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A comparison of the ultrathin Orsiro Hybrid sirolimus-eluting stent with contemporary drug-eluting stents: A meta-analysis of randomized controlled trials☆,☆☆,★

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ABSTRACT

Background: Recent studies suggest the Orsiro sirolimus-eluting stent (O-SES), which has ultrathin struts with a biodegradable sirolimus-eluting polymer coating, performed better than contemporary drug-eluting stents (DES). We performed a meta-analysis to compare clinical outcomes for all randomized controlled trials (RCTs) of O-SES vs contemporary DES.

Methods/materials: PubMed, Cochrane CENTRAL, and meeting abstracts were searched for all RCTs comparing O-SES with contemporary DES. Pooled estimates of longest available clinical outcomes at a minimum of one-year follow-up, presented as odds ratios (OR) [95% confidence intervals], were generated with random-effect models.

Results: We included 8 RCTs with a total of 11,176 patients (5444 O-SES and 5732 contemporary DES [3537 EES, 1295 ZES, and 1264 BP-BES) with a mean age of 65 ± 11, 74% were male, 40% underwent PCI for stable angina, and 56% for ACS. We assessed outcomes comparing O-SES vs. everolimus-eluting stents, vs. permanent-polymer DES, and vs. all DES including biodegradable-polymer DES. Orsiro performed comparably in all categories with a trend toward a reduction in myocardial infarction (0.83 [0.68, 1.02], p = 0.07) and stent thrombosis (0.75 [0.54, 1.04], p = 0.08).

Conclusion: Overall, the Orsiro SES had similar clinical outcomes to contemporary DES with a trend toward reduction in myocardial infarction and stent thrombosis.

1. Introduction

Significant advances have been made over the past 30 years in coronary stent technology. While the addition of a drug-eluting polymer to the coronary stent marked a major advance in combating restenosis, the addition of a polymer increased strut thickness and brought unintended consequences such as delayed healing and increased inflammation [1]. This raises the obvious question of whether development of biodegradable-polymer drug-eluting stents (DES) will improve outcomes. However, a recent meta-analysis of RCTs comparing biodegradable-polymer DES versus permanent-polymer DES did not demonstrate a significant reduction in adverse clinical outcomes, though there was a trend toward reduction in stent thrombosis [2]. Another question is whether reduction in strut thickness may further improve outcomes as stents with greater strut thickness appear to be at higher risk for stent thrombosis due to delayed re-endothelialization [3]. It is important to note that there is significant variability in the strut thickness of available biodegradable-polymer DES, which may account for the failure of biodegradable-polymer DES to demonstrate improvement over permanent-polymer DES.

The Orsiro Hybrid sirolimus-eluting stent (O-SES) (Biotronik AG, Buelach, Switzerland) has the potential to improve outcomes through both a biodegradable polymer and having an ultrathin strut thickness (60 μm for 2.25–3.0 mm diameter and 80 μm for 3.5–4.0 mm diameter). The results of the recently published BIOFLOW V trial are encouraging and suggest placement of O-SES during percutaneous coronary intervention (PCI) reduces target lesion failure (TLF) and myocardial infarction (MI) compared with patients who received the Xience everolimus-eluting stent (EES) (Abbott Vascular, Santa Clara, CA) [4]. However, it is important that these comparisons are assessed in the entirety of the available randomized controlled trial data. Therefore, we performed a meta-analysis of all available randomized controlled trials comparing clinical outcomes of the O-SES with all contemporary DES.

Abbreviations: ACS, acute coronary syndrome; BP-BES, biolimus-eluting stent with biodegradable polymer; DES, drug-eluting stent; EES, everolimus-eluting stent; O-SES, Orsiro sirolimus-eluting stent; PCI, percutaneous coronary intervention; RCT, randomized controlled trial; ZES, zotarolimus-eluting stent.

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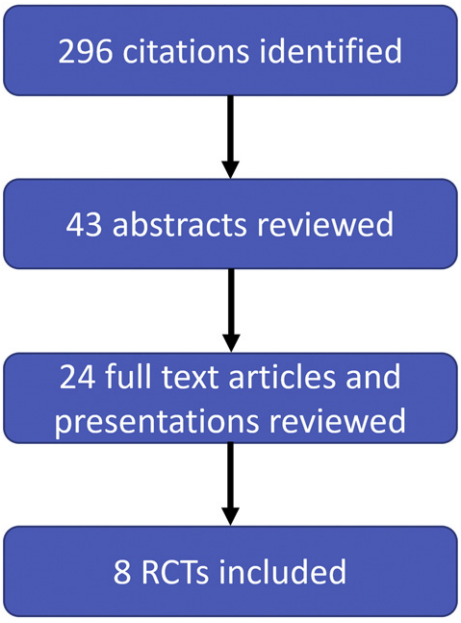

Fig. 1. Flow diagram - Diagram demonstrating the selection process illustrating the number of citations, abstracts, and full-text manuscripts that were evaluated in determining which randomized controlled trials were included in our meta-analysis

2. Materials and methods

2.1. Study search, selection, and abstraction

Two independent reviewers (MJL and BJF) systematically searched (from 2003 to October 2017) Medline/PubMed and available abstract data, applying the search terms "Orsiro" OR "Sirolimus" AND "Stent" AND "Biodegradable polymer" OR "Bioabsorbable polymer" OR "Bioresorbable polymer". We also obtained presentation slides of the late-breaking clinical trials, specifically data from BIOFLOW IV [5]. We included 1) randomized controlled clinical trials comparing 2) the Orsiro Hybrid stent composed of a cobalt chromium alloy covered with an amorphous silicon carbide layer and further with a sirolimus-eluting bioresorbable PLLA polymer coating (Biotronik AG, Buelach, Switzerland) and contemporary newer-generation DES 3) with clinical follow-up. Data were abstracted by the same two investigators (MJL and BJF) in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [6]. We created three groups a priori to compare with O-SES: 1) Comparison with EES, 2) Comparison with permanent-polymer DES, and 3) comparison with all newer-generation DES. We collected outcome data for all-cause mortality, cardiac death, myocardial infarction (MI), clinically driven target lesion revascularization (TLR), clinically driven target vessel revascularization (TVR), target lesion failure (TLF), target vessel failure (TVF), definite or probable stent thrombosis, and major adverse cardiovascular events (MACE), which was typically defined as the composite of cardiac death, myocardial infarction, or repeat revascularization. We utilized TLR or TVR if clinically driven TLR or clinically driven TVR was not available, respectively. We utilized the longest follow-up data when available.

Table 3
Procedural characteristics.

Study	LAD (%)	LCX (%)	RCA (%)	Direct Stenting (%)	Total stent Length (mm)	Stent diameter (mm)
BIOFLOW 2	43	25	31	45	22 ± 11	2.8 ± 0.5
BIOFLOW 4	39	26	34	19	NR	3.0 ± 0.4
BIOFLOW 5	41	26	33	3	28 ± 16	2.6 ± 0.5
BIO-RESORT	40	23	33	17	31	2.8 ± 0.6
BIOSCIENCE	63	34	45	29	29	3.0 ± 0.5
ORIENT	47	25	24	27	37 ± 23	2.8
PRISON IV	30	15	55	0	52 ± 27	3.2 ± 0.4
SORT-OUT VII	54	27	42	14	25 ± 16	3.2 ± 0.6

LAD: left anterior descending coronary artery, LCX: left circumflex coronary artery, RCA: right coronary artery.

Table 1
Study characteristics.

Study	Follow-up	DES comparator	Orsiro patients	DES patients	Total patients	Orsiro lesions	DES lesions
BIOFLOW 2	1 year	Xience EES	298	154	452	332	173
BIOFLOW 4	1 year	Xience EES	354	176	530	409	202
BIOFLOW 5	1 year	Xience EES	884	450	1334	1051	561
BIO-RESORT	1 year	ZES/BP-EES	1169	1173/1172	3514	1551	1580/1532
BIOSCIENCE	2 years	Xience EES	1063	1056	2119	1217	1153
ORIENT	1 year	ZES	250	122	372	345	176
PRISON IV	1 year	Xience EES	165	165	330	165	165
SORT-OUT VII	2 years	Nobori BP-BES	1261	1264	2525	1590	1588

DES: drug-eluting stent, EES: everolimus-eluting stent, ZES: zotarolimus-eluting stent, BP: biodegradable polymer, BES: biolimus-eluting stent.

Table 2
Patient characteristics.

Study	Age	Male sex (%)	Hypertension (%)	Hyperlipidemia (%)	Diabetes mellitus (%)	Smoker (%)	Previous MI (%)	ACS (%)	Stable angina (%)
BIOFLOW 2	63 ± 10	77	78	70	28	27	27	NR	NR
BIOFLOW 4	65 ± 10	74	76	69	31	23	31	29	64
BIOFLOW 5	65 ± 10	74	80	90	35	23	27	51	48
BIO-RESORT	64 ± 11	72	46	38	18	30	19	70	30
BIOSCIENCE	66 ± 12	77	68	67	23	29	20	53	31
ORIENT	65 ± 11	72	65	54	26	27	NR	45	55
PRISON IV	63 ± 10	78	92	96	20	33	30	17	70
SORT-OUT VII	65 ± 11	75	56	56	19	30	18	53	44

ACS: Acute coronary syndrome.

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