

Clinical outcomes of ultrathin biodegradable polymer-coated sirolimus-eluting stents in an all-comer population: One-year results from the T-FLEX registry including high-risk subgroups

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ABSTRACT

Objective: T-Flex registry was designed to investigate the safety and clinical performance of the ultrathin (60 µm) strut biodegradable polymer-coated sirolimus-eluting stent (SES) with a unique long dual Z (LDZ) link design on a cobalt-chromium stent platform (Sahajanand Medical Technologies Pvt. Ltd., Surat, India) in a real-world all-comer population including high-risk subgroups.

Methods: This was an observational, multicenter, single-arm, and investigator-initiated retrospective registry. A total of 1,203 patients treated with an ultrathin biodegradable polymer-coated SES, irrespective of lesion complexity, comorbidities, and acute presentation were analyzed from May 2016 to January 2017. The primary endpoint was the one-year incidence of target lesion failure (TLF), a composite of cardiac death, target-vessel myocardial infarction (TV-MI), and clinically-indicated target lesion revascularization (CI-TLR). Stent thrombosis was assessed as an additional safety endpoint.

Results: At the one-year follow-up, TLF was observed in 3.8% [95% confidence interval (CI) 2.9–5.1] patients, composed of 0.6% (95% CI: 0.3–1.3) cardiac death, 1.3% (95% CI: 0.8–2.2) TV-MI, and 1.9% (95% CI: 1.3–2.9) CI-TLR. In the high-risk subgroups, TLF at one-year was 6.8% (95% CI: 4.6–9.8) in patients with diabetes, 5.2% (95% CI: 3.4–8) in patients with small-vessel disease, 6.1% (95% CI: 3.9–9.6) in patients with ST-elevation myocardial infarction, and 4.5% (95% CI: 2.4–8.3) in patients with total occlusion. During follow-up, stent thrombosis was reported in 0.8% (95% CI: 0.4–1.5) patients in the overall population.

Conclusion: Low event rates of TLF and stent thrombosis at one-year follow-up indicate that this ultrathin biodegradable polymer-coated SES has encouraging safety and clinical performance in real-world all-comer populations as well as in high-risk subgroups.

Keywords: biodegradable polymer, percutaneous coronary intervention, sirolimus-eluting stent, stent thrombosis, target lesion failure, ultrathin strut

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Introduction

Since its inception, percutaneous coronary intervention for the treatment of coronary artery disease has undergone a continuous transition to achieve an optimal stent design. The

breakthrough discovery of drug-eluting stents (DES) significantly reduced neointimal proliferation and high rates of restenosis compared with those of bare-metal stents (BMS). However, it raised long-term safety issues related to late and very late stent thrombosis, attributable to chronic inflamma-



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HIGHLIGHTS

- Since its inception, percutaneous coronary intervention for the treatment of coronary artery disease has undergone a continuous transition to achieve an optimal stent design. New stent engineering aims to improve means of deliverability and safety profile.
- Thinner stent struts are associated with lowered crimp profile, increased flexibility, improved stent deliverability, and trackability in the severely calcified and tortuous path of complex coronary lesions, and improved clinical performance.
- The T-Flex registry yielded low one-year target lesion failure and stent thrombosis rates. These results clearly depict excellent safety and clinical performance of this ultrathin biodegradable polymer-coated sirolimus-eluting stent in real-world all-comer populations as well as in high-risk subgroups with coronary artery disease.

tion or delayed hypersensitivity reaction caused by the persistent presence of polymers in DES (1-3). Subsequent innovations in DES components have been made to overcome the limitations of prior generation DES (4). Accordingly, the newer generation DES have evolved from durable polymers to biodegradable polymers and from thick strut to ultrathin strut with newer anti-proliferative agents to develop a stent with maximal safety and efficacy profiles and improved performance (5-7).

The major clinical advantage of a biodegradable polymer is that it undergoes degradation after the drug has been eluted, thereby reducing local inflammatory reaction and irritation leaving only a metal stent in adhesion with neointima and endothelium. Similarly, thinner stent struts have been developed to enhance the biocompatibility, which resulted in lower restenosis rates after stent placement (8, 9). Moreover, thinner struts are also associated with lowered crimp profile, increased flexibility, improved stent deliverability, and trackability in the severely calcified and tortuous path of complex coronary lesions, and improved clinical performance (10, 11). Although sirolimus-eluting cobalt-chromium stents have demonstrated excellent long-term safety and efficacy outcomes in a wide range of studies (12-21), new stent engineering is aimed at improving its means of deliverability and safety profile. The ultrathin (60 μm) biodegradable polymer-coated sirolimus-eluting stent (SES) (Sahajanand Medical Technologies Pvt. Ltd., Surat, India) is one such latest-generation coronary stent with unique “long dual Z (LDZ) link” on a cobalt-chromium stent platform. The T-Flex registry presents one-year safety and clinical performance outcomes for this ultrathin SES in patients with coronary artery disease in a real-world all-comer population as well as high-risk subgroups, such as patients with diabetes mellitus, small coronary vessels (≤ 2.5 mm), ST-elevation myocardial infarction (STEMI), and total occlusions.

Methods

Study design and patient population

T-Flex registry was an observational, multicenter, single-arm, investigator-initiated retrospective registry conducted at seven tertiary-care centers in India. The registry population comprised real-world all-comer patients with coronary artery disease, who were treated with at least one ultrathin biodegradable polymer-coated SES designed with a LDZ link, between May 2016 and January 2017. As the registry was aimed at studying a real-world and all-comer population, no specific clinical or angiographic exclusion criteria were defined; and all consecutive patients satisfying the inclusion criteria were examined, irrespective of lesion complexity, comorbidities, and acute presentation. The study protocol was approved by the Institutional Ethics Committee. The registry, design, and procedures conformed to the principles of Good Clinical Practice (22) and the Declaration of Helsinki (23). Signed informed consent for data collection and its analysis for research purposes was obtained from each patient.

Description of the study stent

The ultrathin biodegradable polymer-coated SES has the latest-generation Tetrinium L-605 cobalt-chromium alloy with a strut thickness of 60 μm as its stent platform (Sahajanand Medical Technologies Pvt. Ltd., Surat, India). The multi-layer coating on the conformal surface of the SES contains 1.4 $\mu\text{g}/\text{mm}^2$ of sirolimus drug blended with a biodegradable polymeric matrix comprising a combination of hydrophilic and hydrophobic polymers, containing poly (L-lactide) (PLLA), poly (L-lactide-co-caprolactone) (PLCL), and polyvinylpyrrolidone (PVP). These polymers provide elastomeric property to the coating to aid with the metal expansion mechanism and control the drug elution from the stent coating. SES is designed to release the drug at a sustained rate. Nearly 80% of the drug is released within four weeks in biological media. The remaining drug is programmed to be released at a slow rate in approximately three months. Figure 1 represents the *in vitro* percentage cumulative drug release profile of SES. After releasing the drug, biodegradable polymers undergo hydrolysis and then gradually degrade into biologically

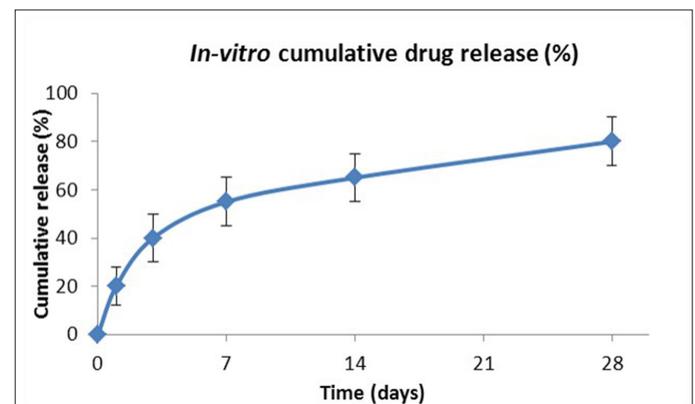


Figure 1. *In vitro* drug release profile of the ultrathin biodegradable polymer-coated sirolimus-eluting stent

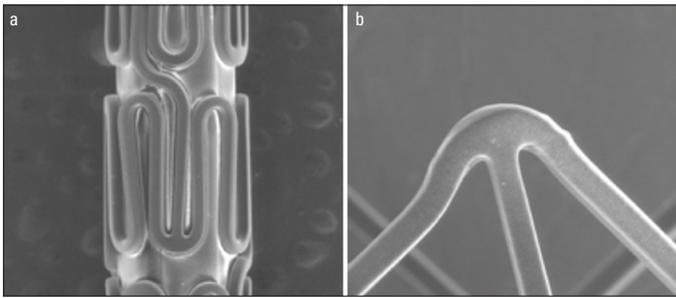


Figure 2. Scanning electron microscopy images of (a) crimped and (b) expanded ultrathin biodegradable polymer-coated sirolimus-eluting stents

acceptable molecules that are metabolized and removed from the body via normal metabolic pathways. The average coating thickness of SES is between 4 and 6 μm . The unique coating matrix offers excellent coating adhesion with a stent surface. The multi-layer coating technology offers precise control over drug release to accommodate arterial drug requirements post stent implantation. Further, the unique blend of biodegradable polymers in each layer aids in achieving controlled drug release and offers unmatched coating integrity. Moreover, the drug-free top layer comprised hydrophilic polymers with antioxidants tends to improve product shelf life and protect coating layers during implantation. The scanning electron microscopy images of sterile crimped stents and expanded stents are displayed in Figure 2, revealing a smooth and uniform coating surface without any coating anomalies and defects such as webbing, bridging, and strut-to-strut contact, even after expansion of the stent. During the study period, the SES was made available in lengths of 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48 mm and diameters of 2.00, 2.25, 2.50, 2.75, 3.00, 3.50, 4.00, and 4.50 mm.

Coronary intervention procedure and adjunctive medications

Coronary interventional procedures and adjuvant medications were performed per the standard guidelines (24). Dual antiplatelet therapy (DAPT) including a loading dose of aspirin (300 mg) and clopidogrel (600 mg) or prasugrel (60 mg) or ticagrelor (180 mg) was given to each patient. Procedural anticoagulation was achieved either with heparin or bivalirudin. However, administration of intra-procedural glycoprotein IIb/IIIa inhibitor was at the investigator's discretion. All the patients were advised to maintain DAPT (aspirin 75–300 mg daily indefinitely and clopidogrel 75 mg daily or prasugrel 10 mg daily or ticagrelor 90 mg twice daily for at least 12 months) after the procedure.

Data collection and patient follow-up

All data including demographic information, cardiovascular history, comorbidities, clinical presentation, lesions, and procedural characteristics were obtained from the hospital records of each study center. Follow-up data were obtained retrospectively either by extraction from existing databases in a consecutive fashion where index and follow-up data existed or were obtained by telephonic contact one year after stent implantation. During these follow-ups, information about patients' clinical

conditions and the occurrence of any adverse events or hospitalizations were collected. Whenever an event occurred, attempts were made to obtain copies of medical records or any other relevant documents to adjudicate the event. Long-term follow-up will be done for up to three years.

Study endpoints

The primary endpoint of the T-Flex registry was the incidence of target lesion failure (TLF), which was defined as a composite endpoint of cardiac death, target-vessel myocardial infarction (TV-MI), and clinically-indicated target lesion revascularization (CI-TLR) by percutaneous or surgical methods after one year. Secondary endpoints included device success, procedural success, and incidence of all separate components of the primary endpoint. At each follow-up, events of stent thrombosis were evaluated as an additional safety endpoint, which was classified into definite, probable, and possible stent thrombosis on the basis of criteria defined by the Academic Research Consortium (ARC) (24).

Study definitions

For this registry, any death due to a cardiac cause such as myocardial infarction (MI), low-output failure, lethal arrhythmia or unwitnessed death, death of unknown reason, and all procedure-related deaths linked to concomitant treatment was stated as cardiac death, whereby non-cardiac death included any death where a non-cardiac cause was well established. MI was defined according to the third universal definition (25). TV-MI was defined as an MI with evidence of myocardial necrosis in the vascular territory of the previously treated target vessel. CI-TLR was described as any revascularization procedure in the target lesion with stenosis $>50\%$ in association with clinical or functional ischemia (positive functional study, electrocardiographic changes, or ischemic symptoms), or stenosis $>70\%$ in the absence of clinical or functional ischemia. Device success was defined as successful delivery, deployment, and withdrawal of the assigned device at the intended target lesion with a final in-stent residual stenosis of $<30\%$ by visual estimation. Procedural success was defined as device success of all intended target lesions without the occurrence of TLF during the index procedure hospital stay.

Statistical analysis

All data were analyzed with the IBM Statistical Package for Social Sciences for Windows, version 20.0. (Armonk, NY: IBM Corp., USA). Data were presented using descriptive statistical methods. Continuous variables were presented as mean \pm standard deviation, and categorical variables were expressed as frequency and percentages. The TLF event curve was obtained using the Kaplan-Meier method.

Results

Baseline, lesion, and procedural characteristics

The T-Flex registry analyzed a total of 1,203 patients. The mean age of the study population was 56.6 ± 10.7 years with male

Table 1. Baseline characteristics for overall study patient population and high-risk subgroups implanted with ultrathin biodegradable polymer-coated sirolimus-eluting stents

Characteristics	Total patients (n=1,203)	Diabetes mellitus (n=387)	Small vessel (≤ 2.5 mm) (n=374)	Total occlusion (n=208)	ST-elevation myocardial infarction (n=291)
Age (years), mean \pm SD	56.6 \pm 10.7	55.74 \pm 9.88	58.30 \pm 9.75	57.38 \pm 10.25	55.42 \pm 11.62
Male, n (%)	884 (73.5)	268 (69.3)	249 (66.6)	143 (68.8)	225 (77.3)
Cardiovascular risk					
Hypertension, n (%)	516 (42.9)	249 (64.3)	152 (40.6)	98 (47.1)	105 (36.1)
Hypercholesterolemia, n (%)	402 (33.4)	169 (43.7)	116 (31.0)	79 (38.0)	74 (25.4)
Diabetes mellitus, n (%)	387 (32.2)	387 (100.0)	141 (37.7)	61 (29.3)	85 (29.2)
Smoking, n (%)	236 (19.6)	56 (14.5)	59 (15.8)	37 (17.8)	78 (26.8)
Family history of coronary artery disease, n (%)	38 (3.2)	18 (4.7)	16 (4.3)	12 (5.8)	9 (3.1)
Previous myocardial infarction, n (%)	70 (5.8)	21 (5.4)	23 (6.1)	17 (8.2)	20 (6.9)
Coronary artery bypass grafting, n (%)	14 (1.2)	7 (1.8)	5 (1.3)	3 (1.4)	3 (1.0)
Previous percutaneous coronary intervention, n (%)	92 (7.6)	32 (8.3)	33 (8.8)	20 (9.6)	15 (5.2)
Previous stroke, n (%)	26 (2.2)	14 (3.6)	6 (1.6)	2 (1.0)	7 (2.4)
Renal insufficiency, n (%)	14 (1.2)	5 (1.3)	6 (1.6)	2 (1.0)	4 (1.4)
Cardiogenic shock, n (%)	33 (2.7)	8 (2.1)	9 (2.4)	4 (1.9)	0 (0.0)
Clinical presentation					
Stable angina, n (%)	312 (25.9)	117 (30.2)	91 (24.3)	47 (22.6)	-
Unstable angina, n (%)	432 (35.9)	145 (37.5)	144 (38.5)	83 (39.9)	-
ST-elevation myocardial infarction, n (%)	291 (24.2)	84 (21.7)	80 (21.4)	53 (25.5)	291 (100.0)
Non-ST-elevation myocardial infarction, n (%)	168 (14.0)	41 (10.6)	59 (15.8)	25 (12.0)	-

Data presented as percentages (95% confidence interval).
SD - standard deviation

preponderance (n=884; 73.5%). Consistent with a real-world all-comer and high-risk patient population, 516 (42.9%), 402 (33.4%), 387 (32.2%), 106 (8.8%), and 596 (49.5%) patients had hypertension, hypercholesterolemia, diabetes mellitus, history of revascularization, and multi-vessel coronary artery disease, respectively. A total of 1,624 SES (1.4 \pm 0.5 stent/patient) were implanted to treat 1,430 coronary lesions (1.1 \pm 0.4 stent/lesion). Of these lesions, 1,194 (83.5%) were complex (i.e. type B2/C) and 208 (17.3%) were total occlusions. Of the 208 occlusions observed, 67 (32.2%) were chronic total occlusions. The mean length and diameter of implanted SES were 26.0 \pm 8.8 mm and 2.9 \pm 0.3 mm, respectively. Device success was achieved in 1,417 (99.1%) lesions, and procedural success was achieved in 1,194 (99.3%) patients. There was no stent fracture observed during the procedure. One case of dissection during post-dilatation and no cases of rupture during pre- and post-dilatation were recorded. At hospital discharge, 1,181 (98.2%) patients adhered to aspirin, whereas 1,165 (96.8%) patients adhered to DAPT. Clopidogrel followed by ticagrelor and prasugrel were the most common

P2Y₁₂ inhibitors adhered to by 703 (59.0%), 347 (29.1%), and 131 (11.0%) patients, respectively. The baseline characteristics for the overall study population and the high-risk subgroups are detailed in Table 1. The lesion and procedural details for the overall study population are outlined in Table 2.

Clinical outcomes

The one-year follow-up data were obtained for 1,143 (95.0%) patients. The primary endpoint of TLF at one year was 3.8% [95% confidence interval (CI) 2.9–5.1], composed of 0.6% (95% CI: 0.3–1.3) cardiac death, 1.3% (95% CI: 0.8–2.2) TV-MI, and 1.9% (95% CI: 1.3–2.9) CI-TLR. In the high-risk subgroups, TLF at one year was 6.8% (95% CI: 4.6–9.8) in the diabetes mellitus, 5.2% (95% CI: 3.4–8) in the small-vessel disease, 6.1% (95% CI: 3.9–9.6) in the STEMI, and 4.5% (95% CI: 2.4–8.3) in total occlusion subgroups. The additional safety endpoint, stent thrombosis, occurred in nine (0.8%) patients in the overall population comprising of three (0.3%), four (0.3%), and two (0.2%) patients with definite, probable, and possible stent thrombosis, respectively.

Table 2. Lesion and stent characteristics for overall study population implanted with ultrathin biodegradable polymer-coated sirolimus-eluting stents

Characteristics	Patients (n=1,203)
Disease vessel (1,203 patients)	
Single-vessel disease, n (%)	607 (50.5)
Double-vessel disease, n (%)	479 (39.8)
Triple-vessel disease, n (%)	117 (9.7)
Target coronary artery (1,430 lesions)	
Left anterior descending artery, n (%)	721 (50.4)
Right coronary artery, n (%)	431 (30.1)
Left circumflex artery, n (%)	270 (18.9)
Left main, n (%)	4 (0.3)
Saphenous vein graft, n (%)	4 (0.3)
Lesion details (1,430 lesions)	
Type A*, n (%)	74 (5.2)
Type B1*, n (%)	162 (11.3)
Type B2*, n (%)	201 (14.1)
Type C*, n (%)	993 (69.4)
Total occlusion, n (%)	208 (17.3)
Pre-dilatation, n (%)	1,074 (89.3)
Maximum balloon length, mm (mean ± SD)	16.8±3.8
Maximum balloon diameter, mm (mean ± SD)	2.7±0.60
Post-dilatation, n (%)	991 (82.4)
Device success, n (%)	1,417 (99.1)
Procedural success, n (%)	1,194 (99.3)
Stent details (1,624 stents)	
No. of stents deployed per patient, (mean ± SD)	1.4±0.5
No. of stents deployed per lesion, (mean ± SD)	1.1±0.4
Stent length, mm (mean ± SD)	26.0±8.8
Stent diameter, mm (mean ± SD)	2.9±0.3
Dual antiplatelet therapy	
At hospital discharge (1,203 patients)	
Aspirin, n (%)	1,181 (98.2)
P2Y ₁₂ inhibitors, n (%)	1,192 (99.1)
Clopidogrel, n (%)	703 (59.0)
Ticagrelor, n (%)	347 (29.1)
Prasugrel, n (%)	131 (11.0)
Aspirin + P2Y ₁₂ inhibitors, n (%)	1,165 (96.8)
At 1-year (1,143 patients)	
Aspirin, n (%)	1,039 (87.2)
P2Y ₁₂ inhibitors, n (%)	1,087 (91.2)
Clopidogrel, n (%)	641 (56.1)
Ticagrelor, n (%)	291 (25.5)
Prasugrel, n (%)	109 (9.5)
Aspirin + P2Y ₁₂ inhibitors, n (%)	1,023 (85.8)

*According to American College of Cardiology (ACC)/American Heart Association (AHA) lesion morphology criteria.
Data presented as percentages (95% confidence interval).
SD - standard deviation

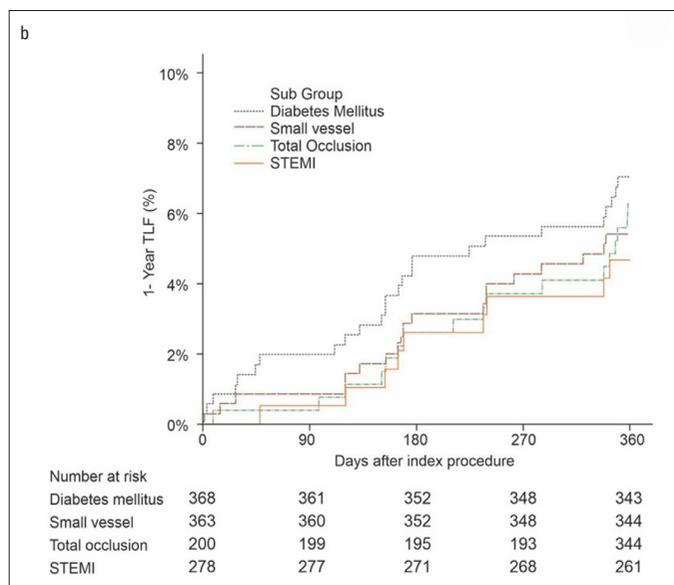
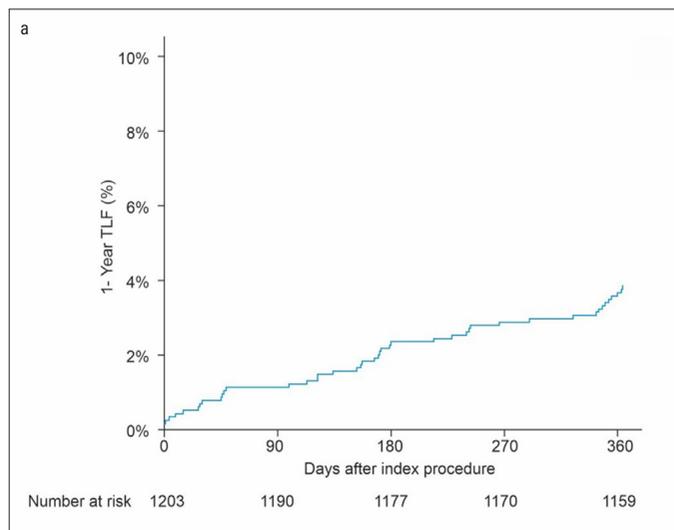


Figure 3. Kaplan-Meier event curve for cumulative target lesion failure during one-year follow-up for (a) overall patients and (b) high-risk subgroup

At one-year follow-up, 1,039 (87.2%) patients adhered to aspirin, and 1,023 (85.8%) patients adhered to DAPT. The trend of clopidogrel followed by ticagrelor and prasugrel being the most common P2Y₁₂ inhibitors remained as at hospital discharge. The clinical outcomes at one year are demonstrated in Table 3. Cumulative TLF-free survival for the overall study population and high-risk subgroups at the one-year follow-up determined by the Kaplan-Meier method are illustrated in Figures 3a and 3b, respectively.

Discussion

The T-Flex registry reported 3.8% one-year TLF for the overall study population. This outcome is acceptable when compared with 2.8–5.1% TLF rates in the BIOFLOW-III Canada Registry (26), S-FLEX UK Registry (27), BIOFLOW-III Italian Satellite Registry (28), ULISSE Registry (29), and the BIOFLOW-

Table 3. Clinical outcomes for overall study population and high-risk subgroups at one-year follow-up

	At 1-year follow-up				
	Total patients (n=1,203)	Diabetes mellitus (n=387)	Small vessel (≤ 2.5 mm) (n=374)	Total occlusion (n=208)	ST-elevation myocardial infarction (n=291)
No. of patients at follow-up, n (%)	1,143 (95.0)	368 (95.1)	363 (97.1)	200 (96.2)	278 (95.5)
No. of patients lost to follow-up, n	60	19	11	8	13
All-cause death, (%)	1.1 (0.7–1.9)	1.4 (0.6–3.1)	1.4 (0.6–3.2)	1.5 (0.5–4.3)	1.4 (0.6–3.6)
Cardiac death, (%)	0.6 (0.3–1.3)	0.5 (0.1–2.0)	0.6 (0.2–2)	1.0 (0.3–3.6)	1.1 (0.4–3.1)
Non-cardiac death, (%)	0.5 (0.2–1.1)	0.8 (0.0–2.4)	0.8 (0.3–2.4)	0.5 (0.1–2.8)	0.4 (0.1–2.0)
All myocardial infarction, (%)	2.1 (1.4–3.1)	2.4 (1.3–4.6)	5.2 (3.4–8.0)	4.0 (2.0–7.7)	4.7 (2.8–7.8)
TV-MI, (%)	1.3 (0.8–2.2)	2.4 (1.3–4.6)	2.5 (1.3–4.6)	1.5 (0.5–4.3)	2.2 (1.0–4.6)
CI-TLR, (%)	1.9 (1.3–2.9)	3.8 (2.3–6.3)	2.2 (1.1–4.3)	2.0 (0.8–5.0)	2.9 (1.5–5.6)
Overall stent thrombosis, (%)	0.8 (0.4–1.5)	1.1 (0.4–2.8)	1.9 (0.9–3.9)	0.5 (0.1–2.8)	1.1 (0.4–3.1)
TLF, (%)	3.8 (2.9–5.1)	6.8 (4.6–9.8)	5.2 (3.4–8.0)	4.5 (2.4–8.3)	6.1 (3.9–9.6)

Data presented as percentages (95% confidence interval).
CI-TLR – clinically-indicated target lesion revascularization; TLF - target lesion failure; TV-MI – target-vessel myocardial infarction

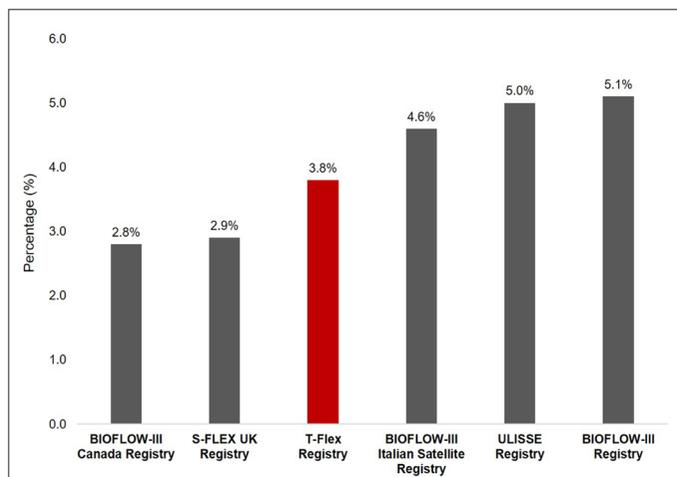


Figure 4. One-year target lesion failure rates of contemporary biodegradable polymer-coated ultrathin and very thin sirolimus-eluting stents

III Registry (16). The comparison of one-year TLF among these registries is displayed in Figure 4. All these studies were prospective multicenter registries assessing the safety and performance of very thin and ultrathin biodegradable polymer SES in all-comer populations.

Meta-analyses including earlier, first, and second-generation DES have proven limus-eluting drugs, more specifically SES, to be superior to other DES in terms of safety and clinical performance (30, 31). However, the diabetic population reveals the “Achilles’ heel” of DES. Thus, as anticipated, the primary endpoint of one-year TLF was 6.8% in the T-Flex registry diabetic subgroup. This finding is similar to those of other studies assessing safety and clinical performance in a diabetic population implanted with limus-eluting stents that reported 6.7% (32), 6.9% (28), 7.8% (33), and 7.8% (34) one-year TLF rates as shown in Figure 5a. The SUGAR trial (35) is the first randomized head-to-

head trial comparing second-generation DES in an all-comer diabetic population. The outcomes of this trial are expected to weigh in on the discussion regarding the treatment of the spectrum of diabetic patients with coronary artery disease.

Small-vessel coronary artery disease has been synonymous with restenosis, thrombosis, and other adverse events in the past. However, improved outcomes in this patient subgroup are not attributable to modifications in drug, drug release kinetics, polymers, metal alloys, or coating biocompatibility but rather to strut thickness. Thick strut cross-sections protrude further into the arterial lumen contributing more significantly to stent-induced luminal obstruction as opposed to thin strut cross-sections. The proven benefit of ultrathin new-generation DES becomes more pronounced in small coronary arteries in which thicker struts and smaller minimum in-stent lumen diameter serve as surrogates of in-stent restenosis. Clinical evidence of the aforementioned observation has been validated by the small-vessel subgroup of the BIO-RESORT trial (36), which compared ultrathin (60 μ m), very thin (74 μ m), and thin (91 μ m) strut stents. The primary endpoint of one-year TLF occurred in 4.0%, 4.3%, and 5.0% patients, respectively. The T-Flex Registry one-year TLF rate was 5.2% in the small vessel (≤ 2.5 mm) subgroup. However, the higher prevalence of small coronary artery disease among women and diabetics should be taken into account (36). The T-Flex registry small-vessel subgroup comprised 33.4% women and 37.7% diabetics, whereas the BIO-RESORT small-vessel subgroup implanted with an ultrathin SES comprised 30.1% women and 19.2% diabetics. Furthermore, in the context of other studies on ultrathin and thin DES, the one-year TLF rate of the present registry compares well with the CENTURY II trial (37) and RESOLUTE ONYX 2.0 mm Clinical Study (38), which reported 6.9% and 5.0% 1-year TLF, respectively, as illustrated in Figure 5b.

Patients with STEMI are most prone to suffer early and late adverse events post percutaneous coronary intervention.

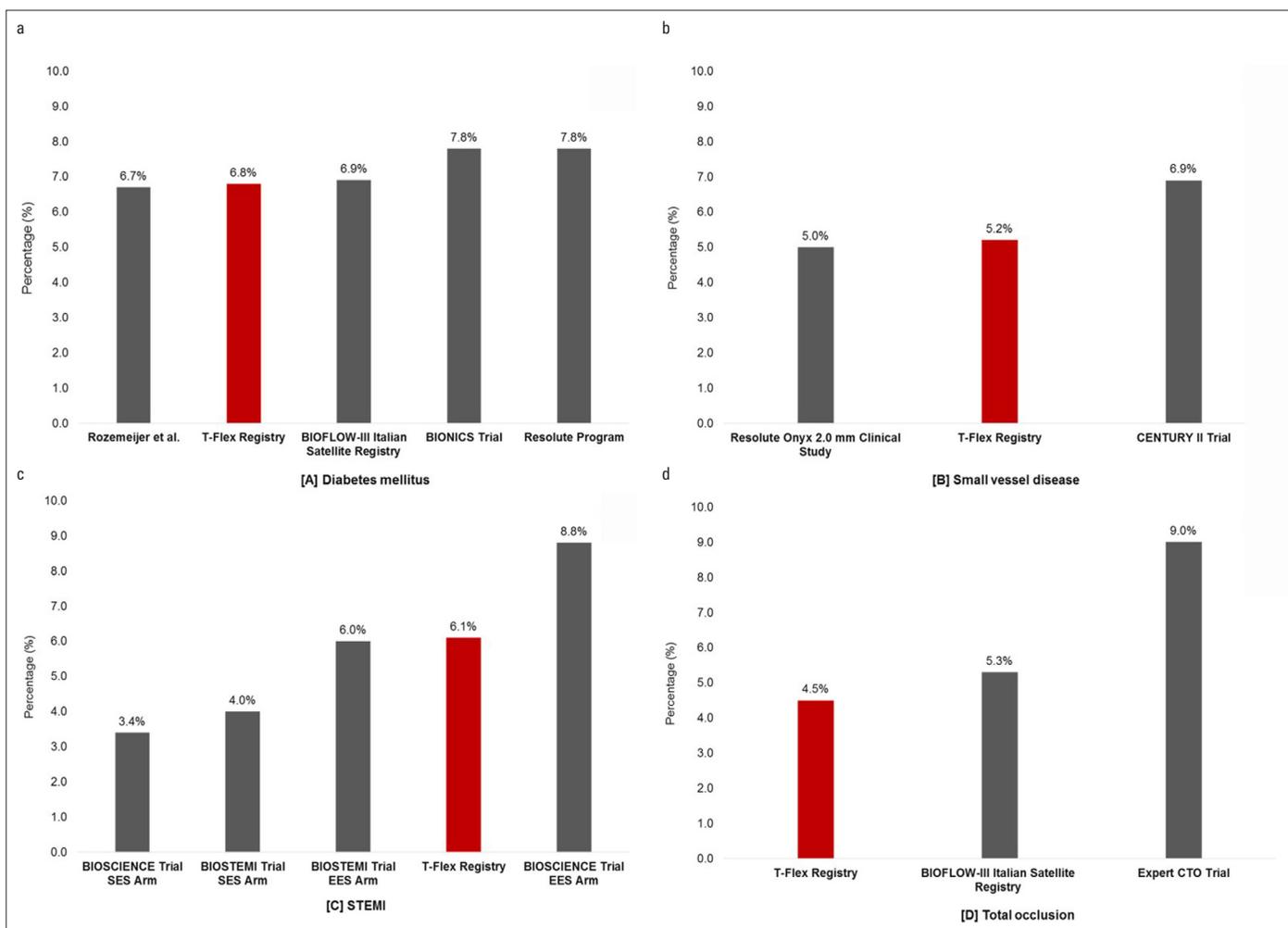


Figure 5. Comparison of one-year target lesion failure rates in high-risk subgroups in the present registry and other registries and trials for (a) diabetes mellitus; (b) small-vessel disease; (c) ST-segment elevation myocardial infarction; and (d) total occlusions

A triad of vulnerable plaque, heightened thrombotic burden and recurrent episodes of inflammation predispose these patients to delayed vascular healing with positive remodeling consequencing sequelae such as stent thrombosis and other cardiac events (39). After a decade of the plethora of head-to-head non-inferiority trials assessing stents differing in polymer, strut thickness, and drug in all-comer populations (17, 40-42), further insights specifically for patients with STEMI have been provided by the BIOSTEMI trial. This landmark trial (43) was the first head-to-head randomized controlled trial powered for superiority comparing an ultrathin biodegradable polymer SES over a thin durable polymer everolimus-eluting stent (EES) in a STEMI population. The primary endpoint of one-year TLF occurred in 4.0% in the biodegradable polymer SES arm and 6.0% in the durable polymer EES arm. Similarly, one-year TLF occurred in 3.4% in the biodegradable polymer SES arm and 8.8% in the durable polymer EES arm in the BIOSCIENCE STEMI subgroup (44) as indicated in Figure 5c. The current registry reported a one-year TLF of 6.1% in the STEMI subgroup. Although this finding is comparable to the other trials, it is higher than that of other high-risk groups and represents an arena that warrants further research.

The early era of percutaneous coronary intervention depicted a grim picture of chronic total occlusions. Labeled the most challenging lesion subset, these lesions had been plagued by lower procedural success rates, higher rates of procedural complications, and restenosis compared with non-occlusive lesions. However, advances in guidewires, devices, procedural approaches, and skilled operators have paved the way to higher procedural success rates and favorable clinical outcomes (45). Recently, the ERCTO Registry (45) and J-CTO Registry (46) reported 82.9% and 86.6% procedural success, respectively. Furthermore, the T-Flex Registry, BIOFLOW-III Italian Satellite Registry (28), and EXPERT CTO trial (47) reported 4.5%, 5.3%, and 9.1% one-year TLF rates in patients with total occlusion, respectively, as demonstrated in Figure 5d. Although these findings are encouraging, older age and more comorbidities in this patient subset should be taken into consideration (48). The T-Flex registry total occlusion subgroup reflects this observation comprising 47.1% patients with hypertension, 38.0% with hypercholesterolemia, 29.3% with diabetes, and 11.0% with previous revascularization. In addition, the vast spectrum of influential factors determining the clinical outcomes in these patients should be acknowledged.

Overall, the results with the ultrathin SES in this T-Flex registry are consistent with those observed in previous studies on biodegradable polymer-coated as well as durable polymer DES. Further follow-up is intended to assess the long-term safety and clinical performance with the ultrathin SES.

Study limitations

The major limitation of this registry was the retrospective, single-arm, and observational study design. All the patients were not followed up through clinic visits; and thus, some clinically-indicated revascularizations might have been missed. Another limitation was the lack of head-to-head comparison with other latest-generation stents, which could have provided better insights into the outcomes. Further, the results of this registry cannot be directly compared with the results from any other registry or trial. Different DES may have different drug load, biodegradable polymer composition, polymer coating, and release kinetics, which may all ultimately influence the final DES performance. Nevertheless, our results are consistent with other studies.

Conclusion

The low event rates of one-year TLF and stent thrombosis clearly depict excellent safety and clinical performance of this ultrathin biodegradable polymer-coated SES in real-world all-comer populations as well as in high-risk subgroups with coronary artery disease. Future studies with comparative analysis and long-term follow-up are warranted.

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