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Impact of acute coronary syndrome on clinical outcomes after revascularization with the dual-therapy CD34 antibody-covered sirolimus-eluting Combo stent and the sirolimus-eluting Orsiro stent

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Abstract

Objectives: To compare the efficacy and safety of the dual-therapy CD34 antibody-covered sirolimus-eluting Combo stent (DTS) and the sirolimus-eluting Orsiro stent (O-SES) in patients with and without acute coronary syndrome (ACS) included in the SORT OUT X study.

Background: The incidence of target lesion failure (TLF) after treatment with modern drug-eluting stents has been reported to be significantly higher in patients with ACS when compared to patients without ACS. Whether the results from the SORT OUT X study apply to patients with and without ACS remains unknown.

Methods: In total, 3146 patients were randomized to stent implantation with DTS ($n = 1578$; ACS: $n = 856$) or O-SES ($n = 1568$; ACS: $n = 854$). The primary end point, TLF, was a composite of cardiac death, target-lesion myocardial infarction (MI), or target lesion revascularization (TLR) within 1 year.

Results: At 1 year, the rate of TLF was higher in the DTS group compared to the O-SES group, both among patients with ACS (6.7% vs. 4.1%; incidence rate ratio: 1.65 [95% confidence interval, CI: 1.08–2.52]) and without ACS (6.0% vs. 3.2%; incidence rate ratio: 1.88 [95% CI: 1.13–3.14]). The differences were mainly explained by higher rates of TLR, whereas rates of cardiac death and target lesion MI

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did not differ significantly between the two stent groups in patients with or without ACS

Conclusion: Compared to the O-SES, the DTS was associated with a higher risk of TLF at 12 months in patients with and without ACS. The differences were mainly explained by higher rates of TLR.

KEYWORDS

acute coronary syndrome, randomized controlled trial, stent comparison, target lesion failure

1 | INTRODUCTION

Patients presenting with acute coronary syndrome (ACS) have a worse prognosis after percutaneous coronary intervention (PCI) when compared to patients with chronic coronary syndrome (CCS).[1–4] To reduce the risk of adverse events after PCI, attempts have been made to further improve early stent healing and to reduce neointima hyperplasia. The dual-therapy CD34 antibody-covered sirolimus-eluting Combo stent (DTS) (OrbusNeich Medical) combines an abluminal, bioabsorbable polymer with a luminal CD34+ antibody designed to capture endothelial progenitor cells. The DTS appears to promote endothelialization while reducing neointima hyperplasia and inflammation as compared to bare metal stents in a porcine model[5] and was found to be noninferior to first- and second-generation drug-eluting stents (DES) in three randomized controlled trials including a total of 815 patients.[6–8] Only two nonrandomized studies have compared outcomes after treatment with the DTS in patients with and without ACS.[9,10] One year after DTS implantation, significantly higher rates of TLF were seen in patients with ACS compared to patients with CCS.[9] The study used registry-based data and did not compare outcomes after DTS treatment with outcomes after treatment with another DES.

The randomized SORT OUT X study was the first study to compare the DTS to a modern DES, the sirolimus-eluting Orsiro stent (O-SES) (Biotronik),[11] and showed that the DTS was inferior to the O-SES for target lesion failure (TLF) at 12 months mainly due to a higher incidence of target lesion revascularization (TLR) in the DTS group. Whether the results from the SORT OUT X study apply to patients with and without ACS remains unknown. The aim of the present study (a predefined substudy of SORT OUT X) was to compare the efficacy and safety of the DTS compared to the O-SES in patients with and without ACS.

2 | MATERIALS AND METHODS

SORT OUT X[11] was a two-arm randomized, multicenter, all-comer, noninferiority trial with blinded end points, comparing the DTS to the O-SES in the treatment of coronary artery lesions. The inclusion period was from June 2017 to December 2019. A detailed study protocol has previously been provided.[12] Briefly, patients were eligible if they were ≥18 years old, had chronic CCS or ACS, and ≥1 coronary lesion with >50% diameter stenosis. If multiple lesions were treated, the allocated study stent was used in all lesions. There were no restrictions in the number of treated lesions, number of treated vessels, or lesion length. Exclusion criteria were life expectancy of <1 year, allergy to aspirin, clopidogrel, ticagrelor, prasugrel, sirolimus, or biolimus; participation in other randomized stent trials; or inability to provide written informed consent.

The investigators enrolled the patients, who were randomly allocated to treatment after diagnostic coronary angiography and before PCI. Block randomization by center (permuted blocks of random sizes [2/4/6]) was used to assign patients in a 1:1 ratio to receive the DTS or the O-SES. The allocation sequence stratified by sex and the presence of diabetes was computer-generated by an independent organization. Patients were assigned to treatment through a web-based randomization system. All individuals who were involved in the clinical event detection were blinded, whereas operators were not blinded to treatment assignment.

Stents were implanted in accordance with standard techniques. Full lesion coverage was attempted by implanting one or more stents. DES other than the allocated stent and bare-metal stents were not allowed unless the allocated study stent could not be implanted. In such situations, balloon angioplasty alone or other stents were allowed. Patients were on acetylsalicylic acid (loading dose of 300 mg) before stent implantation and loaded with either ticagrelor 180 mg, clopidogrel 600 mg, or prasugrel 60 mg. The choice of dual antiplatelet therapy was left to the discretion of the participating centers. Dual antiplatelet therapy was recommended for 6 months in patients with CCS and for 12 months in patients with ACS (unstable angina pectoris or acute myocardial infarction [MI]). An unfractionated heparin dose (70–100 IU/kg) was given before the procedure. Glycoprotein IIb/IIIa inhibitors, bivalirudin, or cangrelor were used at the operator's discretion.

2.1 | Outcome measures

Definitions of end points are provided in the main publication.[11] The primary end point of this substudy was TLF, defined as a composite of cardiac death, target lesion MI (not related to other than the index lesion[s]), or clinically indicated TLR within 12 months of stent

implantation. Individual components of the primary end point comprised the secondary end points: cardiac death, target lesion MI, clinically indicated TLR, all-cause death (cardiac and noncardiac), target vessel revascularization (TVR), and definite, probable, and overall stent thrombosis according to the Academic Research Consortium definition[13]; and a patient-related composite end point (all-cause death, all MIs, or any revascularization).

2.2 | Clinical event detection

The study was based on clinically driven event detection, and no dedicated follow-up was scheduled. At 12 months follow-up, data on mortality, hospital admission, coronary angiography, repeat PCI, and coronary artery bypass surgery (CABG) were obtained from the following national Danish administrative and healthcare registries: the Civil Registration System, the Western Denmark Heart Registry, and the Danish National Registry of Patients. The latter maintains records of all hospitalizations in Denmark. The National Health Service provides tax-funded healthcare, guaranteeing unfettered access to medical care. All acute medical conditions are exclusively treated at public hospitals in Denmark. The Danish Civil Registration System has kept electronic records on sex, birth date, residence, emigration date, and vital status changes since 1968, with daily updates. The 10-digit civil registration number assigned at birth and used in all registries allows accurate record linkage. Loss to follow-up was minimized in the study, as vital status data for our study participants was provided by the Civil Registration System. The Danish National Registry of Patients provided information on diagnoses assigned by the treating physician during hospitalizations (coded according to the International Classification of Diseases, 10th revision).[14] The way Danish hospitals report data to the Danish National Registry of Patients changed on January 1, 2019. The data reported since January 2019 has not been validated. Thus, registry-based follow-up data regarding MI were not available for the entire follow-up period for 2224 patients. Instead, all discharge letters regarding these patients were evaluated to detect MI.

An independent event committee reviewed all end points and source documents to adjudicate causes of death, reasons for hospital admission, and diagnosis of MI. Two dedicated operators at each participating center reviewed cine films for the event committee to classify stent thrombosis, TLR, and TVR (with either PCI or CABG). The independent event committee was blinded to study stent-type assignments during the adjudication process. This methodology has been used in the previous SORT OUT studies.[15–18]

2.3 | Statistical analysis

Distributions of continuous variables were compared between study groups using two-sample *t*-test (or Cochran's test for cases of unequal variance) or Mann–Whitney *U*-test depending on whether the data followed a normal distribution. Distributions of categorical variables were compared using χ^2 test. In analyses of every end point, follow-up continued until the date of an end point event, death, emigration, or 12 months after stent implantation, whichever came first. Survival curves were constructed based on cumulated incidences, accounting for death as a competing risk.[19] Incidence rate ratios were calculated using patients

TABLE 1 Baseline patient characteristics

	Patients with ACS			Patients with CCS			*p* Value ACS versus CCS
Variable	DTS (*n* = 856)	O-SES (*n* = 854)	*p* Value	DTS (*n* = 722)	O-SES (*n* = 714)	*p* Value	
Age (years)	65.9 (±11.3)	65.5 (±11.6)	0.46	68.5 (±9.8)	68.2 (±9.9)	0.51	0.00010
Male gender	657 (76.8%)	641 (75.1%)	0.41	556 (77.0%)	567 (79.4%)	0.27	0.13
Arterial hypertension	343 (44.1%)	410 (48.9%)	0.05	462 (65.2%)	461 (65.9%)	0.78	<0.00001
Hypercholesterolemia	316 (37.4%)	323 (38.5%)	0.64	467 (65.7%)	460 (65.3%)	0.89	<0.00001
Current smoker	292 (38.1%)	273 (35.5%)	0.29	118 (18.4%)	156 (24.5%)	0.0078	<0.00001
Body mass index (kg/m^2)	28.0 (±4.9)	28.0 (±4.8)	0.85	28.1 (±4.6)	27.8 (±4.6)	0.20	0.82
Previous myocardial infarction	101 (12.0%)	102 (12.2%)	0.88	139 (19.4%)	119 (17.3%)	0.29	<0.00001
Previous PCI	114 (13.5%)	129 (15.4%)	0.27	181 (25.3%)	174 (24.9%)	0.85	<0.00001
Previous CABG	35 (4.1%)	32 (3.8%)	0.27	76 (10.6%)	57 (8.2%)	0.11	<0.00001
Killip class			0.57			-	0.00001
Class 1	842 (98.4%)	838 (98.2%)		722 (100)	714 (100)		
Class 2	14 (1.6%)	14 (1.6%)		0	0		
Class 3 or 4	0	2 (0.2%)		0	0		

Note: Data are presented as mean ± SD, median (interquartile range), or the number of patients (%).

Abbreviations: ACS, acute coronary syndrome; CABG, coronary artery bypass graft surgery; CCS, chronic coronary syndrome; DTS, dual-therapy CD34 antibody-covered sirolimus-eluting stent; O-SES, sirolimus-eluting stent; PCI, percutaneous coronary intervention.

TABLE 2 Baseline lesion and procedure characteristics

Variable	Patients with ACS			Patients with CCS			
	DTS (*n* = 856 patients; 1055 lesions)	O-SES (*n* = 854 patients; 1069 lesions)	*p* Value	DTS (*n* = 722 patients; 953 lesions)	O-SES (*n* = 714 patients; 913 lesions)	*p* Value	*p* Value ACS versus CCS
Target lesion			0.024			0.77	0.021
Left main artery	21 (2.0%)	22 (2.1%)		33 (3.5%)	28 (3.1%)		
Left anterior descending artery	437 (41.5%)	483 (45.2%)		422 (44.3%)	422 (46.2%)		
Left circumflex artery	231 (21.9%)	261 (24.4%)		208 (21.8%)	179 (19.6%)		
Right artery	355 (33.7%)	289 (27.1%)		284 (29.8%)	278 (30.4%)		
Saphenous vein graft	10 (0.9%)	13 (1.2%)		6 (0.6%)	6 (0.7%)		
Lesion type			0.35			0.47	<0.00001
A	74 (7.0%)	90 (8.4%)		110 (11.5%)	120 (13.1%)		
B1	299 (28.4%)	317 (29.7%)		268 (28.1%)	268 (29.4%)		
B2	254 (24.1%)	229 (21.4%)		177 (18.6%)	174 (19.1%)		
C	427 (40.5%)	432 (40.4%)		398 (41.8%)	351 (38.4%)		
Chronic total occlusion lesions	14 (1.3%)	16 (1.5%)	0.74	75 (7.9%)	87 (9.5%)	0.21	<0.00001
Bifurcation lesions	236 (22.4%)	244 (22.8%)	0.80	245 (25.7%)	207 (22.7%)	0.82	0.23
Stent technique			0.90			0.43	0.12
First stent technique	126 (12.0%)	140 (13.1%)		129 (13.6%)	122 (13.3%)		
Second stent technique	43 (4.1%)	39 (3.7%)		31 (3.2%)	19 (2.1%)		
Unknown	67 (6.3%)	65 (6.0%)		85 (8.9%)	66 (7.3%)		
Lesion length > 18 mm	523 (49.6%)	539 (50.5%)	0.70	476 (49.9%)	451 (49.4%)	0.81	0.82
Lesion length (mm)	18.0 (13–28)	20.0 (13–28)	0.50	18.0 (12.0–30.0)	18.0 (12.0–30.0)	0.30	0.47
Reference vessel size (mm)	3.5 (±0.6)	3.5 (±0.6)	0.67	3.4 (±0.6)	3.4 (±0.6)	0.93	0.0038
No. of stents per lesion	1.3 (±0.6)	1.3 (±0.6)	0.10	1.3 (±0.7)	1.3 (±0.7)	0.40	0.036
No. of stents per patient	1.6 (±0.9)	1.7 (±1.0)	0.12	1.8 (±1.1)	1.7 (±1.1)	0.29	0.00013
Total stent length per lesion (mm)	27.3 ± 16.4	28.0 ± 17.1	0.39	28.9 ± 19.5	28.7 ± 19.4	0.81	0.042
Total stent length per patient (mm)	33.9 ± 22.8	35.2 ± 26.1	0.30	38.4 ± 27.9	37.5 ± 29.5	0.52	0.00041
Direct stenting	125 (11.9%)	125 (11.7%)	0.87	111 (11.7%)	102 (11.2%)	0.77	0.71
Stent delivery failure	31 (2.9%)	33 (3.1)	0.84	17 (1.8%)	28 (3.1)	0.071	0.24
Maximum pressure (atm)	18.4 (±3.8)	18.3 (±4.0)	0.75	18.8 (±3.8)	18.5 (±4.1)	0.056	0.011
Length of procedure (minutes)	26.9 (±19.7)	26.5 (±20.4)	0.73	36.1 (±33.1)	34.4 (±29.9)	0.29	0.00010
Flouro time (min)	8.7 (±8.7)	8.5 (±8.7)	0.59	13.2 (±15.1)	12.8 (±14.9)	0.60	0.00010
Contrast (ml)	83.8 (±48.2)	87.2 (±55.5)	0.18	106.1 (±71.9)	108.1 (±78.8)	0.62	0.00010
Use of glycoprotein IIb/IIIa inhibitor	11 (1.3%)	27 (3.2%)	0.0085	10 (1.4%)	9 (1.3%)	0.84	0.060
Use of bivalirudin	26 (3.1%)	20 (2.4%)	0.37	5 (0.7%)	4 (0.6%)	0.75	0.00001

Note: Data are presented as mean ± SD, median (interquartile range), or the number of patients (%).

Abbreviations: ACS, acute coronary syndrome; CCS, chronic coronary syndrome; DTS, dual-therapy CD34 antibody-covered sirolimus-eluting stent; O-SES, sirolimus-eluting stent.

who received the O-SES as the reference group. The intention-to-treat principle was used in all analyses. A two-sided *p* value of less than 0.05 indicated statistical significance. Analyses were conducted using SAS 9.4 (SAS Institute). This trial is registered with ClinicalTrials.gov, number NCT03216733.

3 | RESULTS

Between June 2017 and December 2019, 3146 patients were randomly assigned to receive either the DTS (1578 patients [2008 lesions]) or the O-SES (1568 patients [1982 lesions]) Table 2. In total, 1710 patients had ACS of whom 856 were treated with the DTS and 854 were treated with the O-SES. Six patients emigrated and were censored at the time of emigration (total follow-up: 99.8%).

Baseline patient characteristics (Table 1) and procedural characteristics (Table 2) were well balanced in both patients with ACS and with CCS treated with DTS versus O-SES. The only exception was a higher frequency of glycoprotein IIb/IIIa inhibitor treatment in patients with ACS treated with an O-SES when compared to patients with ACS treated with a DTS. Compared to patients with ACS, patients with CCS were older, more frequently treated for hypertension or hypercholesterolemia, and they had a higher rate of previous coronary artery bypass graft surgery (CABG), previous MI, and previous PCI, whereas fewer were current smokers. Patients with CCS had less complex lesions, more chronic total occlusions, a longer total stent length, higher maximum pressure, longer procedure times, longer flouro times, and a higher contrast volume when compared to patients with ACS.

TLF and the secondary end points are presented in Table 3 and Figures 1 and 2. In patients with ACS, TLF occurred in 57 (6.7%) in the DTS group and in 35 (4.1%) in the O-SES group at 12 months of follow-up (incidence rate ratio: 1.65 [95% confidence interval, CI: 1.08–2.52]). This difference was mainly explained by a higher rate of TLR in the DTS group compared to the O-SES group. Furthermore, in-stent restenosis was more frequent in the DTS group (22 [2.6%] vs. 8 [0.9%]; incidence rate ratio: 2.78 [95% CI: 1.24–6.25]) when compared to the O-SES group.

In patients with CCS, TLF occurred in 74 (5.7%) in the DTS group and in 45 (3.5%) of the patients in the O-SES group (incidence rate ratio: 1.67 [95% CI: 1.15–2.42]). Again, this difference was mainly explained by a higher rate of TLR in the DTS group when compared to the O-SES group. Furthermore, when compared to the O-SES group, the rate of TVR and in-stent restenosis was higher in the DTS group.

Of the 1710 patients with ACS, 744 (43.5%) presented with ST-elevation MI (STEMI). There was no statistically significant difference in TLF rate after treatment with the DTS versus O-SES in the STEMI patients (18 [4.6%] vs. 10 [2.8%]; incidence rate ratio: 1.66 [95% CI:

TABLE 3 Clinical outcomes at 12 months in patients presenting with ACS and CCS

	Patients with ACS				Patients with CCS			
Variable	DTS (*n* = 856)	O-SES (*n* = 854)	IRR (95% CI)	*p* Value	DTS (*n* = 722)	O-SES (*n* = 714)	IRR (95% CI)	*p* Value
Target lesion failure	57 (6.7%)	35 (4.1%)	1.65 (1.08–2.52)	0.021	43 (6.0%)	23 (3.2%)	1.88 (1.13–3.14)	0.015
Death								
All-cause mortality	21 (2.5%)	20 (2.3%)	1.05 (0.57–1.94)	0.87	25 (3.5%)	15 (2.1%)	1.66 (0.87–3.14)	0.12
Cardiac	15 (1.8%)	14 (1.6%)	1.07 (0.52–2.23)	0.85	11 (1.5%)	10 (1.4%)	1.09 (0.46–2.58)	0.84
Noncardiac	6 (0.7%)	6 (0.7%)	1.00 (0.32–3.11)	1.00	14 (1.9%)	5 (0.7%)	2.78 (1.00–7.72)	0.049
Target lesion myocardial infarction	29 (3.4%)	18 (2.1%)	1.62 (0.89–2.92)	0.11	14 (1.9%)	11 (1.5%)	1.27 (0.58–2.81)	0.55
Myocardial infarction	35 (4.1%)	24 (2.8%)	1.46 (0.87–2.47)	0.15	20 (2.8%)	15 (2.1%)	1.33 (0.68–2.62)	0.40
Stent thrombosis (all)	8 (1.1%)	4 (0.6%)	1.99 (0.60–6.63)	0.26	8 (1.1%)	4 (0.6%)	1.99 (0.60–6.63)	0.26
Definite	4 (0.5%)	3 (0.4%)	1.33 (0.30–5.97)	0.71	4 (0.6%)	3 (0.4%)	1.33 (0.30–5.96)	0.71
Possible	3 (0.4%)	6 (0.7%)	0.50 (0.13–2.00)	0.33	3 (0.4%)	1 (0.1%)	2.98 (0.31–28.6)	0.34
Probable	1 (0.1%)	1 (0.1%)	1.00 (0.06–16.0)	1.00	1 (0.1%)	0		
Definite or probable	5 (0.6%)	4 (0.5%)	1.25 (0.33–4.66)	0.74	5 (0.7%)	3 (0.4%)	1.66 (0.40–6.97)	0.49
Target vessel revascularization	41 (4.8%)	30 (3.5%)	1.37 (0.85–2.21)	0.19	39 (5.4%)	14 (2.0%)	2.83 (1.53–5.23)	0.00089
Target lesion revascularization	25 (2.9%)	14 (1.6%)	1.80 (0.93–3.46)	0.080	28 (3.9%)	10 (1.4%)	2.82 (1.37–5.82)	0.0050
In-stent restenosis	22 (2.6%)	8 (0.9%)	2.78 (1.24–6.25)	0.013	23 (3.2%)	6 (0.8%)	3.84 (1.56–9.43)	0.0034

Note: Data are presented as the number of patients (%).

Abbreviations: ACS, acute coronary syndrome; CCS, chronic coronary syndrome; CI, confidence interval; DTS, dual-therapy CD34 antibody-covered sirolimus-eluting stent; IRR, incidence rate ratio; O-SES, sirolimus-eluting stent.

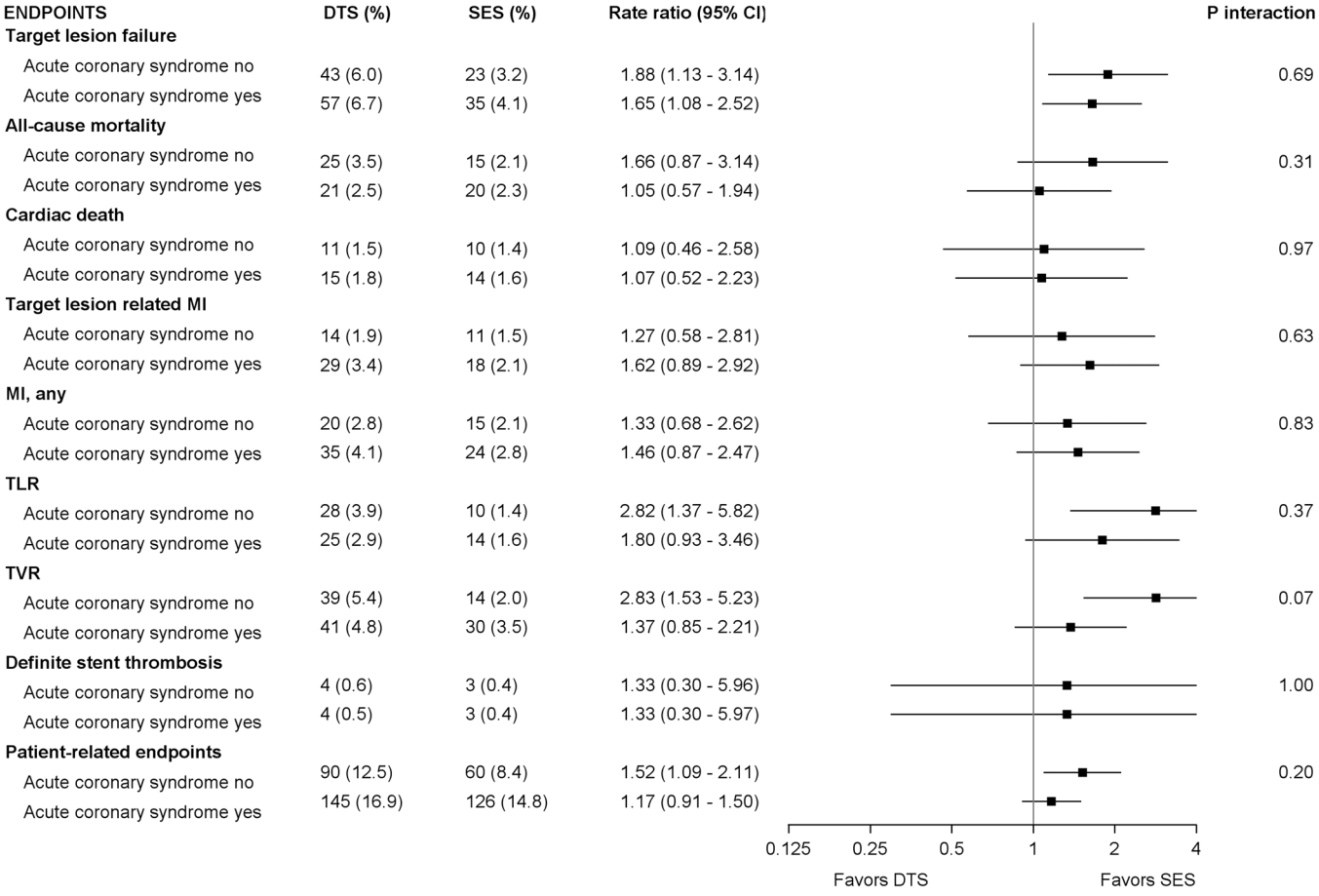


FIGURE 1 One-year clinical outcomes in randomized patients with and without acute coronary syndrome treated with a DTS or an O-SES. Values are presented as the number of patients (%). CI, confidence interval; DTS, dual-therapy CD34 antibody-covered sirolimus-eluting Combo stent; MI, myocardial infarction; O-SES, sirolimus-eluting Orsiro stent; TLR, target lesion revascularization; TVR, target vessel revascularization.

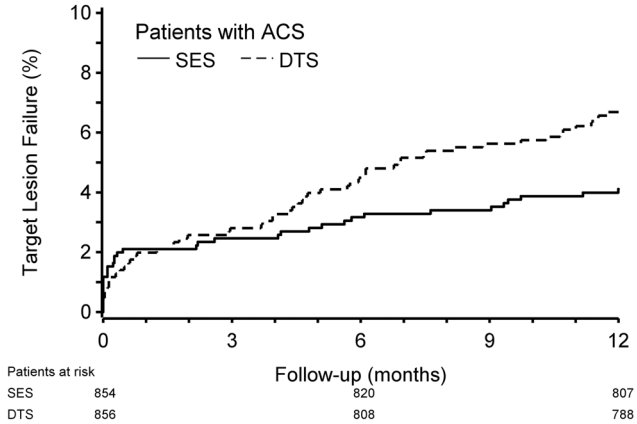
0.76–3.62]). However, in the NSTEMI patients, the rate of TLF was higher after treatment with the DTS compared to the O-SES (39 [8.4%] vs. 11 [2.2%]; incidence rate ratio: 1.70 [95% CI: 1.02–2.82]).

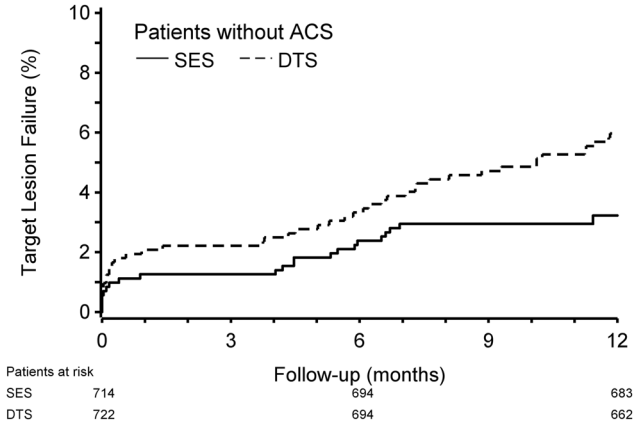
4 | DISCUSSION

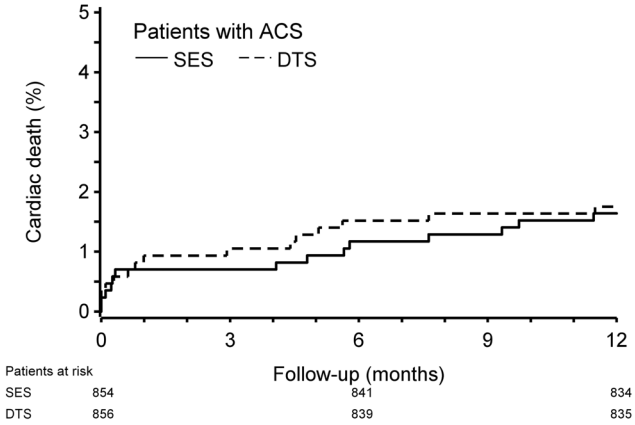
This SORT OUT X substudy provides a 12-month head-to-head comparison of the DTS and the O-SES in patients presenting with ACS and CCS. The study showed that in both patient groups, the patients treated with the DTS had a significantly worse outcome at the 12-month follow-up when compared to patients treated with the O-SES. The difference in patients presenting with ACS was mainly driven by a significant difference among patients with non-STEMI (NSTEMI), while no significant differences were seen in patients with STEMI.

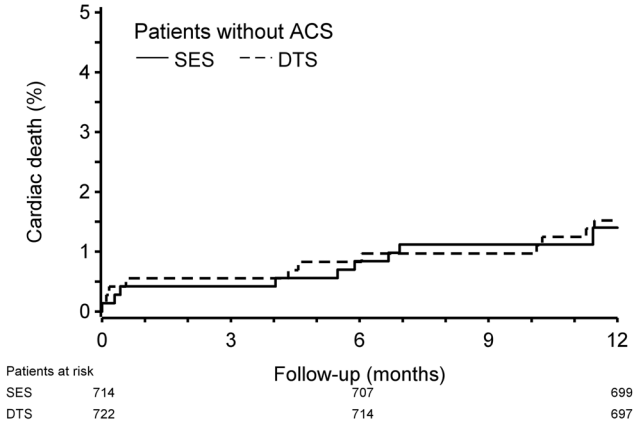
Only two previous studies have evaluated the prognosis after DTS implantation in patients presenting with ACS.[9,10] Both studies were based on registry data and none of the studies compared the outcome after DTS implantation with another DES. Chandrasekhar et al.[9] found a TLF rate of 4.5% in patients with ACS, which was significantly higher than the 3.3% TLF rate among patients with CCS. Based on registry data with no control group, Kalkman et al.[10] concluded that the DTS is a safe and efficient device for patients presenting with ACS with a TLF rate of 7.1%. These reported TLF rates are overall in line with our findings.

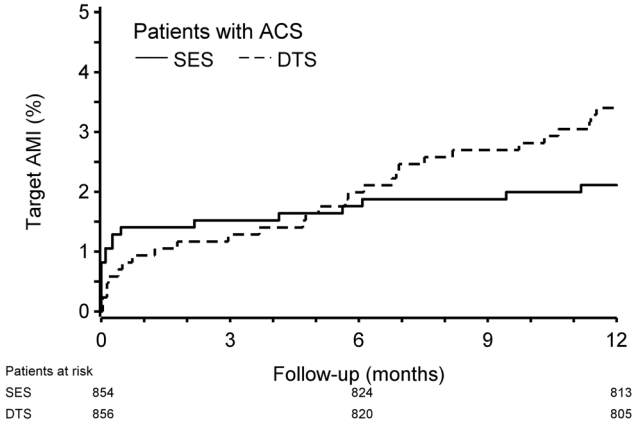
As discussed in the main SORT OUT X publication,[11] there are important differences in the DES technologies between the two study stents that may contribute to the higher TLF rates observed in the DTS group in the present study. First, the DTS has a murine, monoclonal, antihuman CD34 antibody attached to the polymer. Unfortunately, there are no randomized studies using optical coherence tomography (OCT) to compare the DTS and the O-SES. Two studies[8,20] compared the vascular healing of the O-SES and the X-EES (Xience) stent in patients with ACS. The proportion of covered strut was significantly higher in the O-SES group than in the X-EES group and the O-SES group had significantly thinner neointima compared to the X-EES group. On the other hand, there was no difference in the frequency of malapposed strut. Furthermore, in the EGO-Combo Study,[21] the authors found that the DTS showed a unique late neointimal regression that has not been reported for any other DES. Only 3% of the patients included in this study presented with ACS, and STEMI was an exclusion criterion. None of the OCT findings mentioned above have translated into differences in clinical outcomes when compared to other DES[6,22–24] and the results also

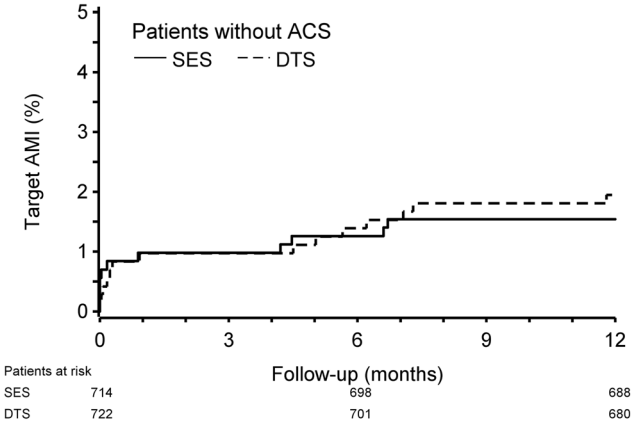


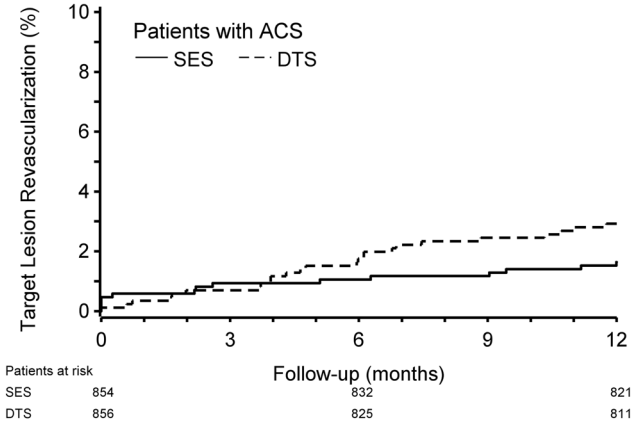












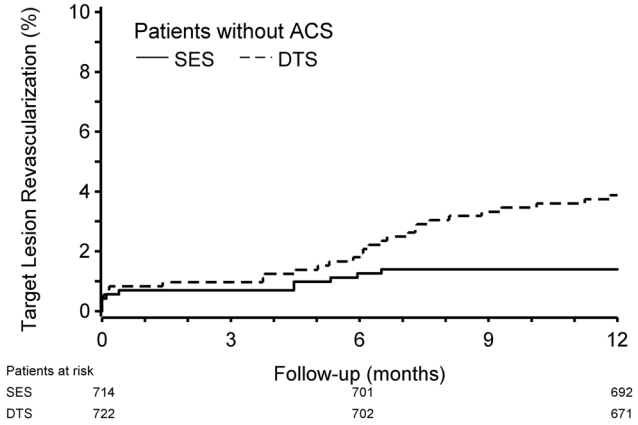


FIGURE 2 (See caption on next page)

appear to be in contrast with the findings of the present study. There are no reports suggesting that the murine, monoclonal, antihuman CD34 antibody attracts cells other than progenitor endothelial cells, leading to more restenosis. Two animal studies evaluating the endothelialization of the DTS using OCT, histology, and scanning electron/confocal microscopy analysis reported no such findings.[5,25]

Second, the DTS has thicker stent struts (100 μm) than the O-SES (60–80 μm). Two recent meta-analyses including 10 and 16 randomized trials, respectively, with a total of more than 34,000 patients with a high percentage of patients presenting with ACS compared newer-generation ultrathin strut DES versus thicker strut DES.[26,27] In one of the meta-analyses, the newer-generation ultrathin strut DES was associated with a 16% reduction in TLF (relative risk: 0.84 [95% CI: 0.72–0.99]) when compared with the older second-generation thicker strut DES. In contrast to our findings, the difference in TLF was mainly driven by a lower risk of MI, with similar risks of cardiovascular death and ischemia-driven TLR. The second study found that the ultrathin-strut DES reduced the risk of TLF compared with thicker-strut second-generation DES in patients undergoing PCI, a difference caused by a lower risk of ischemia-driven TLR.[27] The latter result is in line with our findings.

Third, the study stents have different drug-eluting kinetics. The biodegradable polymer attached to the DTS is completely absorbed within 90 days (compared with 12–24 months for the SES) and the drug release is faster (1 vs. 3 months). Based on registry data, Iqbal et al.[28] compared the Endeavor stent and the Resolute stent. Of the patients included in the study, 72% presented with ACS. The two stents were based on the same stent platform, both stents were zotarolimus-eluting stents but had different polymer coatings resulting in different drug release times. The Endeavor stent released 95% of the drug within 2 weeks and the Resolute stent released 85% of the drug within 60 days and the remainder by 180 days. The longer drug release time resulted in significantly lower 2-year mortality and TLR.

4.1 | Limitations

The SORT OUT X trial, in line with the previous SORT OUT trials,[13–16] relied on registry-based outcome ascertainment without study-related angiographic or clinical follow-up. However, new data showed a high degree of concordance between investigator-reported and adjudicated end points in a randomized trial.[29] Patient care complied with standard clinical practice usually with a single hospital outpatient visit 1–3 months after stent implantation. Although the Danish healthcare databases capture events of sufficient severity for patients to seek medical attention, these records might underestimate event rates compared with clinical follow-up by dedicated trial staff. However, this potential should not influence differences detected between treatment groups. Biomarkers were not routinely measured in relation to the procedure, and thus we could not assess potential differences in periprocedural MI. Furthermore, we did not monitor bleeding complications.

5 | CONCLUSION

The DTS was associated with an increased risk of TLF at 12 months in both patients with and without ACS compared to the O-SES. The differences were explained by higher rates of TLR, whereas rates of cardiac death and MI did not differ significantly between the two stent groups in patients with and without ACS.

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CONFLICTS OF INTEREST

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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FIGURE 2 Event rates of target lesion failure and the individual components (cardiac death, target lesion myocardial infarction, and target lesion revascularization) in patients with and without acute coronary syndrome after implantation with a DTS (dotted line) or O-SES (solid line) during 12-month follow-up. AMI, acute myocardial infarction; DTS, dual-therapy CD34 antibody-covered sirolimus-eluting Combo stent; O-SES, sirolimus-eluting Orsiro stent.

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