Ultrathin (60 µm), ultralong (≥ 40 mm) sirolimus-eluting stent: study of clinical and safety profiles among real-world patients

Santosh Kumar Sinha, Puneet Aggarwal[1], Umeshwar Pandey, Mahmodullah Razi, Awdesh Kumar, Vinay Krishna

Department of Cardiology, LPS Institute of Cardiology; Kanpur-*India*
[1]Department of Cardiology, Dr. Ram Manohar Lohia Institute of Cardiology; New Delhi-*India*

Abstract

Objective: Although thin-strut drug-eluting stents (DES) with a more flexible design are easily obtainable, data regarding using ultralong DES (≥40 mm) for long coronary lesions are limited in the literature. Therefore, the current study assessed the safety and efficacy of an ultralong (≥40 mm) and ultrathin (60 µm) biodegradable polymer-coated sirolimus-eluting stent (SES), Supralimus Grace, with a unique Long Dual Z-link (LDZ-link) design (Sahajanand Medical Technologies Pvt. Ltd., Surat, India) in real-world patients with long coronary lesions.

Methods: The assigned stents were implanted in 684 patients. The primary endpoint was target lesion failure (TLF), which is a composite of cardiovascular death, target vessel myocardial infarction (MI), and target lesion revascularization (TLR), whereas periprocedural secondary endpoints included device failure (failure of stent delivery, change of stent, and stent fracture) and patient-oriented composite endpoint (POCE), which is a composite of all deaths, any MI, and any revascularization, and stent thrombosis (ST). These outcomes were analyzed at one-year follow-up and during the procedure.

Results: The patients' mean age was 52.7±15.9 years; 537 (78.5%) were males. 626 (91.5%) patients suffered from acute coronary syndrome and 58 (8.5%) patients from chronic coronary syndrome (CSS). 989 lesions were removed. The mean numbers of lesions and stents implanted per patient were 1.3±0.2 mm and 1.4±0.3 mm, respectively. TLF occurred in 42 (6.1%) as a result of cardiac death, target vessel MI, and TLR in 9 (1.3%), 20 (2.9%), and 13 (1.9%) patients, respectively. POCE was observed in 131 patients (19.1%) at one-year follow-up, mainly in 63 (9.2%) patients because of any revascularization. Stent failure was seen in 21 patients (3.1%) as a result of delivery failure (2.2%), edge dissection (0.8%), and fracture (0.1%). Definite and probable ST were observed in 8 (1.1%) and 9 (1.3%) patients, respectively.

Conclusion: Ultralong (≥40 mm), ultrathin (60 µm) Supralimus Grace stent can be safely implanted in vessels having long and multiple lesions.

Keywords: drug-eluting stent, ultrathin stent, ultralong stent, target lesion failure, stent thrombosis, percutaneous coronary intervention, target lesion revascularization

Cite this article as: *Sinha SK, Aggarwal P, Pandey U, Razi M, Kumar A, Krishna V. Ultrathin (60 µm), ultralong (≥40 mm) sirolimus-eluting stent: study of clinical and safety profiles among real-world patients. Anatol J Cardiol 2021; 25: 111-9.*

Introduction

The interventional cardiology field had undergone metamorphological improvements, over the last four decades. Older generation DES had major technical problems such as trackability and deliverability because they were short and thick; however, with ultrathin struts and more flexible stent design, the new-generation DES have resolved these drawbacks. Therefore, the use of new-generation DES in treating more diffuse and calcified long lesions has been exponentially increased with good clinical outcomes (1-3). Long lesions accounted for 20% of coronary artery diseases. Treating long lesions usually requires long and multiple stents to provide sufficient coverage, thus rendering the percutaneous coronary intervention (PCI) a difficult procedure due to the higher risk of adverse events such as restenosis and stent thrombosis (4, 5). In general, multiple overlapping stents have been implanted in long diffuse coronary lesions; however, they had the following complications: triggering typical inflammatory reactions, delayed vascular healing, incomplete endothelization, and excessive contrast use with implantation

Address for correspondence: Santosh Kumar Sinha, MD, Department of Cardiology, LPS Institute of Cardiology; Kanpur-*India*
Phone: 9670220088 E-mail: fionasan@rediffmail.com

Accepted Date: 24.08.2020 **Available Online Date:** 03.01.2021

DOI:10.14744/AnatolJCardiol.2020.40909

Anatol J Cardiol 2021; 25: 111-9
DOI:10.14744/AnatolJCardiol.2020.40909

HIGHLIGHTS

- Ultra long and ultrathin Supralimus Grace bioresorbable polymer, sirolimus eluting stent is safe and effective across all substrate of lesion including full metal jacket stenting of chronic total occlusion, possibly non CTO, and diffusely diseased vessels. It may reduce the risk of repeated revascularization in small vessel lesions giving a positive effect on the patients 'comfort and morbidity as well as health care expenditures. By virtue of this stent, one may expect that PCI with DES implantation will be even more frequently the therapy of choice in patients with lesions in small and very small coronary arteries.

of multiple overlapping stents with earlier generation DES and bare-metal stents (6-9). However, latest-generation DES with thinner struts and more flexible design overcome the complications associated with multiple overlapping stents. Moreover, it has been observed that the risks of stent thrombosis and lesion recurrence are increased in the case of thicker struts (10). Also, thicker strut with minimal in-stent lumen diameter is an independent predictor of future in-stent restenosis (11). The ultrathin struts make the stents flexible enhancing the deliverability and trackability across the complex lesion, especially in small vessels (<2.75 mm) (12). The latest addition in the Supra family, Supralimus Grace (Sahajanand Medical Technologies Pvt. Ltd, Surat, India) SES, is an ultrathin (60 µm) biodegradable polymer-coated DES on cobalt-chromium (Co-Cr) platform with a unique Long Dual Z-link (LDZ-link). The safety and efficacy of this ultrathin SES have already been proved in various real-world populations with coronary artery diseases (10, 13-15); however, in coronary arteries with long lesions, they have not been reported. Thus, the safety and efficacy of an ultralong (≥40 mm) ultrathin (60 µm) Supralimus Grace SES with LDZ-link in patients with long coronary lesions are evaluated in this study.

Methods

Study design and participants

This was a prospective, single-arm, investigator-initiated study conducted at the LPS Institute of Cardiology, G.S.V.M. Medical College, Kanpur, Uttar Pradesh, India, a tertiary referral hospital, between January 2016 and July 2017. 684 consecutive patients (age ≥18 years), who had undergone PCI using one or more ultralong (≥40 mm) Supralimus Grace SES with LDZ-link, were enrolled in this study.

Inclusion criteria were as follows: (1) acute coronary syndrome (ACS) including ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina (UA); (2) chronic coronary syndrome refractory to guideline-directed medical therapy; (3) in-stent restenosis (ISR); (4) bifurcation lesion (dedicated stenting of both vessels based on the Medina classification); (5) graft vessel PCI after coronary artery bypass surgery. All STEMI patients who underwent primary and pharmacoinvasive strategies and those who presented late but have ongoing angina were included in the study. The patients' baseline demographics were recorded including the following: clinical data such as age, sex, clinical presentation, and indications for surgical intervention; angiographic outcomes such target lesion and lesions' type and characteristics; procedural data such as guiding catheter's type, guidewire, stent, and lesion preparation. An assessment of coronary angiogram was carried out using visual estimation and quantitative coronary angiography (QCA). Lesions were categorized into types A, B1, B2, and C according to the American Heart Association/American College of Cardiology (AHA/ACC) criteria including length, calcification, chronicity, angulation, and tortuosity (16). Irrespective of the anatomical location, the cutoff values for significant stenosis and reference vessel diameter were ≥70% and ≥2.25 mm, respectively. In terms of the bifurcation lesions, only those patients where dedicated stenting was carried out and a long stent was implanted in the vessel (≥40 mm) were included, irrespective of the diameter of the side branch stent. The bifurcation strategy was planned according to the side branch caliber and its angle. The target vessel, length and number of lesions, and the number of stents have been left to the operator's discretion. Exclusion criteria were as follows: intolerance to antiplatelet drugs (e.g., aspirin, clopidogrel, ticagrelor, and prasugrel), heparin, and sirolimus; expected major surgery within 6 months after PCI; life expectancy <12 months; disease of the left main vessel either in isolation or involving left anterior descending or circumflex artery where the implanted stent length is <40 mm; having cardiogenic shock. All patients signed informed consent before performing the procedures; the Institutional Ethics Committee approved the study's protocol. The study strictly complied with the Good Clinical Practice principles and Declaration of Helsinki.

Study device (Fig. 1)

Supralimus Grace is an ultrathin (60 µm) biodegradable polymer-coated SES designed with a unique LDZ-link on a Tetrinium L605 Co-Cr platform with in-phase strut design. This latest-generation stent has a multilayer conformal coating on the surface, that is, sirolimus drug mixed with a matrix of biodegradable polymers containing a combination of hydrophilic and hydrophobic polymers (poly(L-lactide), poly(L-lactide-co-caprolactone), and polyvinylpyrrolidone). Moreover, this special biodegradable polymers' mixture in each layer plays an integral role in controlling drug release and ensuring the integrity of the coating. Furthermore, a drug-free top layer consisting of hydrophilic polymers and antioxidants enhance the shelf life of the products, in addition to protecting the coating layers during implantation. 80% of sirolimus is eluted in one month; then, the rest is slowly released over a period of three months. Regard-

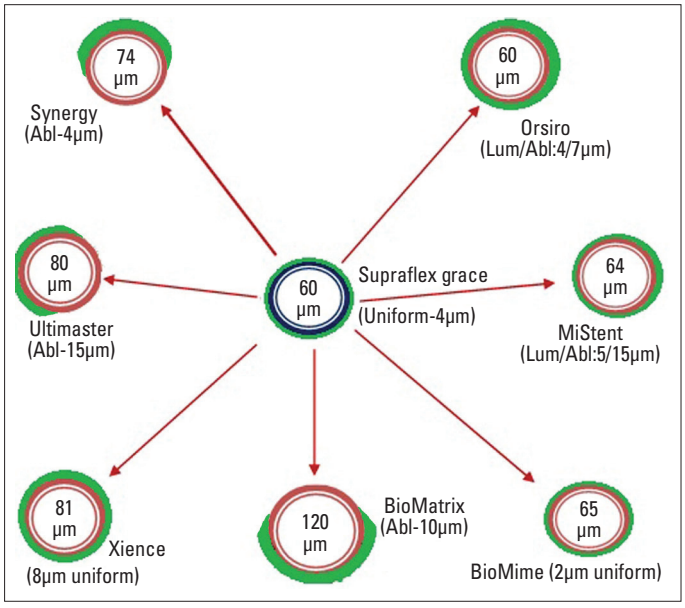

Figure 1. Schematic representation of strut and polymer thickness of contemporary stents. Green color indicates the thickness of the polymer
Lum - luminal; Abl - abluminal

less of the diameter of the stent, the average coating thickness (5-6 µm) remains the same. It takes 9 to 12 months for the polymer to be fully degraded.

Percutaneous coronary intervention protocol and follow-up

Following standard techniques, the procedures were carried out via a transfemoral or transradial route using a 6F guiding catheter; however, in cases of dedicated bifurcation lesion and chronic total occlusion, a 7F guiding catheter was utilized. Unfractionated heparin was used as an anticoagulant (dose=70–100 U/kg). Predilatation with semicompliant, noncompliant, or cutting balloon was performed to modify the lesions, except in direct stenting cases where thrombus-laden lesions appeared to be very soft. Thrombosuction was performed using Thrombuster II 6F catheter (Kaneka Medix Corporation, Japan) to decrease the thrombus burden, in cases of total occlusion. Similarly, postdilatation was conducted using a noncompliant balloon accordingly. During the index procedure, multivessel intervention was done, except in ACS patients where culprit artery-only revascularization was performed followed by other vessels within 4 weeks. All patients were pretreated with aspirin and a P2Y12 inhibitor (ticagrelor, prasugrel, or clopidogrel); dual antiplatelet therapy was continued for at least 12 months, then aspirin as a monotherapy indefinitely. Ticagrelor was the preferred antiplatelet agent, followed by prasugrel and clopidogrel depending on the economy and drug availability. The stent was delivered in a standard fashion; if failed, a buddy wire with or without balloon anchoring was employed. GuideZilla extension catheter (GEC) was used in refractory cases due to various technical challenges (17). In case delivering the stent failed, another stent was chosen according to the operator's preference. Cardiac biomarkers (creatine kinase-myocardial band and troponins I and T) were measured 24 h before and within 8 h after the intervention to diagnose periprocedural MI. All patients were followed up clinically (history, electrocardiogram, and echocardiogram) at one week, one month, six months, and 12 months; check angiogram was performed only if the patient was symptomatic or presented with ASC.

Study endpoints

The primary endpoint of this study was TLF, which is a composite of cardiac death, target vessel MI, and ischemia-driven TLR assessed at 12 months. Secondary endpoints were as follows: all-cause mortality (cardiac and noncardiac), cardiac death, any revascularization, ischemia-driven TLR, ischemia-driven target vessel revascularization (TVR), ST, periprocedural and spontaneous MI, and device failure (composite of stent delivery failure, changing stent, and stent fracture). POCE is the composite endpoint of all-cause mortality, any MI, and any revascularization. ST and periprocedural and spontaneous MI were defined according to the Academic Research Consortium (ARC) criteria (18), World Health Organization definition (19), and Third Universal Definition of Myocardial Infarction (20), respectively. Based on the clinical presentation, laboratory data, and the electrocardiogram and angiographic findings, target vessel-related MI was attributed to the target vessel or could not be related to another vessel (21). Revascularization was performed when diameter stenosis was ≥70% with subjective evidence of ischemia. Device success was defined as successful trackability, deliverability, and deployment of the stent at the target lesion with final residual stenosis ≤30% after postdilatation, if any.

Statistical evaluation

The Statistical Package for Social Sciences program, version 20 (SPSS 20; Chicago, IL, USA), was used to analyze the data. Mean±standard deviation and frequency (percentage) represented the continuous and categorical variables, respectively. A Kaplan–Meier method was used for estimating the event and survival rates at 12-month follow-up.

Results

During the index period, 6789 patients underwent revascularization, where ultralong (≥40 mm) Supralimus Grace stents were implanted in 684 patients. All patients were followed up according to the study's protocol; finally, at 12 months, 632 patients (93.1%) completed the follow-up (Fig. 2). The patients' baseline demographic characteristics are shown in Table 1. The mean age of patients was 52.7±15.9 years; the majority (n=484; 70.7%) were males. 28.4% of the patients were smokers, while 21.8% were hypertensive. Various indications for PCI were STEMI (n=284; 46.2%), NSTEMI (n=201; 32.8%), UA (n=78; 12.6%), and CCS (n=52;

Anatol J Cardiol 2021; 25: 111-9
DOI:10.14744/AnatolJCardiol.2020.40909

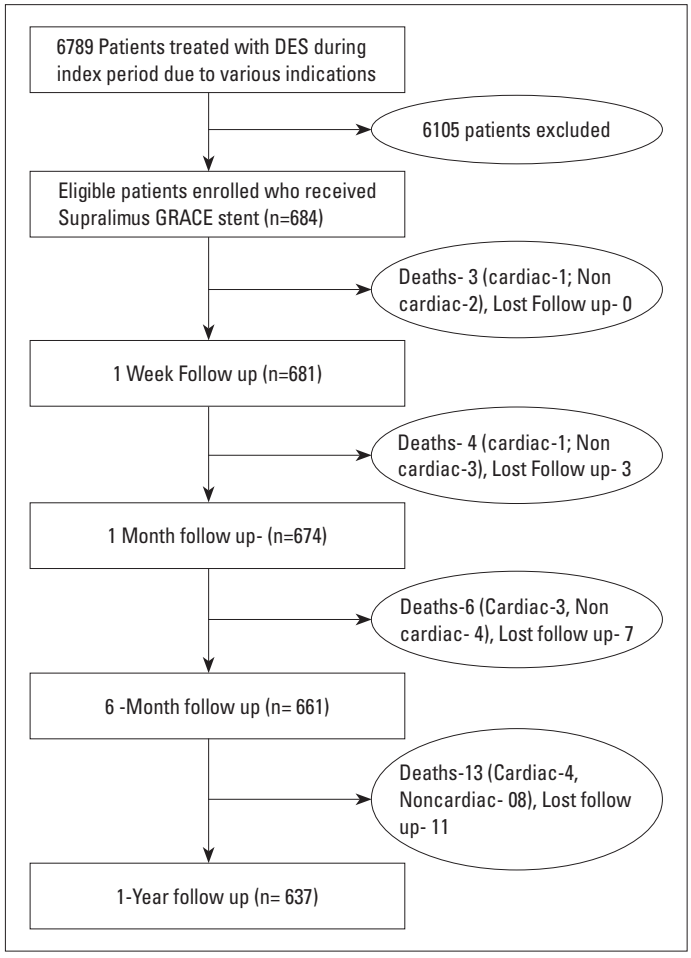

Figure 2. Flowchart of patients enrolled in the study (n=684)

8.4%). Most STEMI patients were thrombolysed (n=127; 18.5%) and infarct-related artery intervention was done within 24 hours as pharmacoinvasive PCI. 108 (15.8%) patients who presented after 18 hours of infarction and suffered persistent angina were managed with infarcted-artery PCI. Only 81 (11.8%) patients underwent PCI.

The angiogram revealed the following: single-vessel disease found in 531 (77.6%) patients; left anterior descending artery in 239 (34.9%), right coronary artery (RCA) in 191 (27.9%), and left circumflex artery in 101 (14.8%). Similarly, double-vessel and triple-vessel diseases were reported in 92 (13.5%) and 61 (8.9%) patients, respectively. Relative preservation of left ventricular ejection fraction was observed (>45%) in the majority of patients (n=493; 72.1%). After PCI, 674 (98.6%) patients received aspirin and 10 (1.4%) patients developed gastrointestinal bleed. Most patients were given clopidogrel (n=401; 58.6%), whereas only 108 (15.8%) patients took ticagrelor (Table 1) because it could be locally unavailable and not cost-effective.

Procedural details (Table 2)

Most procedures were carried out via the transfemoral route (n=521; 76.1%) using the 6F guiding catheter (n=538; 78.7%), whereas the 7F guiding catheter was employed in cases of chronic total

Table 1. Baseline characteristics of patients (n=684)

Characteristics	n (%) or mean±SD
Age (years)	52.7±15.9
Male	484 (70.7%)
Female	200 (29.3%)
BMI (kg/m^2)	24.7±2.9
Serum creatinine (mg/dL)	1.3±0.4
CAD risk factors	
Hypertension	150 (21.8%)
Diabetes mellitus	125 (18.4%)
Smokers	195 (28.4%)
Family history of CAD	25 (3.6%)
Dyslipidemia	137 (20.1%)
Post-CABG	17 (2.4%)
Clinical presentation	
STEMI	316 (46.2%)
a. Primary PCI (pPCI)	81 (11.8%)
b. Pharmacoinvasive	127 (18.5%)
c. Delayed presentation (>12 hours)	108 (15.8%)
NSTEMI	224 (32.8%)
UA	86 (12.6%)
CCS	58 (8.4%)
LVEF (%)	
>45%	493 (72.1%)
35–45%	100 (14.6%)
<35%	91(13.3%)
Medications	
Tenecteplase	127 (18.5%)
Aspirin	674 (98.6%)
Clopidogrel	401 (58.6%)
Prasugrel	175 (25.6%)
Ticagrelor	108 (15.8%)
Statin	666 (97.5%)
Beta-blocker	490 (71.7%)
ACEI/ARB	638 (93.3%)
CCB	134 (19.7%)
Aldosterone antagonist	86 (12.6%)
Angiographic severity of CAD (target vessel location)	
1. SVD	531 (77.6%)
LAD	239 (34.9%)
LCx	101 (14.8%)
RCA	191 (27.9%)
2. DVD	92 (13.5%)
3. TVD	61 (8.9%)

Data are represented as mean±standard deviation or number (percentage). BMI - body mass index; CAD - coronary artery disease; DM - diabetes mellitus; PCI - percutaneous coronary intervention; CABG - coronary artery bypass graft; STEMI - ST-segment elevation myocardial infarction; NSTEMI - non-ST-segment elevation myocardial infarction; UA - unstable angina; CCS - chronic coronary syndrome; LVEF - left ventricular ejection fraction; ACEI - angiotensin-converting enzyme inhibitor; ARB - angiotensin receptor blocker; CCB - calcium channel blocker; SVD - single-vessel disease; LAD - left anterior descending coronary artery; LCx - left circumflex coronary artery; RCA - right coronary artery; DVD - double-vessel disease; TVD - triple-vessel disease

Table 2. Procedural characteristics of patients (n=684)

Variables	Values, n (%)
Transradial approach	163 (23.8%)
Transfemoral approach	521 (76.2%)
Size of vessels	
a. 2.25–2.5 mm	131 (19.1%)
b. 2.5–3 mm	105 (15.4%)
c. 3–3.5 mm	351 (51.3%)
d. 3.5–4 mm	97 (14.2%)
Number of vessels stented	
1	531(77.6%)
2	92(13.5%)
3	61(8.9%)
Lesion characteristics	
a. At least 1 complex lesion	593 (86.7%)
b. At least 1 bifurcation lesion	39 (5.7%)
c. At least 1 chronic total occlusion	107 (15.6%)
d. At least 1 ostial lesion	25 (3.7%)
e. At least 1 calcified lesion	28 (4.1%)
f. In-stent restenosis (ISR)	14 (2.1%)
Lesions per patient, mm (mean±SD)	1.3±0.2
Lesion length (mm)	34 (32-46)
Stents per patient, mm (mean±SD)	1.4±0.3
Median stent length per patient (mm)	62±14
Median stent length per lesion (mm)	54±12
Stent diameter, mm (mean±SD)	2.7±0.3
Procedural details	
Thrombosuction	61 (8.9%)
Glycoprotein IIb/IIIa inhibitor	88 (12.8)
Lesion modification	
a. Direct stenting	17 (2.4%)
b. Predilataion with semicompliant balloon	632 (92.4%)
c. Cutting balloon	35 (5.1%)
Stent delivery	
a. Direct	600 (87.8%)
b. Buddy wire	33 (4.8%)
c. GuideZilla mother-in-child system	36 (5.2%)
Implantation of assigned stents (>40 mm) only	669 (97.8%)
TIMI flow before the procedure	
a. Grade 0	121 (17.6%)
b. Grade 1	52 (7.6%)
c. Grade 2	38 (5.6%)
d. Grade 3	473 (69.2%)
TIMI flow after the procedure	
a. Grade 0	00 (00%)
b. Grade 1	05 (0.7%)
c. Grade 2	47 (6.8%)
d. Grade 3	632 (92.4%)

occlusion (n=146; 21.3%) and bifurcation lesions (n=39; 5.7%). Seventeen (2.4%) patients belonged to post-CABG (coronary artery bypass graft) group: the majority presented with NSTEMI (n=12; 1.7%), while the rest (n=5; 0.7%) had CCS. They had degenerated venous graft with median age of 13.4 years and underwent graft vessel PCI of RCA (n=12; 1.7%) and obtuse marginal artery (n=5; 0.7%). Moreover, they were pretreated with intracoronary diltiazem to decrease no-reflow. For the bifurcation lesions (n=39; 5.7%), various techniques were employed as follows: mimicrush (n=11; 1.9%), step crush (n=09; 1.7%), culotte (n=07; 1.1%), DK crush (n=05; 0.7%), and TAP (n=07; 1.1%). In the culotte technique, there was no difficulty in rewiring the side branch and tracking the long main branch stent through strut of the side branch stent.

989 lesions were treated. 17 (2.4%) patients underwent direct stenting with primary PCI as the lesions appeared to be soft and thrombotic. The stent was delivered over the workhorse wire in 615 patients (89.9%), whereas resistant lesions were managed using the buddy wire (n=33; 4.8%) and GuideZilla mother-in-child system (n=36; 5.3%). Supralimus Grace was used in all lesions except in a few side branches and device failure (n=21; 3.1%).

Clinical outcomes (Table 3)

TLF, the primary endpoint, was noticed in 42 (6.1%) patients, contributed by cardiac death, target vessel MI, and TLR in 9 (1.3%), 20 (2.9%), and 13 (1.9%) patients, respectively (Fig. 3). POCE was observed in 131 (19.1%) patients at the 12-month follow-up, mainly as a result of any revascularization in 63 (9.2%) patients. Stent (≥40 mm) could not be delivered to target lesion in 15 (2.2%) patients; this was managed by deploying two smaller overlapping stents in 10 (1.5%) patients and implanting a different stent in the other 5 (0.7%) patients (XIENCE Prime everolimus-eluting stent; Abbott Vascular, USA). In 5 (0.8%) patients, edge dissection was noticed: proximal in one case and distal in four cases; among them, three required other short overlapping stents to prevent the acute threatening of the vessel. Stent fracture (Grade II) was observed in one asymptomatic patient.

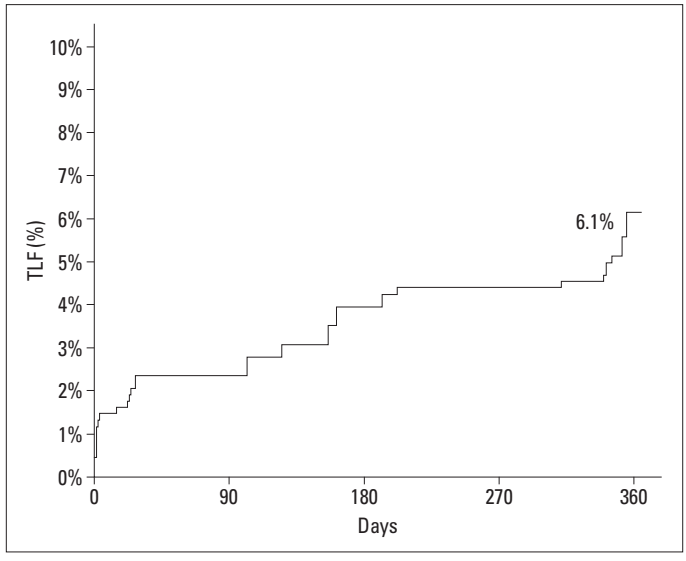

Figure 3. Cumulative incidence of TLF at a 12-month period

Anatol J Cardiol 2021; 25: 111-9
DOI:10.14744/AnatolJCardiol.2020.40909

Table 3. Periprocedural endpoints and clinical events during at 1-year follow-up (n=684)

Variables	Values, n (%)
Target lesion failure	42 (6.1%)
a. Target vessel MI	20 (2.9%)
b. Ischemia-driven TLR	13 (1.9%)
c. Cardiac death	9 (1.3%)
Device failure (secondary)	21 (3.1%)
a. Failure of stent delivery	15 (2.2%)
b. Edge dissection	5 (0.8%)
c. Stent fracture	1 (0.1%)
TVF	59 (8.6%)
POCE	131 (19.1%)
All-cause mortality	26 (3.8%)
Periprocedural MI	8 (1.1%)
Any MI	42 (6.1%)
Any revascularization	63 (9.2%)
Ischemia-driven TVR	30 (4.4%)
Definite stent thrombosis	8 (1.1%)
a. Acute (0-1 days)	2 (0.3%)
b. Subacute (2–30 days)	3 (0.4%)
c. Late (31–360 days)	3 (0.4%)
Definite or probable ST	9 (1.3 %)
a. Acute (0-1 days)	3 (0.4%)
b. Subacute (2–30 days)	2 (0.3%)
c. Late (31–360 days)	4 (0.5%)

MI - myocardial infarction; TLR - target lesion revascularization; TVF - target vessel failure (composite of cardiac death, target vessel MI, and ischemia-driven TVR);
POCE - patient-oriented composite endpoint (composite of all-cause mortality, any MI, and any revascularization); ST - stent thrombosis; TVR - target vessel revascularization

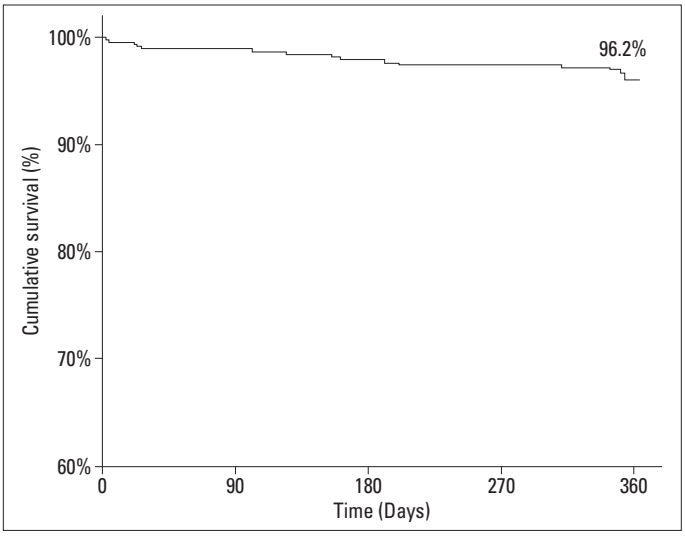

Figure 4. Kaplan–Meier survival curves of patients over a 12-month follow-up period

Definite and probable ST were observed in 8 (1.1%) and 9 (1.3%) patients, respectively. Regarding definite ST, in three patients, acute ST occurred as a result of stent malapposition circumvented by postdilatation using an oversized noncompliant balloon, while subacute and late ST occurred in two and three cases, respectively, resolved by implanting HETERO-DES (XIENCE Prime everolimus-eluting stent; Abbott Vascular, USA). Figure 3 displays the Kaplan–Meier curve of TLF at 12 months. Figure 4 demonstrates the Kaplan–Meier survival curves of patients over a 12-month period. Seventeen deaths were due to noncardiac conditions (e.g., stroke, malignancy, renal failure, sepsis, and pneumonia), while nine deaths were attributed to cardiac conditions such as stent thrombosis (n=5; 56%), heart failure because of progressive pump dysfunction (n=3; 33%), and MI (n=1; 11%). Those who died because of heart failure had systolic dysfunction at baseline which did not improve after PCI.

Discussion

The primary outcomes in this study were as follows: (a) treating coronary artery disease with ultralong (≥40 mm) Supralimus Grace resulted in acceptable clinical events, that is, TLF of 6.1% and definite ST of 1.1% at 12-month follow-up; (b) cardiovascular death, target vessel MI, and ischemia-driven TLR rates were 1.3%, 2.9%, and 1.9%, respectively, at 12-month follow-up. These findings were in agreement with event rates in previous studies that reported the use of contemporary third-generation DES such as Orsiro (6%) in Kandzari et al. (13) and Synergy SES (7.5%) in Lam et al. (21).

Ultrathin strut (60 µm) is one of the factors contributing to the favorable results. The LDZ-link design makes the stent swiftly trackable and deliverable across the lesion compared to the other two ultrathin stents, Orsiro (Biotronik, Bülach, Switzerland) and BioMime (Merrill Life Sciences, Gujarat, India). The uniform drug coating of the Supralimus Grace is another which further minimizes its thickness to 68–70 µm (strut plus coating)feature, which further minimizes its thickness to 68–70 µm (strut plus coating), compared to differential coating (more on the abluminal side) in Orsiro and BioMime. The duration of drug-release kinetics and polymer degradation is shorter (over 9–12 months) compared to these two stents (21).

Device success (96.7%) was acceptable and little better than the current-generation stents such as Firehawk (92.4%) and XIENCE group (94.8%) as reported in the TARGET All Comer study (22). A number of underlying factors contributed to stent delivery by overcoming the resistance across were as follows: the unique design, aggressive predilatation, lesion modification using cutting/scoring balloon, buddy wire, and the GuideZilla mother-in-child system. In only 0.8% of patients, crossover to another stent was performed which was only in refractory cases. Stent fracture (Grade II) was observed in only one case, which was attributed to postdilatation in the angulated obtuse marginal branch. These factors support the safety and efficacy of the stent, as the median length of implantation was 54 mm.

In this study, TVF was 8.6% was comparable to the results in other contemporary trials as it was 9.9% in the Firehawk group and 9.6% in the XIENCE group in the TARGET All Comers trial (23). In the BIO-RESORT clinical trial, which compared thin, very thin, or ultrathin strut, biodegradable or durable polymer-coated DES, TVF was reported to be 8.5%, 8.8%, and 10% for Orsiro SES, Synergy EES, and Resolute Integrity zotarolimus-eluting stent (ZES) (24), whereas it was 5.4% in the TALENT trial using the Supraflex SES (23).

In this study, POCE was 19.1% which was quite similar to those reported in the Firehawk and the XIENCE groups, 19.3% and 17.8%, respectively, in the TARGET All Comers trial (23); however it was higher than the POCE reported in the TALENT trial, that is 9.9% (25). This could be attributed to the higher rates of all deaths (3.8% vs. 2%) and all MI (6.1% vs. 3.1%), which are the result of higher comorbidities, a higher proportion of complex lesion, a higher transfemoral intervention, and longer mean length of stent per lesion. Another trial of ultrathin SES from South Korea by Youn et al. (26) reported that TVF was much lower (3.9%) because of the higher transradial intervention (79.1% vs. 23.9%) and lower proportion of chronic total occlusion (4.2% vs. 15.6%) compared to our study.

In this study, ST (both definite and probable) was higher (2.4%) than those for Orsiro SES (1.1%), Synergy EES (1.1%), and Resolute Integrity ZES (0.9%) (24), which could be due to longer stent, impaired left ventricular systolic function, bifurcation stenting, small stent diameter (mean diameter <3.0 mm), and lesser number of patients receiving potent P2Y12 inhibitors such as ticagrelor and prasugrel. This agrees with Lim et al.'s study (27). Furthermore, the other predictors of ST were multiple stents, the left anterior descending stenting, and small vessel diameter at baseline (28), as similarly noted in our study. The percentage of chronic total occlusion (15.6%) in our study could be another contributing factor to the higher rate of ST as a result of malapposition, incomplete stent endothelialization, the subintimal passage of a guidewire, creation of false lumen, eccentric plaque compression, and multiple stent implantation (28, 29). The incidence of late ST (0.4%) was consistent with the findings reported in the TALENT trial using ultrathin SES (Supraflex) but with different design and drug kinetics (25); this could be possibly attributed to the reduced long-term inflammation as biodegradable polymer minimizes the polymer volume and sirolimus drug concentrations in the vessel.

A pooled meta-analysis of 11,658 patients in various trials comparing ultrathin-strut stents (Orsiro, MiStent, and BioMime) with thicker-strut stents (XIENCE, Resolute, and Nobori) revealed that ultrathin stents were associated with a reduced risk (16%) of TLF at 1-year follow-up. Moreover, the prevalence of ST was lower although not significant (30).

The median length per lesion in our study was 54±12 mm which could be concerning in terms of safety. Thus, full lesion coverage with multiple and longer stents is essential for preventing in-stent restenosis (at edges) which might sometimes result in full-metal jacketing (FMJ) (>60 mm) (31). In a study of 1,107 consecutive patients who underwent chronic total occlusion procedures by Lee et al. (32), FMJ was performed in 406 (36.7%) patients using overlapping stents with stent length ≥60 mm. In their study, the median length was 76.8±14.6 mm (range: 60–122 mm). TLF at the end of a 5-year follow-up period was 8.6% which was similar to that reported in this study at 12 months (7% vs. 6.1%). Furthermore, definite ST in our study was comparable to Lee et al.'s study (32) (71.2 vs. 1.1%). Amirzadegan et al.'s study (6) included 124 patients who received ≥40 mm of BioMime SES (Merrill Life Sciences, Gujarat, India), another ultrathin stent, in long lesion (42.20±2.73 mm) proving its safety.

Using Supralimus Grace in smaller vessels was another safety concern dealt with in our study; conventionally, smaller vessels have a diameter of ≤2.75 mm (15). The prevalence of this issue is 20–30% of patients with symptomatic coronary artery disease and it is particularly higher in those having diabetes and underlying renal dysfunction. PCI in these vessels is associated with an increased risk of adverse effects such as restenosis and thrombosis (15). Revascularization offers an increase in minimum lumen diameter which is later offset by late lumen loss as a result of vessel recoil and intimal hyperplasia (15). As Supralimus Grace is very thin (60 µm), the polymer is biodegradable, and the late luminal loss ranges 0.05–0.10 mm for all DES, the small vessels are not significantly affected which is, in fact, a potential benefit of these ultrathin strut stents in such lesions. In this study, the TLF and ST are 7.2% and 1%, respectively which is in agreement with the BIONICS trial, as reported by Kandzari et al. (33), at one-year follow-up in 787 patients who had small vessels (reference diameter ≤2.5 mm), suggesting its safety in treating these subsets of patients. Currently, with the availability of DES with a 2.25 mm diameter, even very small coronary arteries are being managed with PCI (24, 33). Similarly, in BIO-RESORT trial, which compared contemporary DES in small vessels, 1506 out of 3514 (42%) patients had reference vessel <2.5 mm, in whom 2.25 mm and 2.5 mm stents were implanted in 484 (32.1%) and 754 (50.1%) patients, respectively. TLF and ST at 12 months were 4% and 0.8%, respectively, similar to our findings (24). Therefore, it may be concluded that these ultrathin struts are quite safe in small vessel lesions, which could have a positive effect on the patients' comfort, morbidity, and healthcare expenditures. Consequently, strut thickness should be taken into consideration when choosing DES for treating small vessel lesions.

Imaging modalities, such as intravascular ultrasound (IVUS) and optical coherence tomography (OCT), either before the procedure or after the procedure, were not utilized in this study. Our analysis was based on the angiographic parameters alone. In most of the contemporary trials using ultrathin stents such as BIO-RESORT (24), only 26 out of 1506 patients were subjected to IVUS, that is, 1.7%. Using imaging could have provided a better insight, but also it is not cost-effective.

In India, nearly 25% of deaths in the third to seventh decade of age are caused by cardiovascular diseases (34). Up to 40% of patients have to bear their medical expenses in the absence of

Anatol J Cardiol 2021; 25: 111-9
DOI:10.14744/AnatolJCardiol.2020.40909

an organized insurance system. In lieu of the skyrocketing costs of multivessel PCI, many young people opt for coronary artery bypass (35). Recently, with the government capping stent prices and the availability of ultralong stent (≥40 mm), multivessel intervention has become cheaper so that complete revascularisation could be achieved in more patients. More importantly, our study also sheds light on the safety of ultrathin (60 μm) and ultralong (≥40 mm) stents in long lesions in the Indian population where diffuse vessel disease is not so infrequent.

Study limitations

This study was an observational study including a small-size population. Moreover, patients with the left main coronary ar-tery disease and cardiogenic shock were not included. Imaging modalities such as IVUS and OCT were not utilized which could have provided better insight like strut coverage and healing score. Furthermore, comparison with other stents was not con-ducted in terms of efficacy and safety in long lesions. Long-term follow-up (>5 years) would have provided further safety data.

Conclusion

The outcomes of the present study proved the safety and effectiveness of ultralong (≥40 mm) and ultrathin (60 μm) Supralimus Grace biodegradable polymer-coated SES in all substrates of the lesion including FMJ stenting of chronic total occlusion and possibly nonchronic total occlusion diffusely diseased vessels. It may reduce the risk of repeated revascularization in small vessel lesions, possibly resulting in positive effects in terms of the patients' comfort, morbidity, and healthcare expenses. As a result of introducing this stent innovation, it is expected that PCI with DES implantation will be the therapy of choice in patients with lesions in small and very small coronary arteries.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept – S.K.S., P.A., U.P., M.R., A.K., V.K.; Design – S.K.S., P.A., U.P., M.R., A.K., V.K.; Supervision – S.K.S., P.A., U.P., M.R., A.K., V.K.; Fundings – S.K.S., P.A., U.P., M.R., A.K., V.K.; Materials – S.K.S., P.A., U.P., M.R., A.K., V.K.; Data collection and/or processing – S.K.S., P.A., U.P., M.R., A.K., V.K.; Analysis and/or interpretation – S.K.S., P.A., U.P., M.R., A.K., V.K.; Literature search – S.K.S., P.A., U.P., M.R., A.K., V.K.; Writing – S.K.S., P.A., U.P., M.R., A.K., V.K.; Critical review – S.K.S., P.A., U.P., M.R., A.K., V.K.

References

1. Schunkert H, Harrell L, Palacios IF. Implications of small reference vessel diameter in patients undergoing percutaneous coronary revascularization. J Am Coll Cardiol 1999; 34: 40–8.
2. van der Heijden LC, Kok MM, Danse PW, Schramm AR, Hartmann M, Löwik MM, et al. Small-vessel treatment with contemporary newer-generation drug-eluting coronary stents in all-comers: Insights from 2-year DUTCH PEERS (TWENTE II) randomized trial. Am Heart J 2016; 176: 28–35.
3. Wöhrle J, Markovic S, Rottbauer W, Muramatsu T, Kadota K, Vázquez-González N, et al. Bioresorbable polymer sirolimus-eluting coronary stent compared with permanent polymer everolimus-eluting coronary stent implantation for treatment of small vessel coronary artery disease: CENTURY II trial. EuroIntervention 2016; 12: e167–74.
4. Claessen BE, Smits PC, Kereiakes DJ, Parise H, Fahy M, Kedhi E, et al. Impact of lesion length and vessel size on clinical outcomes after percutaneous coronary intervention with everolimus- versus paclitaxel-eluting stents pooled analysis from the SPIRIT (Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System) and COMPARE (Second-generation everolimus-eluting and paclitaxel-eluting stents in real-life practice) Randomized Trials. JACC Cardiovasc Interv 2011; 4: 1209–15.
5. Elezi S, Dibra A, Mehilli J, Pache J, Wessely R, Schömig A, et al. Vessel size and outcome after coronary drug-eluting stent placement: results from a large cohort of patients treated with sirolimus- or paclitaxel-eluting stents. J Am Coll Cardiol 2006; 48: 1304–9.
6. Amirzadegan A, Hasanabadi M, Saadatagah S, Afarideh M, Omidi N, Aghajani H, et al. Single Long Stents versus Overlapping Multiple Stents in the Management of Very Long Coronary Lesions: Comparisons of Procedures and Clinical Outcomes. J Tehran Heart Cent 2019; 14: 94–102.
7. Stefanini GG, Taniwaki M, Windecker S. Coronary stents: novel developments. Heart 2014; 100: 1051–61.
8. Stefanini GG, Byrne RA, Serruys PW, de Waha A, Meier B, Massberg S, et al. Biodegradable polymer drug-eluting stents reduce the risk of stent thrombosis at 4 years in patients undergoing percutaneous coronary intervention: a pooled analysis of individual patient data from the ISAR-TEST 3, ISAR-TEST 4, and LEADERS randomized trials. Eur Heart J 2012; 33: 1214–22.
9. Smits PC, Hofma S, Togni M, Vázquez N, Valdés M, Voudris V, et al. Abluminal biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent (COMPARE II): a randomised, controlled, non-inferiority trial. Lancet 2013; 381: 651–60.
10. Bangalore S, Toklu B, Patel N, Feit F, Stone GW. Newer-Generation Ultrathin Strut Drug-Eluting Stents Versus Older Second-Generation Thicker Strut Drug-Eluting Stents for Coronary Artery Disease. Circulation 2018; 138: 2216–26.
11. Briguori C, Sarais C, Pagnotta P, Liistro F, Montorfano M, Chieffo A, et al. In-stent restenosis in small coronary arteries: impact of strut thickness. J Am Coll Cardiol 2002; 40: 403–9.
12. Biondi-Zoccai G, Moretti C, Abbate A, Sheiban I. Percutaneous coronary intervention for small vessel coronary artery disease. Cardiovasc Revasc Med 2010; 11: 189–98.
13. Kandzari DE, Mauri L, Koolen JJ, Massaro JM, Doros G, Garcia-Garcia HM, et al.; BIOFLOW V Investigators. Ultrathin, bioresorbable polymer sirolimus-eluting stents versus thin, durable polymer everolimus-eluting stents in patients undergoing coronary revascularisation (BIOFLOW V): a randomised trial. Lancet 2017; 390: 1843–52.
14. Kolandaivelu K, Swaminathan R, Gibson WJ, Kolachalama VB, Nguyen-Ehrenreich KL, Giddings VL, et al. Stent thrombogenicity early in high-risk interventional settings is driven by stent design and deployment and protected by polymer-drug coatings. Circulation 2011; 123: 1400–9.

15. von Birgelen C, Zocca P, Buiten RA, Jessurun GAJ, Schotborgh CE, Roguin A, et al. Thin composite wire strut, durable polymer-coated (Resolute Onyx) versus ultrathin cobalt-chromium strut, bioresorbable polymer-coated (Orsiro) drug-eluting stents in allcomers with coronary artery disease (BIONYX): an international, single-blind, randomised non-inferiority trial. Lancet 2018; 392: 1235–45.
16. Chan PH, Alegria-Barrero E, Foin N, Paulo M, Lindsay AC, Viceconte N, et al. Extended use of the GuideLiner in complex coronary interventions. EuroIntervention 2015; 11: 325–35.
17. Chen CY, Huang YY, Tang L, Hu XQ, Fang ZF, Zhou SH. Guidezilla extension catheter for percutaneous interventional therapy of complex lesions via a transradial approach: Case series from a single-center experience. Cardiol J 2018; 25: 171–8.
18. Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, et al.; Academic Research Consortium. Clinical end points in coronary stent trials: a case for standardized definitions. Circulation 2007; 115: 2344–51.
19. Vranckx P, Cutlip DE, Mehran R, Kint PP, Silber S, Windecker S, et al. Myocardial infarction adjudication in contemporary all-comer stent trials: balancing sensitivity and specificity. Addendum to the historical MI definitions used in stent studies. EuroIntervention 2010; 5: 871–4.
20. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD et al.; Joint ESC/ACCF/AHA/WHF Task Force for Universal Definition of Myocardial Infarction; Authors/Task Force Members Chairpersons. Third universal definition of myocardial infarction. J Am Coll Cardiol 2012; 60: 1581–98.
21. Lam MK, Sen H, Tandjung K, van Houwelingen KG, de Vries AG, Danse PW, et al. Comparison of 3 biodegradable polymer and durable polymer-based drug-eluting stents in all-comers (BIO-RESORT): rationale and study design of the randomized TWENTE III multicenter trial. Am Heart J 2014; 167: 445–51.
22. Lansky A, Wijns W, Xu B, Kelbæk H, van Royen N, Zheng M, et al.; TARGET All Comers Investigators. Targeted therapy with a localised abluminal groove, low-dose sirolimus-eluting, biodegradable polymer coronary stent (TARGET All Comers): a multicentre, open-label, randomised non-inferiority trial. Lancet 2018; 392: 1117–26.
23. Modolo R, Chichareon P, Kogame N, Asano T, Chang CC, de Winter RJ, et al. A prospective multicentre randomised all-comers trial to assess the safety and effectiveness of the thin-strut sirolimus-eluting coronary stent SUPRAFLEX: rationale and design of the Thin Strut Sirolimus-eluting Stent in All Comers Population vs Everolimus-eluting Stent (TALENT) trial. EuroIntervention 2019; 15: e362–9.
24. Buiten RA, Ploumen EH, Zocca P, Doggen CJM, van der Heijden LC, Kok MM, et al. Outcomes in Patients Treated With Thin-Strut, Very Thin-Strut, or Ultrathin-Strut Drug-Eluting Stents in Small Coronary Vessels: A Prespecified Analysis of the Randomized BIO-RESORT Trial. JAMA Cardiol 2019; 4: 659–69.
25. Zaman A, de Winter RJ, Kogame N, Chang CC, Modolo R, Spitzer E, et al.; TALENT trial investigators. Safety and efficacy of a sirolimus-eluting coronary stent with ultra-thin strut for treatment of atherosclerotic lesions (TALENT): a prospective multicentre randomised controlled trial. Lancet 2019; 393: 987–97.
26. Youn YJ, Yoo SY, Lee JW, Ahn SG, Lee SH, Yoon J, et al. Safety and Efficacy of a New Ultrathin Sirolimus-Eluting Stent with Abluminal Biodegradable Polymer in Real-World Practice. Korean Circ J 2020; 50: 317–27.
27. Lim S, Koh YS, Kim PJ, Kim HY, Park CS, Lee JM, et al. Incidence, Implications, and Predictors of Stent Thrombosis in Acute Myocardial Infarction. Am J Cardiol 2016; 117: 1562–8.
28. van Werkum JW, Heestermans AA, Zomer AC, Kelder JC, Suttorp MJ, Rensing BJ, et al.Predictors of coronary stent thrombosis: the Dutch Stent Thrombosis Registry. J Am Coll Cardiol 2009; 53: 1399–409.
29. Cook S, Wenaweser P, Togni M, Billinger M, Morger C, Seiler C, et al. Incomplete stent apposition and very late stent thrombosis after drug-eluting stent implantation. Circulation 2007; 115: 2426–34.
30. Bouras G, Jhamnani S, Ng VG, Haimi I, Mao V, Deible R, et al. Clinical outcomes after PCI treatment of very long lesions with the XIENCE V everolimus eluting stent; Pooled analysis from the SPIRIT and XIENCE V USA prospective multicenter trials. Catheter Cardiovasc Interv 2017; 89: 984–91.
31. Lee CW, Ahn JM, Lee JY, Kim WJ, Park DW, Kang SJ, et al.; OPERA Steering Committee and Investigators. Long-term (8 year) outcomes and predictors of major adverse cardiac events after full metal jacket drug-eluting stent implantation. Catheter Cardiovasc Interv 2014; 84: 361–5.
32. Lee PH, Lee SW, Yun SC, Bae J, Ahn JM, Park DW, et al. Full Metal Jacket With Drug-Eluting Stents for Coronary Chronic Total Occlusion. JACC Cardiovasc Interv 2017; 10: 1405–12.
33. Kandzari DE, Smits PC, Love MP, Ben-Yehuda O, Banai S, Robinson SD, et al. Randomized Comparison of Ridaforolimus- and Zotarolimus-Eluting Coronary Stents in Patients With Coronary Artery Disease: Primary Results From the BIONICS Trial (BioNIR Ridaforolimus-Eluting Coronary Stent System in Coronary Stenosis). Circulation 2017; 136: 1304–14.
34. Prabhakaran D, Jeemon P, Roy A. Cardiovascular Diseases in India: Current Epidemiology and Future Directions. Circulation 2016; 133: 1605–20.
35. Kaul U. The new pricing policy for coronary stents in India: a boon or a bane? EuroIntervention 2017; 13: 267–8.