Biodegradable polymer sirolimus-eluting stents vs durable polymer everolimus-eluting stents in patients undergoing percutaneous coronary intervention: A meta-analysis of individual patient data from 5 randomized trials

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Abstract

Background Newest generation drug-eluting stents combine biodegradable polymers with ultrathin stent platforms in order to minimize vessel injury and inflammatory response. Evidence from randomized controlled trials suggested that differences in stent design translate into differences in clinical outcome. The aim of the present study was to evaluate the safety and efficacy of ultrathin strut, biodegradable polymer sirolimus eluting stents (BP SES) compared with thin strut, durable polymer everolimus-eluting stents (DP EES) among patients undergoing percutaneous coronary intervention (PCI).

Methods We pooled individual participant data from 5 randomized trials (NCT01356888, NCT01939249, NCT02389946, NCT01443104, NCT02579031) including a total of 5,780 patients, and performed a one-stage meta-analysis using a mixed effects Cox regression model.

Results At a median duration of follow-up of 739 days (interquartile range 365-1,806 days), target-lesion failure occurred in 337 (10.3%) and 304 (12.2%) patients treated with BP SES and DP EES (HR 0.86, 95%CI 0.71-1.06, $P = .16$). There were no significant differences between BP SES and DP EES with regards to cardiac death (111 (3.4%) vs 102 (4.1%); HR 1.05, 95%CI 0.80-1.37, $P = .73$), target-vessel myocardial infarction (136 (4.1%) vs 126 (5.0%), HR 0.79, 95%CI 0.62-1.01, $P = .061$), and clinically-driven target-lesion revascularization (163 (5.0%) vs 147 (5.9%); HR 0.94, 95%CI 0.75-1.18, $P = .61$). The effect was consistent across major subgroups. In a landmark analysis, there was no significant interaction between treatment effect and timing of events.

Conclusions In this patient-level meta-analysis of 5 randomized controlled trials, BP SES were associated with a similar risk of target-lesion failure compared with DP EES among patients undergoing PCI.

Study registration PROSPERO registry (CRD42018109098). (Am Heart J 2021;000:1–9.)

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Abbreviations: BP SES, biodegradable-polymer sirolimus-eluting stents; DES, drug-eluting stents; DP EES, durable-polymer everolimus-eluting stents; HR, hazard ratio; IPD, individual participant data; PCI, percutaneous coronary intervention; TLF, target lesion failure.

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Background

Refinements in stent design involving strut thickness, polymer matrix and antiproliferative substance improved clinical outcomes of patients undergoing percutaneous coronary intervention (PCI). The polymer matrix controls the release of the antiproliferative substance and has been associated with a chronic inflammatory response and delayed vascular healing in patients treated with early generation stents, clinically manifesting in the occurrence of very late stent thrombosis.[1,2] Biodegradable polymers have been developed to mitigate the risk of late events and have been combined with different stent platforms.

Randomized trials designed to test the safety and efficacy of ultrathin strut biodegradable-polymer sirolimus-eluting stents (BP SES) with respect to thin strut durable-polymer everolimus-eluting stents (DP EES) yielded conflicting findings. The BIOFLOW-V trial and the BIOSTEMI trial indicated a lower rate of target-lesion failure (TLF) at 1 year in patients treated with BP SES as compared to DP EES, whereas the BIOFLOW-II, PRISON IV, BIOSCIENCE, and BIORESORT trials showed noninferiority with regards to primary angiographic or composite clinical end points without significant differences between the 2 treatment arms.[3,4,5,6,7,8]

Against this background, we aimed to evaluate the safety and efficacy of ultrathin strut BP SES vs DP EES through a collaborative, individual participant data (IPD) meta-analysis, and examine the consistency of the findings across prespecified subgroups.

Methods

We developed and followed a standard protocol for this IPD meta-analysis. A detailed report that summarizes methods, search strategies, and additional information was published in PROSPERO registry (CRD42018109098). This protocol-based systematic review and IPD meta-analysis was conducted in accordance with the Preferred Reporting Items for a Systematic Review and Meta-analysis of Individual Participant Data (PRISMA-IPD) Development Group[9] and the Cochrane guidelines for IPD meta-analyses.[10] Patients and members of the public were not involved in the study. All individual studies included into the present analysis obtained ethics committee approval at each participating site. Only anonymized data were provided in patient level by the investigators of the original studies.

Information sources and search strategy

We developed a literature search strategy in PubMed by using medical subject headings (MeSH) and text words related to PCI. The search was supplemented by scrutinizing for potentially eligible trials in the reference lists of the selected trials. We developed a specific search algorithm by combining relevant key words and terms (supplemental material).

Study design and participants

Multicenter randomized controlled clinical trials (RCTs) comparing ultrathin strut biodegradable polymer sirolimus-eluting stents (BP SES vs durable polymer everolimus-eluting stents (DP EES) with at least 100 participants per study arm were deemed eligible. We included RCTs examining the general adult population (18 years or older) presenting with symptoms suggestive of either stable coronary artery disease (CAD) with indication for invasive coronary angiography and/or PCI or acute coronary syndrome (ACS) undergoing invasive management with timing of intervention consistent with existing recommendations at the time the study was conducted. We excluded prematurely stopped RCTs, nonrandomized and quasi-RCT studies. Trials solely recruiting patients with successfully recanalized chronic occlusions were excluded. We did not include unpublished trials or trials that have not undergone peer-review and been reported in full at the time of the systematic review.

Data collection process

We followed the recommended approach to contact the included study's authors.[11] Specifically, we contacted the corresponding authors of eligible trials explaining the study purpose and requesting their data. All IPD were saved on a secure server adhering to the Personal Health Information Protection Act (PHIPA).

Data items

We applied methods of standardizing and translating variables within the IPD data sets to ensure common scales or measurements across the included trials. We asked the contributing authors to provide data on patient-level on the following variables: ***patient characteristics*** (age, gender, diabetes mellitus, hypertension, hypercholesterolemia, smoking status, previous PCI, previous MI, previous coronary artery bypass graft (CABG), chronic kidney disease (CKD), hemodialysis, smoking status, diabetes mellitus (DM), previous stroke or TIA, renal failure, left ventricular ejection fraction, and indication to the procedure (ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEACS), stable CAD); ***anatomical and procedural characteristics*** (number of lesions, target-vessel location, Thrombolysis in Myocardial Infarction (TIMI) grade flow at presentation in the target lesion(s), number of implanted stents, total stent length per patient, stent diameter, lesion characteristics).

End point definitions and follow-up

The primary outcome of this IPD meta-analysis is target-lesion failure (TLF), a composite end point of cardiac death, target-vessel myocardial infarction (MI), and

clinically indicated target-lesion revascularization (TLR). The latter events were defined as device-related events. Secondary outcomes were: cardiac death, target-vessel MI, clinically-indicated TLR, all-cause death, any MI, any TLR, definite stent thrombosis, and definite or probable stent thrombosis. The definitions of the individual end points in the different trials are detailed in the supplemental material (Supplemental Table I). All serious adverse events in the individual trials have been independently adjudicated by a clinical events committee. Maximum available follow-up was 5 years for the BIOFLOW-II and the BIOSCIENCE trials, 3 years for the BIOFLOW-IV trial, 2 years for the BIOFLOW-V trial, and 1 year for the BIOSTEMI trial.

IPD integrity

We checked the data sets of individual trials for missing, invalid, out-of-range, or inconsistent items, or for any baseline imbalance and for discrepancies with any trial publication. Any discrepancies were resolved with the trial's personnel, to improve data quality and ensure that trials are represented accurately.

Statistical analysis

Individual patient data were pooled into a single data set and we performed the analysis according to the intention-to-treat principle including all randomized patients. Categorical variables were reported as counts and percentages and compared using multilevel random effect logistic regression or multilevel random effect ordered logistic regression in case of ordered variables to account for variation between trials. Continuous variables were reported as means and standard deviations and were compared using random effect linear regression. We performed an IPD meta-analysis with a one-stage approach by making an average inference across all trials while accounting for the clustering of participants within trials.[12] We assessed the outcomes using a mixed effects Cox regression model with baseline hazards stratified by trial and a random intercept to account for variation between trials in baseline risk, and a random slope to account for variation between trials in treatment effect.[13,14] Treatment effects are presented as hazard ratios and 95% confidence intervals (CI). We tested proportional-hazards assumptions after stratification by trial using Schoenfeld residuals.

Prespecified subgroup analyses of the primary outcome were performed according to age (≥65 years vs <65 years), sex, diabetes at baseline, clinical presentation (stable CAD vs ACS) and the presence of long lesion or small vessel. We separated out within-trial and across-trial interactions and based tests for subgroup-by-treatment interactions on within-trial interactions.[15] We performed a landmark analysis of the primary outcome with hazard ratios calculated separately for events that occurred up to 30 days, between 30 days and 1 year, between 1 year and 2 years, and between 2 years and 5 years after stent implantation. Landmark analyses were accompanied by a test for interaction between treatment and time (first 30 days vs subsequent periods). We conducted the analyses using R version 3.4.3 (R Foundation for Statistical Computing, Vienna, Austria) and Stata Release 14.2 (Stata Corp, College Station, TX).

Role of funding source

The BIOSCIENCE trial and the BIOSTEMI trial were investigator-initiated studies supported by an unrestricted grant from Biotronik, Bülach, Switzerland. The BIOFLOW-II, BIOFLOW-IV and BIOFLOW-V trials were industry-sponsored studies. No extramural funding was used to support this work. Biotronik had no role in data analysis, data interpretation, writing of the report, and the decision to submit for publication. The authors are solely responsible for the design and conduct of this study, all study analyses and drafting and editing of the paper.

Results

A total of 5 randomized controlled trials qualified for inclusion and provided data in individual patient-level in the present analysis (Supplemental Figure 1). We summarized IPD of the BIOFLOW-II, BIOFLOW-IV, BIOFLOW-V, BIOSCIENCE and BIOSTEMI trials. The study designs of the 5 individual trials have been detailed previously.[4,5,16,17,18] Patients undergoing PCI were randomly allocated to treatment with BP SES or DP EES in a 1:1 (BIOSCIENCE, BIOSTEMI) or 2:1 (BIOFLOW-II, BIOFLOW-IV, BIOFLOW-V) ratio. Inclusion and exclusion criteria of the individual trials are summarized in the supplemental material (Supplemental Table II). Each trial was approved by the institutional ethics committees of all participating sites and complied with the declaration of Helsinki. All participants provided written informed consent. The trials are registered with Clinicaltrials.gov (NCT01356888, NCT01939249, NCT02389946, NCT01443104, NCT02579031).

A total of 5,780 patients with 7,629 lesions undergoing PCI were randomly allocated to BP SES ($n = 3,279$, 4,300 lesions) or DP EES ($n = 2,501$, 3,329 lesions) between July 2011 and March 2018. The median duration of follow-up was 739 days (interquartile range 365-1, 806 days). Follow-up data at 5 years was available in 1,361 patients receiving BP SES and in 1,210 patients receiving DP EES. Completeness of follow-up at the longest reported duration of follow-up was 94.7%. Clinical and angiographic characteristics at baseline are summarized in Tables I and II. The mean age of patients amounted to 64.4 ± 11.1 years and 64.8 ± 11.2 years ($P = .25$) in patients treated with BP SES and DP EES, and 3,315 patients (57.4%) presented with an acute coronary syndrome. A

Table I. Baseline clinical characteristics

	Biodegradable polymer sirolimus-eluting stent N = 3,279	Durable polymer everolimus-eluting stent N = 2,501	*P* value
Age—yrs ± SD	64.4 ± 11.1	64.8 ± 11.2	.2525
Male gender—no. (%)	2504 (76.4)	1880 (75.2)	.2603
Diabetes mellitus—no. (%)	831 (25.4)	580 (23.2)	.9705
Insulin dependent—no. (%)	245 (7.5)	168 (6.7)	.7014
Hypertension—no. (%)	2232 (68.3)	1612 (64.7)	.6777
Hypercholesterolemia—no. (%)	2174 (66.4)	1637 (65.5)	.1804
Current smoker—no. (%)	981 (30.1)	742 (29.9)	.1432
Previous MI—no. (%)	692 (21.2)	436 (17.5)	.1315
Previous PCI—no. (%)	960 (29.3)	613 (24.6)	.0969
Previous CABG—no. (%)	191 (5.8)	129 (5.2)	.0855
Previous stroke or TIA—no. (%)	160 (4.9)	125 (5.0)	.3629
Renal failure—no. (%)	351 (10.9)	266 (11.0)	.3485
Left ventricular ejection fraction—%	56.1 ± 11.3	55.3 ± 12.1	.9321
Acute coronary syndrome—%	1817 (55.4)	1498 (59.9)	.3611
ST-segment elevation myocardial infarction—%	860 (26.2)	847 (33.9)	.4521

Hypercholesterolemia is defined as total cholesterol >5.0 mmol or 190 mg/dL or requiring treatment. MI, myocardial infarction. Renal failure as defined as eGFR <60 mL/min.

Table II. Angiographic and procedural characteristics

	Biodegradable polymer sirolimus-eluting stent N = 3,279	Durable polymer everolimus-eluting stent N = 2,501	*P* value
Number of lesions	4300	3329	
Target-vessel location per lesion—no. (%)			
Left main artery	40 (0.9)	36 (1.1)	.7813
Left anterior descending artery	1742 (40.5)	1437 (43.2)	.0598
Left circumflex artery	983 (22.9)	745 (22.4)	.7720
Right coronary artery	1493 (34.7)	1064 (32.0)	.0230
Multivessel disease	444 (13.7)	360 (14.6)	.6064
Number of treated lesions per patient—no. (%)			.7865
One	2477 (75.6)	1836 (73.5)	
Two	621 (19.0)	518 (20.7)	
Three	143 (4.4)	128 (5.1)	
≥Four	36 (1.1)	17 (0.7)	
Minimum TIMI flow pre per patient—no. (%)			.6767
0 or 1	698 (21.3)	702 (28.1)	
2	442 (13.5)	333 (13.3)	
3	2116 (64.7)	1448 (58.0)	
Number of stents per patient—mean (SD)	1.6 ± 0.9	1.7 ± 1.0	.1570
Total stent length per patient—mm (SD)	31.8 ± 21.3	35.4 ± 24.4	.0094
Maximum stent diameter—mm	3.3 ± 0.9	3.3 ± 0.9	.3122
Long lesion (at least 1 lesion >20 mm)	1859 (57.0)	1527 (61.2)	.8536
Small vessel (at least 1 vessel ≤3 mm)	2080 (63.6)	1611 (64.5)	.3367
Bifurcation lesion	507 (15.5)	420 (16.8)	.7010

considerable proportion of lesions was long lesions or located in small vessels (Table II). The distribution of lesion location, number of lesions and stents, and thrombolysis in myocardial infarction grade flow are summarized in Table II.

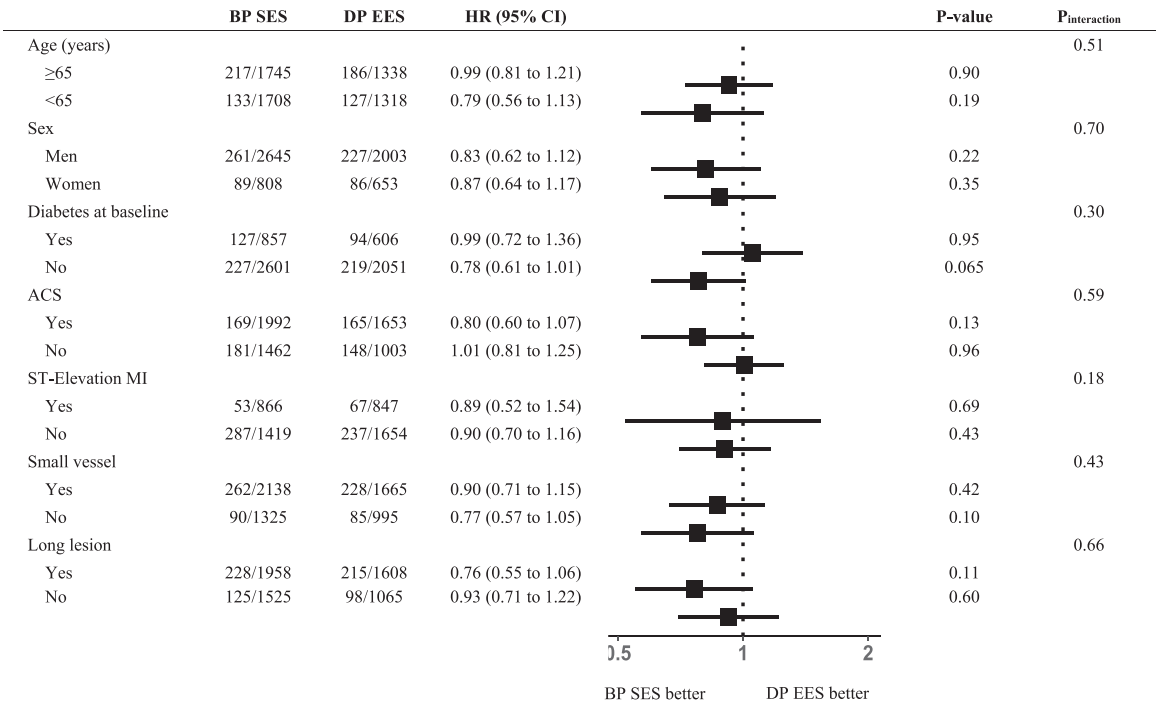
At longest follow-up, TLF occurred in 337 (10.3%) and 304 (12.2%) patients randomized to BP SES and DP EES (HR 0.86, 95%CI 0.71-1.06, $P = .16$) (Table III). For the individual components of TLF, the risk of cardiac death and clinically indicated TLR was comparable between the 2 treatment arms. However, there was a trend toward a lower rate of target-vessel MI among patients randomized to BP SES compared with DP EES (136 (4.1%) vs 126 (5.0%); HR 0.79, 95%CI 0.62-1.01, $P = 0.061$) (Table III).

A stratified analysis of the primary end point TLF demonstrated consistent findings across major sub-

Table III. Clinical outcomes at maximal follow-up after stent implantation

	Biodegradable polymer sirolimus-eluting stent *N* = 3,279	Durable polymer everolimus-eluting stent *N* = 2,501	Hazard Ratio [BP SES/DP EES] (95% CI)	*P* value	*P* value for proportional hazards test
Target-lesion failure	337 (10.3%)	304 (12.2%)	0.86 (0.71-1.06)	.16	.033
Cardiac death	111 (3.4%)	102 (4.1%)	1.05 (0.80-1.37)	.73	.41
Target vessel myocardial infarction	136 (4.1%)	126 (5%)	0.79 (0.62-1.01)	.061	.46
Clinically driven target lesion revascularization	163 (5%)	147 (5.9%)	0.94 (0.75-1.18)	.61	.89
Patient oriented clinical outcome	650 (19.8%)	525 (21%)	0.98 (0.88-1.11)	.79	.80
All-cause mortality	209 (6.4%)	161 (6.4%)	1.15 (0.93-1.41)	.19	.97
Any myocardial infarction	201 (6.1%)	188 (7.5%)	0.83 (0.68-1.01)	.066	.59
Any revascularization	386 (11.8%)	313 (12.5%)	0.98 (0.84-1.14)	.82	.11
Definite stent thrombosis	32 (1%)	31 (1.2%)	0.87 (0.53-1.44)	.59	.15
Probable stent thrombosis	52 (1.6%)	65 (2.6%)	0.81 (0.56-1.16)	.25	.91
Definite or probable stent thrombosis	82 (2.5%)	94 (3.8%)	0.83 (0.61-1.11)	.21	.52

Figure 1

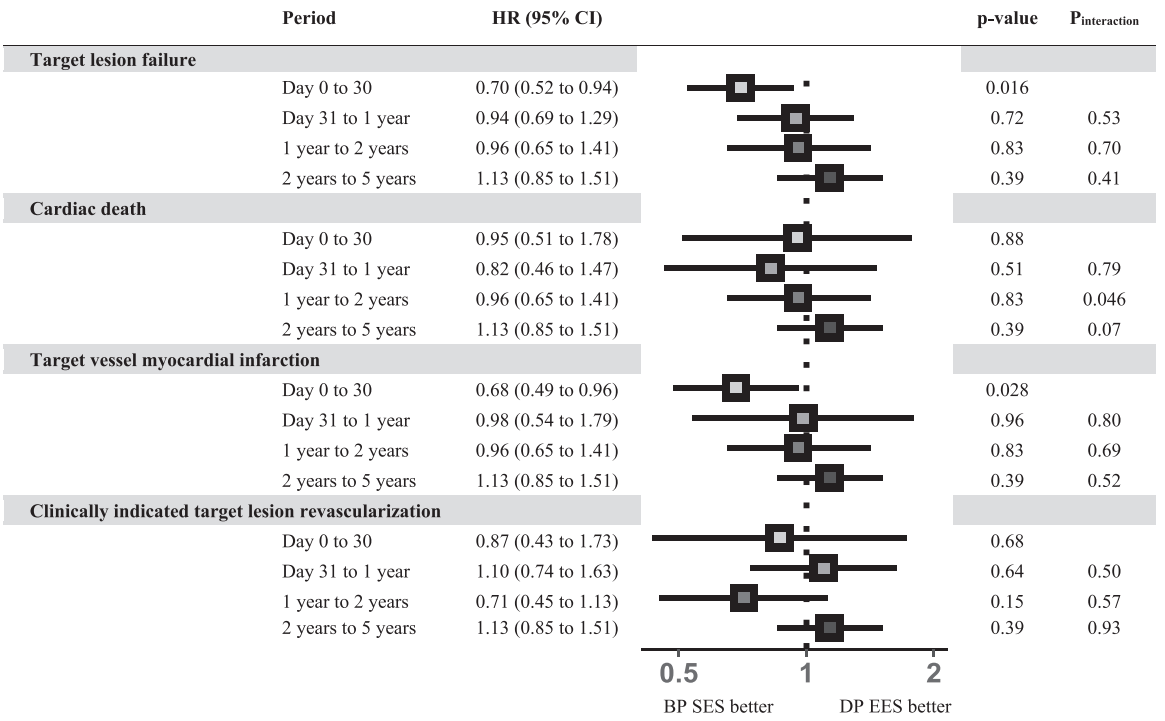


Subgroup analyses of the primary composite end point of target lesion failure. Post hoc subgroup analyses of the primary outcome are shown according to age (≥65 years vs <65 years), sex, diabetes status at presentation, clinical presentation (stable CAD vs ACS), long lesion and small vessel. Small vessels are defined as stent diameter in any lesion ≤3.0 mm. Long lesions are defined as total stent length in ay lesion ≥20 mm. *P* values are for within-trial interaction.

groups (Figure 1). There was no significant interaction between treatment effect and presentation with acute coronary syndrome.

A landmark analysis of the primary end point TLF and its components showed no significant interaction between treatment effect and time (Figure 2). There was no difference in rates of definite stent thrombosis between patients treated with BP SES vs DP EES during the first year after PCI (HR 1.23, 95% CI 0.64-2.40), nor between

Figure 2



Analysis of the primary composite end point of target lesion failure and its components. The hazard ratios are shown according to the time from randomization (30 days or less, 31 days to 1 year, 1 year to 2 years, and 2 years to 5 years). The black boxes represent hazard ratios for 30 days or less after randomization, the dark gray boxes represent hazard ratios for day 31 to 1 year from randomization, the light gray boxes represent hazard ratios for 1 to 2 years from randomization, and the white boxes represent hazard ratios for 2 to 5 years from randomization. Arrows indicate that the end of the confidence interval is more than 2. For the analyses from 30 days or less and 31 days to 1 year 5,780 patients were available, for the analysis from 1 year to 2 years 4,480 patients were available, and for the analysis from 2 years to 5 years a maximum of 3,146 patients were available.

1 and 5 years (HR 0.53, 95% CI 0.24-1.17) (*P* for interaction = .13).

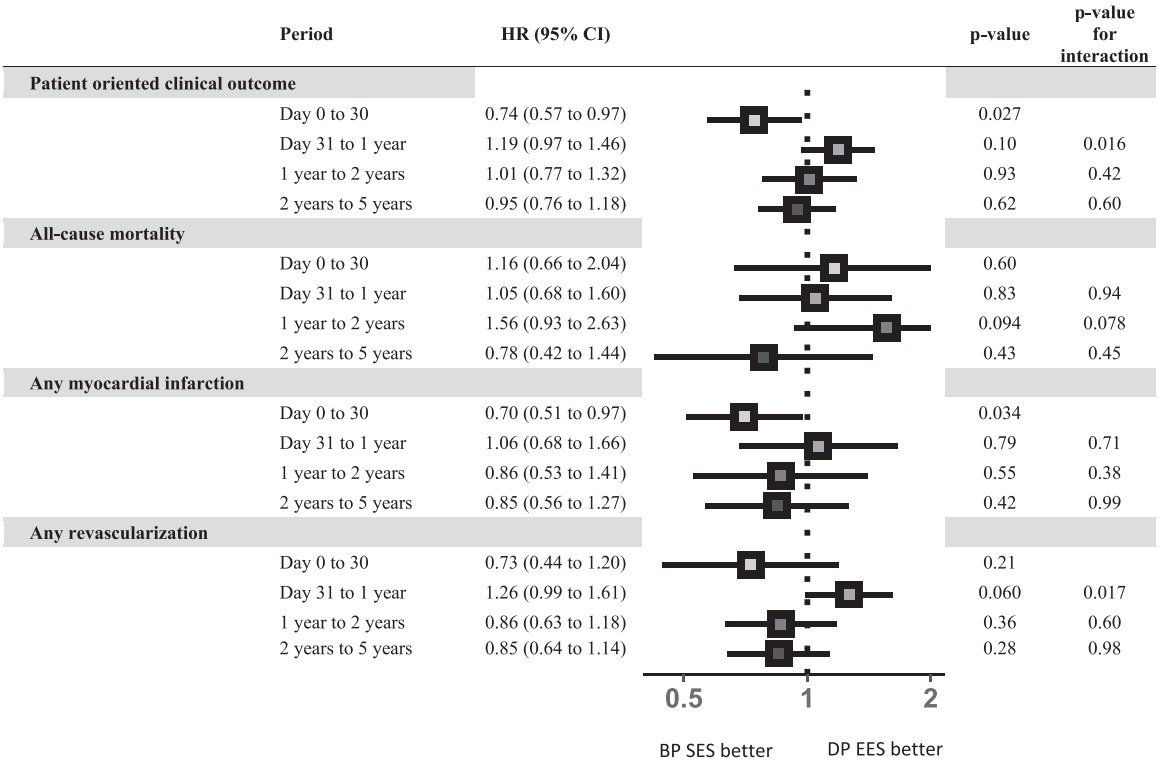
All-cause mortality was comparable between the 2 treatment arms. There was a trend toward a lower risk of any MI among patients randomized to BP SES compared with DP EES (201 (6.1%) vs 188 (7.5%); HR 0.83, 95% CI 0.68-1.01, *P* = .066). In a landmark analysis of patient-oriented clinical outcomes and its individual components, the treatment effect of BP SES on the occurrence of myocardial infarction was consistent across time (Figure 3).

Discussion

The main findings of the present IPD meta-analysis of 5 randomized trials can be summarized as follows: (1) among patients with stable coronary artery disease or acute coronary syndrome undergoing PCI, the risk of TLF and its individual components was similar between BP SES and DP EES without significant interactions across major subgroups. (2) Device-related events accounted for roughly half of all clinical events occurring throughout maximum duration of follow-up.

The present analysis represents the largest randomized data set of individual patients with stable coronary artery disease or acute coronary syndromes randomly allocated to treatment with Orsiro BP SES or Xience DP EES. Our findings demonstrate a similar risk of TLF among patients undergoing PCI with BP SES and DP EES at variance with the individual findings of the BIOFLOW-V trial and the BIOSTEMI trial.[4,19] In BIOFLOW-V, a significant difference in the risk of TLF at 1 year was driven by a lower rate of MI.[19] A reduction in clinically-indicated target lesion revascularization with BP SES compared with DP EES emerged beyond 1 year of follow-up.[20] While we didn't observe a difference in clinically-indicated target lesion revascularization in the present study, we ob-

Figure 3



Analysis of the primary composite end point of patient oriented clinical outcomes and its components. The black boxes represent hazard ratios for 30 days or less after randomization, the dark gray boxes represent hazard ratios for day 31 to 1 year from randomization, the light gray boxes represent hazard ratios for 1 to 2 years from randomization, and the white boxes represent hazard ratios for 2 to 5 years from randomization. Arrows indicate that the ends of the confidence interval are either less than 0.35 or more than 2.

served a trend toward a reduction in the risk of target vessel MI among patients randomized to BP SES as compared to DP EES which may point toward differences in neointimal healing. In view of the fact that this difference emerged before complete degradation of the polymer this effect may be related to the stent platform. Specifically, different mechanisms may account for a potential difference in the occurrence of MI according to strut thickness. Smaller strut thickness may result in less arterial injury, reduced inflammatory response, and improved endothelialization.[21] Thinner struts may furthermore have a lower thrombogenicity as compared to thicker strut stent platforms due to less local flow disturbances.[21] Finally, thinner stent struts may decrease the risk of side branch occlusion, which may result in periprocedural MI. Of interest, the findings of our IPD meta-analysis are in line with those of an aggregate meta-analysis of 10 trials that compared 3 different ultrathin strut drug-eluting stents with thicker strut second generation drug-eluting stents and showed a 28% relative risk reduction of MI among patients treated with ultrathin strut stents, which translated into a significant reduction of TLF.[22] The findings were largely driven by the Orsiro BP SES. However, it is important to acknowledge that only BP SES with a diameter of equal to or less than 3.0 mm feature a strut thickness of 60 μm, whereas BP SES with a diameter of more than 3.0 mm have a strut thickness of 80 μm, which is in the range of the strut thickness of DP EES. As a consequence, and based on the considerations above, we may expect a particularly marked difference in the occurrence of MI in patients treated with smaller stent diameters. By contrast, we found no significant interaction of the primary end point as a function of vessel size.

As opposed to the invariable effect of stent strut thickness, the benefit of the biodegradable polymer may take effect only after its complete resorption. An increased risk of very late stent thrombosis in patients treated with first generation durable polymer DES as compared to biodegradable polymer DES has been attributed to delayed arterial healing secondary to a chronic inflammatory response.[1,23,24] The present IPD meta-analysis

showed no evidence of a trend toward a differential in timing of the occurrence of definite stent thrombosis in patients treated with BP SES or DP EES. In contrast, 3-year outcome of the BIOFLOW-V trial indicated a lower incidence of definite late or very late stent thrombosis in patients treated with BP SES as compared with DP EES.[20]

Another important finding of the present study is that device-related events accounted for approximately half of all clinical events over maximum duration of follow-up. Consequently, such finding which seems to be unchanged compared with older randomized trials underscore the importance of secondary prevention measures in order to mitigate stent- and nonstent-related adverse events.

The present analysis importantly differs from a meta-analysis investigating a class effect of ultrathin strut vs thin strut DES irrespective of platform material, polymer characteristics, and antiproliferative substance of the individual stents.[22] In contrast, the present analysis is confined to RCTs comparing the Orsiro BP SES with the Xience DP EES and is based on individual participant data of 5 RCTs. It is important to note, that the Orsiro BP SES is not the only newer generation DES combining an ultrathin stent platform with a biodegradable polymer eluting sirolimus.[25,26] However, while different stent platforms share some properties of strut thickness and polymer degradation, they differ with regards to stent strut geometry, time to complete degradation of the polymer and drug-elution kinetics.

Limitations

The present analysis needs to be interpreted in light of the methodological differences between the individual trials. First, definitions of individual end points slightly vary across trials. We refrained from readjudicating the reported events and used the events as independently adjudicated for each single trial. Second, the 5 trials differed in terms of inclusion and exclusion criteria, hence introducing selection bias to different degree. The BIOSCIENCE and the BIOSTEMI trial were the only trials including patients with ST-segment elevation MI and complex coronary artery disease, and contributed the highest numbers of events. In addition, the use of intravascular imaging has not been prospectively recorded and may have introduced bias. Third, there were significant differences with regards to the extent of data monitoring between trials. The industry-sponsored BIOFLOW trials were subjected to a greater extent of data monitoring in order to comply with regulatory requirements, whereas the BIOSCIENCE trials was an investigator-initiated study. Fourth, data from the PRISON IV trial comparing BP SES with DP EES in 330 patients with successfully recanalized chronic occlusions was not included in the present meta-analysis. The study missed its primary noninferiority end point of in-segment late lumen loss for BP SES vs DP EES at 9 months, and there was a higher incidence of TLR in patients treated with BP SES. However, there was no significant difference between the 2 treatment arms with regards to target vessel failure, cardiac death, myocardial infarction and stent thrombosis, respectively. Fifth, follow-up was not complete; 5.3% of patients were lost to follow-up across all trials at the maximum duration of reported follow-up. In addition, follow-up throughout 5 years was limited to 2 trials. Hence, the precision in the risk estimates of rare events, such as definite stent thrombosis, may be limited. And finally, while the present IPD meta-analysis represents the largest study of patients treated with BP SES and DP EES, a larger sample size of approximately 12,000 o 15,000 individuals would be needed to detect a 20% relative difference in TLF between the 2 stents. Furthermore, the individual patient-level rather than study-level analysis reduces the effect of heterogeneity between trials.

Conclusions

In conclusion, the IPD meta-analysis of 5 randomized trials demonstrated a similar risk of TLF among patients undergoing PCI with BP SES compared with DP EES.

Funding

None.

Conflict of interest

TP has received research grants to the institution from Biotronik and Boston Scientific, and Research grants to the institution from Edwards Lifesciences, speaker fees from Biotronik and Boston Scientific, and consultancy from HighLife SAS, he is a proctor for Medtronic and Boston Scientific. *DEK* received institutional research/grant support from Biotronik, Boston Scientific, cardiovascular Systems, Inc., Medtronic; and personal consulting honoraria from Cardiovascular Systems, Inc., and Medtronic. *SW* received research grants to the institution from Amgen, Abbott, Biotronik, Boston Scientific, Edwards Lifesciences, Medtronic, Terumo and St Jude. All other authors have reported that they have no relationships to disclose.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ahj.2021.02.009.

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