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Original Article

Predictors of Outcome in the treatment of In-Stent Restenosis with Drug-Eluting Balloons

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ABSTRACT

The prognosis of coronary revascularization in patients has been significantly altered by the Interventional cardiology. With the advancement of the novel drugs and stent technology the new complications i.e., in-stent restenosis, have emerged. **Objective:** To analyze the predictors of outcome in the treatment of in-stent restenosis with drug-eluting balloons. **Methods:** It was a retrospective study conducted at Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences Gambat for the duration of one year from August 2021 to July 2022. The patients older than 18 years were eligible for the trial. The patients who have undergone coronary intervention with a drug-eluting balloon during the duration of the study were also eligible. This study received approval from the institution's research ethics board. The patient demographic features, procedure complications and operative results were recorded. **Results:** The mean age of patients was 65 years. There were 62 male participants. There were 54 patients that had history of diabetes mellitus, 87 had hypertension, 32 reported about smoking habits. There were 91 patients that reported about history of percutaneous coronary intervention (PCI), 72 about myocardial infraction (MI) and 30 reported about coronary artery bypass graft (CABG). Kidney related inflammation or infection was found in case of 19 patients. **Conclusions:** This single center study showed significantly low rate of target lesion revascularization (TLR) for a period of one year and moderate rate was found at five years.

INTRODUCTION

The prognosis of coronary revascularization patients has been significantly altered by the Interventional cardiology. The continuous efforts in this field have ultimately leads to the advancement. With the advancement of the novel drugs and stent technology the new complications i.e., in-stent restenosis, have emerged. The possible solution to such complications is drug-eluting balloons [1, 2]. For the percutaneous intervention of stenotic coronary arteries, the standard balloon angiography is usually recommended. However, there are few limitations associated with its flow-restricting dissections and recoil. The bare metal stents have emerged as more effective in the past years as it decreases plain old balloon angiography (POBA's) initial recoil, dissection, and recurring intimal constriction [3, 4]. The drug-eluting stents has been created by combining the scaffolding of bare metal stents (BMS) with an anti-proliferative agent. Bare metal stent is emerged to be the optimal treatment for all patients with coronary artery disease (CAD). There are few limitations that has add to the medical expenses and associated complications of BMS, such as the inability of stents to fit in small channels, long-term dual antiplatelet medication and the installation of a second stent layer. This has made drug-eluting stents- in-stent restenosis (DES-ISR) treatment challenging. The

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stent fracture, misplacement and under expansion leads to the DES-ISR. DES-ISR patients exhibited poorer clinical outcomes than bare metal stents-in-stent restenosis BMS-ISR patients, according to research [5, 6]. These concerns have sparked a discussion on whether recurrent stenting is the most effective treatment for ISR. DEBs are now a realistic alternative. Interventional cardiology has significantly altered the prognosis of patients requiring coronary revascularization. Bare metal stents (BMS) evolved as an effective treatment, offering a framework for the coronary artery's support and reducing POBA's initial recoil, dissection, and recurring intimal constriction [7, 8]. Restenosis continued to occur in vessels treated with BMS despite an improvement over POBA. It has been found that DES-ISR patients had worse clinical results than BMS-ISR patients. These concerns have prompted the debate of whether repeat stenting is the most effective treatment for ISR. DEBs have become a viable option. Randomized controlled trials have demonstrated that both DES and DEB are efficacious in treating BMS and DES-ISR [9, 10].

METHODS

The study was carried out to analyze 113 lesions found in 92 patients that were treated with paclitaxel- eluting balloon. It is a retrospective study conducted at Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences Gambat for the duration of one year from August 2021 to July 2022. The patients older than 18 years were eligible for the trial. The patients who have undergone coronary intervention with a paclitaxel-eluting balloon during the duration of the study was also eligible. This study received approval from the institution's research ethics board. The data of the patients treated in the cardiac catheterization in laboratory were assembled in the health information system database, which was consulted for this study. The patient demographic features, procedure complications and operative results were documented. The repeat vascularization report was also documented. For unfavorable outcomes repeat catheterization angiograms were examined. The baseline characteristics of population were reported as the mean and median for continuous variables, and as the frequency for categorical variables. Kaplan–Meier plots were used for plotting mortality major adverse cardiovascular events (MACE) results. The TLR outcomes were characterized. The cumulative incidence function was used for this purpose. TLR was determined. Survival rates were calculated. In cases of likelihood function non-convergence, Firth's penalized maximum likelihood technique for reducing bias was applied. The overall model selection strategy stated by Collet was used. Then, using automatic backward selection, a multivariable model was fitted with all significant univariable predictors, and those predictors that were not significant at the 0.10 level were discarded. The univariable and multivariable models were summarized. In cases of likelihood function non-convergence, Firth's penalized maximum likelihood technique for reducing bias was applied. Unless otherwise noted, the criterion for statistical significance was a two-sided value of 0.05. All analyses were conducted using SAS statistical software version 9.4 (SAS Institute Inc., Cary, North Carolina, United States) or R version 3.6.1 with the coxphf.

RESULTS

There were 54 patients that had history of diabetes mellitus, 87 had hypertension, 32 reported about smoking habits. There were 91 patients that reported about history of PCI, 72 about MI and 30 reported about CABG. The baseline features of the patients are shown in table 1. Kidney related inflammation or infection was found in case of 19 patients.

Baseline features	Total patients n=92
Age average (SD)	65
Sex, male	62
Diabetes mellitus	54
Hypertension	87
Dyslipidemia	89
Smoking	32
History of percutaneous coronary intervention	91
History of myocardial infraction	72
Prior coronary artery bypass graft (CABG)	30
Kidney disease	19

Table 1: Demographic features of the patients

ISR was carried out for all the patients and IRS was followed by DES in 75 of the participants. STEMI was reported in 3 individuals, stable angina was found in 22 patients and unstable angina was found in 38 participants as shown in table 2.

STEMI	3
NSTEMI	23
Stable angina	22
Unstable angina	38
Other	2
Graft disease	9
IRS, DES	75

Table 2: Signs for procedure

Mostly the vessel that was intervened was right coronary artery (RCA) in case of 31 patients. It was then followed by LAD and then Cx. SVG was also intervened in 9 patients. In 80 patients no. of vessels used was 1. In 10 patients there were 2 vessels used for 10 patients as shown in table 3.

List of data	No. of patients
Lesion restenosis	
<50%	3
50-70%	6
Greater than 70%	74

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100%	8
Intervention stage	
Pre-treatment	2
Primary	78
Adjunct	6
Missing	3
Target vessel	
Cx n	19
LAD	24
RCA	31
SVG	9
LMS	5
No. of vessel PCI	
1 vessel	80
2 vessels	10
3 vessels	2
Bifurcation	12
Angiographic failure	3
Angiographic success	91
No. of lesions (%)	
1%	81
≥ 2 n (%)	11

Table 3: Data required for procedure

There were 91 patients that were discharged on ASA, 76 were discharged on clopidogrel and 14 patients were discharged on ticagrelor. The follow-up of almost 37 weeks was carried out for all the patients. Univariable and multivariable analysis was also carried out for MACE as shown in table 4.

Variable	Univariable		Multivariable	
	H.R. (95% CI)	p HR	H.R. (95% CI)	p HR
Age	1.055 (1.005,1.078)	0.0752	1.04 (1.55,1.012)	0.015
Balloon length (mm)	1.015 (0.563,1.095)	0.2635		
Sex, female	1.50	0.0567		
Vessel lesion	(0.962,4.763)	0.3451		
Cx reference	0.959 (0.387,2.798)			
LAD	2.880 (0.695,1.075)	0.0831		
LMS	1.0508	0.0312		
RCA	(0.769,8.6)	0.387		
SVG	2.95 (0.71,8.071)	0.128		
Hypertension	2.681(0.312,18.91)	0.376		
Diabetes	1.11(1.012, 0.128)	0.165		
Smoker	0.9(0.405,1.88)	0.834		
Dyslipidemia	2.31(0.05,3.078)	0.438		
Prior MI	2.155 (0.512,3.078)	0.659	2.131 (1.173.4.134)	0.0131
Prior CABG	2.41(1.23,0.478)	0.0129		
Graft failure	0.813(1.121,1.912)	0.723		
ISR-DES	1.61(1.13,0.78)	0.356		
ISR-BMS	0.813 (1.175,1.882)	0.368		

Table 4: Univariable multivariable analysis for MACE

DISCUSSION

This study was carried out to find the occurrence and predictors of the consequences found in the treatment of in-stent restenosis by making use of drug-eluting balloons. This is a real-life single center study that was carried out on 92 patients. The use of DEB in CAD along with the significant follow-up was analyzed. In this study it was found that the clinical consequences in DEB for treating ISR are in accordance with the length of lesion and number of balloons used. The risk of DEBs was analyzed prior to this work in RIBSIV and other procedures. Although only one-year outcome was analyzed in this study which is not enough for DES, still it did well for mortality and the rate of MACE was found to be quite reasonable. As per our study the mortality rate came out to be high as compared to other studies carried out for one year. Our study showed results more comorbid with high ratio of patients with diabetes mellitus and previous history of myocardial infection. If we compare the demographic data of both RIBS DEB and DES arm to this study, the participants were of same age [11]. But as far as comorbidities are concerned there was high rate of diabetes, hypertension and dyslipidemia in our study. There was quite different presentation found in these patients, as most of them were presented with stable angina pain. And the rest of them showed symptoms of acute coronary syndrome. In our study it was found that there were 76% patients that were released on clopidogrel and 15% were discharged on tricagrelor. This study demonstrates that the use of long balloon or multiple balloons can't be used as a prognostic marker, and there is a link of MACE risk and ultimate death with age and past history of bypass surgery. The vessels intervened in previous studies were predominantly LAD, then it was followed by RCA and Cx [12, 13]. In our studies there was some contrast found in the vessel as the highest intervened vessel was RCA and then it was followed by LAD and LCX. As per some previous studies the five-year outcomes of DEBs in ISR vs DES were studied [14]. In a retrospective study the five-year comparison was done and the mortality rate came out to be 18% as compared to 21% in our study. There five-year MACE was 47% which is greater than that found in our study. The univariable and multivariable analysis was carried out by making us of hazard ratio (HR) which is similar to that used by previous studies [15, 16]. 95% confidence interval and a p-value less than 0.05 was kept for statistical analysis. As per some studies the link of MACE and death with the history of bypass surgery can help doctors decide what sort of cases of ISR should be given treatment through DEB so that death rate can be reduced [17]. The main findings of this study are that DEB angioplasty in ISR gives effective results even in a significantly comorbid population. Some of the features studied in this study were balloon's length and no. of vessels used. In case of multivariable analysis, the total length of the lesion was insignificant. However, it was observed that DEBs per vessel value was significant. This indicates that long length lesions that require the use of various DEBs are difficult to perform and can result in failure. This prognostic

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marker can be studied more precisely for future studies [18]. This indicates that the use of multiple DEBs where only one can be used is not a favorable approach. Univariate analysis has shown that the main determinants in this study were age and the patient's history of CABG. Similar results were obtained on multivariate analysis as well. As per studies the use of (drug eluting balloons) DES is not an ideal solution especially in case of patients suffering from coronary artery disease [19-21]. There are certain limitations of this study, one limitation can be the retrospective design of study and the small sample size. As this study was retrospective so the part of selection bias can't be ignored. Secondly, due to the small sample size, it is difficult to comment on intervention of lesion.

CONCLUSIONS

This single center study showed significantly low rate of TLR for a period of one year and moderate rate was found at five years. This study demonstrates that the use of drug-eluting balloon for in-stent restenosis (DES-ISR) treatment is safe and can be considered as effective treatment even in case of high comorbid population. This study also demonstrates that the factors like length of balloons and use of various balloons is not a prognostic marker. This study can help clinicians to make precise decisions to select which ISR patient can be treated with DEB.

Conflicts of Interest

The authors declare no conflict of interest.

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