e. late stent thrombosis, risk of bleeding due to need of prolonged use of Dual Antiplatelet Therapy (DAPT) and inability to address complex lesions like small vessel disease.[5] Even by using new generations of stents the incidence of ISR is still high at 12% after 6 months of stent placement.[6]

Drug Eluting Balloon (DEB) has been introduced in recent years in the treatment of CAD to overcome limitations of DES.[7] It is a non-stent technology in which an anti-proliferative medication is administered through an inflated balloon to the vessel wall.[8]

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Without inserting a long-lasting foreign object, this procedure restores luminal vascularity to cure atherosclerosis, in-stent restenosis, and lowers the risk of late thrombosis.[7,8] DEB rapidly delivers liquid formulation of submicron particles of protected drug directly into the target lesion minimizing the concerns of creating embolic material that can block vessels downstream. Proprietary bio-absorbable particle technology enables sustained release of the drug with higher arterial tissue concentration and the same elusion can add as a proven drug DES without the need for a permanent implant by delivering the drug during standard angioplasty without embolic particles.[8,10] Most DEBs used today deliver Paclitaxel or Sirolimus using different carriers and excipients.

DEB when used alone or in combination with DES play an important role in the treatment of coronary artery disease. Many clinical and experimental studies have persuasively demonstrated that DEB PCI is safe and effective in selected de novo coronary lesions, small vessel disease (SVD) and bifurcation lesions.[4,8] Aim of current study was to identify the short-term outcome of DEB PCI in patients with CAD.

METHODOLOGY

This Analytical Cross-sectional study was conducted at Armed Forces Institute of Cardiology, National Institute of Heart Diseases, Rawalpindi, from Jan 2022 to July 2022, after ethical approval from Institutional Ethical Review Board (letter no. 10/2/R&D/2022/157).

AFIC/NIHD being tertiary cardiac care center had introduced this new technique of treating patients with DEB PCI. Therefore, current study enrolled all the patients (referred from all over the Pakistan) who underwent DEB procedure during 6-months of study duration and total sample size accounted for n=62.

Inclusion Criteria: A total of 62 patients between age 20-90 years irrespective of gender, who had history of CAD and were treated with DEB PCI alone were selected during 6-months study.

Exclusion Criteria: Patients who had complex Triple Vessel Coronary Artery Disease (TVCAD) with history of multi-vessel PCI, patients with complex anatomy of cardiac vessels and patients suffering from Chronic Kidney Disease (CKD) or liver disease were excluded from the study.

All the patients who underwent DEB PCI during 6-month duration at a tertiary care hospital were chosen using Universal sampling technique. Comprehensive information of the study was provided to all patients, and their informed written consent was obtained. Prior to enrollment, all recruited individuals underwent a thorough evaluation consisting of a detailed medical history assessment, clinical examination, electrocardiography (ECG), and echocardiography. Symptomatic patients were evaluated by conventional coronary angiography, while asymptomatic patients were assessed by using computed tomography angiography (CT angiography). Primary outcome assessed in this study was restenosis rate on angiographic follow-up, Patients having <30% visually estimated stenosis in the DEB treated artery were considered as to be having satisfactory results of DEB PCI whereas those patients who had >30% stenosis were deemed to have unsatisfactory results.

Data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 26:00. Means and standard deviations were calculated for numerical variables specifically age and ejection fraction. Qualitative variables like gender, hypertension, smoking, and diabetes were recorded in terms of frequency and percentage. Pearson chi-square test was applied to find the association of study's variables with DEB outcome. *p*-value <0.05 was considered statistically significant.

RESULTS

Among 62 total study participants, 60(96.8%) were males and only 2(3.2%) were females. Mean age was 60.45±10.08 years. Out of 62, 29(46.8%) patients were hypertensive, 16(25.8%) were diabetic and 4(6.5%) were smokers. Majority of the patients had multi vessel disease (n=46, 74.1%). Angina was noted in 28(45.2%). Mean ejection fraction was 52.5±9.27%. Major bulk of patients 46(74.2%) were scanned by coronary angiography. A total of 63 lesions were treated with DEB. DEB outcome was satisfactory in majority of our study participants 48(77.4%) (Table-I).

Figure is illustrating that DEB was used in diagonal branch in majority of the cases i.e., 17(26.9%). There was only 1 case of trifurcation 1(1.6%) due to high tortuosity of vessel.

Furthermore, 13(20.6%) lesions were treated with DEB in OM branch, 6(9.4%) in AV Circ, 3(4.8%) in PLV and PDA. Among the large vessels; 6(9.4%) in LCX, 10(15.9%) in LAD and 4(6.3%) in RCA were treated with DEB. No mortality or other complications related to procedure or device were reported among the study participants.

Table-I: Baseline Characteristics, Comorbids and DEB outcome (n=62)

Variables		Mean±SD
Age (years)		60.45±10.08
Ejection Fraction (%)		52.50±9.27
		Frequency(%)
Gender	Male	60(96.8%)
	Female	2(3.2%)
Hypertension	Yes	29(46.8%)
	No	33(53.2%)
Diabetes Mellitus	Yes	16(25.8%)
	No	46(74.2%)
Smoking Stats	Yes	4(6.5%)
	No	58(93.5%)
Multi vessel Disease	Yes	46(74.1%)
	No	16(25.8%)
Angina	Yes	28(45.2%)
	No	34(54.8%)
Dyspnea	Yes	2(3.2%)
	No	60(96.8%)
Diagnostic Parameters	Coro Angiography	46(74.2%)
	CT Angiography	16(25.8%)
DEB Outcome	Satisfactory (<30%)	48(77.4%)
	Unsatisfactory (>30%)	14(22.6%)

LV=Left Ventricle; DEB=Drug Eluting Balloon

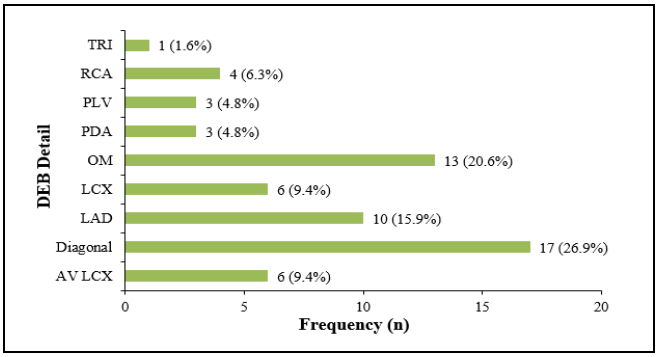

Figure: Frequency of Drug Eluting Balloon usage among target vessels (n=62)

TRI=Trifurcation branch, RCA=right coronary artery, PLV=posterior left ventricular, PDA=posterior descending artery, OM=obtuse marginal, LCX=left cir-cumflex artery, LAD=left anterior descending artery, AV Circ=AV Circumflex Artery

Out of total 62, 14(22.6%) patients showed unsatisfactory results with significant angiographic stenosis. Among these, 14 patients, 8(13%) patients were further treated with angioplasty and the remaining 6(9.6%) were left on optimal medical therapy. 33(78.5%) showed satisfactory results of DEB in small vessels (<2.5mm diameter),[9] while 15(71.4%) patients had satisfactory results of DEB in large vessels (>2.7mm diameter),[9] (Table-II).

Table-III illustrated insignificant association of co-morbid with DEB outcome as the *p*-value was >0.05. However, significant association of multi vessel disease involvement with DEB outcome was noted (*p*=0.02). Overall, there were satisfactory results of DEB in a majority of the patients.

Table II: Association of DEB outcome with vessel size (n=62)

Variable	Frequency (%)	DEB Outcome		
		Satisfactory (n=48)	Unsatisfactory (n=14)	*p*-value
Small vessel	42(66.6%)	33(78.5%)	9(21.5%)	1.00
Large vessel	21(33.3%)	15(71.4%)	6(28.5%)	

Table-III: Cross-tabulation of study variables and DEB outcome (n=62)

Variables		DEB Outcome		*p*-value
		Satisfactory (n=48) Frequency(%)	Unsatisfactory (n=14) Frequency(%)	
Hypertension	Yes	20(41.6%)	9(64.2%)	0.13
	No	28(58.3%)	5(35.7%)	
Diabetes Mellitus	Yes	11(22.9%)	5(35.7%)	0.48
	No	37(77.1%)	9(64.2%)	
Smoker	Yes	4(8.3%)	3(21.4%)	0.71
	No	44(91.7%)	11(78.6%)	
Multi vessel disease	Yes	29(60.4%)	7(50.0%)	0.02
	No	19(39.6%)	7(50.0%)	

DEB = Drug Eluting Balloon

DISCUSSION

The primary objective of existing study was to evaluate the short-term effectiveness of DEB PCI in the treatment of CAD. The study yielded positive results, indicating that DEB is a viable and efficient alternative for CAD treatment. The outcomes of DEB PCI were deemed satisfactory for the majority of the study participants. It is noteworthy that the treatment predominantly targeted lesions located in the smaller branches of the coronary artery which implied that DEB PCI was successful in treating small vessel disease in coronary arteries.

Yu *et at.*, reported successful use of drug-coated balloons (DCBs) in the endovascular treatment of short femoro popliteal artery illness.[11] Another study named "one-year results of drug-coated balloons for long and occlusive Femoro popliteal artery disease" demonstrated the effectiveness and safety of DCBs in long and totally occluded femoro popliteal artery disease.[12] Our study of DEB outcomes in coronary artery also resulted in favorable DEB outcomes in majority of the patients 48(77.4%).

Returning to balloon-only lesion treatment while also administering medication to reduce restenosis and increase the likelihood of beneficial remodeling is another reductionist strategy. When evaluating the rate of restenosis, DCB studies have demonstrated equivalent or superiority to DES in single or multi vessel disease and ISR. On the other hand another research in patients with a high bleeding risk showed that DCB was not inferior to DES after a year.[13] Our study also revealed satisfactory results of DEB alone in a good number 46(74.1%) of patients with multi-vessel disease.

The treatment of CAD with a DCB-only approach has shown favorable results in small vessel CAD, with clinical outcomes comparable to DES results. Positive remodeling and greater clinical relevance are two advantages of drug elution to a vascular lesion in the absence of a foreign-body placement, such as a stent.[14] In most of our patients, DEB was used in small vessels 42(66.6%) and the DEB outcome was satisfactory 33(78.5%) in majority of these patients.

A study conducted in Milan reported the role of DEB alone and in combination with DES in treatment of CAD. The study identified that the mean age of the study participants was 66.5±10.4 years in DEB and DES while 66.1±8.4 years in DEB alone.[15] Our study showed mean age of the study participants with Drug Eluting Balloon was 60.45±10.08 years. Several studies have shown that combining BMS with a DEB is superior to using BMS alone. In our study, we specifically excluded lesions that underwent simultaneous treatment with both drug-eluting balloons (DEB) and drug-eluting stents (DES), however, this study revealed satisfactory results of DEB alone in a large number 48(77.4%) of patients.

Diabetes affects a large percentage of CAD patients, and these patients typically have extensive and widespread vessel lesions. Patients with diabetes and CAD who were treated with DES alone have poor clinical outcomes including mortality and recurrent revascularization which is related to stent thrombosis and ISR.[16] In diabetic patients, DCBs have several advantages, they offer a smaller profile, enabling better access to smaller vessels, which are a frequent site of pathology in that patient group. They also permit the anti-proliferative medication to be distributed evenly along the vessel wall and improve its effectiveness.[17] In our study sample 16(25.8%) patients were diabetic and the DEB outcome was satisfactory in 11, while 5 diabetics had unsatisfactory DEB outcome. However, the association between diabetes and DEB outcome was not statistically significant (p-value=0.48)

Bifurcation and SVD lesions, which ranges from 15-18% of CAD, are typically associated with a high incidence of ISR and frequently result in a high probability of revascularization, in spite of the significant advancements in DES treatment of CAD. However, the treatment therapy of In-Stent Restenosis by Paclitaxel-Coated Balloon Catheters (PACCOCATH ISR) study, demonstrated that DEB was significantly more effective at reducing ISR than the conventional balloon angioplasty (POBA), suggesting that DEB may be useful in treating CAD. Paclitaxel is currently used extensively in DEB for PCI due to its high lipophilic property.[16] Another study named "Drug-coated balloon angioplasty: predicting outcomes based on different patterns of DES restenosis" demonstrated that DEB effectively lowers the rate of recurrent restenosis in focal DES-ISR.[18]

Numerous earlier studies only showed the DEB's promising effects in small coronary arteries. However, the study titled "Short-term outcomes from drug-coated balloon for coronary de novo lesions in large vessels" focused on evaluating the effectiveness of drug-coated balloon (DCB) treatment for coronary de novo lesions specifically located in large vessels. The majority of patients showed positive results, indicating that DCB was successful in addressing the lesions in large vessels.[19] In our study, 21(33.3%) lesions were treated in large vessels and majority 15(71.4%) showed satisfactory results.

Our study on DEB treatment yielded valuabl insights into its short-term efficacy, it is important to acknowledge that the study duration was relatively short. As a result, the long-term outcomes of DEB treament for CAD remains to be fully explored. In light of this, we are currently in the planning phase of a follow-up study, designated as Phase-2 study, which aims to investigate the long-term effects of DEB treatment in these participants. This forthcoming study will involve a 3-year and 5-year follow-up of these patients, enabling us to assess the durability of DEB outcomes and monitor potential late-stage complications or adverse events. By undertaking this extended research, we aim to provide a more comprehensive understanding of the long-term benefits and risks associated with DEB treatment and improve patient outcomes in the management of CAD.

LIMITATIONS OF STUDY

The study was conducted at a single center with restricted financial resources and a relatively small sample size. Additionally, our investigation focused on evaluating the short-term effectiveness of DEB, within a six-month

timeframe and the patients included were all Asian. As a result, the long-term outcomes of DEB treatment for CAD remains to be fully explored. Further, Randomized Control Trials (RCTs) and large cohort studies are needed to comprehensively evaluate the extended effectiveness and safety profile of DEB over a longer period.

CONCLUSION

Study findings emphasized the safety and effectiveness of DEB as a possible treatment option for atherosclerotic Coronary Artery Disease, essentially in small vessels, offering potential benefits in improving patient outcomes without metal mesh network in their arteries.

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Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript:

MA, AN & FUR: Study concept, Manuscript writing, Editing, Study design, Final approval, critical review.

SS, IA & NA: Data collection, Proof reading, Data management, Critical review, Data analysis, approval of the final version to be published.

MBS, JK: Intellectual contribution, Data interpretation, critical review, Approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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