Am J Cardiovasc Dis 2020;10(4):317-328
www.AJCD.us /ISSN:2160-200X/AJCD0114427

Original Article

Clinical safety and efficacy of World's thinnest (50 μm), very long (>40 mm) Everolimus Eluting Stent (SES) among real world patients

Santosh Kumar Sinha[1], Mukesh Jitendra Jha[2], Vikas Mishra[3], Umeshwar Pandey[1], Mahmodullah Razi[1], Awadesh Kumar Sharma[1], Puneet Aggarwal[1], Ramesh Thakur[1], Vinay Krishna[1]

[1]Department of Cardiology, LPS Institute of Cardiology, G.S.V.M. Medical College, Kanpur, Uttar Pradesh, India; [2]Department of Cardiology, Sri Aurobindo Institute of Medical Sciences, Indore, MP, India; [3]Department of Cardiology, Netaji Subhash Chandra Bose Medical College, Jabalpur, MP, India

Received May 16, 2020; Accepted August 22, 2020; Epub October 15, 2020; Published October 30, 2020

Abstract: Background: Safety and efficacy of newer-generation and World's thinnest everolimus eluting stent (Evermine 50) in patients with very long and multiple lesions. Method: Total of 711 patients received >40 mm long, World's thinnest (50 μm) Evermine 50 Everolimus eluting stent (Meril Life Sciences Pvt. Ltd., India) for various indications at LPS Institute of Cardiology, GSVM Medical College, Kanpur, UP, India between August 2017 and December 2018. Primary outcome as Device-oriented composite outcome (DOCO)- composite of cardiovascular death, target vessel myocardial infarction, and target lesion revascularization, secondary end points including periprocedural device failure (failure of stent delivery, change of stent, edge dissection, stent fracture), target vessel failure (TVF), Global Cardiovascular End Points (GCEP)- composite of all-cause death, any MI, and any revascularization, and stent thrombosis (ST) were evaluated at 1-year follow-up. Result: Mean age was 52.7±15.9 years and majority (78.6%) were male. Indications for implantation were STEMI (n=284; 46.2%), NSTEMI (n=201; 32.8%), UA (n=78; 12.6%), and CCS (n=52; 8.4%). Total of 989 lesions were treated among 711 patients. Median length of stent per lesion was 54±14 mm. DOCO occurred in 47 (6.6%) which was contributed by target vessel MI and TLR in 23 (3.2%) and 15 (2.1%) patients respectively. GCEP was observed in 117 (16.4%) at 12-month follow-up mainly attributed by any revascularization 60 (8.4%). Stent failure was seen in 36 (5.1%) patients mainly as result of failure of assigned stent delivery (n=18; 2.5%), and edge dissection (n=15; 2.1%). Definite and probable ST were observed in 8 (1.1%) and 6 (0.8%) patients respectively. Conclusion: Evermine 50 Everolimus eluting stent is safe and effective to treat unduly long and multiple lesions.

Keywords: Ultrathin stent, device-oriented composite outcome, global cardiovascular end points, stent thrombosis, evermine 50

Introduction

In the last four decades, world of percutaneous coronary intervention (PCI) has witnessed plain only balloon angioplasty, bare metal stent, drug eluting stent (DES), and finally bioresolvable vascular scaffold but the quest for best is still going on. Bare metal stent are associated with higher rate of restenosis and repeat revascularization. These complications were reduced by drug eluting stents. Higher long-term mortality secondary to stent thrombosis was one of concern of DES [1-3]. Diffuse, calcified lesions and complex high risk interventions (CHIP) are frequently being performed now. Older generation of DES had technical issues like trackibility and deliverability as they were shorter and bulkier because of their design. Current generation of DES, because of their profile (thinner struts) and different design (biodegradable vs. biostable polymer), has reduced the risk of stent thrombosis by nearly 50% [4]. Longer lesion, smaller reference vessel diameter (RVD), and diabetes are most important determinants of adverse outcome following revascularization. The prevalence of coronary artery disease in small vessel is 30%-50% among India population [5-7]. Lesions among such patients are

mostly multiple and often diffuse which sometimes requires longer and multiple stents for optimal coverage, which makes PCI not only technically challenging but also carries higher risk of adverse cardiovascular outcome as a result of repeated revascularization [8, 9]. In those patients, superiority of single long stent over overlapping multiple stents is not well defined [10].

The design of a typical DES consists of a metallic platform (stainless steel, cobalt chromium etc.) of variable thickness and polymer coating (biodegradable vs. biostable) which elutes antiproliferative drugs (sirolimus, paclitaxel, everolimus, zotarolimus) to prevent lesion recurrence [11]. The durable polymer carries potential of late or very late stent thrombosis (≥ 1-year) as it acts as a nidus for chronic inflammation, delayed arterial healing and neo-atherosclerosis. These risks were subsequently mitigated by introduction of biodegradable polymer stent as they disappear after releasing the drug over a certain period of time, thereby leaving only bare metal stent-like platform [12-15]. Pooled analysis from multiple trials has shown superiority of biodegradable polymer stent over durable polymer stent [16]. As stents with thicker struts are associated with increased risk of stent thrombosis and lesion recurrence, there was a quest for stents with thinner struts. Ultrathin stents (strut thickness <70 μm) with biodegradable polymer have replaced first-generation drug-eluting stents as older generation stents were relatively thicker (struts thickness- 120 μm). Ultrathin stents are more flexible, trackable and easily deliverable across complex lesions especially in smaller vessels (2.25-2.5 mm) [17]. The present study was undertaken to assess clinical safety and efficacy of World's thinnest (50 μm) and very Long (>40 mm) Evermone-50 Everolimus Eluting Stent (SES) in spectrum of coronary lesions among real world patients.

Material and method

Study design and participants

This was a prospective, observational study conducted among patients who received Evermine 50 (Meril Life Sciences Pvt. Ltd., India) between August 2017 and December 2018 at LPS Institute of Cardiology, GSVM Medical College, Kanpur, UP, India. Indications for implantation were- (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 (CCS) refractory to guideline directed medical treatment, (3). In-stent restenosis (ISR), (4). Bifurcation lesion (true and provisional lesion based on Medina classification), and (5). Intervention of degenerated grafts following post coronary artery bypass graft surgery. Baseline demographics of patients including clinical (age, sex, clinical presentation and indication for intervention), angiographic outcome (target lesion, type and character of lesion) and procedural data (type of guiding catheter, guidewire, stent, lesion preparation) were recorded. Lesion was classified as type A, B1/B2, or C as per the American Heart Association/American College of Cardiology (AHA/ACC) criteria [18]. Cut-off for significant stenosis and reference vessel diameter were ≥70% and ≥2.25 mm respectively. Among bifurcation lesion, vessel receiving long stent (≥40 mm) was included irrespective of diameter of side branch. Procedures were performed after obtaining signed informed consent from all patients and study protocol was approved by institutional ethical committee. Major exclusion criteria were intolerance to antiplatelet agents (aspirin, clopidogrel, ticagrelor, prasugrel), heparin, and sirolimus, expected major surgery within 6-months following PCI, life expectancy <12 months, and patient having cardiogenic shock.

Device description and procedural details

Evermine 50, the world's thinnest stent having strut thickness of 50 μm, is combination product of a device (L-605 cobalt chromium alloy as stent platform) and drug (formulation of everolimus with blend of *biocompatible - biodegradable copolymer* acting as drug reservoir and drug releasing platform). The polymeric matrix coating consists of 50:50 mixture of lactide (poly-L-lactic acid) and glycolide (poly-lactic-co-glycolic acid) based biodegradable polymers. It has a unique hybrid cell design because of open cells in mid segment and closed cells at edges. The minimal balloon overhang (0.5 mm) with abrupt balloon shoulder further minimizes balloon induced trauma at edges. It elutes everolimus at 1.25 μg/mm^2 of stent area. The average thickness of coating is 2 μm which

remains same irrespective of stent diameter. It completely elutes the drug within 7 weeks while polymer takes 10 weeks to get completely degraded. The currently available diameter and length are 2-4.5 mm and 8-48 mm respectively. The thin-strut provides low-crossing profile which translates into excellent deliverability, crossability and conformability across the lesion.

The procedures were performed either through transfemoral or transradial route following standard techniques using unfractionated heparin (70-100 U/kg) as anticoagulant. Lesion modification was done using semicompliant, noncompliant, or cutting balloon except in cases of very soft lesion (thrombus laden) where direct stenting was performed. Post dilatation was performed accordingly. Multi vessel intervention was performed during index procedure except in ACS where revascularization of only culprit artery was performed followed by other vessels within 4 weeks. All patients were pretreated with aspirin and P2Y12 inhibitors (ticagrelor, prasugrel, or clopidogrel) and dual antiplatelet (DAPT) were continued for at least 12-months followed by aspirin alone indefinitely. Preference of antiplatelet agent was ticagrelor, followed by prasugrel and clopidogrel depending on economy and drug availability. In cases of failure of stent delivery due to various technical challenges, buddy wire with or without balloon anchoring, and rarely GuideZilla extension catheter (GEC) were used [19]. In refractory cases, different stent was chosen as per operator's preference. Cardiac biomarkers (creatine kinase-myocardial band, troponin- I and T) were measured 24 hr before and within 8 hr following intervention to diagnose periprocedural MI. All patients were followed up clinically (history, electrocardiogram, and echocardiogram) at 1 week, and then at 1, 3, 6, 9, and 12 months period. Check angiogram was performed only if they were symptomatic or when presented with acute coronary syndrome.

Study endpoints

The primary endpoint of the study was device-oriented composite outcome (DOCO), a composite of cardiac death, target vessel myocardial infarction, and target lesion revascularization driven by ischemia (TLR) which was assessed at 12 months. Secondary endpoints included individual components of primary end point, all-cause death (cardiac and non-cardiac), any revascularization, ischemia-driven target vessel revascularization (TVR), stent thrombosis, periprocedural and spontaneous MI, and device failure (composite of failure of delivery of assigned, change of stent, edge dissection, coronary perforation and stent fracture). Global cardiovascular end point (GCEP) was defined as composite of all-cause death, any MI, and any revascularization. Stent thrombosis, periprocedural MI, and spontaneous MI were defined using criteria proposed by Academic Research Consortium (ARC) [20], World Health Organization [21], and third universal definition of MI [22] respectively. Target vessel MI was attributed to entire territory (upstream and downstream) of coronary artery having target lesion or when could not be assigned to another vessel on basis of clinical presentation, laboratory data, electrocardiogram and angiographic findings [20]. Device success was defined as successful trackibility, delivery and deployment of assigned stent at target lesion with final residual stenosis ≤ 30% following post dilatation if any.

Statistical evaluation

Statistical analyses were performed using SPSS 19.0 (SPSS Inc., Chicago, IL, USA). Baseline characteristics of patients were presented as frequencies and percentages for categorical variables and mean (SD) for continuous variables. Kaplan-Meier estimate was used to construct survival curve for time-to-event variables. For it, confidence interval on each survival proportion was calculated which led to confidence curve enclosing survival curve. 95% confidence interval (CI) was calculated after deducing value of standard error of estimate (SEE) for every death at a given time. Landmark analysis of survival was performed by using 1-year landmark after censoring patients who lost follow up at various stages.

Results

During index period, revascularization was performed in 6991 patients of whom 711 patients received Evermine 50. They were followed as per protocol and finally 665 (93.5%) of them completed the follow up at 12-months (**Figure 1**). Baseline characteristics of the patients are presented in **Table 1**. Mean age of patients was 51.4±16.6 years and majority (n=454; 72.3%) were male. Risk factor were smoking (n=228; 31.9%) either in form of ciggarette/bidi (n=120;

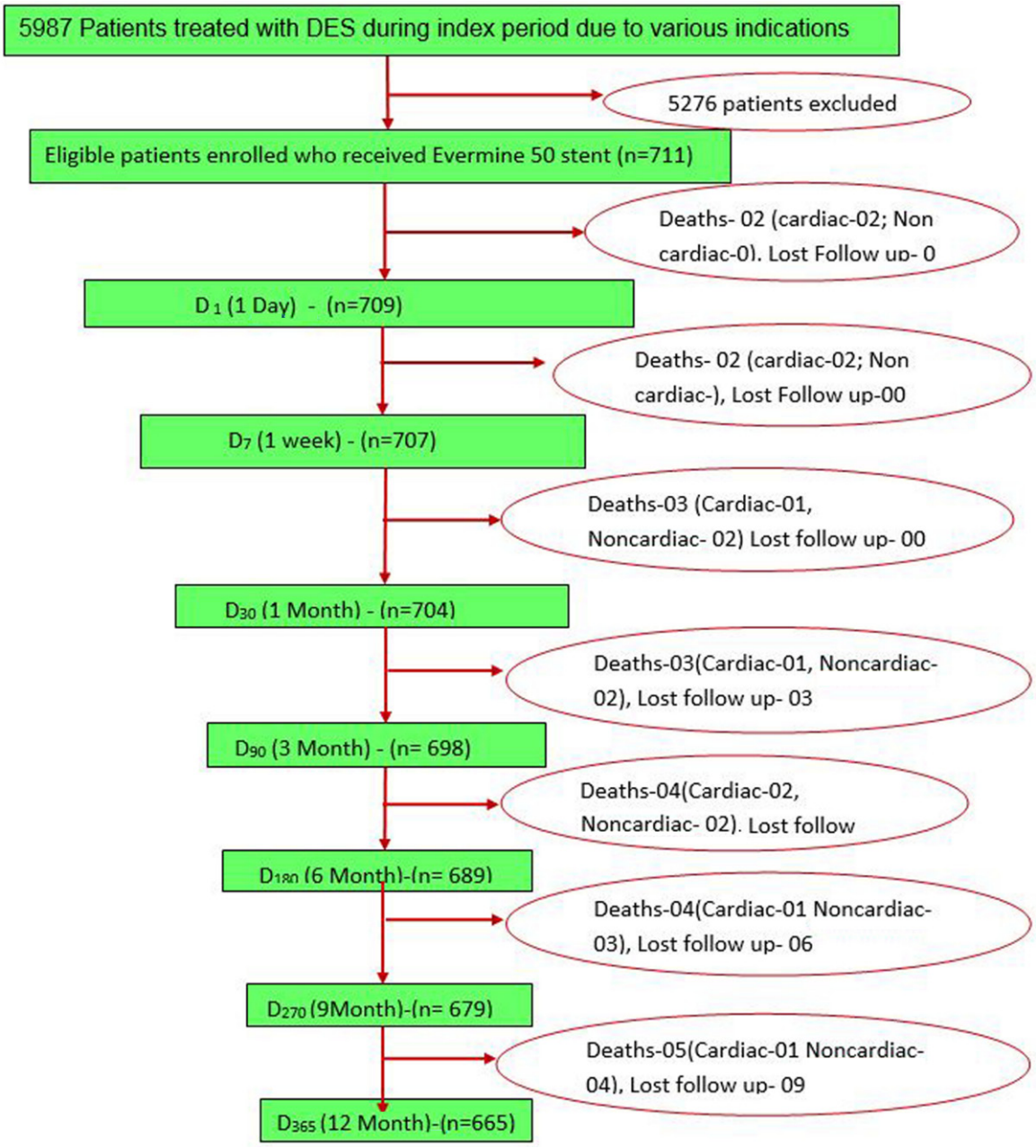

Figure 1. Flow chart of patients enrolled in the study with follow up over 12 months (N=711).

16.8%) or smokeless tobacco (n=108; 15.1%) [37] followed by hypertension (n=161; 22.6%) and dyslipidemia (n=157; 22.1%). Various indications for PCI were STEMI (n=318; 44.7%), NSTEMI (n=225; 31.6%), UA (n=103; 14.5%), and CCS (n=65; 9.2%). On angiogram, SVD was found in 438 (61.7%) patients where left anterior descending artery (LAD), right coronary artery (RCA) and left circumflex artery (LCx) were involved in 200 (28.1%), 151 (21.2%), and 87 (12.2%) patients respectively. Similarly, DVD and TVD were reported in 176 (24.7%) and 91 (13.6%) patients respectively.

*Procedural details (**Table 2**)*

Most of procedures were performed through transfemoral route (n=588; 82.7%). 6F guide catheter was used in 615 patients (86.5%) while rest were performed using 7F guide catheter which included CTO (n=93; 13.1%) and bifurcation lesions (n=30; 4.2%). Majority of

Table 1. Baseline and demographic characteristics of patients (N=711)

Characteristic	No (%)
Age (years)	51.4±16.6
Male	454 (72.3%)
Female	197 (27.7%)
BMI (kg/m^2)	23.8±3.6
Serum creatinine (mg/dL)	1.2±0.3
CAD risk factors	
Hypertension	161 (22.6%)
Diabetes mellitus	136 (19.1%)
Smokers (Ciggerette/Bidi)	120 (16.8%)
Smokeless tobacco	108 (15.2%)
Family history of CAD	34 (4.8%)
Dyslipidemia	157 (22.1%)
Clinical Presentation	
STEMI	318 (44.7%)
NSTEMI	225 (31.6%)
UA	103 (14.5%)
CCS	65 (9.2%)
LVEF (%)	
>45%	487 (68.5%)
35-45%	123 (17.3%)
<35%	101 (14.2%)
Medications	
Aspirin	699 (98.3%)
Clopidogrel	403 (56.7%)
Prasugrel	206 (28.9%)
Ticagrelor	102 (14.4%)
Statin	697 (98.1%)
Beta-blocker	492 (69.2%)
ACEI/ARB	649 (91.3%)
CCB	62 (8.7%)
Ivabradine	69 (9.7%)
Aldosterone antagonist	99 (13.9%)
Angiographic severity of CAD (Target vessel location)	
1. SVD	438 (61.7%)
a. LAD	200 (28.1%)
b. LCx	87 (12.2%)
c. RCA	151 (21.2%)
2. DVD	176 (24.7%)
3. TVD	97 (13.6%)

Data presented as mean ± standard deviation or number (percentage). BMI-Body mass index; CAD = Coronary artery disease; DM = Diabetes mellitus; PCI-Percutaneous Coronary Intervention; 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.

patients underwent single-vessel PCI (n=553; 77.8%). LAD was most commonly intervened artery in 200 (28.1%) patients followed by RCA and LCx in 151 (21.2%) and 87 (12.2%) patients respectively. Total of 998 lesions were treated. Direct stenting was performed in 25 (3.5%) patients. Assisted stent delivery was performed in 47 (6.5%) patients using buddy wire (n=28; 3.9%) and GuideZilla mother-in-child system (n=19; 2.6%). The lesion belonged to LCx (n=27; 57%) and RCA (n=20; 43%) as a result of tortuosity, angulation, and shepherd crook origin. Evermine 50 was used to treat all lesions except in few side branches and in cases of device failure (n=18; 2.5%).

*Clinical outcomes (**Table 3**)*

The primary endpoint, DOCO, observed in 47 (6.6%) patients, was mainly attributed by target vessel MI (n=23; 3.2%) and TLR (n=15; 2.1%). GCEP was observed in 117 (16.4%) patients at 12-month follow-up mainly because of any revascularization (n=60; 8.4%) and any MI (n= 34; 4.7%). Assigned stent (≥40 mm) could not be delivered to target lesions in 18 (2.9%) subjects which were finally dealt by deploying shorter and overlapping stents in 6 (0.5%) patients and different stent (Yukon Choice Sirolimus eluting stent; Translumina, Germany) in 12 (1.6%) patients. Edge dissection was observed in 15 (2.1%) patients among whom site was proximal in 4 (0.5%) patients while distal in 11 (1.5%) patients. Another stent (shorter and overlapping with previous stent) was implanted in 6 (0.8%) patients to bail out them from threatened vessel closure. Stent fracture (Grade II) was seen in one patient who was asymptomatic. Definite ST was observed in 08 (1.1%) patients while probable or possible ST was reported in 06 (0.8%) patients. Among those with definite ST, acute cases were caused by malposition of stent which was finally dealt by post dilatation using oversized non-compliant balloon. Sub-acute and late ST was responsible in three and two cases respectively which were dealt by implantation of hetero DES (Xience Prime Everolimus eluting stent; Abott Vascular, USA). **Figure 2** illustrates the Kaplan-Meier survival curves of patients over 12 months period which standard error of estimate was 0.0069 with 95% CI of 0.9521-0.9792. Of all deaths, fourteen deaths were attributed to non-cardiac conditions (eg, stroke, malignancy, renal failure, sepsis, and pneumonia).

Table 2. Procedural characteristics of patients (N=711)

Variables	Values (No; %)
Intervention (transfemoral/Radial)	588 (82.7%)/123 (17.3%)
Catheter size (6 F/7 F)	615 (86.5%)/96 (13.5%)
Size of vessels	
a. 2.25-2.5 mm	176 (24.7%)
b. 2.5-3 mm	215 (30.2%)
c. 3-3.5 mm	242 (34%)
d. 3.5-4 mm	78 (11.1%)
TIMI flow pre procedure	
a. Grade 0	103 (14.5%)
b. Grade 1	52 (7.3%)
c. Grade 2	27 (3.8%)
d. Grade 3	529 (74.4%)
Number of vessels stented	
a. 1	553 (77.8 %)
b. 2	103 (14.5%)
c. 3	55 (7.7%)
Lesion characteristics	
a. At least 1 complex lesion	638 (89.8%)
b. At least 1 bifurcation lesion	30 (4.2%)
c. At least 1 chronic total occlusion	93 (13.1%)
d. At least 1 osteo-proximal lesion	87 (12.2%)
e. At least 1 calcified lesion	33 (4.6%)
f. In-stent restenosis (ISR)	17 (2.3%)
Stents per patient	1.4±0.3
Lesions per patient (total lesion = 998)	1.4
Number of stents used per lesion	1.1
Median Stent length per lesion (mm)	49±0.8
Stent diameter (mm)	2.8±0.3
Procedural details	
Lesion Modification	
a. Direct Stenting	25 (3.5%)
b. Predilataion (semi/noncompliant balloon)	686 (96.5%)
c. Cutting Balloon	43 (6.1%)
Stent Delivery	
a. Direct (On workhorse wire alone)	647 (93.4%)
b. Buddy Wire	28 (3.9%)
c. GuideZilla mother-in-child system	19 (2.6%)
Patients who received assigned stents only (≥40 mm)	693 (97.4%)
Post-dilation	692 (97.3%)
TIMI flow post procedure	
a. Grade 0	06 (0.8%)
b. Grade 1	03 (0.4%)
c. Grade 2	18 (2.5%)
d. Grade 3	688 (96.2%)

Discussion

The key findings in our study were: (a) PCI using ultra long and thinnest stent "Evermine 50" resulted in acceptable level of primary end point (DOCO-6.6%) and its individual components which included cardiac death (1.2%), target vessel MI (3.2%), and ischaemia driven TLR

Table 3. Peri-procedural End Point and Clinical Events during 1-Year Follow-Up (N=711)

Variables	Value (No; %)
Device-oriented composite outcome (DOCO)	47 (6.6%)
a. Cardiac death	09 (1.2%)
b. Target vessel MI	23 (3.2%)
c. TLR	15 (2.1%)
Device Failure (Secondary)	36 (5.1%)
a. Failure of assigned stent delivery	18 (2.5%)
b. Edge dissection	15 (2.1%)
c. Coronary perforation	02 (0.2%)
d. Stent fracture	01 (0.1%)
Target Vessel Failure (TVF)	55 (7.7%)
Global Cardiovascular End Point (GCEP)	117 (16.4%)
All-cause death	23 (3.2%)
Any MI	34 (4.7%)
Any revascularization	60 (8.4%)
Ischemia-driven TVR	23 (3.2%)
Definite stent thrombosis	08 (1.1%)
a. Acute (≤ 24 hours)	03 (0.4%)
b. Subacute (>24 hours to 30 days)	04 (0.5%)
c. Late (>30 days to 1 year)	01 (0.1%)
Probable or possible ST	06 (0.8 %)
a. Acute (≤ 24 hours)	03 (0.4%)
b. Subacute (>24 hours to 30 days)	02 (0.2%)
c. Late (>30 days to 1 year)	01 (0.1%)

MI-Myocardial infarction; TLR-Target lesion revascularization; TVF-Target vessel failure (composite of cardiac death, target vessel MI, and ischemia-driven TVR); Global Cardiovascular End Points (GCEP)-composite of all-cause death, any MI, and any revascularization; ST-Stent thrombosis; TVR-Target vessel revascularization.

(2.1%) along with definite ST (1.1%) at the end of 12-month. These findings were consistent with event rates reported using contemporary third generation DES such as Orsiro (6%) as reported by Kandzari [14] and Synergy SES (7.5%) as reported by Lam [23].

Ultrathin strut (50 μm) may be one of the factors behind favourable result. The unique design (thinnest strut with hybrid cell) makes it swiftly trackable and deliverable across the various lesions when compared to currently available other ultrathin stents like Orsiro (Biotronik, Bülach, Switzerland)- 60 μm, Synergy Everolimus Eluting Platinum Chromium stent (Boston Scientific, USA)- 74 μm, Firehawk (Shanghai Micro Port Medical Group, Shanghai, China)- 86 μm, Supraflex Cruise SES (Sajahanand Medical Technology, Gujarat, India)- 60 μm, and MiStent SES (MiCell Technologies, Durham, NC, USA)- 64 μm. Another distinguishing feature is its unique drug elution kinetics which has shortest presence of drug (7 weeks) and polymer (10 weeks) in the vessels [24].

Thinner struts cause minimal encroachment of vessel lumen leading to maximum in-stent luminal gain, lesser turbulence with minimum eddy current formation causing lower shear stress, lower metal density, and easy strut nesting following implantation. Lower shear stress causes less platelet activation and neointimal hyperplasia. All these factors contribute to fewer acute events in form of early stent thrombosis and in-stent restenosis in longer term as thicker struts and smaller minimum in-stent lumen diameter are known independent predictors of in-stent restenosis [25]. Furthermore, thinnest strut gives more flexibility and conformability which made the stent easily trackable and deliverable during implantation [26]. These were evident in our study as only 2.6% of patients required GuideZilla mother-in-child system to assist the delivery of stent and most of them were in left circumflex vessel which had an angulated origin.

Device success (93.6%) was comparable to current generation stents like FIREHAWK (92.4%) and Xience group (94.8%) as reported in the TARGET all-comer Trial [27] but little lower than Supraflex Cruise (99.6%) as reported in TALENT Trial [28] and Orsiro SES (97.9%), Synergy EES (98.5%) as reported in BIORESORT Trial [23]. Slightly lower rate of device success in our study was because multiple parameters (including all procedural complications) were taken into consideration to define device failure while successful delivery of stent was considered as the only parameter for device success in contemprory studies [23, 27, 28].

Edge dissection in our study was 1.8% which was concordant with finding from TALENT Trial where it was reported as 2.8% and 2.2% for Supraflex Cruise and XIENCE respectively [28]. This was based on angiographic criteria alone. Our finding was also consistent with results from ILUMIEN II study which was based on intravascular ultrasound (IVUS) and optical coherence tomography (OCT) among patients

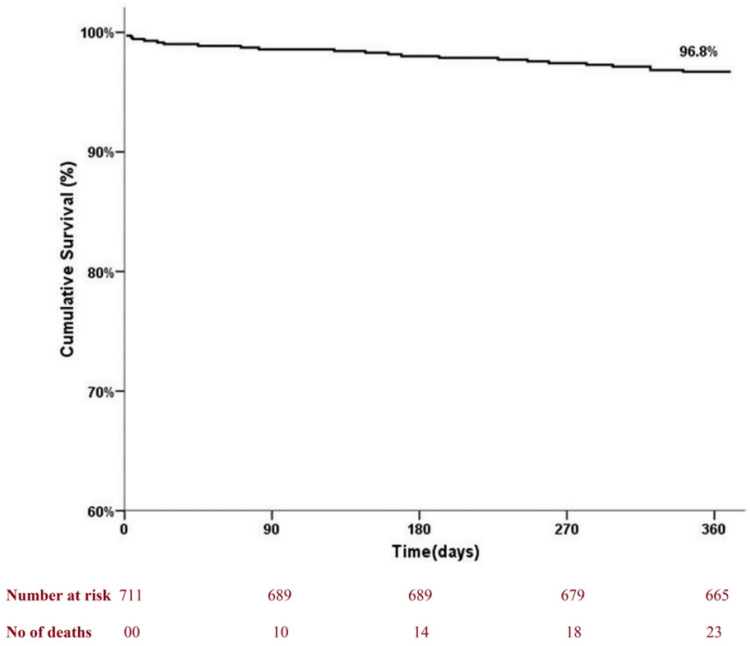

Figure 2. Kaplan-Meier survival curve of patients over 12 months period of follow up.

receiving XIENCE where incidence was 2.4% and 2.8% respectively [29]. These factors support safety and efficacy of Evermine 50 further as median length of implantation in our study was 49 mm and sizeable proportion (24.7%) of patients had vessel size ≤ 2.5 mm which are known predictors of edge dissection.

Target vessel failure in our study (7.7%) was comparable to other contemporary trials which reported it as 9.9% in FIREHAWK group while 9.6% in Xience group in TARGET all-comer trial [27]. In BIO-RESORT trial which compared thin, very thin, or ultrathin strut stents using Orsiro SES, Synergy EES and Resolute Integrity ZES, it was reported as 8.5%, 8.8%, and 10% respectively [30] while it was 5.4% in TALENT trial using Supraflex Cruise stent [28]. It was mainly driven by slightly higher target vessel MI and ischemia-driven TVR as lesion length, median stent length, and proportion of small vessel involvement were higher in our study. Another trial of ultrathin sirolimus eluting stent from South Korea as reported by Youn [31] it was much lower (3.9%) which was mainly driven by higher proportion of transradial intervention (79.1% vs. 17.3%) and lower proportion of chronic total occlusion (4.2% vs. 13.1%) when compared to our study.

Global cardiovascular end point in our study was better than FIREHAWK and Xience stent (16.4% vs. 19.3% vs. 17.8%) as shown in TARGET all-comer trial [27], but higher than 9.9% as reported in TALENT trial [28]. Our finding was also discordant with result from DESSOLVE III trial where it was reported as 13.3% using MiStent [32] and 14.3% for Orsiro SES, 14.9% for Synergy EES and 15.6% for Resolute Integrity ZES as reported in BIO-RESORT study [30]. This was mostly driven by higher rate of all deaths and all myocardial infarction because of higher co-morbidities, complex lesion, higher transfemoral intervention, and longer mean length of stent per lesion.

Stent thrombosis (both definite and probable) was little higher (1.9%) in our study compared to Orsiro SES (1.1%), Synergy EES (1.1%), and Resolute Integrity ZES (0.9%) as reported in BIO-RESORT trial, [30] MiStent (1.1%) in DESSOLVE III trial [32], Supraflex Cruise (1.5%) in TALENT trial [28], and FIREHAWK (1.7%) and Xience stent (2.1%) as shown in TARGET all-comer trial [27]. The interesting point was that most of ST was either acute or sub-acute while late events were the least in our study which makes it quite safe over long term. The possible reasons for slightly higher acute ST may be longer stent and lesser number of patients receiving potent P2Y12 inhibitor like ticagrelor and prasugrel while reasons for lower rate of late ST may be reduced long-term inflammation as biodegradable polymer minimizes polymer volume and everolimus drug concentrations in the vessel.

There was a concern regarding its safety as median length per lesion in our study was 49±8 mm. Full lesion coverage with longer stent is essential to prevent in-stent restenosis (at edges) which often requires more than one stent, sometime resulting into full metal jacketing (>60 mm) [33]. In a study of 1,107 consecutive patients involving CTO procedures as reported by Lee [34], 406 (36.7%) patients underwent FMJ using overlapping stent. In their study, median length was 76.8±14.6 mm

(range: 60-122 mm) which was higher than our study but DOCO was almost similar to our study (6.6% vs. 6.1%).

In India, cardiovascular diseases accounts for one quarter of deaths between 30 yrs to 70-years of population group [35]. Here, nearly half of patients have to bear their medical expenses as an organised insurance system is absent. In lieu of skyrocketing cost of multivessel PCI, many young patients opt for coronary artery bypass surgery because of economic restraint [36]. Recently, the government has drastically braught down the price of stents which carries a capping and with availability of ultra long stent (≥40 mm), cost of multivessel intervention has come down so that a lot more patients can achieve complete revascularisation. Our study also sheds important light regarding safety with ultrathin and ultra long stent in long lesion among Indian population where diffuse vessel disease is not so infrequent.

Limitation

Our study was observational study of not a large population. Moreover, disease of left main coronary artery was not included. Patients with cardiogenic shock were not included. Strut coverage and healing score was not studied using optical coherence tomography. Long term follow up (>5 years) would have provided safety data further.

Conclusion

The findings of the present study provide safety and efficacy of very long (>40 mm), and world's thinnest DES (Evermine 50) which is a bioresorbable polymer, sirolimus eluting stent across all substrate of lesion of coronary artery. It also included full metal jacketing especially in patients with chronic total occlusion and also non-CTO diffusely diseased small vessels as well.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Santosh Kumar Sinha, Department of Cardiology, LPS Institute of Cardiology, G.S.V.M. Medical College, Kanpur, Uttar Pradesh, India. Tel: 91-9670220088; Fax: 91-0512-255659; E-mail: fionasan@rediffmail.com

References

[1] Lagerqvist B, James SK, Stenestrand U, Lindbäck J, Nilsson T and Wallentin L. Long-term outcomes with drug-eluting stents versus bare-metal stents in Sweden. Long-term safety and efficacy of drug-eluting versus bare-metal stents in Sweden. N Engl J Med 2007; 356: 1009-1019.

[2] Nordmann AJ, Briel M and Bucher HC. Mortality in randomized controlled trials comparing drug-eluting vs. bare metal stents in coronary artery disease: a meta-analysis. Eur Heart J 2006; 27: 2784-2814.

[3] Stettler C, Wandel S, Allemann S, Kastrati A, Morice MC, Schömig A and Goy JJ. Outcomes associated with drug-eluting and bare-metal stents: a collaborative network meta-analysis. Lancet 2007; 370: 937-948.

[4] Palmerini T, Biondi-Zoccai G, Della Riva D, Stettler C, Sangiorgi D, D'Ascenzo F and DeWaha A. Stent thrombosis with drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. Lancet 2012; 379: 1393-1402.

[5] Schunkert H, Harrell L and Palacios IF. Implications of small reference vessel diameter in patients undergoing percutaneous coronary revascularization. J Am Coll Cardiol 1999; 34: 40-48.

[6] Zocca P, Kok MM, Tandjung K, Danse PW, Jessurun GAJ, Hautvast RWM, van Houwelingen KG, Stoel MG, Schramm AR, Gin RM, de Man FHAF, Hartmann M, Louwerenburg JHW, Linssen GCM, Löwik MM, Doggen CJM and von Birgelen C. 5-year outcome following randomized treatment of all-comers with zotarolimus-eluting resolute integrity and everolimus-eluting PROMUS element coronary stents: final report of the DUTCH PEERS (TWENTE II) trial. JACC Cardiovasc Interv 2018; 11: 462-469.

[7] Wöhrle J, Markovic S, Rottbauer W, Muramatsu T, Kadota K, Vázquez-González N, Odenstedt J, Serra A, Antoniucci D, Varenne O, Saito S and Wijns W. 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-e174.

[8] Claessen BE, Smits PC, Kereiakes DJ, Parise H, Fahy M, Kedhi E, Serruys PW, Lansky AJ, Cristea E, Sudhir K, Sood P, Simonton CA and Stone GW. 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-elut-

ing and paclitaxel-eluting stents in real-life practice) randomized trials. JACC Cardiovasc Interv 2011; 4: 1209-1215.

[9] Elezi S, Dibra A, Mehilli J, Pache J, Wessely R, Schömig A and Kastrati A. 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: 1304-1309.

[10] Amirzadegan A, Hasanabadi M, Saadatagah S, Afarideh M, Omidi N, Aghajani H, Alidoosti M, Pourhosseini H, Salarifar M and Nozari Y. 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.

[11] Stefanini GG, Taniwaki M and Windecker S. Coronary stents: novel developments. Heart 2014; 100: 1051-1061.

[12] Stefanini GG, Byrne RA, Serruys PW, de Waha A, Meier B, Massberg S, Jüni P, Schömig A, Windecker S and Kastrati A. 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: 1214-1222.

[13] Smits PC, Hofma S, Togni M, Vázquez N, Valdés M, Voudris V, Slagboom T, Goy JJ, Vuillomenet A, Serra A, Nouche RT, den Heijer P and van der Ent M. Abluminal biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent (COMPARE II): a randomised, controlled, non-inferiority trial. Lancet 2013; 381: 651-660.

[14] Kandzari DE, Mauri L, Koolen JJ, Massaro JM, Doros G, Garcia-Garcia HM, Bennett J, Roguin A, Gharib EG, Cutlip DE and Waksman R; 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: 1843-1852.

[15] Kolandaivelu K, Swaminathan R, Gibson WJ, Kolachalama VB, Nguyen-Ehrenreich KL, Giddings VL, Coleman L, Wong GK and Edelman ER. Stent thrombogenicity early in high-risk interventional settings is driven by stent design and deployment and protected by polymer-drug coatings. Circulation 2011; 123: 1400-1409.

[16] Bangalore S, Toklu B, Patel N, Feit F and 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: 2216-2226.

[17] von Birgelen C, Zocca P, Buiten RA, Jessurun GAJ, Schotborgh CE, Roguin A, Danse PW, Benit E, Aminian A, van Houwelingen KG, Anthonio RL, Stoel MG, Somi S, Hartmann M, Linssen GCM, Doggen CJM and Kok MM. 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: 1235-1245.

[18] Chan PH, Alegria-Barrero E, Foin N, Paulo M, Lindsay AC, Viceconte N and Di Mario C. Extended use of the GuideLiner in complex coronary interventions. EuroIntervention 2015; 11: 325-335.

[19] Chen CY, Huang YY, Tang L, Hu XQ, Fang ZF and 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: 171-178.

[20] Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, Steg PG, Morel MA, Mauri L, Vranckx P, McFadden E, Lansky A, Hamon M, Krucoff MW and Serruys PW. Clinical end points in coronary stent trials: a case for standardized definitions. Circulation 2007; 115: 2344-2351.

[21] Vranckx P, Cutlip DE, Mehran R, Kint PP, Silber S, Windecker S and Serruys PW. Myocardial infarction adjudication in contemporary allcomer stent trials: balancing sensitivity and specificity. Addendum to the historical MI definitions used in stent studies. EuroIntervention 2010; 5: 871-874.

[22] Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD; Writing Group on the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction, Thygesen K, Alpert JS, White HD, Jaffe AS, Katus HA, Apple FS, Lindahl B, Morrow DA, Chaitman BA, Clemmensen PM, Johanson P, Hod H, Underwood R, Bax JJ, Bonow RO, Pinto F, Gibbons RJ, Fox KA, Atar D, Newby LK, Galvani M, Hamm CW, Uretsky BF, Steg PG, Wijns W, Bassand JP, Menasché P, Ravkilde J, Ohman EM, Antman EM, Wallentin LC, Armstrong PW, Simoons ML, Januzzi JL, Nieminen MS, Gheorghiade M, Filippatos G, Luepker RV, Fortmann SP, Rosamond WD, Levy D, Wood D, Smith SC, Hu D, Lopez-Sendon JL, Robertson RM, Weaver D, Tendera M, Bove

AA, Parkhomenko AN, Vasilieva EJ and Mendis S; ESC Committee for Practice Guidelines (CPG). Third universal definition of myocardial infarction. Eur Heart J 2012; 33: 2551-2567.

[23] Lam MK, Sen H, Tandjung K, van Houwelingen KG, de Vries AG, Danse PW, Schotborgh CE, Scholte M, Löwik MM, Linssen GC, IJzerman MJ, van der Palen J, Doggen CJ and von Birgelen C. 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; 67: 445-451.

[24] Modolo R, Chichareon P, Kogame N, Asano T, Chang CC, de Winter R J, Kaul U, Zaman A, Spitzer E, Takahashi K, Katagiri Y, Soliman O, van Es GA, Morel MA, Onuma Y and Serruys PW. 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-e369.

[25] Briguori C, Sarais C, Pagnotta P, Liistro F, Montorfano M, Chieffo A, Sgura F, Corvaja N, Albiero R, Stankovic G, Toutoutzas C, Bonizzoni E, Di Mario C and Colombo A. In-stent restenosis in small coronary arteries: impact of strut thickness. J Am Coll Cardiol 2002; 40: 403-409.

[26] Farhatnia Y, Pang JH, Darbyshire A, Dee R, Tan A and Seifalian AM. Next generation covered stents made from nanocomposite materials: a complete assessment of uniformity, integrity and biomechanical properties. Nanomedicine 2016; 12: 1-12.

[27] Lansky A, Wijns W, Xu B, Kelbæk H, van Royen N, Zheng M, Morel MA, Knaapen P, Slagboom T, Johnson TW, Vlachojannis G, Arkenbout KE, Holmvang L, Janssens L, Ochala A, Brugaletta S, Naber CK, Anderson R, Rittger H, Berti S, Barbato E, Toth GG, Maillard L, Valina C, Buszman P, Thiele H, Schächinger V and Baumbach A. 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: 1117-1126.

[28] Zaman A, de Winter R J, Kogame N, Chang CC, Modolo R, Spitzer E, Tonino P, Hofma S, Zurakowski A, Smits PC, Prokopczuk J, Moreno R, Choudhury A, Petrov I, Cequier A, Kukreja N, Hoye A, Iniguez A, Ungi I, Serra A, Gil RJ, Walsh S, Tonev G, Mathur A, Merkely B, Colombo A, Ijsselmuiden S, Soliman O, Kaul U, Onuma Y and Serruys PW. 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: 987-997.

[29] Maehara A, Ben-Yehuda O, Ali Z, Wijns W, Bezerra HG, Shite J, Généreux P, Nichols M, Jenkins P, Witzenbichler B, Mintz GS and Stone GW. Comparison of stent expansion guided by optical coherence tomography versus intravascular ultrasound: the ILUMIEN II study (observational study of Optical Coherence Tomography [OCT] in patients undergoing Fractional Flow Reserve [FFR] and Percutaneous Coronary Intervention). JACC Cardiovasc Interv 2015; 8: 1704-1714.

[30] Buiten RA, Ploumen EH, Zocca P, Doggen CJM, van der Heijden LC, Kok MM, Danse PW, Schotborgh CE, Scholte M, de Man FHAF, Linssen GCM and von Birgelen C. 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: 659-669.

[31] Youn YJ, Yoo SY, Lee WJ, Ahn SG, Lee SH, Yoon J, Park JH, Choi WG, Cho S, Lim SW, Jang YS, Kwon KH, Lee NH, Doh JH, Kang WC, Jeon DW, Lee BK, Heo JH, Hong BK and Choi HH. Safety and efficacy of a new ultrathin sirolimus-eluting stent with abluminal biodegradable polymer in real-world practice. Korean Circ J 2020; 50: 317-327.

[32] de Winter RJ, Katagiri Y, Asano T, Milewski KP, Lurz P, Buszman P, Jessurun GAJ, Koch KT, Troquay RPT, Hamer BJB, Ophuis TO, Wöhrle J, Wyderka R, Cayla G, Hofma SH, Levesque S, Żurakowski A, Fischer D, Kośmider M, Goube P, Arkenbout EK, Noutsias M, Ferrari MW, Onuma Y, Wijns W and Serruys PW. A sirolimus-eluting bioabsorbable polymer-coated stent (MiStent) versus an everolimus-eluting durable polymer stent (Xience) after percutaneous coronary intervention (DESSOLVE III): a randomised, single-blind, multicentre, non-inferiority, phase 3 trial. Lancet 2018; 391: 431-440.

[33] Lee CW, Ahn JM, Lee JY, Kim WJ, Park DW, Kang SJ, Lee SW, Kim YH, Park SW and Park SJ. 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: 361-365.

[34] Lee PH, Lee SW, Yun SC, Bae J, Ahn JM, Park DW, Kang SJ, Kim YH, Lee CW, Park SW and Park SJ. Full metal jacket with drug-eluting

stents for coronary chronic total occlusion. JACC Cardiovasc Interv 2017; 10: 1405-1412.
[35] Prabhakaran D, Jeemon P and Roy A. Cardiovascular diseases in india: current epidemiology and future directions. Circulation 2016; 133: 1605-1620.
[36] Kaul U. The new pricing policy for coronary stents in India: a boon or a bane? EuroIntervention 2017; 13: 267-268.
[37] Piano MR, Benowitz NL, Fitzgerald GA, Corbridge S, Heath J, Hahn E, Pechacek TF and Howard G. American Heart Association Council on Cardiovascular Nursing. Impact of smokeless tobacco products on cardiovascular disease: implications for policy, prevention, and treatment: a policy statement from the American Heart Association. Circulation 2010; 122: 1520-44.