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Research Article

Clinical Outcomes of Biodegradable Polymer Sirolimus-Eluting Stent in Coronary Artery Lesions Patients: A Retrospective Analysis

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Abstract

The aim of this study was to evaluate the safety and efficacy of biodegradable polymer BioMime™ sirolimus-eluting coronary stent (SES) for the treatment of coronary artery disease. This was a retrospective analysis of 73consecutive patients who underwent percutaneous coronary intervention with BioMime SES implantation were included. The clinical endpoint was a major adverse cardiac event (MACE) including cardiac death, myocardial infarction (MI) and target lesion revascularization. The mean patient age was 61.3 ± 12.2 years and 62 (84.9%) were male. A total of 139 lesions were intervened successfully with 73 stents. The average stent length and diameter was 24.4 ± 8.38 mm and 2.79 ± 0.27 mm respectively. The patients characteristics were noted as having 28 (38.4%) diabetics and 36 (49.3%) hypertensive patients. Device and procedural success was 100%. During a mean follow-up at 1.68 ± 0.58 years, the absence of MACE was observed. No stent thrombosis or MI was reported. The present study demonstrated the BioMime SES is safe and effective in "real-world" coronary artery disease patients population.

Keywords: *Biodegradable Polymer; Percutaneous Coronary Intervention; Sirolimus-Eluting Stent*

Abbreviations

CAD: Coronary Artery Disease; DES: Drug-Eluting Stent; MACE: Major Adverse Cardiac Events; MI: Myocardial Infarction; PCI: Percutaneous Coronary Intervention; ST: Stent Thrombosis; TLR: Target Lesion Revascularization

Introduction

Coronary artery disease (CAD) is a major cause of mortality in the arena of global health concern [1]. Drug-eluting stent (DES) implantation is a conventional treatment approach in patients undergoing percutaneous coronary intervention (PCI) over the last few years [2]. Early PCI procedures involved balloon angioplasty with bare-metal stents (BMS) and at present accepted DES technology was introduced [3]. The last 10 years, first-generation DES has extensively used devices worldwide for CAD patients [4]. The first-generation DES has a stainless steel stent platform and more recently, second-generation DES have been developed using a cobalt-chromium (Co-Cr) stent platform with more radiopaque and radial force [4,5]. In contrast to first-generation DES, new-generation DES system have challenged to improve safety, significantly decreased restenosis, neointimal hyperplasia and the need for target vessel revascularization [6-10]. In advance stent technology, use of biocompatible and biodegradable polymers components of new-generation DES system have minimized the risk of late restenosis and thrombus formation [11]. BioMime™ (Meril Life Sciences Pvt. Ltd., Vapi, India) is new-generation DES coated with biodegradable polymer sirolimus-eluting stent (SES). The biodegradable polymer SES delivers sirolimus which releases into the treated vessel during 30 - 40 days after stent implantation [12]. The first in human study of BioMime SES has confirmed exceptional clinical out-

comes with high procedural success (100%) in CAD patients [13]. Thus, DES such as BioMime SES (CE approved) has been developed with a purpose to reduce the adverse effects and restenotic rates in real-world patients.

Aim of the Study

The aim of this study was to evaluate the safety and efficacy of BioMime biodegradable polymer SES in the treatment of CAD patients.

Methods

Study design and patient population

This was a retrospective, single-center, non-randomized and observational study carried out in real-world patients. A total of 73 consecutive patients who underwent PCI with the use of BioMime SES between May 2015 and 2017 at Padmavathy Medical Foundation, Kerala, India, were included in this study. Patients with age 18 years or above, stable or unstable angina or ischemic heart disease, and patients who had undergone PCI with at least use of BioMime™ SES stent were considered for the study. However, patients who refused to provide written informed consent were excluded from the study. The study was performed in accordance with the Helsinki declaration. All patients signed the informed consent form as per the Institutional Review Board or Independent Ethics Committee.

Study device and procedure

The BioMime SES platform is made of L605 cobalt chromium alloy with a hybrid cell design. The stent is available in size of 8, 13, 16, 19, 24, 29, 32, 37, 40, 44, 48 mm lengths and diameters of 2.00, 2.25, 2.50, 2.75, 3.00, 3.50, 4.00, 4.50 mm-cell structure design. The cell design of BioMime stent is a mix of open and closed cells architecture. The strut thickness is 65 µm (ultra-thin). The BioMime SES has a sirolimus-coated 1.25 µg/mm^2 stent surface area. The drug-carrier of BioMime device is a co-polymer composition of biocompatible and biodegradable polymers components, i.e. poly-L-lactic acid (PLLA) and poly-lactic-co-glycolic acid (PLGA).

The coronary angioplasty procedures were performed as per the current standard guidelines [14]. After the procedure, all patients received dual antiplatelet therapy (DAPT) with a loading dose of aspirin (75-325 mg/day) and clopidogrel (75 mg/day) or prasugrel (10 mg/day) or ticagrelor (90 mg/day) for at least 12 months.

Study endpoints and definitions

The clinical end-point of this study was to determine the incidence of major adverse cardiac events (MACE) during the follow-up period after the index procedure. MACE was defined as cardiac death, myocardial infarction (MI) and target lesion revascularization (TLR). Cardiac death is defined as any death due to immediate cardiac cause like MI, arrhythmia, cardiac failure, cardiac arrest, procedure related deaths, unwitnessed death or unexplained cause death. MI is defined as symptomatic or silent ischemic myocardial injury identified by electrocardiogram changes or cardiac enzymes. TLR was defined as repeat percutaneous coronary intervention of the target lesions or bypass grafting of the target vessel executed for other complication or restenosis of the target lesion. The stent thrombosis (ST) was categorized according to the Academic Research Consortium definitions [15]. Procedural success was defined as an angiographic success without MACE during hospitalization [16]. Device success was defined as the ability of device to insert into the target lesion and the ability of < 30% final residual diameter stenosis [17].

Statistical analysis

Statistical analysis was carried out using Microsoft Excel spreadsheet (version 2007, Microsoft Corp, Seattle, Washington). Categorical variables were presented as number with percentages of the total. Values were expressed as a mean ± standard deviation. All data were evaluated with the statistical package for social sciences (SPSS Statistics; Chicago, IL, USA) program, version 15.

Results

Patient characteristics

Among 73 patients, mean patient age was 61.3 ± 12.2 years, and 62 (84.9%) were male. Baseline and demographic characteristics are outlined in table 1. The co-morbidities, i.e. diabetes mellitus and hypertension were presented in 28 (38.4%), and 36 (49.3%) patients respectively. Moreover, history of previous PCI and CAD was observed in 24 (32.9%) and 29 (39.7%) patients respectively. The mean percent left ventricular ejection fraction was 48.3 ± 6.33. The majority of 55 (75.3%) patients had Non-ST- segment elevation myocardial infarction.

Characteristics	Patients (n = 73)
Age (Mean ± SD), Years	61.27 ± 12.23
Gender, n (%)	
Male	62 (84.9%)
Female	11 (15.1%)
BMI kg/m^2, Mean ± SD	24.84 ± 3.63
Heart rate (bpm), Mean ± SD	75.80 ± 13.66
SBP (mmHg), Mean ± SD	137.9 ± 28.9
DBP (mmHg), Mean ± SD	83.19 ± 11.57
Medical history	
Diabetes mellitus	28 (38.4%)
Hypertension	36 (49.3%)
Smoking	9 (12.3%)
Previous PCI	24 (32.9%)
Previous CAD	29 (39.7%)
Angina	3 (4.1%)
COPD	1 (1.4%)
Alcoholic	1 (1.4%)
Other illness	3 (4.1%)
LVEF %, Mean ± SD	48.25 ± 6.33
Cardiac Status, n (%)	
Stable angina	6 (8.2%)
Unstable Angina	6 (8.2%)
STEMI	55 (75.3%)
NSTEMI	6 (8.2%)

Table 1: *Baseline and demographic characteristics of the study population.*

Values are expressed as mean ± standard deviation or frequencies (percentages of the total).

BMI: Body Mass Index; DBP: Diastolic Blood Pressure; SBP: Systolic Blood Pressure; CAD: Coronary Artery Disease; COPD: Chronic Obstructive Pulmonary Disease; PCI: Percutaneous Coronary Intervention; LVEF: Left Ventricular Ejection Fraction; STEMI: ST Segment Elevation Myocardial Infarction; NSTEMI: Non-ST Segment Elevation Myocardial Infarction.

Procedural characteristics

Baseline lesion and procedural characteristics are outlined in table 2. A total of 73 lesions were treated with BioMime SES. The average stent length was 24.4 ± 8.38 mm, and average stent diameter was 2.79 ± 0.27. The average number of lesions was 139. Patients with single, two and three diseased vessels were 25 (34.2%), 30 (41.1%), and 18 (24.7%) respectively. Baseline analysis showed 84.5 ± 18.28 mean percent diameter stenosis. The target vessel was left anterior descending artery 34 (46.58%), followed by the right coronary artery 23 (31.51%) and the left circumflex 16 (21.92%). Device and procedure success were obtained in 100% of patients. A mean follow-up period of 1.68 ± 0.58 years demonstrated the absence of MACE (all-cause death, MI, and TLR) or ST.

Variables	Patients (n = 73)
Disease Vessel, n (%)	
Single Vessel	25 (34.2%)
Double Vessel	30 (41.1%)
Triple Vessel	18 (24.7%)
Lesion location, n (%)	
RCA	23 (31.51%)
LAD	34 (46.58%)
LCx	16 (21.92%)
Procedure characteristics	
Total Number of Lesions	139
Total number of lesion treated with study stent	73
Diameter stenosis %, Mean ± SD	84.51 ± 18.28
Stent length (mm), Mean ± SD	24.37 ± 8.38
Stent Diameter (mm), Mean ± SD	2.79 ± 0.27

Table 2: *Lesion and procedural characteristics.*
Values are expressed as mean ± standard deviation or frequencies (percentages of the total).
LAD: Left Anterior Descending Artery; LCx: Left Circumflex Artery; RCA: Right Coronary Artery.

Discussion

Next generation DES has been an advance discovery in the arena of interventional cardiology. There was a decrease in restenosis rate and revascularization with DES as compared to BMS [7,18]. In the present study, the BioMime SES represented favorable outcomes in the treatment of CAD patients including procedural success and clinical presentation. This study population had a high occurrence of hypertension (49.3%) and diabetes (38.4%). In ISAR-STEREO and ISAR-STEREO-2 trials, thinner-strut stents reduced angiographic and clinical restenosis compared to the thicker-strut stent (140 μm Vs. 50 μm) [19,20]. Furthermore, EXCEL and EXCEL II, cobalt-chromium thin-struts stents were prevent restenosis compared to stainless steel thick-struts stents (120 μm Vs. 88 μm) [21,22]. In addition, ultra-thin struts thickness platforms improved flexibility and deliverability to expedite PCI procedures. The ultra-thin struts thickness BioMime SES is comprised of DES platform using inventive hybrid cell design (combination of open and closed cell architecture) and morphology-mediated expansion. This expansion eradicates the typical dog-boning and gives excellent stent arrangement. Therefore, BioMime SES is associated with enhanced deliverability, clinical outcome, re-endothelialization and reduction of in-stent restenosis compared with thicker strut DES [19,23]. Sirolimus is an anti-proliferative drug which affects the local vessel wall after implantation and common final

pathway of cell division cycle. It decreased neointima formation by inhibiting vascular smooth muscle migration and proliferation [24]. Previous studies reported with novolimus-eluting stents, everolimus-eluting stents, zotarolimus-eluting stents and SES have demonstrated safety and efficacy in the treatment of real-world CAD patients [25-29]. Moreover, biocompatible and biodegradable polymers show to be essential constituents of BioMime SES. The DES with the biodegradable polymer have some advantages such as preventing the issue due to the long-lasting polymeric residue, improving endothelization, vascular healing, decrease the dependence on prolonged DAPT and bleeding events [11,12]. Furthermore, NOBORI 2 clinical study has evaluated the safety and performance of biodegradable polymers in real-world population with more complex lesions [30]. The BioMime SES in meriT-1, meriT-2 and meriT-3 study represented favorable safety and efficacy in real-world CAD patients with high prevalence of diabetes and multiple complex lesions [13,31,32]. The preliminary evaluation of meriT-1 study revealed that there were no safety concerns including the absence of MACE or ST at 1-year follow-up. Similarly, the MACE rate in meriT-2 and meriT-3 study was 15 (6.0%) and 26 (2.35%) at 1-year follow-up. Our finding suggested BioMime SES was associated with the absence of MACE or ST during 1.68 ± 0.58 years mean follow-up period sustain the meriT-1, meriT-2 and meriT-3 results. In sirolimus-eluting Orsiro stent system (BIOFLOW-I), MACE rate was 3 (10.0%) and no MI or ST reported through 1-year follow-up, these findings agree with our results [11]. In addition, sirolimus-eluting Excel II stent, there were similarly no instances of MACE and ST at 12-month follow-up. In this study, BioMime SES incorporates some features such as the ultra-thin struts and sirolimus-coated biodegradable polymer with lower restenotic rates. Therefore, it is observed that combination of an ultra-thin struts and biodegradable polymer has considerable clinical procedure and outcomes of the BioMime SES in real-world patients. The study limitations of our study, this was a single-arm design, non- randomized, retrospective analysis and lack of control group for comparison. The present study is limited by the fact that, the number of patients was relatively less in compare to previously published studies, so further studies on a more number of patients are needed.

Conclusion

In conclusion, the clinical result of BioMime with biodegradable polymer coated sirolimus-eluting stent is safe and effective in real-world coronary artery disease patients, demonstrating the absence of MACE or ST at mean follow-up.

Conflict of Interest

The author declares no conflict of interest.

Bibliography

1. Ma X., *et al*. "Drug-eluting stent coatings". *Interventional Cardiology* 4 (2012): 73-83.

2. Ishii H., *et al*. "Percutaneous coronary intervention with bare metal stent vs. drug-eluting stent in hemodialysis patients". *Circulation Journal: Official Journal of the Japanese Circulation Society* 76 (2012): 1609-1615.

3. Yildiz M., *et al*. "Recent Developments in Drug-Eluting Coronary Stents". *Cardiovascular and Haematological Disorders* 14 (2014): 220-224.

4. Navarese EP., *et al*. "First-generation versus second-generation drug-eluting stents in current clinical practice: updated evidence from a comprehensive meta-analysis of randomised clinical trials comprising 31 379 patients". *Open Heart* (2014).

5. Jaffery Z., *et al*. "Drug-eluting coronary stents - focus on improved patient outcomes". *Patient Related Outcome Measures* 2 (2011): 161-174.

6. Morice M-C., *et al*. "A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization". *The New England Journal of Medicine* 346 (2002): 1773-1780.

7. Moses JW., *et al*. "Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery". *The New England Journal of Medicine* 349 (2003): 1315-1323.

8. Lemos PA., *et al*. "Unrestricted utilization of sirolimus-eluting stents compared with conventional bare stent implantation in the "real world": the Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital (RESEARCH) registry". *Circulation* 109 (2004): 190-195.

9. Stettler C., *et al*. "Outcomes associated with drug-eluting and bare-metal stents: a collaborative network meta-analysis". *The Lancet* 370 (2007): 937-948.

10. Spaulding C., *et al*. "A pooled analysis of data comparing sirolimus-eluting stents with bare-metal stents". *The New England Journal of Medicine* 356 (2007): 989-997.

11. Hamon M., *et al*. "Clinical and angiographic experience with a third-generation drug-eluting Orsiro stent in the treatment of single de novo coronary artery lesions (BIOFLOW-I): a prospective, first-in-man study". *EuroIntervention* 8 (2013): 1006-1011.

12. Seth A., *et al*. "Late angiographic and clinical outcomes of the novel BioMime™ sirolimus-eluting coronary stent with ultra-thin cobalt–chromium platform and biodegradable polymer for the treatment of diseased coronary vessels: results from the prospective, multicentre meriT-2 clinical trial". *AsiaIntervention* 2 (2016): 19-27.

13. Dani S., *et al*. "First-in-human evaluation of the novel Bio Mime sirolimus-eluting coronary stent with bioabsorbable polymer for the treatment of single de novo lesions located in native coronary vessels - results from the meriT-1 trial". *EuroIntervention* 9 (2013): 493-500.

14. Levine GN., et al. "2015 ACC/AHA/SCAI Focused Update on Primary Percutaneous Coronary Intervention for Patients With ST-Elevation Myocardial Infarction: An Update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention and the 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction. A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Society for Cardiovascular Angiography and Interventions". *Catheterization and Cardiovascular Interventions* (2015).

15. Cutlip DE., *et al*. "Clinical End Points in Coronary Stent Trials. A Case for Standardized Definitions". *Circulation* 115 (2007): 2344-2351.

16. Dani S., *et al*. "First-in-human evaluation of the novel Bio Mime sirolimus-eluting coronary stent with bioabsorbable polymer for the treatment of single de novo lesions located in native coronary vessels-results from the meriT-1 trial". *EuroIntervention: journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology* 9 (2013): 493-500.

17. Alaswad K., *et al*. "Transradial approach for coronary chronic total occlusion interventions: insights from a contemporary multicenter registry". *Catheterization and Cardiovascular Interventions* 85 (2015): 1123-1129.

18. Colombo A., *et al*. "Randomized study to assess the effectiveness of slow-and moderate-release polymer-based paclitaxel-eluting stents for coronary artery lesions". *Circulation* 108 (2003): 788-794.

19. Kastrati A., *et al*. " [Intracoronary Stenting and Angiographic Results Strut Thickness Effect on Restenosis Outcome (ISAR-STEREO) Trial] ". *Vestnik Rentgenologii i Radiologii* (2012): 52-60.

20. Pache J., *et al*. "Intracoronary stenting and angiographic results: strut thickness effect on restenosis outcome (ISAR-STEREO-2) trial". *Journal of the American College of Cardiology* 41 (2003): 1283-1288.

21. Wang G., *et al*. "First-in-man study evaluating the safety and efficacy of a second generation biodegradable polymer sirolimus-eluting stent in the treatment of patients with de novo coronary lesions: clinical, Angiographic, and OCT outcomes of CREDIT-1". *Catheterization and Cardiovascular Interventions* 85 (2015): 744-751.

22. Xu K., *et al*. "Efficacy and Safety of A Second Generation Biodegradable-Polymer Sirolimus-Eluting Stent: One Year Results of The CREDIT 2 Trial". *Cardiovascular Therapeutics* 36.3 (2018): e12327.

23. Simon C., *et al*. "Influence of topography on endothelialization of stents: clues for new designs". *Journal of Long-Term Effects of Medical Implants* (2000): 10.

24. Lekshmi KM., *et al*. "Drug- and Gene-eluting Stents for Preventing Coronary Restenosis". *Chonnam Medical Journal* 53 (2017): 14-27.

25. Costa JJ., *et al*. "EXCELLA First-in-Man (FIM) study: safety and efficacy of novolimus-eluting stent in de novo coronary lesions". *EuroIntervention* 4 (2008): 53-58.

26. Taniwaki M., *et al*. "4-year clinical outcomes and predictors of repeat revascularization in patients treated with new-generation drug-eluting stents: a report from the RESOLUTE All-Comers trial (A Randomized Comparison of a Zotarolimus-Eluting Stent With an Everolimus-Eluting Stent for Percutaneous Coronary Intervention) ". *Journal of the American College of Cardiology* 63 (2014): 1617-1625.

27. Pilgrim T., *et al*. "Ultrathin strut biodegradable polymer sirolimus-eluting stent versus durable polymer everolimus-eluting stent for percutaneous coronary revascularisation (BIOSCIENCE): a randomised, single-blind, non-inferiority trial". *The Lancet* 384 (2014): 2111-2122.

28. Waksman R., *et al*. "Safety and efficacy of the XIENCE V everolimus-eluting stent compared to first-generation drug-eluting stents in contemporary clinical practice". *The American Journal of Cardiology* 109 (2012): 1288-1294.

29. Stone GW., *et al*. "Comparison of an everolimus-eluting stent and a paclitaxel-eluting stent in patients with coronary artery disease: a randomized trial". *Journal of the American Medical Association* 299 (2008): 1903-1913.

30. Danzi GB., *et al*. "Clinical performance of a drug-eluting stent with a biodegradable polymer in an unselected patient population: the NOBORI 2 study". *EuroIntervention* 8 (2012): 109-116.

31. Seth A., *et al*. "Late angiographic and clinical outcomes of the novel BioMime™ sirolimus-eluting coronary stent with ultra-thin cobalt-chromium platform and biodegradable polymer for the treatment of diseased coronary vessels: results from the prospective, multi-centre meriT-2 clinical trial". *Asia Intervention* 2 (2016): 19-27.

32. Jain RK., *et al*. "One-year outcomes of a BioMime™ Sirolimus-Eluting Coronary Stent System with a biodegradable polymer in all-comers coronary artery disease patients: The meriT-3 study". *Indian Heart Journal* 68 (2016): 599-603.

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