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Evaluation of novel ultrathin, biodegradable polymer tetriflex (sirolimus-eluting stent) optimization using intravascular ultrasound (IVUS) in short coronary lesion (≤ 20mm) vs. long coronary lesion (≥ 20mm): Tetriflex IVUS study

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Abstract

BACKGROUND: Intravascular ultrasound (IVUS)-guided percutaneous coronary intervention (PCI) is useful for stent optimization. Outcomes of the ultrathin Supralimus Tetriflex stent (Sahajanand Medical Technologies Pvt. Ltd., India) using IVUS were evaluated among patients with short (≤ 20 mm) versus long lesions (≥ 20 mm).

METHODS: A total of 207 patients underwent PCI, and IVUS was performed post-deployment. The primary outcome was optimal stent deployment, defined as (a) mean surface area (MSA) >5.0 mm²; (b) plaque burden <50%; (c) complete apposition; and (d) no edge dissection. Secondary outcomes were target lesion failure (TLF)—a composite of cardiac death, target vessel myocardial infarction (TVMI), and target lesion revascularization (TLR)—stent thrombosis, and major adverse cardiovascular events (MACE; a composite of death, MI, stent thrombosis, and repeat revascularization).

RESULTS: Suboptimal deployment was significantly more frequent among patients with longer lesions (30.1% vs. 23.3%; p=0.03) due to higher rates of malapposition (17.3% vs. 10.6%) and MSA <5 mm² (9.6% vs. 7.7%). Following post-dilatation, suboptimal deployment was observed in 7.6% and 5.8% of patients, respectively. Residual plaque burden was 4.5% and 5.7%, respectively. The MSA in both groups was 6.3 mm² and 6.5 mm². Minimum and mean stent expansions were 82.1% versus 81.7% and 106.3% versus 109.8%, respectively, with no significant differences. TLF and stent thrombosis were observed in 0.9% versus 0.9% and 2.9% versus 3.8% of patients, respectively, with no significant differences. However, MACE was significantly higher (10.5% vs. 8.7%; p=0.05) among patients with longer lesions.

CONCLUSION: Supralimus Tetriflex stent has very good optimal deployment based on angiogram and becomes better with IVUS imaging, making it safe among long lesions (≥ 20mm).

Keywords: Intravascular ultrasound; Major adverse cardiovascular events; Stent optimization; Target lesion failure; Stent thrombosis; Target lesion revascularization

Introduction

Coronary angiography (CAG) is the standard imaging modality used for percutaneous coronary intervention (PCI). It is essentially a luminogram that provides information only about the lumen of the vessel[1]. Since the vessel is a complex three-dimensional structure, angiography lacks details on plaque morphology, composition, burden, and vascular remodeling. It is also inaccurate in detecting calcium. Furthermore, it is suboptimal in identifying stent under-expansion, malapposition, residual dissection, thrombus, and plaque protrusion. These limitations can be addressed by using intracoronary imaging modalities such as intravascular ultrasound (IVUS), virtual histology, infrared spectroscopy, and optical coherence tomography (OCT)[2-4].

As suboptimal stent implantation is associated with adverse periprocedural and long-term major adverse cardiac events (MACE), imaging-based implantation (IVUS/OCT) has been associated with reduced MACE and a lower need for repeat revascularization. This becomes even more critical in cases where lesions are associated with complexities such as long and diffuse lesions, ostial location, underlying calcium, bifurcations, chronic total occlusions, and left main involvement[5-8]. However, despite their proven advantages over conventional angiography, these modalities are still not widely adopted in real-world practice due to the lack of appropriately powered randomized trials, cost considerations, availability, and time consumption[3].

Thus, the present study was designed to evaluate the novel ultrathin, biodegradable polymer Supralimus Tetriflex (Sirolimus-eluting stent) optimization using IVUS among patients with short lesions (≤ 20 mm) and long lesions (≥ 20 mm).

Materials and Methods

Study design and participants

This was a prospective and observational study conducted at the LPS Institute of Cardiology, GSVM Medical College, Kanpur, UP, India, a tertiary-care center, between January 2018 and March 2019. The study enrolled 207 consecutive patients (age ≥18 years) who had undergone PCI using one or more Tetriflex stents, with post-procedural assessment conducted via IVUS.

Enrollment criteria included patients undergoing revascularization for acute coronary syndrome, including recent ST-segment elevation MI (STEMI) ≥24 hours, non-ST-segment elevation MI (NSTEMI), unstable angina (UA), and chronic coronary syndrome refractory to guideline-directed medical treatment. Eligible patients had one or more target lesions located in a native coronary artery with a visually estimated reference vessel diameter (by angiography) of 2.5 mm to 4 mm. Patients with significant involvement of the left main artery, ostium of the right coronary artery, bypass graft, in-stent restenosis, degenerated vein graft following bypass surgery, intolerance to antiplatelet drugs (aspirin, clopidogrel, ticagrelor, prasugrel), heparin, or sirolimus; expected major surgery within six months following PCI; life expectancy <12 months; or cardiogenic shock were excluded.

Baseline demographics of patients—including clinical data (age, sex, and clinical presentation), angiographic findings, and procedural data (type of guiding catheter, guidewire, stent, lesion preparation)—were recorded. Coronary angiograms were assessed by visual estimation and quantitative coronary angiography (QCA). Lesions were classified as type A, B1, B2, or C according to the American Heart Association/ American College of Cardiology (AHA/ACC) criteria[9]. The study strictly adhered to the principles of Good Clinical Practice and the Declaration of Helsinki. The study protocol was approved by the institutional ethics committee, and written informed consent was obtained from all patients.

Study device

The Supralimus Tetriflex sirolimus-eluting stent (Tetrinium™ L605) is an ultrathin (60 µm), biodegradable polymer-coated cobalt-chromium stent, designed with unique LDZ-link and in-phase struts. The multilayer conformal

coating on the stent's surface comprises a blend of sirolimus and a biodegradable polymeric matrix, incorporating a combination of hydrophilic and hydrophobic polymers, including poly-L-lactide, 50/50 poly (D,L-lactide-co-glycolide), and polyvinyl pyrrolidone. These polymers provide an elastomeric property to the coating, aligning with metal expansion and controlling drug elution from the stent's coating. The multilayer coating technology also ensures controlled drug release following stent implantation. Furthermore, the unique blend of biodegradable polymers in each layer facilitates controlled drug release—two-thirds of the drug elutes within the first week, while the remaining one-third elutes over seven weeks—offering exceptional integrity. The polymer completely degrades over a period of nine months to one year.

PCI protocol and follow-up

The procedures were performed through either the transfemoral or transradial route following standard techniques, routinely using a 6F guide and a 7F guide in cases of true bifurcation lesions and chronic total occlusion. Unfractionated heparin was used as an anticoagulant (dose: 70–100 U/kg). Lesion modification was performed using semicompliant, noncompliant, or cutting balloons, except in cases of direct stenting when the lesion appeared very soft. The diameter of the vessel and the length of the lesion (≤ 20 mm or ≥ 20 mm) were determined by angiography. Stent diameter was calculated according to the size of the distal reference vessel. The stent was delivered in the standard fashion at 14 atm pressure, and inflation time was maintained at 30 seconds.

IVUS imaging and analysis

Intravascular ultrasound studies were performed using the Volcano system (Volcano Corporation, CA, USA), incorporating a 45-MHz Eagle Eye catheter after stent deployment. Following the administration of 100–200 µg of intracoronary nitroglycerine with an adequate saline flush, the IVUS transducer was advanced 10 mm beyond the distal edge of the stent, and image acquisition was performed to a point 5 mm proximal to the stent through manual pullback. When evaluating ostial lesions of the left anterior descending artery, the guiding catheter was disengaged before image acquisition. All IVUS recordings were reviewed to evaluate quantitative parameters. The minimal cross-sectional area of the stent (Stent CSA), maximum, minimum, and mean stent diameter, stent expansion, and plaque burden were measured onsite using IVUS.

Stent CSA was defined as the slice with the smallest area bounded by the stent border. Maximum and minimum stent diameters were considered as the longest and shortest diameters through the center of mass of the stent, respectively. Plaque burden was calculated as: (EEM CSA - lumen CSA) / EEM CSA, where EEM is the external elastic membrane. Stent expansion was defined as minimum CSA / reference CSA. Optimal stent deployment was defined as (a) Stent CSA >5.0 mm^2; (b) plaque burden <50% at 5 mm to either edge of the stent; (c) complete apposition to the vessel wall; and (d) no edge dissection involving the media. Malapposition, under-expansion, thrombus protrusion, and plaque prolapse were defined accordingly[6,10–17].

Post-dilatation was performed in cases of malapposition and under-expansion using a noncompliant balloon (balloon/stent diameter = 1:1) at higher pressure (>20 atm). In cases of edge dissection, the implantation of another overlapping stent was determined by flow limitation. All patients were pre-treated with aspirin and a P2Y12 inhibitor (ticagrelor, prasugrel, or clopidogrel) and continued dual antiplatelet therapy (DAPT) for at least 12 months, followed by aspirin alone indefinitely. Cardiac biomarkers (creatine kinase-myocardial band, troponin-I, and troponin-T) were measured 24 hours before and within 8 hours following PCI to diagnose periprocedural MI. All patients were followed up clinically (history, electrocardiogram, and echocardiogram) at 1 week, and at 1, 6, 9, and 12 months, respectively.

Study Endpoints

The primary outcome measure (immediately after stent implantation) was to evaluate optimal stent deployment following stent implantation. Secondary outcome measures included target lesion failure (TLF)—a composite of cardiac death, target vessel myocardial infarction (TVMI), and ischemia-driven target lesion revascularization (TLR)—which was assessed at 12 months. It also encompassed individual components of TLF, periprocedural complications (dissection, no-reflow, thrombus, abrupt closure, and perforation), final IVUS assessment (mean stent diameter, mean stent area, under-expansion, malapposition, dissection), all-cause death, any myocardial infarction (MI), any revascularization, ischemia-driven target vessel revascularization (TVR), stent thrombosis, and major adverse cardiovascular events (MACE; a composite of death, MI, stent thrombosis, or repeat revascularization).

Stent thrombosis, periprocedural MI, and spontaneous MI were defined according to the criteria established by the Academic Research Consortium (ARC)[18], the World Health Organization[19], and the Third Universal Definition of MI[20], respectively. TVMI was attributed to the target vessel or was considered unrelated to another vessel based on clinical presentation, laboratory data, electrocardiogram, and angiographic findings[21]. Revascularization was performed when the diameter stenosis was ≥70%, along with subjective evidence of ischemia.

Statistical Evaluation

All data were analyzed using the Statistical Package for Social Sciences (SPSS; Chicago, IL, USA) program, version 20. Continuous variables were expressed as mean ± standard deviation (SD) for normal distributions and compared using the Student's t-test, whereas variables with non-normal distributions were expressed as median ± SD and compared using the independent t-test. Categorical variables were expressed as frequencies or percentages and compared using the Chi-square test. A p-value of <0.05 was considered statistically significant.

Results

Baseline characteristics of the patients are presented in Table 1. The majority of the participants (n=176; 80.1%) were male. The most common risk factor was tobacco consumption (n=58; 28.4%), followed by hypertension (n=44; 22%) and diabetes (n=37; 18%). Various indications for percutaneous coronary intervention included STEMI (n=95; 45.9%), NSTEMI (n=66; 31.9%), UA (n=33; 15.9%), and CCS (n=17; 8.2%). No significant intergroup differences were observed.

On angiography, single-vessel disease was identified in 144 (69.7%) patients, with the left anterior descending artery (LAD), right coronary artery (RCA), and left circumflex artery (LCx) involved in 110 (53.1%), 53 (25.6%), and 45 (21.7%) patients, respectively. Double-vessel disease and triple-vessel disease were observed in 45 (21.7%) and 18 (8.6%) patients, respectively. Ejection fraction was relatively preserved (LVEF >45%) in the majority of patients (n=113; 54.6%).

Procedural details (Table 2)

Most of the PCI were performed through transfemoral route (n=144; 70.1%) using 6F guide catheter (n=538; 78.7%) while 7F guide catheter was used for chronic total occlusion (n=13; 6.2%) and dedicated bifurcation lesions (n=14; 6.8%). These two substrates were significantly higher in group with longer lesion (11.2% vs 7.8%; p=0.03) and (14.8% vs 6.9%; p=0.04) respectively. Dedicated bifurcation lesions using two stent technique were dealt by mimicrush technique (n=6;46%), step crush (n=02;15%), culotte (n=02;15%), and T stenting and protrusion (n=03;23%).

IVUS assessment (Table 3)

IVUS assessment following stent deployment revealed significantly more suboptimal stent deployment in the group with longer lesions (30.1% vs. 23.3%; p=0.02), whereas those with shorter lesions demonstrated good apposition (Figures 1, 2). This was primarily attributed to higher rates of malapposition (17.3% vs. 10.6%) and MSA <5 mm² (9.6% vs. 7.7%). These

Table 1. Baseline demographic and clinical presentation of patients (N=207)

Variables	Group A (N=103) Short lesion (≤20 mm)	Group B (N=104) Long lesion (≥20 mm)	P value
Age (years)	58.4±8.3	59.8±6.4	0.5
Sex (Male vs Female)	84(81.6%); 19(18.4%)	83(80%); 21(20%)	0.6
CAD risk factors			
HTN	23(22.3%)	21(20.1%)	0.6
DM	19(18.4%)	18(17.3%)	0.6
Tobacco consumption	27(26.2%)	31(29.8%)	0.3
Family history of CAD	4(3.4%)	3(2.8%)	0.8
Dyslipidemia	23(22.3%)	25(24%)	0.6
Clinical Presentation			
STEMI	47(45.8%)	44(39.9%)	0.7
NSTEMI	31(30.1.9%)	35(33.7%)	0.3
UA	16(15.6%)	17(16.3%)	0.2
CCS	09(8.7%)	08(7.8%)	0.5
LVEF (%)			
a. >55	23(22%)	28(26.9%)	0.2
a. 45-55	32(31%)	30(28.8%)	0.4
b. 35-45	32(31%)	27(26%)	0.4
c. <35	16(15%)	19(18.2%)	0.5
Medications			
Tenecteplase	29(28.1%)	32(30.8%)	0.2
Aspirin	103(99.1%)	102(98.1%)	0.8
Ticagrelor	103(100%)	102(98.1%)	0.7
Statin	101(98.44%)	100(96.1%)	0.4
Beta-blocker	60(75%)	64(61.6%)	0.6
ACEI/ARB	84(83.2%)	79(76%)	0.6
CCB	09(11.8%)	12(11.5%)	0.5
Aldosterone antagonist	12(15.2%)	14(13.5%)	0.2
Angiographic severity			
1. SVD	73(70.8%)	71(68.2%)	0.4
2. DVD	22(21.4%)	23(22.1%)	0.5
3. TVD	08(7.8%)	10(9.7%)	0.7
Target vessel involved			
a. LAD	53(51.4%)	57(54.8%)	0.7
b. LCx	23(22.4%)	21(20.2%)	0.5
c. RCA	27(26.2%)	26(25%)	0.4

HTN- Hypertension; DM- Diabetes Mellitus; CAD- Coronary artery disease; DM- Diabetes mellitus; 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; DVD- Double-vessel disease; TVD- Triple-vessel disease; LAD- Left anterior descending coronary artery; LCx- Left circumflex coronary artery; RCA- Right coronary artery; Age was represented as Mean ± SD (standard deviation) while other variables were expressed as number (N) and percentage (%). Categorical variables were compared using Chi-square test. Mean of two group were compared using Independent t-test.

Table 2. Angiographic and procedural characteristics of patients (N=207)

Variables	Group A (N=103) Short lesion (<20 mm)	Group B (N=104) Long lesion (≥20 mm)	P value
Arterial Access			
a. Femoral	71(68.9%)	74(71%)	0.5
b. Radial	32(31.1%)	30(28.1%)	
Size of vessel (mm)			
a. 2.5 - 3	50(48.4%)	48(46.2%)	
b. 3 - 3.5	42(40.9%)	40(38.3%)	0.5
c. 3.5 - 4	12(11.7%)	14(13.5%)	
Lesion characteristics			
a. At least 1 complex lesion	37(35.9%)	81(77.9%)	0.04
b. At least 1 bifurcation lesion	8(7.8%)	12(11.5%)	0.03
c. At least 1 chronic total occlusion	5(4.9%)	15(14.4%)	0.04
d. At least 1 ostial lesion	13(12.6%)	15(14.4%)	0.5
e. At least 1 calcified lesion	3(2.9%)	11(10.6%)	0.05
Lesions per patient (Mean±SD)	1.2±0.2	1.3±0.3	0.5
Lesion length (mm; Mean±Range)	16(12-20)	26(24-42)	0.04
RVD (mm; Mean±Range)	2.65(2.6-4.2)	2.74(2.7-4.1)	0.4
Length of stent (mm; Mean±Range)	22.8(16-26)	36.5(24-54)	0.01
Stent diameter (mm; Mean±SD)	3.1±0.3	3.2±0.2	0.5
Maximum Inflation pressure (atm)	14(100%)	14(100%)	0.7
Inflation Time (sec;Mean±SD)	25.8±5.2	26.2±4.8	0.6
Post dilatation inflation pressure (atm Mean±Range)	22.3(18-28)	21.9(18-39)	0.3

RVD-Reference vessel diameter. Variables were expressed as number (N) and percentage (%). Mean of two group were compared using Independent t-test.

Table 3. Peri-procedural End Point and Clinical Events during 12-months Follow-up (N= 207)

Variables	Group A (N=103) Short lesion (<20 mm)	Group B (N=104) Long lesion (≥20 mm)	P value
Final post-PCI IVUS analysis			
RVD (mm; Mean±range)	2.8(2.7-4)	2.9(2.6-4)	0.8
Mean stent diameter (Mean±SD)	2.95±0.29	2.93±0.39	0.8
Minimum stent expansion (%)	82.1	81.7	0.8
Mean stent expansion (%)	106.3	109.8	0.7
Stent CSA (mm^2; Mean± range)	6.3(5.8- 17.1)	6.4(6.1-16.3)	0.4
Residual Plaque Burden (<50%)	99(95.2%)	98(94.3%)	0.5
Any malapposition			
a. Post stenting	11(10.6%)	18(17.3%)	0.02
b. After balloon dilatation	2(1.9%)	3(2.8%)	
Any underexpansion			
a. Post stenting	4(3.8%)	11(10.5%)	0.7
b. After balloon dilatation	1(0.9%)	2(1.9)	
Sub-optimal Stent Deployment	24(23.3%)	31(30.1%)	
a. Any MSA<5mm^2	8(7.7%)	10(9.6%)	
b. Any Plaque burden > 50%	4(3.8%)	6(5.8%)	0..03
c. Any Malapposition	11(10.6%)	18(17.3%)	
d. Any Underexpansion	4(3.8%)	9(8.7%)	
e. Any Edge dissection	1(0.9%)	1(0.9%)	
Sub-optimal Stent Deployment Following post dilatation	6(5.8%)	8(7.6%)	
Peri procedural complication			
a. Dissection	1(0.9%)	1(0.9%)	
b. Slow flow or no-reflow	9(8.7%)	10(9.6%)	
c. Thrombus	1 (0.9%)	1 (0.9%)	0.7
d. Abrupt closure	0	0	
e. Perforation	0	0	
Post Procedural TIMI III flow	99(96.1%)	101(97.2)	0.7
Target Lesion Failure (TLF)	3(2.9%)	4(3.8%)	
a. Target vessel MI	1(0.9%)	2(1.8%)	0.5
b. Ischemia-driven TLR	1(0.9%)	1(0.9%)	
c. Cardiac death	1(0.9%)	1(0.9%)	
Target Vessel Failure (TVF)	4(3.8%)	6(5.7%)	0.05
MACE	9(8.7%)	11(10.5%)	0.05
All cause death	2(1.9%)	2(1.9%)	0.7
Periprocedural MI	1(0.9)	1(0.9%)	0.8
Any MI	3(2.8%)	4(3.8%)	0.7
Any revascularization	3(2.9%)	4(3.8%)	0.6
Ischemia-driven TVR	2(1.9%)	2(1.9%)	0.4
Definite and Probable ST	1(0.9%)	1(0.9%)	
a. Acute (0-1 days)	0	0	0.7
b. Sub-acute (2-30 days)	1(0.9%)	01(0.9%)	
c. Late (31-360 days)	0	0	

MI- Myocardial infarction; TLR- Target lesion revascularization; RVD- Reference vessel diameter; MLD- Minimum lumen diameter; MLA- Mean luminal area; TVF-Target vessel failure (composite of cardiac death, target vessel MI, and ischemia-driven TVR); TVR- Target vessel revascularization; MACE- Major adverse cardiovascular events (composite of death, MI, stent thrombosis, or repeat revascularisation); ST- Stent thrombosis. Variables were expressed as number and percentage (%). Mean was compared using independent t-test.

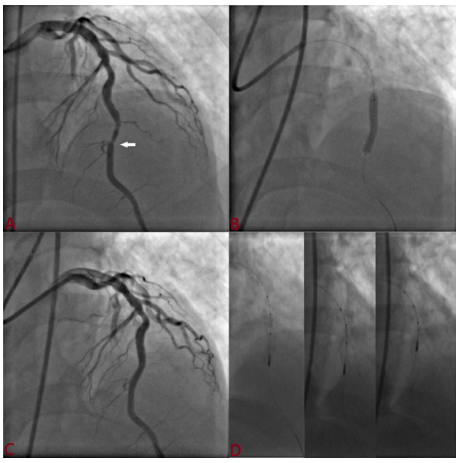

Figure 1. Left anterior descending artery showing critical tubular lesion in mid segment (white arrow;A), Tetriflex 4x20 mm was deployed at 12 atm pressure (B); optimally deployed stent observed on angiogram (C) and its IVUS assessment (D)

issues were mostly observed at the stent edges and overlapping segments in cases of two overlapping stents (Figures 3–6). Post-dilatation was performed using an oversized (≥0.5 mm stent size) non-compliant (NC) balloon at higher pressure. Similarly, patients in the longer lesion group also exhibited significantly higher under-expansion rates (8.7% vs. 3.8%; p=0.02).

In patients with stent under expansion, post-dilatation with an appropriately sized NC balloon (based on reference lumen diameter) was done (Figure 5, 6). Even after aggressive dilatation using NC balloon, there were still few minor under-expansion and malapposition because of fibrotic and calcified plaque which resulted in suboptimal stent optimization in 5.8% and 7.6% patients with shorter and longer lesion respectively. As post IVUS assessment indicated these to be acceptable, overzealous dilatation was not further done. No reflow which were noted following stent deployment were dealt with intracoronary administration of diltiazem and nikorandil.

Clinical outcomes (Table 3)

The primary endpoint, TLF, was higher in patients with longer lesion lengths, although not statistically significant (3.8% vs. 2.9%; p=0.5). Similarly, TVF (5.7% vs. 3.8%; p=0.04) and MACE (10.5% vs. 8.7%; p=0.05) were significantly higher in patients with longer lesion lengths, primarily driven by higher rates of TVMI.

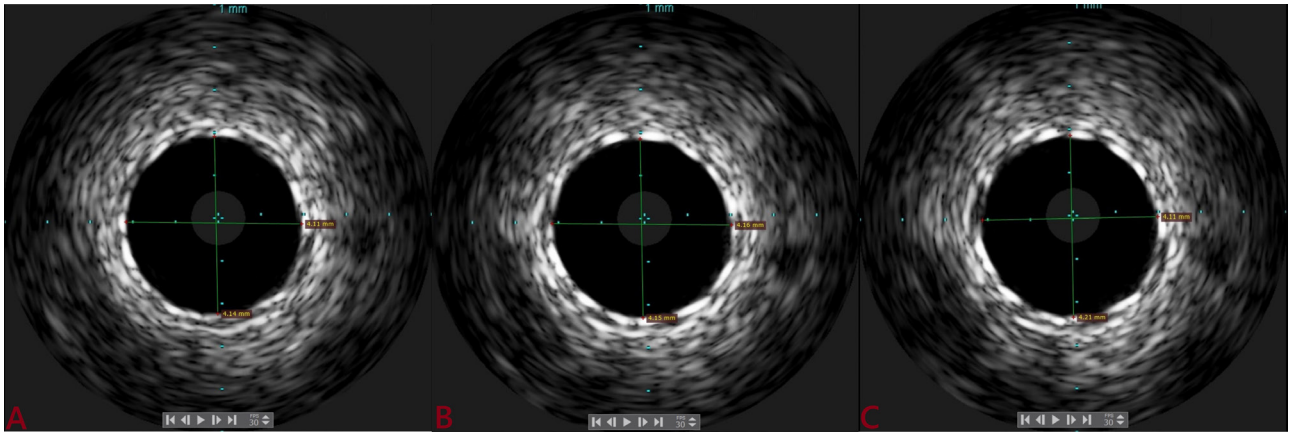

Figure 2. IVUS image showing optimally deployed stent (distal edge-A, mid segment-B; proximal segment-C).

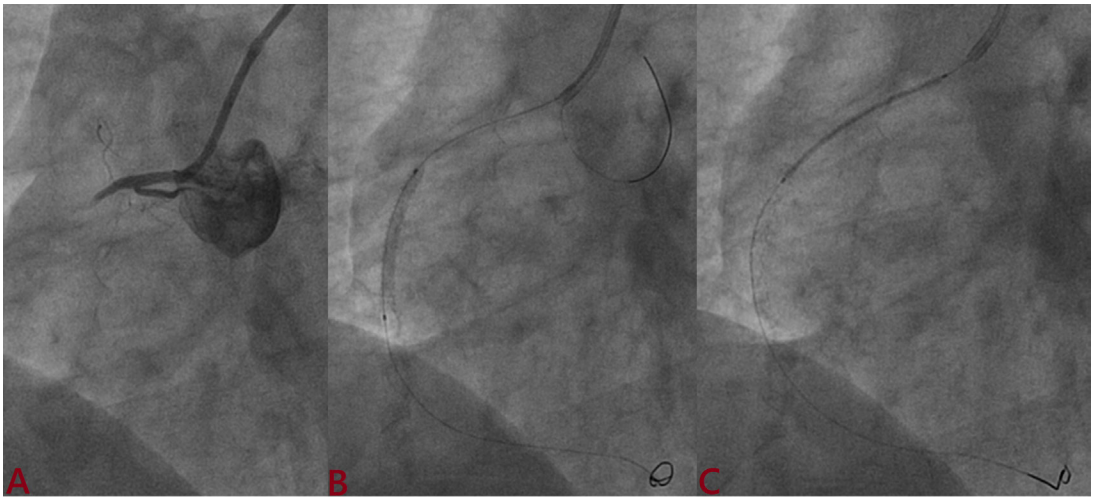

Figure 3. Right coronary artery showing total occlusion in proximal segment (A), 3x28 mm stent was deployed distally (B) and overlapped with 4x32 mm stent proximally (C).

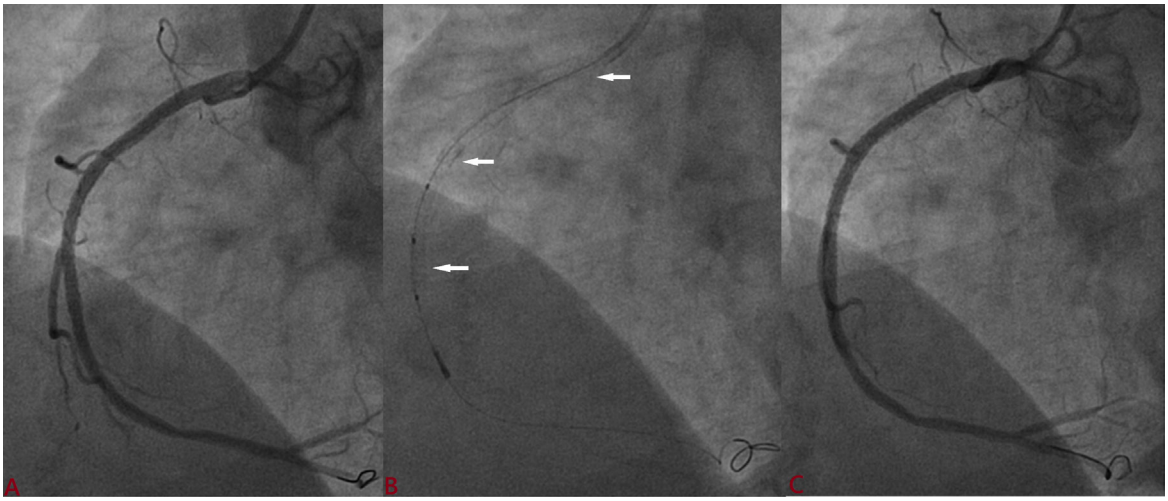

Figure 4. Angiogram showing deployed and overlapped stents in RCA (A); IVUS following deployment (B); Final angiogram well apposed stent following post dilatation using high pressure non-compliant balloon (C).

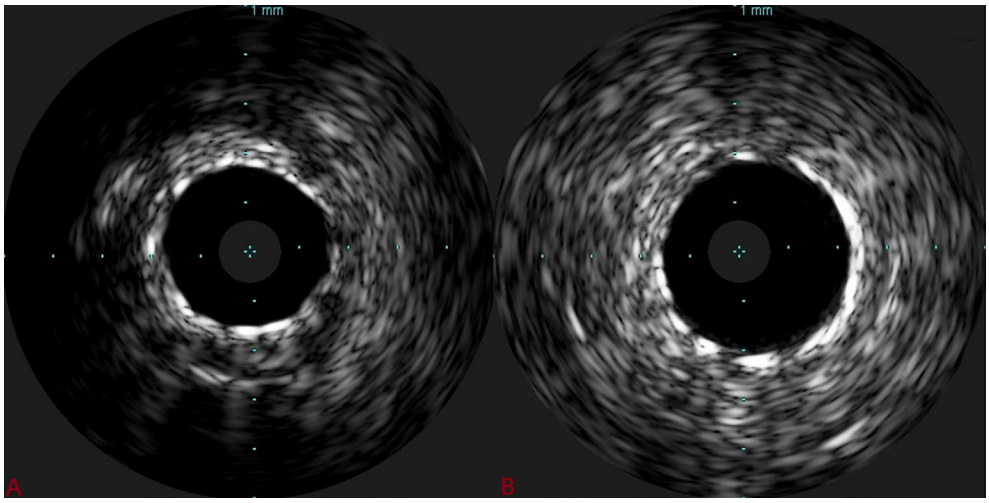

Figure 5. IVUS image showing underexpanded stent at proximal segment (A); well apposed stent following post dilatation (B).

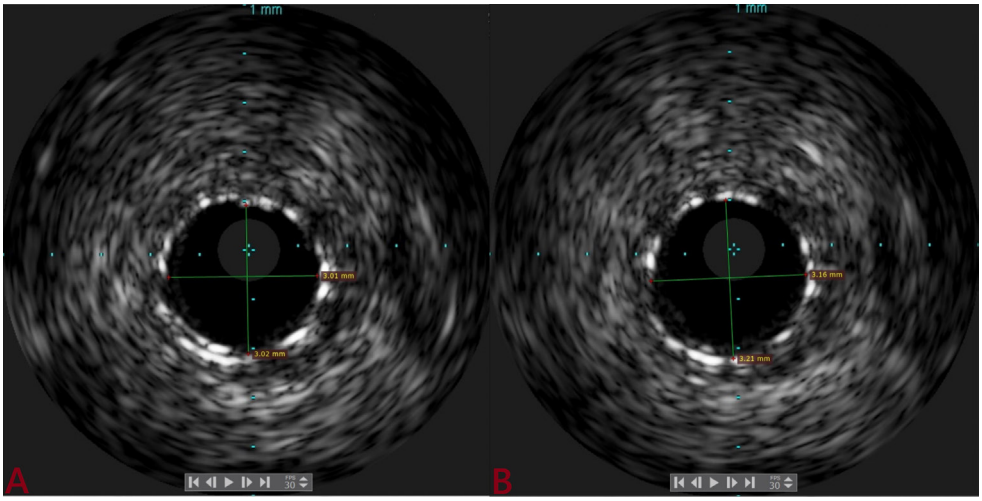

Figure 6. IVUS image of underexpanded stent at overlapping segment (A); well apposed stent following post dilatation (B).

Any ST was observed in 0.9% of patients in both groups, with no significant difference. It was a sub-acute event in both groups. Cardiac deaths in both groups were attributed to progressive pump dysfunction, as patients had impaired systolic function at baseline that did not improve following PCI.

Discussion

The primary findings of our study were as follows: (a) Optimal stent expansion following deployment of Supralimus Tetriflex in shorter and longer lesions was 76.7% and 69.9%, respectively. (b) Treatment of coronary artery disease with these lesions using Supralimus Tetriflex resulted in an acceptable level of clinical event rates, with TLF of 3.3% and any ST of 0.9% at the 12-month follow-up. (c) The rates of cardiovascular death, MI, and TLR were 0.9%, 1.4%, and 0.9%, respectively, with no significant differences between these groups.

These findings are consistent with results obtained using Xience Prime everolimus-eluting stents for long lesions in the IVUS-XPL trial[8]. In this trial, IVUS-based stent implantation was compared to angiography-guided implantation. Our study is unique in that IVUS was performed only after angiographic-guided stent implantation. Periprocedural outcomes in our study were also consistent with the findings from this trial. A higher rate of optimal deployment was notable, despite the fact that complex lesions were observed in 57% of the overall patient population, and 50% of patients had an average stent length of 33 mm.

The minimum cross-sectional area (CSA) of the stent in our study was consistent with findings from the ILUMEIN 3 trial, which compared Everolimus, Zotarolimus, Sirolimus, and Biolimus-eluting stents based on OCT, IVUS, and angiographic assessment[22]. The post-stenting minimal lumen diameter (MLD) in our study (3.1 mm) was also concordant with findings from the ULTIMATE trial (3 mm), which compared Everolimus, Zotarolimus, and Sirolimus-eluting stents[17], and the AIR-CTO trial, which reported an MLD of 3.08 mm[23]. In both of these trials, IVUS was used as the primary imaging modality.

The minimum stent expansion in our study was 81.2%, which was slightly lower than the findings from the ILUMEIN 3 trial[22], where a cut-off of ≥90% was used to define optimal expansion. Post-dilatation was identified as a key corrective measure for achieving optimal deployment. In imaging-based studies, achieving expansion targets of >90% is often challenging, even in simple lesions. Stent expansions of >80% and >90% are considered optimal for straight and tortuous vessels, respectively. In the landmark MUSIC study, the cut-off for optimal expansion was set at 80%[24].

As the minimum stent expansion in both groups in our study was 82%, further aggressive dilatation to achieve >90% expansion was not pursued. It has been demonstrated that IVUS consistently overestimates sizing compared to angiography; thus, even a minimum expansion of >80% is considered acceptable. Moreover, angiographic success is defined as residual stenosis <30%[18], which corresponds to approximately 80% by IVUS criteria. In the AVIO trial, more aggressive criteria for optimal stent deployment led to larger stent dimensions but failed to demonstrate improved clinical outcomes at 24 months[25].

Mean stent expansion (110.3%) in our study was similar to the findings from the ILUMEIN 3 study[22]. Suboptimal expansion in our study was significantly lower in the group with shorter lesions (23.3%) compared to those with longer lesions (30.1%), which was primarily attributed to malapposition and MSA <5 mm^2. Following post-dilatation using a non-compliant balloon, residual suboptimal stent expansion was observed in 5.8% and 7.6% of patients, respectively, as a result of correcting malapposition and achieving an MSA >5 mm^2. These findings were consistent with those reported by Taherioun et al., who noted a suboptimal expansion rate of 22%[26].

Major contributing factors to malapposition included vessel size <2.75 mm and longer lesions >20 mm, which required longer

stents. The ultrathin strut (≤60 µm) may have contributed to the favorable results, while the novel design (LDZ-link) likely provided unique conformability across lesions. In addition to its innovative design, aggressive predilatation, lesion modification using cutting or scoring balloons, higher inflation pressures, and longer inflation times may have played contributory roles. It has been documented that prolonged inflation (≥30 seconds) is associated with greater stent expansion compared to shorter inflation durations[27-30].

In our study, stent deployment pressure was 12 atm, with post-dilatation performed at higher pressures (average: 22 atm). These findings were similar to the POSTIT trial[30], which demonstrated that stent deployment pressures ≤12 atm were associated with a higher frequency of suboptimal stent deployment. Furthermore, selecting an undersized stent for the target lesion may have contributed to stent under-expansion, as IVUS was not performed upfront. Additionally, underlying calcification was a notable factor responsible for suboptimal expansion, as demonstrated by Ribamar et al.[31].

Cumulative target lesion failure in our study (3.3%) was much lower in comparison to contemporary third generation DES such as Orsiro (6%) as reported by Kandzari et al,[32] and Synergy SES (7.5%) as reported by Lam et al.[21], and by Tian et al in AIR-CTO trial[23]. It was concordant with findings from ULTIMATE II trial which reported as 2.8%[17]. It was significantly lower among patients with shorter lesion. Strongest predictor of TLF on IVUS is MSA and residual plaque burden <50%. Studies and meta-analysis have demonstrated that IVUS, compared with coronary angiography alone, is associated with decreased risk of cardiovascular death, MI, TLR and ST[5,33]. As it provides better understanding of vessel anatomical characteristics at the time of PCI, it facilitates better stent optimization, detects any malapposition, under expansion, and identify unrecognized complications, such as edge dissection thereby reduce improve short- and long-term outcomes.

Similarly, target vessel failure (TVF) in our study (4.8%) was significantly lower than that reported in other contemporary trials, including the TARGET All-Comer trial using FIREHAWK (9.9%) and Xience Prime (9.6%)[34], the BIO-RESORT trial using Orsiro SES (8.5%), Synergy EES (8.8%), and Resolute Integrity ZES (10%)[35], and the TALENT trial using the Supraflex Cruse stent (5.4%)[36]. However, the TVF rate in our study was higher compared to the ULTIMATE II trial, which reported a rate of 2.8%[17]. In all IVUS-based trials, the modality was utilized upfront, which resulted in better vessel sizing, as mean vessel size was higher in the ULTIMATE trial[17].

Stent thrombosis (both definite and probable) in our study was not different between the two groups and was observed in 0.9% of patients, comparable to 1.1% for Orsiro SES, 1.1% for Synergy EES, and 0.9% for Resolute Integrity ZES as reported in the BIO-RESORT trial[35]. In another study by Waksman et al., among 884 patients who underwent IVUS-guided DES implantation, ST was reported as 0.7% at 1 year and was significantly higher than in the angiography-guided arm[37]. However, it was higher than the rate reported in the ULTIMATE II trial (0.1%)[17]. Possible reasons for this difference could include impaired left ventricular systolic function, bifurcation stenting, smaller vessel diameter at baseline, and a mean stent diameter <3.0 mm[38].

Our study also addressed the safety of the Supralimus Tetriflex in smaller vessels, defined as those with a diameter ≤2.75 mm[39]. PCI in these vessels is associated with an increased risk of adverse outcomes, including restenosis, thrombosis, and an elevated need for TLR. While PCI leads to an acute gain in minimum lumen diameter, this is later offset by late lumen loss due to vessel recoil and intimal hyperplasia[39]. However, as the Tetriflex stent is ultrathin (60 µm) and its polymer is biodegradable, late lumen loss (0.05 to 0.10 mm) does not significantly impact these smaller vessels.

With improved technology and refinements in hardware, complex, multivessel, and/or left main coronary artery stenting is now frequently being performed. Therefore, the issue of

stent optimization has become even more critical. IVUS unquestionably helps minimize the risk of stent thrombosis resulting from stent malapposition or under-expansion. Most studies have considered the distal reference or mean reference vessel for stent sizing and balloon sizing during post-dilatation; however, this approach minimizes luminal gain, especially in long lesions with overlapping stents or vessels with distal tapering[40]. IVUS-guided DES implantation has been associated with a lower risk of MACE, target vessel revascularization, and has been identified as an independent predictor of freedom from cumulative stent thrombosis at 12 months in complex lesions[41-43].

Conclusion

The findings of the present study demonstrate the safety and effectiveness of the ultrathin Supralimus Tetriflex bioresorbable polymer, sirolimus-eluting stent across all lesion substrates, including chronic total occlusions and diffusely diseased vessels. IVUS imaging indicated optimal deployment in a large proportion of patients, and a very high number of patients achieved optimal deployment following noncompliant balloon dilatation, which led to reduced MACE and stent thrombosis.

Limitation

IVUS in this study was performed only after stent deployment to assess optimization, as pre-intervention imaging assessment was not conducted. Our study was an observational study with a relatively small population, and IVUS-based follow-up was not performed. Third, our analysis included a mix of lesion locations and multivessel disease interventions. Long-term follow-up (>5 years) would have provided additional safety data.

Conflict of interests

The authors declare no conflict of interest.

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Author's Contributions

Study Conception or Design: SKS, MS, MJJ, PS, UP, MR, PA, RKV

Data Acquisition: SKS, NUS, MJJ, UP, AKS, PA, KH

Data Analysis or Interpretation: SKS, MS, PS, MR, RKV

Manuscript Drafting: SKS, NUS, MJJ, UP, MR, AKS, PA, KH, RKV

Critical Manuscript Revision: SKS, MS, PS, MR, AKS, PA, KH

All authors have approved the final manuscript and are responsible for all aspects of the work.

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