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DES strut thickness and clinical outcomes after CTO recanalization: Insights from LATAM CTO registry

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ABSTRACT

Background: Ultra-thin strut drug-eluting stent (UTS-DES) may improve outcomes after percutaneous coronary intervention (PCI) but have received limited study in chronic total occlusion (CTO) PCI.
Aims: To compare of 1-year incidence of major adverse cardiac events (MACE) between patients who underwent CTO PCI with ultrathin (≤ 75 μm) versus thin (>75 μm) strut DES in the LATAM CTO registry.
Methods: Patients were considered for inclusion only if successful CTO PCI was performed and when only one type of stent strut thickness (ultrathin or thin) was used. A propensity score matching (PSM) was computed to produce similar groups in relation to clinical and procedural characteristics.
Results: Between January 2015 and January 2020, 2092 patients underwent CTO PCI, of whom 1466 were included in the present analysis (475 in the ultra-thin and 991 in the thin strut DES). In unadjusted analysis the UTS-DES group had lower rate of MACE (HR: 0.63 95 % CI 0.42 to 0.94, $p = 0.04$) and repeat revascularizations (HR: 0.50 95 % CI 0.31 to 0.81, $p = 0.02$) at 1-year follow-up. After adjustment for confounding factors in a Cox regression model there was no difference in 1-year incidence of MACE between groups (HR: 1.15 95 % CI 0.41 to 2.97, $p = 0.85$). On PSM of 686 patients (343 in each group) the 1-year incidence of MACE (HR 0.68 95 % CI 0.37–1.23; $P = 0.22$) and individual components of MACE did not differ between groups.
Conclusions: One-year clinical outcomes after CTO PCI were similar with ultrathin and thin strut DES.

1. Introduction

Chronic total occlusion (CTO) percutaneous coronary intervention (PCI) is often performed in long lesions in calcified, diffusely diseased, and negatively remodeled vessels and often requires implantation of multiple overlapping stents. Despite use of drug eluting stent (DES),

Abbreviations: CTO, Chronic total occlusion; MI, Myocardial infarction; PCI, Percutaneous coronary interventions; LATAM, Latin American; MACE, Major adverse cardiovascular events; TVF, Target vessel failure; TVR, Target vessel revascularization.

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the incidence of major adverse cardiac events (MACE) after CTO PCI remains high [1–3] and may be improved by intravascular imaging.

Compared with first generation metal stents, newer generation DES have thinner structures and more biocompatible polymers, which reduce inflammation and vascular injury, promote faster reendothelialization and reduce neointimal proliferation and thrombogenicity [4–8]. Bench tests have been shown the increment in foreign material, flow stagnation and reattachment are proportional to the increase in strut thickness. [8] Thus, Ultrathin Strut DES (UTS-DES) have potential to improve clinical outcomes, especially regarding reduction of acute myocardial infarction [9] and target lesion failure (TLF) at 1 year and in the long term after PCI [10–12]. However, the clinical impact of stent struts thickness has received limited study in the setting of CTO PCI. We used a multicenter CTO PCI registry to compare the clinical outcomes after CTO PCI with ultrathin strut versus thin struts DES.

2. Methods

2.1. Study population

The present work assessed clinical outcomes from the Latin American (LATAM) CTO registry which has been described elsewhere [13]. The LATAM CTO registry is an ongoing international observational study from 57 centers from Latin America (Brazil, Argentina, Ecuador, Mexico, Chile, Puerto Rico, Costa Rica, and Colombia). There is no specific requirement regarding CTO PCI volume and operators experience for entering data into the registry. But regarding centers volume, hospitals with <50 cases per year were 87 % of the participating Centers, as follows: 65 % in Brazil, 10 % in Mexico, 10 % in Argentina, 5 % in Chile and Ecuador and 2.5 % in Colombia and Costa Rica. The CTO volume of center between 50 and 500 cases/year: 13 % of the Centers, being: 6.5 % Brazilian Centers and the other 6.5 % distributed among Buenos Aires, Mexico, and Puerto Rico.

2.2. Data collection

CTO PCI data was included in an online platform coordinated by the group of investigators, in partnership with the Brazilian Society of Interventional Cardiology and managed by the Instituto de Cardiologia do Rio Grande do Sul, Brazil. Access to the database was available via research electronic data capture (REDCap), a secure and free-access web application developed by the Vanderbilt University that meets international standards and requirements from the Brazilian National Agency for Sanitary Surveillance. All investigators received standardized instructions for data entry in REDCap, and clinical, procedural, angiographic information, and postprocedural clinical outcomes were collected in the same platform. The centers received online support for questions regarding inclusion or completion of cases, and monthly feedback for missing data and discrepant values. The clinical follow-up was done uniformly among centers at 1-, 6- and 12- and 24-months. The information could be obtained from the patient's medical record (outpatient or emergency room care) or from a phone call. When there was any doubt, the presence of the patient or a companion could be requested to bring a record referring to any medical event that may have occurred during that period.

2.3. Definitions

We compared clinical outcomes of patients according to the type of DES implanted (thin- or ultrathin strut) during successful CTO recanalization. CTO was defined was as a 100 % occlusion of a major coronary artery present for at least 3 months based on clinical or angiographic features, such as previous imaging. Demographic, clinical, angiographic, procedural and postprocedural outcomes used standard definitions from the LATAM CTO registry [13].

Technical success of the CTO PCI was defined as <30 % residual stenosis and TIMI flow 3 without significant side branch occlusions.

DES were categorized as ultrathin (strut thickness ≤ 75 μm) and thin (strut thickness > 75 μm). We excluded patients who received bare-metal stents, bioresorbable scaffolds or those with mixed stent (thin- and ultra-thin struts) implantation. Fig. 1 depicts patient selection for the present analysis. The UTS-DES group included Orsiro™ (Biotronik, Bulach, Switzerland), Supra Flex Star™ (Sahajanand Medical Technologies Pvt. Ltd., Gujarat, India), Metafor™ (Meril Life Sciences Pvt. Ltd., Vapi), Biomime™ (Meril Life Sciences Pvt. Ltd., Gujarat, India), Sinergy™ (Boston Scientific, Natick, Massachusetts, USA) and Inspiron™ (Scitech Medical, Goiás, Brazil). The thin-struts DES (TS-DES) group included Ultimaster™ (Terumo, Tokyo, Japan), Xience™ (Abbott. Vascular, California, USA), Promus™ (Boston Scientific, Natick, Massachusetts, USA), Resolute Onyx™ (Medtronic Inc., Santa Rosa, California, USA), DESyne™ (Elixir Medical Corporation, Sunnyvale, USA), Firehawk™ (Shanghai Micro Port Medical Group, Shanghai, China), Endeavor™ (Medtronic, Santa Rosa, California, USA), Resolute Integrity™ (Boston Scientific, Natick, Massachusetts, USA), Biomatrix™ (Biosensors International, Morges, Switzerland) and Nobori (Terumo, Tokyo, Japan). The total number of patients and type of stents implanted are described in the supplemental material (Online Table 1).

MACE was defined as the composite of all cause death, myocardial infarction (MI) and repeated revascularizations. MI was defined using the universal definition of MI (type 4a MI). [14] Target vessel failure (TVF) was defined as a combined primary endpoint, consisting of reocclusion, restenosis, and target vessel revascularization (TVR). TVR was defined as any repeat PCI in the target vessel. All revascularizations were defined as any type of revascularization, including both percutaneous and surgical procedures, and irrespective of the revascularized vessel. And all cause of death referred to the measure of death from all causes, regardless of the specific disease or condition that led to death.

2.4. Data analysis

Continuous variables were summarized using mean ± standard deviation (SD) and median (interquartile range) and compared using the *t*-test or Mann–Whitney test, as appropriate. Categorical variables were summarized using absolute and relative frequencies and were compared with the chi-square test. A two-tailed $p < 0.05$ was considered statistically significant for all tests. Since, in clinical practice, patients undergoing stent implantation with different types of thickness struts tend to be different, a propensity score matching (PSM) was used to adjust for confounding variables. For the creation of the PSM, the dependent variable was the thickness of the struts of the DES and all variables of interest were candidates for inclusion in the model. The pairing was performed without substitution, in a 1: 1 ratio and with a target caliper of 0.01. The standardized mean difference between the groups before and after pairing was compared to verify the quality of the fit. The variables used in the final pairing model were age, sex, previous peripheral vascular disease, previous PCI, previous heart failure, previous chronic kidney disease, hypercholesterolemia, and the use of intracoronary imaging. A standardized mean difference of up to 0.01 was considered satisfactory. Characteristics and outcomes of procedures that used ultrathin struts were compared to those that used thin struts. The incidence of clinical outcomes at 1-year follow-up was calculated using the Kaplan-Meier method and compared using the log-rank test. Comparison of events rates between groups were adjusted for confounding factors in a Cox regression model. The variables we used for the adjusted comparison were: hypertension, previous heart failure, previous chronic kidney disease, presence of ischemia >10 % as an indication for recanalization, family history of coronary artery disease, procedure duration, volume of contrast used, vascular access, PCI in non CTO vessel, ostial lesion, extension of chronic occlusion, location of recanalization in the territory of the anterior descending artery, location of recanalization in the territory of the right coronary, strategy used retrograde wire escalation and

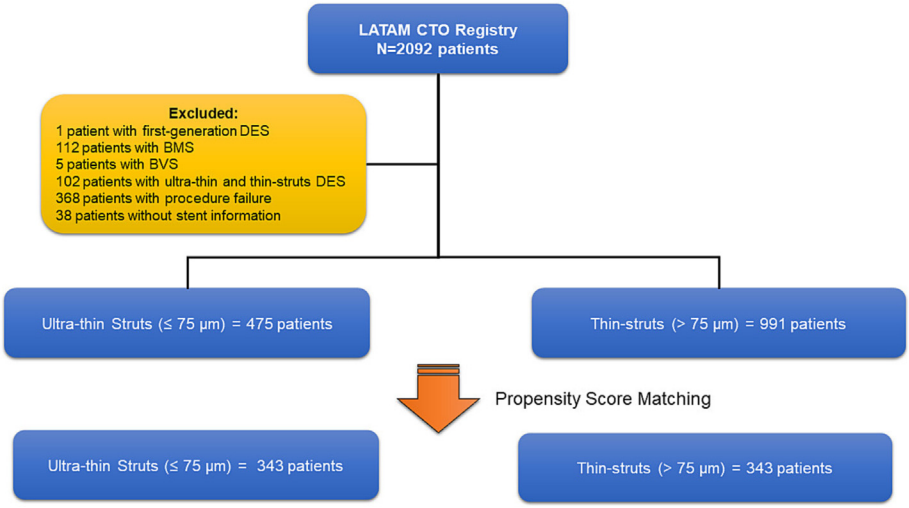

Fig. 1. Study flowchart demonstrating patients included in the present analysis. DES = drug eluting stent; BMS = bare metal stent; BVS = bioresorbable scaffold.

intravascular image use. The subgroup analysis for MACE during the first 1-year after recanalization of CTO was performed using an exponential model. A p interaction <0.05 was considered statistically significant for the Cox regression. The data was analyzed by SPSS version 26 (IBM Research, Armonk, New York) and Medcalc version 20 for Windows (Medcalc Software bv, Ostend, Belgium). In accordance with Brazilian legislation, research data cannot share.

3. Results

3.1. Population

Between January 2015 to January 2020, 2092 CTO PCIs were included in the LATAM CTO registry. After exclusion of patients who did not meet the inclusion criteria, 1466 patients were included in the present analysis (Fig. 1). Table 1 depicts baseline demographics and clinical characteristics of ultra-thin and thin struts group from the LATAM CTO Registry. Overall, the mean age was 64.1 (63.8 to 64.4) years, 78.5 % were male, 37.9 % were diabetics and 12.4 % had heart failure. Hypercholesterolemia (81.1 % vs 71.7 %, $p < 0.001$), heart failure (18.7 % vs 9.5 %, $p < 0.001$), chronic kidney disease (11.4 % vs 5.7 %, $p < 0.001$) and use of nitrates (37.3 % vs 26.3 %, $p < 0.001$) and new oral anticoagulants (2.5 % vs 1.0 %, $p = 0.037$) before CTO PCI was more common among patients who received ultrathin struts DES. The principal revascularization indication in both groups was angina control (82.9 % vs 82.3 %, $p = 0.826$). The revascularization indication by large ischemic area in non-invasive ischemic test (38.5 % vs 31.3 %, $p = 0.007$) and by heart failure (12.4 % vs 8.6 %, $p = 0.024$) was higher in UTS-DES group.

Table 2 shows the angiographic and procedural characteristics between ultrathin and thin struts group. The median CTO duration was higher in the TS-DES group (8.0 vs 6.0 months $p = 0.014$). The right coronary artery (RCA) was the most common CTO target vessel (40.9 %). Previous attempt to recanalize CTO has been performed in 12.8 %, moderate/severe calcification was present in 42.8 % of CTOs, ostial location in 18.9 %, CTO at bifurcation in 32.9 %, in-stent CTO in 12.5 % and use of the retrograde approach in 12.0 %. The median J-CTO score was 2.0 (1.0–3.0) and the median PROGRESS CTO score was 1.0 (0–1.0). The most common successful strategy for CTO crossing was anterograde wire escalation (79.8 %). Retrograde wire escalation was more often performed in the UTS-DES group (6.6 % vs 3.8 %, $p = 0.023$). The duration of the

Table 1
Baseline Demographics and Clinical Characteristics Between Ultrathin and Thin Struts Group from the LATAM CTO Registry.

	Overall (1466 patients)	Ultra-thin Struts (475 patients)	Thin Struts (991 patients)	*p* value
Age, years ± SD	64.1 ± 0.3	64.7 ± 0.5	63.8 ± 0.3	0.182
Male Gender, n (%)	1151 (78.5 %)	368 (77.5 %)	783 (79.0 %)	0.498
Body mass index, Kg/m^2 ± SD	28.6 ± 0.3	28.7 ± 0.5	28.6 ± 0.4	0.557
Current smoker, n (%)	275 (19.0 %)	97 (21.0 %)	178 (18.1 %)	0.196
Hypercholesterolemia, n (%)	1082 (74.7 %)	378 (81.1 %)	704 (71.7 %)	<0.001
Hypertension, n (%)	1263 (87.0 %)	416 (89.3 %)	847 (85.9 %)	0.080
Heart Failure, n (%)	170 (12.4 %)	80 (18.7 %)	90 (9.5 %)	<0.001
Diabetes mellitus, n (%)	550 (37.9 %)	186 (39.9 %)	364 (37.0 %)	0.297
CKD, n (%)	103 (7.5 %)	49 (11.4 %)	54 (5.7 %)	<0.001
Peripheral vascular disease, n (%)	154 (11.2 %)	43 (10.0 %)	111 (11.7 %)	0.406
History of cerebrovascular accident, n (%)	46 (3.3 %)	16 (3.7 %)	30 (3.2 %)	0.628
Previous myocardial infarction, n (%)	593 (43.1 %)	186 (43.5 %)	407 (43.0 %)	0.906
Previous PCI, n (%)	659 (47.7 %)	203 (47.0 %)	456 (48.1 %)	0.728
Previous CABG, n (%)	187 (13.6 %)	63 (14.6 %)	124 (13.1 %)	0.446
Revascularization Indication:				
Angina control, n (%)	1210 (82.5 %)	394 (82.9 %)	816 (82.3 %)	0.826
Large ischemic area, n (%)	493 (33.6 %)	183 (38.5 %)	310 (31.3 %)	0.007
Heart Failure, n (%)	144 (9.8 %)	59 (12.4 %)	85 (8.6 %)	0.024
Ventricular Arrhythmia, n (%	16 (1.1 %)	7 (1.5 %	9 (0.9 %)	0.420
Family History of CAD, n (%)	381 (27.0 %)	106 (23.7 %)	275 (28.5 %)	0.062

CKD: Chronic Kidney Disease; PCI: Percutaneous Coronary Intervention; CABG: Coronary Artery Bypass Grafting; ACE: Angiotensin converting enzyme; CAD: Coronary Artery Disease.

Table 2
Baseline Angiographic and Procedural Characteristics Between Ultra-thin and Thin Struts Group from the LATAM CTO Registry.

	Overall (1466 patients)	Ultra-thin Struts (475 patients)	Thin Struts (991 patients)	p value
CTO duration, months – median (Q1 – Q3)	8 (4–15)	6 (3—12)	8 (4–18)	0.014
Duration of the Procedure, min – median (Q1 – Q3)	82.0 (55.0–130.0)	108.0 (60.0–170.0)	73.0 (50.0–120.0)	<0.001
Fluoroscopy Time, min – median (Q1 – Q3)	31.0 (21.0–51.0)	37.2 (23.0–66.0)	30 (19.0–46.0)	<0.001
Contrast Volume, ml – median (Q1 – Q3)	223 (160–300)	250 (200–350)	200 (150–290)	<0.001
CTO Previous Attempt, n (%)	185 (12.8 %)	63 (13.5 %)	122 (12.5 %)	0.614
Access				
Radial, n (%)	809 (55.8 %)	252 (53.6 %)	557 (56.8 %)	0.259
Femoral, n (%)	1017 (69.8 %)	331 (70.0 %)	686 (69.6 %)	0.951
Other, n (%)	31 (2.2 %)	21 (4.6 %)	10 (1.0 %)	<0.001
Dual Injection, n (%)	790 (54.3 %)	273 (58.2 %)	517 (52.5 %)	0.043
Number of vessels with lesions > 70 %, median (Q1 – Q3)	2 (1–2)	2 (1–3)	2 (1–2)	0.346
Attempted non-CTO vessel PCI, n (%)	342 (23.5 %)	97 (20.6 %)	245 (24.9 %)	0.065
CTO territory location				
Left Main Coronary Artery, n (%)	9 (0.6 %)	3 (0.6 %)	6 (0.6 %)	1.000
LAD Coronary Artery, n (%)	520 (35.5 %)	151 (31.8 %)	369 (37.2 %)	0.041
Left Circumflex Coronary Artery, n (%)	277 (18.9 %)	86 (18.1 %)	191 (19.3 %)	0.618
Right Coronary Artery, n (%)	600 (40.9 %)	219 (46.1 %)	381 (38.4 %)	0.005
Other or Unknown, n (%)	18 (1.2 %)	4 (0.8 %)	14 (1.4 %)	0.453
Ostial CTO	269 (18.9 %)	98 (21.4 %)	171 (17.6 %)	0.096
CTO Length, mm – median (Q1 – Q3)	20.0 (15.0–30.0)	24.0 (15.3–30.0)	20.0 (15.0–30.0)	0.006
J-CTO score ≥ 3, n (%)	427 (31,6 %)	278 (30,4 %)	149 (34,2 %)	0.165
Bifurcation, n (%)	439 (32.9 %)	144 (33.0 %)	295 (32.9 %)	1.000
Calcification moderate/severe (%)	612 (42.8 %)	204 (44.5 %)	408 (41.9 %)	0.360
In-stent CTO, n (%)	178 (12.5 %)	54 (11.8 %)	124 (12.8 %)	0.607
Successful strategy				
AWE	1161 (79.8 %)	368 (78.1 %)	793 (80.7 %)	0.264
ADR	144 (9.9 %)	45 (9.6 %)	99 (10.1 %)	0.779
RWE	68 (4.7 %)	31 (6.6 %)	37 (3.8 %)	0.023
RDR	81 (5.6 %)	27 (5.7 %)	54 (5.5 %)	0.903
Use of the Retrograde Approach, n (%)	173 (12.0 %)	65 (14.0 %)	108 (11.0 %)	0.118
Time for the guidewire to cross the CTO, min – median (Q1 – Q3)	20.0 (10.0–41.0)	23.0 (12.0–60.0)	20.0 (9.5–39.0)	<0.001
Total Stent Length, mm – median (Q1 – Q3)	52.0 (33.0–75.5)	56.0 (37.0–80.0)	49.0 (32.0–71.0)	<0.001
Maximum Stent Diameter, mm – median (Q1 – Q3)	3.0 (2.75–3.5)	3.0 (2.75–3.5)	3.0 (2.75–3.5)	0.001
Use of Stent diameter ≤ 2.5 mm (%)	334 (23.0 %)	97 (20.6 %)	237 (24.1 %)	0.143
Use of Guide Extension Catheters, n (%)	204 (16.4 %)	86 (21.7 %)	118 (14.0 %)	0.001
Intracoronary Imaging, n (%)	277 (22.4 %)	144 (36.2 %)	133 (15.8 %)	<0.001

CTO: Chronic Total Occlusion; PCI: Percutaneous Coronary Intervention; AWE: Anterograde Wire Escalation; ADR: Anterograde Dissection and *Re*-entry; RWE: Retrograde Wire Escalation; RDR: Retrograde Dissection and Re-entry;

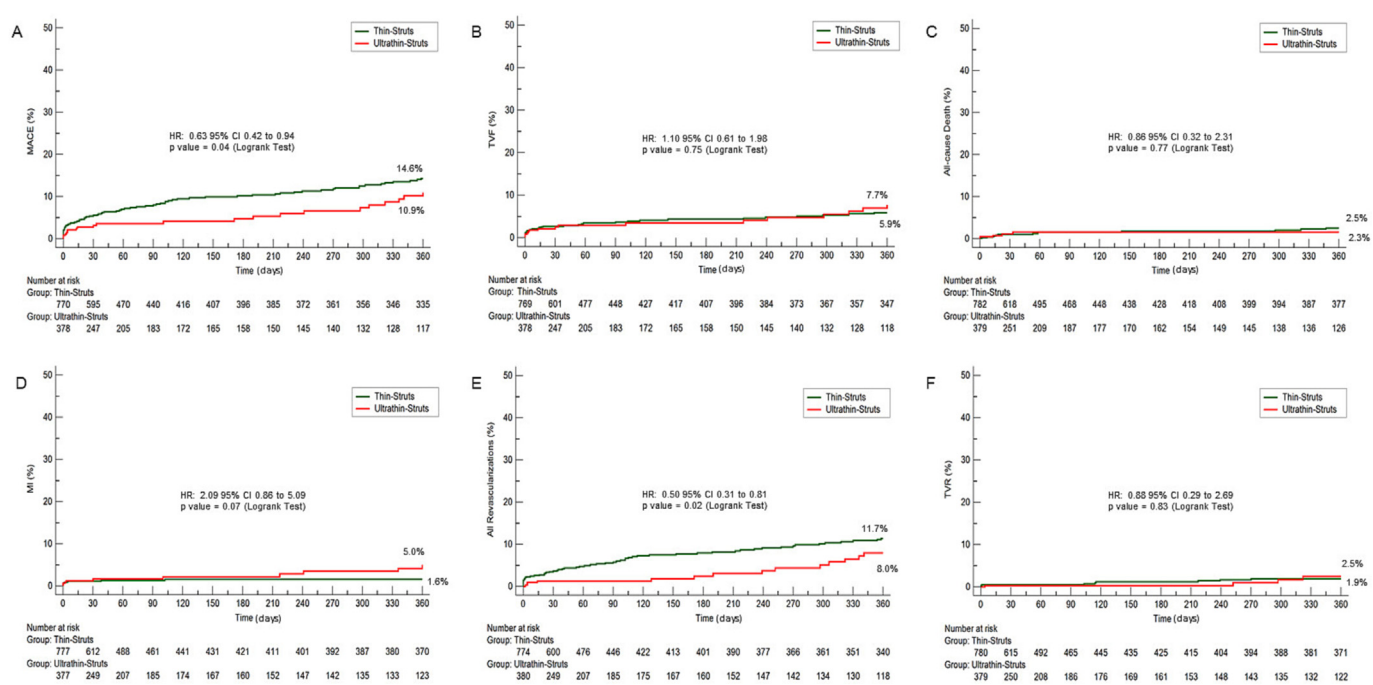

Fig. 2. Kaplan-Meier curves representing the incidence of major adverse cardiac events (MACE) (A), target vessel failure (TVF) (B), all-cause death (C), myocardial infarction (MI) (D), all-revascularization (E) and target vessel revascularization (TVR) (F) from the LATAM CTO Registry. Cumulative event rates up to 1-year for the different subgroups: ultra-thin struts and thin struts.

procedure, use of fluoroscopy, contrast volume, CTO crossing time and device utilization (over the wire balloon, microcatheter, guide extension catheters, cutting balloons, rotational atherectomy and intracoronary imaging) were higher in the UTS-DES group.

In unadjusted analysis patients in ultrathin group had lower incidence of MACE (HR: 0.63 95 % CI 0.42 to 0.94, $p = 0.04$) and any revascularization (HR: 0.50 95 % CI 0.31 to 0.81, p = 0.02) at one-year follow-up (Fig. 2). After adjusted for confounding factors in a Cox regression model there was no difference for 1-year MACE (Fig. 3) between groups (HR: 1.15 95 % CI 0.41 to 2.97, $p = 0.85$).

3.2. Propensity score matching comparison

Propensity score matching generated 343 pairs of patients with ultrathin and thin struts DES. The baseline demographics and clinical characteristics (Table 3) as well as the angiographic characteristics and procedural metrics (Table 4) were similar in the ultrathin and thin strut groups, except for the use other access, dual injection, moderate/severe calcification, and procedural strategy.

After propensity score matching, the 1-year incidence of MACE (HR: 0.68 95 % CI 0.37 to 1.23, $p = 0.22$); TVF (HR 1.12 95 % CI 0.48 to 2.58, $p = 0.79$); all-cause death (HR 0.80 95 % CI 0.18 to 3.54, $p = 0.77$); MI (HR 3.37 95 % CI 1.00 to 10.46, $p = 0.05$); any revascularization (HR: 0.58 95 % CI 0.29 to 1.16, $p = 0.14$) and TVR (HR: 0.48 95 % CI 0.11 to 2.11, $p = 0.37$) were similar between groups (Fig. 4). Moreover, in subgroup analysis there was no significant interaction according to stent strut thickness (Fig. 5) for MACE after 1-year follow-up.

4. Discussion

The main finding of the present study is that patients undergoing successful CTO PCI with UTS-DES had lower unadjusted incidence of MACE and revascularization when compared with those receiving TS-DES at 1-year follow-up, but there was no significant difference after adjustment for confounding factors in a Cox regression model and after a propensity score matching.

To the best of our knowledge the present study was the largest comparison of the impact of stent thickness on clinical outcomes after CTO PCI. Second-generation DES significantly improved PCI outcomes compared with first-generation DES by reducing the risk of restenosis, stent thrombosis and acute myocardial infarction [4–7]. Improvements in the second-generation DES included thinner struts, more biocompatible polymers and advancements in the metallic alloys and platforms, promoting less inflammation, vascular injury and a faster reendothelialization. All of these have associated with a reduction in neointimal proliferation and thrombogenicity [8]. However, clinical outcomes with second-generation DES, while notable, have remained stable over the past decade [6,15]. Recently, UTS-DES were introduced with the aim to further reduce vascular injury and accelerate reendothelialization even more [9]. Large randomized clinical trials (RCTs) demonstrate similar results of newer generation ultra-thin compared to thin struts DES [16–18]. In the BIORESORT trial, very thin struts DES with dissimilar biodegradable polymer coatings (eluting either everolimus or sirolimus) were non-inferior to the durable polymer stent (eluting zotarolimus) in treating allcomers with a high proportion of patients with acute coronary syndromes at 12-month follow-up [16]. In SORT OUT VII trial, the thin-strut sirolimus-eluting Orsiro™ stent was noninferior to the biolimus-eluting Nobori™ stent in unselected patients for target lesion failure at 1 year [17]. In the BIOSCIENCE trial, a patient population with minimum exclusion criteria and high adherence to dual antiplatelet therapy, biodegradable sirolimus-eluting stents were non-inferior to durable polymer everolimus-eluting stents for the combined safety and efficacy outcome target lesion failure at 12 months [18]. More recently, Azzaini et al. observed comparable rates of MACE and definite/probable ST in patients undergoing PCI with cobalt-chromium (CoCr) - durable-polimer (DP) -everolimus (EES) (Xience™), platinum-chromium (PtCr)-DP-EES (Promus™), or PtCr - bioresorbable-polymer (BP)-EES (Synergy™) in the same period of follow-up. Results were not altered among patients undergoing complex PCI ($n = 2894/5446$–53.1 %). [19] And in BIODEGRADE trial, in patients with a high prevalence of acute coronary syndrome, Orsiro™ stents were not inferior to target lesion failure to BioMatrix™ stent. Both showed good clinical outcomes. [20]

A meta-analysis of 10 RCTs with a total of 11,658 patients showed that ultra-thin struts DES had 16 % less target vessel failure (TVF) than second-generation DES group at 1-year follow up [9]. This was mainly due to less acute myocardial infarction. The subgroup analysis demonstrated consistency in the results among the three ultra-thin struts DES evaluated (Orsiro™ – 60 μm, MiStent™ – 64 μm and Biomime™ –

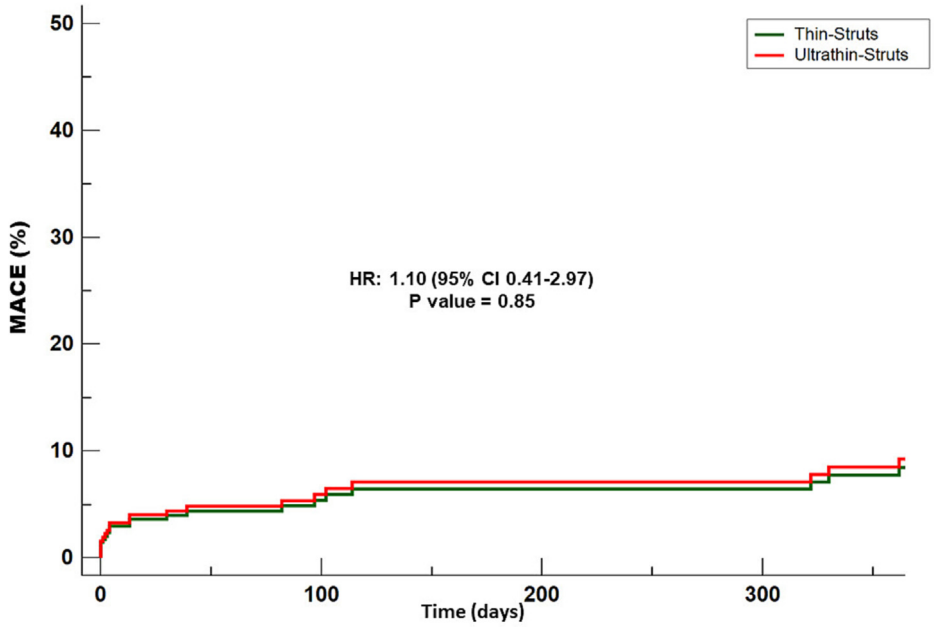

Fig. 3. Cumulative event of major adverse cardiac events (MACE) rates up to 1-year for the different subgroups (ultra-thin struts and thin struts) after adjustment for confounding factors in a Cox regression model.

Table 3
Baseline Demographics and Clinical Characteristics Between Ultra-thin and Thin Struts Group from the LATAM CTO Registry After Propensity Score Matching.

	Overall (686 patients)	Ultra-thin Struts (343 patients)	Thin Struts (343 patients)	p value
Age, years ± SD	64.8 ± 0.4	64.7 ± 0.6	64.9 ± 0.6	0.639
Male Gender, n (%)	533 (77.7 %)	261 (76.1 %)	272 (79.3 %)	0.359
Body mass index, Kg/m^2 ± SD	28.4 ± 0.4	28.8 ± 0.7	28.2 ± 0.3	0.880
Current smoker, n (%)	126 (18.4 %)	70 (20.5 %)	56 (16.4 %)	0.168
Hypercholesterolemia, n (%)	558 (81.3 %)	280 (81.6 %)	278 (81.0 %)	0.922
Hypertension, n (%)	593 (86.4 %)	304 (88.6 %)	289 (84.3 %)	0.118
Heart Failure, n (%)	107 (15.6 %)	57 (16.6 %)	50 (14.6 %)	0.528
Diabetes mellitus, n (%)	263 (38.3 %)	127 (37.0 %)	136 (39.7 %)	0.530
CKD, n (%)	62 (9.0 %)	33 (9.6 %)	29 (8.5 %)	0.690
Peripheral arterial disease, n (%)	79 (11.5 %)	37 (10.8 %)	42 (12.2 %)	0.633
History of cerebrovascular accident, n (%)	24 (3.5 %)	9 (2.6 %)	15 (4.4 %)	0.299
Previous myocardial infarction, n (%)	288 (42.1 %)	147 (43.1 %)	141 (41.1 %)	0.642
Previous PCI, n (%)	316 (46.1 %)	157 (45.8 %)	159 (46.4 %)	0.939
Previous CABG, n (%)	113 (16.5 %)	53 (15.5 %)	60 (17.5 %)	0.537
Revascularization indication:				
Angina control, n (%)	547 (79.7 %)	287 (83.7 %)	260 (75.8 %)	0.013
Large ischemic area, n (%)	289 (42.1 %)	136 (39.7 %)	153 (44.6 %)	0.216
Heart Failure, n (%)	79 (11.5 %)	33 (9.6 %)	46 (13.4 %)	0.151
Ventricular Arrhythmia, n (%)	8 (1.2 %)	4 (1.2 %)	4 (1.2 %)	1.000
Family History of CAD, n (%)	178 (26.7 %)	81 (24.6 %)	97 (28.8 %)	0.255

CKD: Chronic Kidney Disease; PCI: Percutaneous Coronary Intervention; CABG: Coronary Artery Bypass Grafting; ACE: Angiotensin converting enzyme; CAD: Coronary Artery Disease.

65 μm) with the different comparators of second-generation DES. Recently, another meta-analysis with all RCTs comparing ultrathin-strut DES to conventional 2nd-generation TS-DES with 20,701 patients and at a mean 2.5-year follow-up was published. UTS- DES were associated with a 15 % reduction in long-term TLF compared with conventional 2nd-generation thin-strut DES [relative risk (RR) 0.85, 95 % confidence interval (CI) 0.76–0.96; $P = 0.008$] driven by a 25 % reduction in clinically driven target lesion revascularization (RR 0.75, 95 % CI 0.62–0.92; $P = 0.005$). There were no significant differences between stent types in the risks of MI, ST, cardiac death, or all-cause mortality. [10] This

Table 4
Baseline Angiographic and Procedural Characteristics Between Ultra-thin and Thin Struts Group from the LATAM CTO Registry After Score Propensity Matching.

	Overall (686 patients)	Ultra-thin Struts (343 patients)	Thin Struts (343 patients)	p value
CTO duration, months – median (Q1 – Q3)	6 (3–12)	8 (3–12)	8 (3–18)	0.071
Duration of the Procedure, min – median (Q1 – Q3)	116.5 (67.0–159.8)	120.0 (61.0–180.0)	110.0 (69.0–150.0)	0.240
Fluoroscopy Time, min – median (Q1 – Q3)	40.0 (24.0–67.3)	38.5 (23.0–68.0)	40.1 (25.0–66.0)	0.441
Contrast Volume, ml – median (Q1 – Q3)	250 (190–330)	250 (200–350)	250 (180–318)	0.107
CTO Previous Attempt, n (%)	102 (15.0 %)	50 (14.7 %)	52 (15.2 %)	0.915
Access				
Radial, n (%)	380 (55.9 %)	189 (55.9 %)	191 (56.0 %)	1.000
Femoral, n (%)	459 (67.1 %)	240 (70.4 %)	219 (63.8 %)	0.074
Other, n (%)	26 (3.9 %)	18 (5.4 %)	8 (2.4 %)	0.046
Dual Injection, n (%)	391 (57.2 %)	208 (61.2 %)	183 (53.4 %)	0.044
Number of vessels with lesions > 70 %, median (Q1 – Q3)	2 (1–3)	2 (1–2)	2 (1–3)	0.459
Attempted non-CTO vessel PCI, n (%)	159 (22.2 %)	77 (21.5 %)	82 (22.8 %)	0.719
CTO territory location				
Left Main Coronary Artery, n (%)	7 (1.0 %)	2 (0.6 %)	5 (1.5 %)	0.451
LAD Coronary Artery, n (%)	230 (33.5 %)	106 (30.9 %)	124 (36.2 %)	0.169
Left Circumflex Coronary Artery, n (%)	132 (19.2 %)	67 (19.5 %)	65 (19.0 %)	0.923
Right Coronary Artery, n (%)	290 (42.3 %)	157 (45.8 %)	133 (38.8 %)	0.075
Other or Unknown, n (%)	7 (1.0 %)	3 (0.9 %)	4 (1.2 %)	1.000
Ostial CTO	151 (22.5 %)	70 (21.1 %)	81 (23.8 %)	0.460
CTO Length, mm – median (Q1 – Q3)	22.0 (15.0–30.0)	22.0 (15.0–30.0)	21.0 (16.0–30.0)	0.688
J-CTO score ≥ 3, n (%)	247 (38,8 %)	112 (35,4 %)	135 (42,1 %)	0.087
Bifurcation, n (%)	230 (35.2 %)	103 (31.7 %)	127 (38.7 %)	0.071
Calcification moderate/severe (%)	345 (51.1 %)	153 (45.9 %)	192 (56.1 %)	0.009
In-stent CTO, n (%)	77 (11.5 %)	40 (12.1 %)	37 (10.9 %)	0.717
Successful strategy				
AWE	480 (70.4 %)	255 (74.8 %)	225 (66.0 %)	0.015
ADR	99 (14.5 %)	40 (11.7 %)	59 (17.3 %)	0.050
RWE	45 (6.6 %)	22 (6.5 %)	23 (6.7 %)	1.000
RDR	58 (8.5 %)	24 (7.0 %)	34 (10.0 %)	0.216
Use of the Retrograde Approach, n (%)	114 (16.8 %)	50 (14.8 %)	64 (18.07)	0.183
Time for the guidewire to cross the CTO, min – median (Q1 – Q3)	25.0 (13.0–60.0)	24.5 (13.0–60.0)	29.0 (13.3–54.8)	0.865
Total Stent Length, mm – median (Q1 – Q3)	56.0 (38.0–81.0)	56.5 (38.0–83.0)	56.0 (38.0–80.0)	0.702
Maximum Stent Diameter, mm – median (Q1 – Q3)	3.0 (2.75–3.5)	3.0 (2.75–3.5)	3.0 (2.75–3.5)	0.812
Use of Stent diameter ≤ 2.5 mm (%)	129 (18.9 %)	63 (18.5 %)	66 (19.4 %)	0.845
Use of Guide Extension Catheters, n (%)	178 (26.2 %)	72 (21.2 %)	106 (31.1 %)	0.004
Intracoronary Imaging, n (%)	235 (34.3 %)	114 (33.2 %)	121 (35.3 %)	0.628

CTO: Chronic Total Occlusion; PCI: Percutaneous Coronary Intervention; AWE: Anterograde Wire Escalation; ADR: Anterograde Dissection and *Re*-entry; RWE: Retrograde Wire Escalation; RDR: Retrograde Dissection and Re-entry;

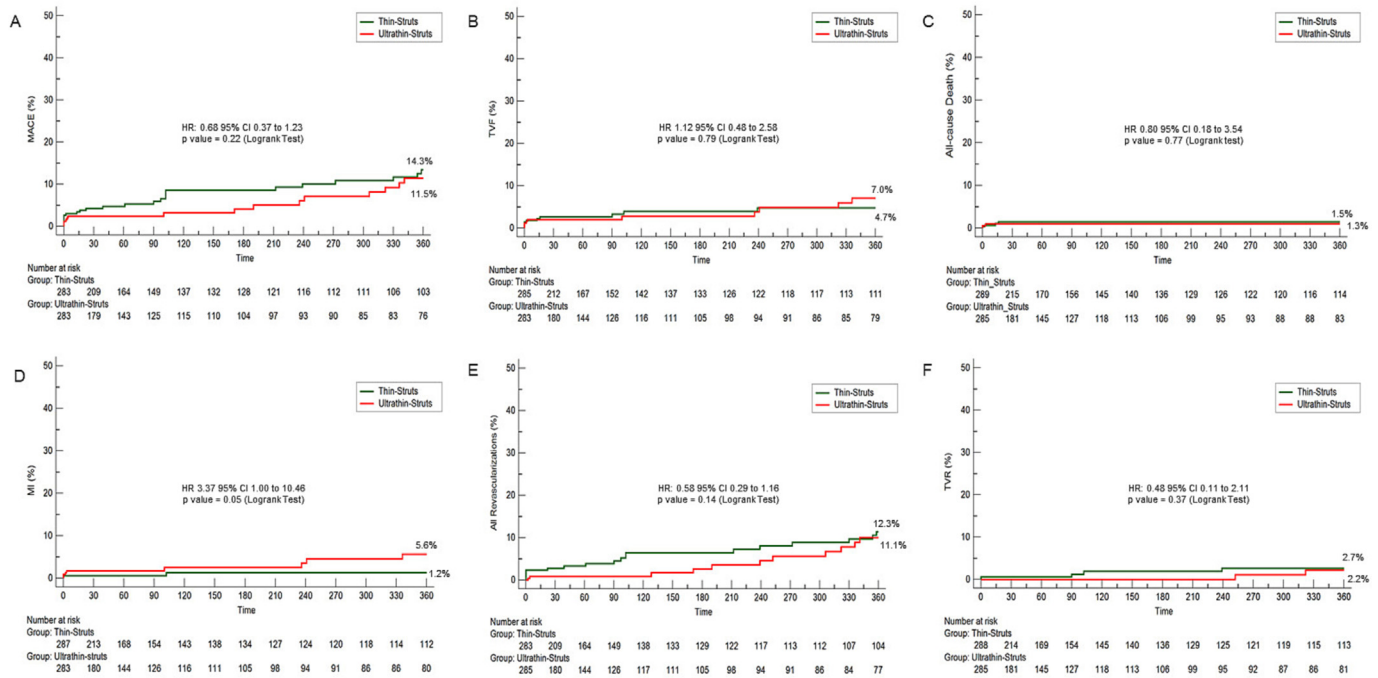

Fig. 4. After propensity score matching Kaplan-Meier curves representing the incidence of major adverse cardiac events (MACE) (A), target vessel failure (TVF) (B), death (C), myocardial infarction (MI) (D), all-revascularization (E) and target vessel revascularization (TVR) (F) from the LATAM CTO Registry. Cumulative event rates up to 1-year for the different subgroups: ultra-thin struts (red line) and thin struts (green line). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

same result was evidenced in another two meta-analysis of longer-term follow-up. [11,12]

The use of UTS-DES compared to conventional second-generation DES for the treatment of CTOs has received limited study [9]. In 2017, Markovic et al. conducted a study comparing angiographic and clinical results 24 months after recanalization of CTO using the ultrathin Orsiro™ DES and the second-generation Resolute DES. In a prospective series, 57 patients with CTO underwent PCI with Resolute™ followed by 74 patients treated with Orsiro™. Patients who underwent PCI with the UTS-DES had significantly less late lumen loss, but similar clinical results in 24 months [21]. The use of UTS-DES for the treatment of CTO appears to be feasible in a high proportion of procedures. [1] In contrast in the PRISON IV RCT the ultrathin Orsiro™ stent had higher incidence of in-stent/in-segment restenosis compared with the Xience™ DES (8.0 % versus 2.1 %; $p = 0.028$) with similar incidence of target vessel/lesion revascularization (9.2 % versus 4.0 %; $p = 0.08$ and 9.2 % versus 6.0 %; $p = 0.33$), target vessel failure (9.9 % versus 6.6 %; $p = 0.35$) and definite or probable stent thrombosis (0.7 % versus 0.7 %; $p = 1.0$). [22] Our

	Ultra-thin Struts	Thin Struts	HR (95%CI)	p	p interaction
MACE	**11.5%**	**14.3%**	**1.62 (0.70 – 3.73)**	**0.26**	**0.61**
≤ 65 y	10.5%	10.1%	1.17 (0.45 – 3.04)	0.75	
> 65 y	12.10%	18.1%	1.64 (0.71 – 3.80)	0.24	
MACE	**11.5%**	**14.3%**	**0.81 (0.12 – 5.28)**	**0.83**	**0.51**
Male	12.3%	12.2%	1.29 (0.62 – 2.68)	0.50	
Female	8.8%	20.9%	2.13 (0.65 – 6.94)	0.21	
MACE	**11.5%**	**14.3%**	**1.05 (0.10 – 10.58)**	**0.97**	**0.75**
No diabetes	11.5%	15.5%	1.60 (0.75 – 3.38)	0.22	
Diabetes	11.2	12.4%	1.27 (0.42 – 3.80)	0.67	
MACE	**11.5%**	**14.3%**	**1.26 (0.03 – 47.85)**	**0.90**	**0.93**
No CKD	10.9	13.5%	1.50 (0.77 – 2.90)	0.23	
CKD	19.2	24.4%	1.24 (0.20 – 7.48)	0.82	
MACE	**11.5%**	**14.3%**	**0.35 (0.03 – 4.15)**	**0.40**	**0.24**
no CHF	8.5	14.0%	1.90 (0.90 – 4.01)	0.09	
CHF	25.4	15.0%	0.79 (0.24 – 2.60)	0.70	
MACE	**11.5%**	**14.3%**	**1.43 (0.74 – 2.78)**	**0.29**	**0.57**
CTO length ≤ 56 mm	10.9	13.4	1,44 (0.74 – 2.80)	0.28	
CTO length > 56 mm	25.0%	36.8%	4.57 (0.39 – 53.99)	0.23	
MACE	**11.5%**	**14.3%**	**1.56 (0.81 – 3.00)**	**0.18**	**0.34**
No in-stent CTO	11.1%	14.3%	1.56 (0.81 – 3.01)	0.18	
In-stent CTO	18.7	9.1%	0.46 (0.04 – 5.04)	0.52	
MACE	**11.5%**	**14.3%**	**1.33 (0.68 – 2.60)**	**0.41**	**0.52**
No ostial CTO	12.0%	14.6%	1.33 (0.68 – 2.61)	0.41	
Ostial CTO	9.6%	12.3%	2.50 (0.48 – 12.95)	0.27	
MACE	**11.5%**	**14.3%**	**1.19 (0.58 – 2.46)**	**0.63**	**0.34**
No bifurcation CTO	12.5%	14.0%	1.19 (0.58 – 2.45)	0.64	
Bifurcation CTO	9.3%	13.5%	2.57 (0.69 – 9.48)	0.16	
MACE	**11.5%**	**14.3%**	**0.84 (0.33 – 1.14)**	**0.72**	**0.16**
No / mild calcification	13.7%	9.8%	0.82 (0.32 – 2.08)	0.67	
Mod / severe calcification	8.3%	18.3%	2.20 (0.88 – 5.52)	0.09	
MACE	**11.5%**	**14.3%**	**1.81 (0.89 – 3.70)**	**0.10**	**0.17**
No intravascular imaging use	12.1%	17.0%	1.82 (0.89 – 3.72)	0.10	
Intravascular imaging use	9.7%	7.4%	0.59 (0.14 – 2.48)	0.48	
MACE	**11.5%**	**14.3%**	**1.40 (0.69 – 2 83)**	**0.35**	**0.89**
Max. stent diameter ≤ 2,5 mm	11.0%	22.3%	1.34 (0.35 – 5.16)	0.67	
Max. stent diameter > 2,5 mm	11.5%	10.9%	1.40 (0.69 – 2.84)	0.35	

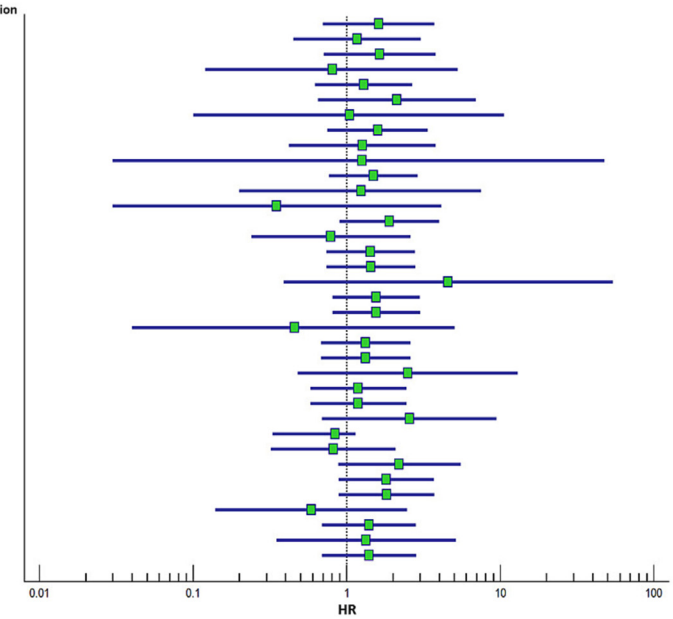

Fig. 5. Subgroups analysis for MACE during the first 1-year after recanalization of CTO with ultra-thin or thin struts DES of patients included in the individual participant data analysis after propensity score matching.

study, differently the PRISON IV, showed no difference in MACE, TVF, all-death, all-revascularization and TVR between ultrathin and thin strut DES 1-year after CTO PCI. This difference may have been due to the large amount of Synergy™ in our UTS-DES group when compared to the PRISON IV study that used Orsiro™ exclusively in the UTS-DES group. Another important fact is that in our group of TS-DES, we have a quarter of Ultimaster™ and Resolute Onyx™ stents (newer generation stent, but with thick thickness struts).

UTS-DES may be more deliverable than TS-DES, which can be a significant advantage when treating complex lesions, such as CTOs. The fact that UTS-DES were used more after the retrograde approach and procedural metrics were worse in this group clearly hints at a higher procedural complexity of these procedures and is probably the result of selection bias (i.e., tougher cases were tackled by experienced operators who also decided to use UTS-DES). Similarly, intravascular image use was more than two-fold higher in the ultra-thin group, which again hints at a selection bias and might have influenced the outcomes (e.g., higher image intravascular use could have optimized the result in ultra-thin DES to such an extent that it could have masked inferior absolute performance compared to thin-strut DES, as shown in PRISON IV). This is something to keep in mind and a potential source of residual confounder even after multivariable adjustment and PSM.

4.1. Limitations

To the best of our knowledge the present study was the largest comparison of the impact of stent thickness on clinical outcomes after CTO PCI, but our study has important limitations. First, we cannot exclude residual confounding, even after adjustment of baseline differences through PSM. Although our findings are hypothesis-generating, a "real world" data always provide regional tendencies and insights regarding CTO PCI. Like other studies that evaluated the impact of the thickness of the DES struts, both groups have a mixed DES bag, with different drugs, with different polymers, with different platforms and with different types of quality. The issue of differences between various DES is still unresolved in simpler settings than a CTO, and it gets more complex and multifactorial biased in complex lesions. Moreover, there was no core angiographic laboratory analysis. All angiographic characteristics are site-reported and differences in angiographic appraisal between centers may be present. A randomized clinical trial examining the impact of DES strut thickness on MACE in patients undergoing CTO PCI would be ideal but likely challenging to perform. Assuming a MACE rate of 11.5 % (UTS-DES) and 14.3 % (TS-DES) as observed in our study, 4498 patients would be required to have 80 % power with an alpha of 0.05.

5. Conclusion

CTO PCI using ultrathin struts DES demonstrated lower unadjusted incidence of MACE and revascularization when compared with those receiving thin-struts DES. The adjusted comparison in a Cox regression model or propensity score matching did not show difference in outcomes according to stent struts.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.carrev.2023.03.002.

Declaration of competing interest

Carlos M. Campos received consultant honoraria and lectures from Abbott, Terumo and Teleflex. Emmanouil S Brilakis reports consulting/speaker honoraria from Abbott Vascular, American Heart Association (associate editor, Circulation), Boston Scientific, Cardiovascular Innovations Foundation (Board of Directors), CSI, Elsevier, GE Healthcare, InfraRedx, and Medtronic; research support from Regeneron and Siemens; shareholder in MHI Ventures; Board of Trustees for the Society of Cardiovascular Angiography and Interventions. Alexandre Quadros received honoraria from Boston Scientific. And research funds from Boston Scientific and Terumo. The remaining authors report no conflicts of interest regarding the content herein.

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