Cardiovascular Revascularization Medicine 20 (2019) 865–870

Contents lists available at ScienceDirect

Cardiovascular Revascularization Medicine

Biodegradable-Polymer Versus Polymer-Free Drug-Eluting Stents for the Treatment of Coronary Artery Disease☆

Jason Nogic [a], Paul Thein [a], Sam Mirzaee [a], Andrea Comella [a], Kean Soon [b], James D. Cameron [a], Nick E.J. West [c], Adam J. Brown [a,*]

[a] Monash Cardiovascular Research Centre, Monash University and MonashHeart, Monash Health, Melbourne, Victoria, Australia
[b] Department of Cardiology, Eastern Health, Melbourne, Victoria, Australia
[c] Department of Interventional Cardiology, Royal Papworth Hospital, Cambridge, UK

ARTICLE INFO

Article history:
Received 7 November 2018
Received in revised form 7 December 2018
Accepted 11 December 2018

Keywords:
Drug-eluting stent
Biodegradable-polymer stent
Polymer-free stent
Coronary artery disease
Percutaneous coronary intervention

ABSTRACT

Background/purpose: Biodegradable-polymer (BP) and polymer-free (PF) drug eluting stents (DES) were developed to reduce the risk of delayed arterial healing observed with durable-polymer (DP) platforms. Although trials demonstrate BP-DES and PF-DES are non-inferior to DP-DES, there is limited data directly comparing these technologies. We performed a meta-analysis to assess the efficacy and safety of BP-DES versus PF-DES for the treatment of coronary artery disease.
Methods/materials: Electronic searches were performed identifying randomized trials comparing BP-DES with PF-DES. Co-primary efficacy endpoints were target vessel revascularization (TVR), target lesion revascularization (TLR) and angiographic in-stent late lumen loss (LLL). Co-secondary safety endpoints were all-cause death, myocardial infarction (MI) and stent thrombosis (ST).
Results: Of 208 studies, 5 met inclusion criteria including 1975 patients. At mean follow-up (14 ± 5 months), BP-DES were associated with significantly reduced rates of TVR (OR 0.58, 95%CI 0.37–0.92, $p = 0.02$), TLR (4.7% vs 9.5%) (OR 0.48, 95%CI 0.31–0.75, $p = 0.001$) and in-stent LLL (pooled mean difference −0.20 mm, 95%CI −0.24 to −0.16, $p < 0.001$). There was no difference in safety, including all-cause death (OR 1.24, 95%CI 0.68–2.28, $p = 0.48$), MI (OR 0.92, 95%CI 0.54–1.56, $p = 0.75$) or ST (OR 1.58, 95%CI 0.67–3.73, $p = 0.30$).
Conclusions: These data suggests that BP-DES are more efficacious when compared with PF-DES for the treatment of CAD.

1. Introduction

Chronic inflammation, endothelial dysfunction, delayed arterial healing and neoatherosclerosis are well-documented sequelae after implantation of durable polymer-coated (DP) drug eluting stents (DES) and may lead to premature in-stent restenosis (ISR) or stent thrombosis (ST) [1]. Although the mechanisms underlying both ISR and ST are multi-factorial [2], the durable polymer coating applied during stent manufacture to aid anti-proliferative drug elution is thought to contribute to DES failure [3]. Animal and human studies have demonstrated that DP can provoke increased arterial wall eosinophilic infiltration and chronic inflammation, leading to impaired healing and inadequate neointimal tissue strut coverage [4,5].

Biodegradable polymer (BP) and polymer-free (PF) DES were developed in an attempt to mitigate adverse clinical events associated with DP-DES [6]. With the purpose of controlling drug elution, through either simultaneous/subsequent dissolution or absence of the carrier polymer entirely, these devices were designed to eliminate the stimulus for chronic arterial inflammation. Thus, such technologies aimed to return the DES to a biologically inert bare metal stent (BMS) after the period of drug elution was complete. Multiple BP-DES and PF-DES platforms have been developed and undergone clinical use, with recent meta-analyses of randomized controlled trials (RCTs) showing both BP-DES and PF-DES to be safe and non-inferior in terms of efficacy when compared with conventional DP-DES [7,8]. However, as the number of BP- and PF-DES continues to grow, there is an increasing need for direct comparisons between these two new and competing technologies.

To date there have only been a limited number of studies comparing BP-DES with PF-DES, with pooled data of clinical outcomes comparing these two DES-coating strategies lacking. We therefore performed a systematic review and meta-analysis of all available randomized controlled trials to assess the efficacy and safety of BP-DES compared with PF-DES for the treatment of coronary artery disease (CAD).

☆ Conflict of interestNEJW reports having received consultancy fees from Abbott Vascular and Boston Scientific.AJB reports having received speaker fees from Abbott Vascular.All other authors report no conflict of interest.

* Corresponding author at: Monash Cardiovascular Research Centre and MonashHeart, Monash Health, 246 Clayton Road, Clayton, Melbourne, Victoria, Australia.
E-mail address: ajdbrown@me.com (A.J. Brown).

https://doi.org/10.1016/j.carrev.2018.12.010
1553-8389/

2. Methods

2.1. Data sources and search strategy

Comprehensive searches were performed of the electronic PubMed, MEDLINE, EMBASE and clinical trial databases through to June 2018. The search strategy also involved manual searches of major cardiovascular conference proceedings and reference lists of potential articles with no language restriction applied. Searches were performed using Medical Subject Heading (MeSH) and keywords that included but were not limited to; 'coronary artery disease', 'drug eluting stent', 'polymer-free', 'biodegradable-polymer' and 'percutaneous coronary intervention'. Results were combined with Boolean operators to refine search results. The study protocol was prospectively registered with PROSPERO (CRD42018100617) and adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [9]. An example search strategy, and results of the MEDLINE database search are provided in Supplementary Table S1.

2.2. Study selection

The inclusion criteria for studies were as follows: 1) randomized controlled trial, 2) studies comparing BP-DES with PF-DES for the treatment of de novo atherosclerotic coronary artery disease, and 3) studies reporting clinical and/or angiographic outcomes. Studies were excluded if bare-metal, durable-polymer or bioresorbable scaffolds were used as the comparator stent platform or the study was undertaken in an animal or experimental model.

2.3. Data items and collection process

Two review authors (JN and PMT) independently conducted literature searches based on the pre-specified selection criteria to identify potential trials for inclusion. All citations returned were first screened at the title and abstract level to determine suitability for inclusion. Full-text articles and/or conference proceedings were then retrieved and reviewed with studies meeting the inclusion criteria included in the analysis. Two authors (JN and PMT) independently extracted data from each included study. Baseline patient characteristics, treatment variables, indication for intervention, cardiovascular risk factors, sample size of trials, duration of dual anti-platelet therapy (DAPT) and clinical follow up were all recorded. The patient inclusion/exclusion criteria for each of the included trials are provided in Supplementary Table S2. Stent specific data was also extracted, including stent used (both arms of trials), scaffold material, eluted drug and biodegradation kinetics along with strut thickness where available. The senior author (AJB) verified the extracted data with any discrepancies resolved by consensus. Risk of bias for each trial included in the analysis was assessed by two authors (JN and AC) using the Cochrane Collaboration Assessment Tool [10]. Full details of the risk of bias assessment are presented in Supplement Fig. S1.

2.4. Study endpoints

Pre-specified efficacy and safety endpoints were determined prior to literature search with the primary efficacy co-endpoints being target vessel revascularization (TVR), target lesion revascularization (TLR)

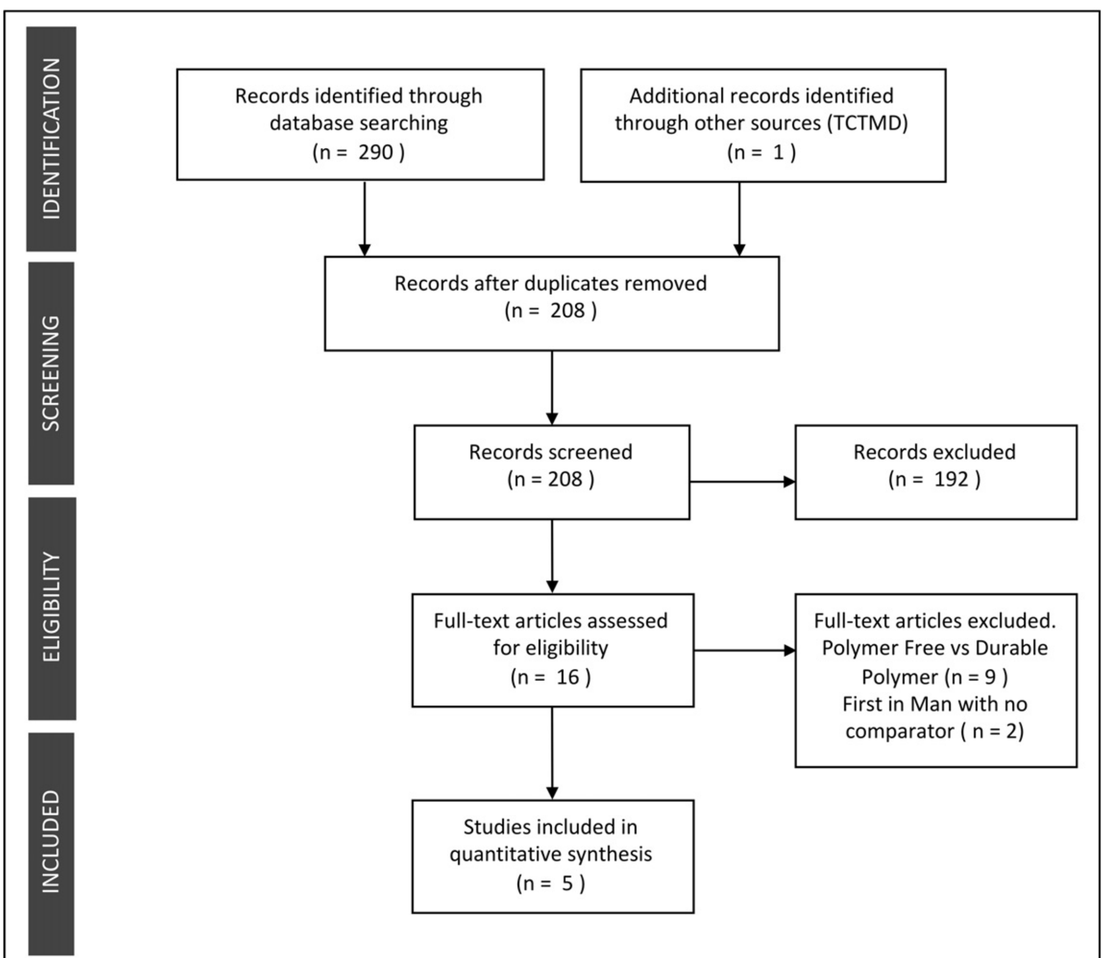

Fig. 1. Study flow chart. PRISMA flow diagram of review process and study selection.

and angiographic in-stent late lumen loss (LLL). Secondary safety co-endpoints consisted of all-cause mortality, myocardial infarction (MI), and definite or probable ST. Available study specific definitions are detailed in Supplemental Table S3.

2.5. Statistical analysis

Statistical analysis was performed using Review Manager (RevMan) version 5.3 in line with recommendations from the Cochrane Collaboration and PRISMA guidelines. Outcomes were analyzed using a Peto random effect model due to expected low event rates and summary estimates reported as pooled odds ratios (OR) with 95% confidence intervals (CI). Statistical heterogeneity was quantified with the I^2 statistic. Heterogeneity was defined as low, moderate or high based on I^2 values of 25%, 50% and 75% respectively as previously reported [11]. Analysis was performed on an intention-to-treat basis and publication bias was estimated visually by funnel plot assessment and the Harbord test. A two-sided p-value of <0.05 was considered significant.

3. Results

As shown in Fig. 1, of the 208 studies returned in the search, 5 studies were included in the final analysis. These RCTs included 1975 patients with 995 (50.4%) patients receiving BP-DES and 980 (49.6%) patients receiving PF-DES. Mean duration of follow up was 14 ± 5 months. The five trials included were; Individual Drug-Eluting Stent to Abrogate Restenosis (ISAR-TEST 3) [12], the RECOVERY trial [13], one single center trial [14] and two multi-center trials [15,16]. Baseline characteristics of the included trials are outlined in Table 1. The prevalence of acute coronary syndrome as the presenting complaint in the included studies ranged from 32 to 86%, and 20–32% of patients had diabetes mellitus. Full clinical and angiographic characteristics are presented in Tables 2 and 3 respectively.

3.1. Efficacy outcomes

Four trials reported the occurrence of TVR. In patients receiving the BP-DES there were 29 (3.7%) events compared with 49 (6.3%) events in patients receiving PF-DES. Pooled analysis demonstrated that patients receiving BP-DES had significantly lower rates of TVR when compared with patients receiving PF-DES (OR 0.58, 95%CI 0.37–0.92, $p = 0.02$, $I^2 = 67\%$) (Fig. 2A). Three studies reported rates of TLR, with 28 (4.7%) and 56 (9.5%) events in the BP-DES and PF-DES groups respectively. Similarly, this was associated with reduction in the rates of TLR for patients who had received BP-DES (OR 0.48, 95%CI 0.31–0.75, $p = 0.001$, $I^2 = 34\%$) (Fig. 2B). Finally, angiographic in-stent LLL was assessed in three trials at a time period that ranged between 6 and 13 months. The pooled mean difference (mm) between BP-DES and PF-DES was −0.20 mm (95%CI −0.24 to −0.16, $p < 0.0001$), demonstrating that BP-DES were associated with less in-stent LLL than PF-DES (Fig. 2C). All these results were replicated on sensitivity analysis with the removal of paclitaxel-based platforms with BP-DES associated with a reduction in TLR, TVR and in-stent LLL when compared with the PF-DES (Supplemental Fig. S2).

3.2. Safety outcomes

All five trials reported the occurrence of all-cause death, with an event rate of 24 (2.4%) in the BP-DES group compared with 19 (1.9%) in the PF-DES group at latest follow up. There was no significant difference in the rate of all-cause death between stent technologies (OR 1.24, 95% CI 0.68–2.28, $p = 0.48$, $I^2 = 0\%$) (Fig. 3A). Similarly, all five trials reported the occurrence of MI, with 27 (2.7%) and 29 (3.0%) events reported in the BP-DES and PF-DES cohorts respectively. Again, pooled analysis demonstrated no significant difference between the treatment strategies (OR 0.92, 95%CI 0.54–1.56, $p = 0.32$, $I^2 = 0\%$) (Fig. 3B). Finally, all five trials reported the occurrence of ST, with 13 (1.3%) and 8 (0.8%)

Table 1
Included study characteristics.

Author	Trial	Journal	Year	PF-DES (drug eluted)	PFS patients	BP-DES (drug eluted)	BPS patients	Total patients	Setting	DAPT duration	Primary endpoint	Follow-up (months)
Byrne	ISAR-TEST 3	Heart	2009	Cypher (sirolimus)	201	Cypher (sirolimus)	202	403	SA/UA	12 months (ASA/clopidogrel)	2 year TLR	24
Zhang	N/A	IJC	2012	YINYI (paclitaxel)	90	EXCEL (sirolimus)	90	180	SA/ACS	12 months (ASA/clopidogrel)	MACE	12
Chen	N/A	CT	2012	Dual-DES (sirolimus & probucol)	173	EXCEL (sirolimus)	173	346	SA/ACS	6 months (ASA/clopidogrel)	TVR	12
Zhang	N/A	IJC	2013	YINYI (paclitaxel)	327	EXCEL (sirolimus)	341	668	SA/ACS	12 months (ASA/clopidogrel)	2 year MACE	24
Tao	RECOVERY	TCT 2017	2017	NANO (sirolimus)	216	COMBO (sirolimus)	216	532	SA/UA	NR	In segment LLL 9 months	12

ACS: acute coronary syndrome, ASA: aspirin, BP-DES: biodegradable polymer drug eluting stent, CTI: cardiovascular therapeutics, DAPT: dual antiplatelet therapy, DES: drug-eluting stent, IJC: International Journal of Cardiology, IVUS: intravascular ultrasound, JIC: Journal of Interventional Cardiology, LLL: late lumen loss, SA: stable angina, MACE: major adverse cardiovascular event, MI: myocardial infarction, NSTEMI: non-ST segment elevation myocardial infarction, STEMI: ST elevation myocardial infarction, TCT: transcatheter cardiovascular therapeutics, TLR: target lesion revascularization, TVR: target vessel revascularization, UA: unstable angina.

Table 2
Patient baseline demographics.

Study	Age (yrs)	Male	Smoker	HTN	HChol	LVEF (%)	Diabetes	Prior MI	Prior PCI	Prior CABG	ACS presentation
Byrne 2009	67/66	78/78	18/16	67/72	71/71	54/54	27/29	33/32	NR/NR	13/10	32/32
Zhang 2012	64/67	49/58	45/47	60/69	49/58	68/67	30/28	10/7	4/4	0/0	46/51
Chen 2012	63/64	79/78	29/27	70/67	30/32	60/59	29/27	12/19	16/23	0/0	89/88
Zhang 2013	65/68	65/69	41/44	65/68	35/58	67/67	25/32	5/6	8/9	0/1	76/70
Tao 2017	58/59	68/63	45/43	54/60	13/17	60/60	20/21	NR/NR	10/9	NR/NR	87/86

ACS: acute coronary syndrome, CABG: coronary artery bypass grafting, HChol: hypercholesterolaemia, HTN: hypertension, LVEF: left ventricular ejection fraction, MI: myocardial infarction, NA: not applicable, NR: not-reported, PCI: percutaneous coronary intervention.
Data are reported as % or mean PF-DES/BD-DES.

events in the BP-DES and PF-DES groups, respectively, with no significant difference between the two platforms (OR 1.58, 95% CI 0.67–3.73, $p = 0.30$, $I^2 = 0\%$) (Fig. 3C). These results were replicated on sensitivity analysis with the removal of paclitaxel-based platforms with again no significant difference observed in all-cause death, MI and ST observed between the two groups (Supplemental Fig. S3).

3.3. Publication bias

Publication bias was estimated via visual funnel plot assessment and the Harbord Test with no clear evidence of bias demonstrated. However, the small number of trials included somewhat diminishes interpretation of publication bias.

4. Discussion

To our knowledge, this is the first meta-analysis of randomized controlled trials directly comparing clinical outcomes between BP-DES versus PF-DES for the treatment of coronary artery disease. We find that BP-DES have superior clinical efficacy at medium term follow-up when compared with PF-DES, as demonstrated by significantly lower rates of both TVR and TLR with corresponding less angiographic in-stent LLL. We also find that there was no significant difference in safety outcomes between DES platforms, as rates of all-cause death, MI and ST were similar. These results are important to practicing clinicians who are considering changing their default stent platforms to these increasingly available technologies.

The addition of anti-proliferative agents to bare metal stents heralded the arrival of DES, with clear reductions in the rates of angiographic and clinical restenosis [17,18]. Initial experience with paclitaxel and sirolimus revealed the importance of optimal drug dosing and release kinetics to maximize the anti-restenotic benefit [19]. However, the engineering challenges were clear, with the amount of drug adhering to the metallic stent surface minimal coupled with limited control of the rate or amount of drug eluted. Durable inert synthetic polymers were soon utilized to aid drug elution kinetics, allowing adequate drug loading and controlled drug elution [5]. However, data soon arose suggesting that the durable polymer coatings promoted a chronic arterial inflammatory response, resulting in delayed vascular healing and the pre-disposition for increased late clinical events [4,20]. This led to the development of biodegradable polymer and novel polymer free DES in an attempt to either remove, or limit polymer exposure and thus reducing chronic inflammation while still allowing steady and controlled drug elution over a set time period. However, this approach may have affected drug elution kinetics.

We find that BP-DES are associated with significantly reduced rates of TVR, TLR and angiographic LLL when compared with PF-DES. BP-DES typically have biodegradable polymers consisting of either poly-ι-lactic acid (PLLA) or poly(lactic-co-glycolic) acid (PLGA) that act to adhere the drug to the metallic stent while allowing for controlled and sustained delivery. Previous work has shown that in using biodegradable polymers, the majority of the drug is released within 1–6 months, with complete polymer degradation by 6–12 months [1]. In contrast, PF-DES have no polymer at all and instead use novel engineering techniques including textured microporous surfaces, crystallisation and even reservoirs to aid drug adherence, deposition and release kinetics [21]. Although pre-clinical and first-in-human testing of PF-DES have been favorable, the lack of any polymer coating in these technologies may have potential to impact the duration and intensity of drug delivery, especially when these devices are applied in more diverse patient cohorts. For example, previous studies have demonstrated that DES architecture and integrity can be disrupted during stent delivery to a calcified target lesion and has potential to lead to an increased risk of restenosis [22]. This effect may be even more relevant in PF-DES, where subtle changes to the stent surface may severely impact on the ability of the platform to retain the drug. Although exploration of this as a possible mechanism for our results is outside the scope of this study, it may explain the reduced efficacy of PF-DES seen in our analysis. Further research is now required to assess neointimal healing patterns in PF-DES, especially in challenging patient and lesion subsets.

Importantly, our analysis demonstrates that both PF-DES and BP-DES are equally safe platforms, with both having similar rates of all-cause death, MI and ST at latest follow up. Our findings mirror results of previous pooled analyses comparing different DES polymer coating strategies. In a recent meta-analysis of 16 RCTs including 19,886 patients comparing BP-DES with second generation DP-DES, no significant difference was observed between the two platforms in regards to the safety outcomes of cardiac death, MI or ST at a mean follow up of 26 months [7]. Although not as extensively studied, PF-DESs have shown similar results. We have recently shown that PF-DES are again as safe as DP-DES in an analysis of 12 RCTs including 6943 patients at a mean follow up of 43 months in regards to the safety co-endpoints of all cause death, ST and MI [8]. These results should reassure clinicians that although PF-

Table 3
Angiographic characteristics.

Study	LMCA	LAD	LCx	RCA	CTO	Bifurcation	Pre-dilation	Post-dilatation	PF-LL (mm)	BP-LL (mm)	PF-RVD (mm)	BP-RVD (mm)	Mean number of stents
Byrne 2009	0/0	40/46	30/22	31/32	7/8	25/23	NR/NR	NR/NR	14.3 ± 5.1	13.9 ± 7.2	2.75 ± 0.45	2.74 ± 0.49	NR/NR
Zhang 2012	0/0	72/71	25/25	33/29	NR/NR	NR/NR	N/R/NR	NR/NR	22.3 ± 11.3	22.3 ± 11.0	3.25 ± 0.48	3.16 ± 0.46	$1.28 \pm 0.49/1.27 \pm 0.52$
Chen 2012	6/7	77/79	10/9	7/6	7/5	NR/NR	54/51	100/100	31.4 ± 8.6	31.2 ± 8.9	2.74 ± 0.26	2.73 ± 0.27	$1.4 \pm 0.4/1.4 \pm 0.6$
Zhang 2013	0/0	49/48	22/20	29/31	NR/NR	NR/NR	84/87	19/20	27.9 ± 17.1	29.2 ± 16.6	3.28 ± 2.09	3.26 ± 2.40	$1.57 \pm 0.67/1.61/0.75$
Tao 2017	0/0	52/47	19/24	29/29	0/0	NR/NR	92/92	74/72	16.3 ± 7.2	17.1 ± 7.7	2.89 ± 0.52	2.89 ± 0.50	$1.2 \pm 0.4/1.2 \pm 0.4$

CTO: chronic total occlusion, DES: drug eluting stent, LAD: left anterior descending artery, LCx: left circumflex artery, LL: lesion length, LMCA: left main coronary artery, PFS: polymer-free stent, PPS: permanent polymer stent, RCA: right coronary artery, RVD: reference vessel diameter.
Data are reported as % or mean PF-DES/BD-DES.

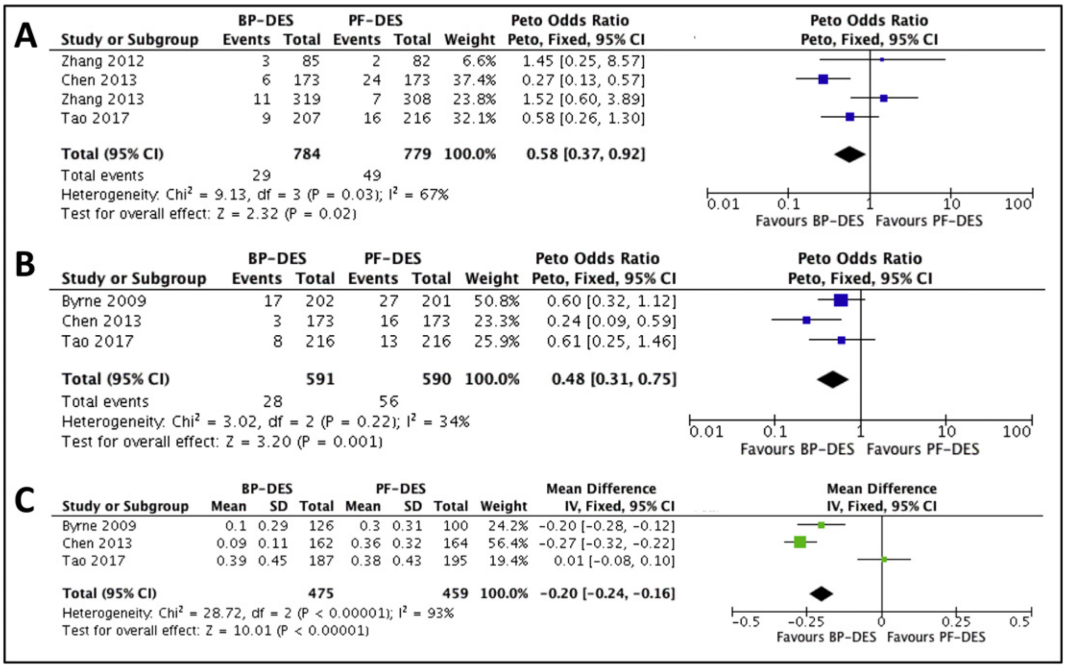

Fig. 2. Efficacy outcomes. Forest plot displaying summary odds ratio (OR) and 95% confidence intervals (CI) for the occurrence of (A) target vessel revascularisation (TVR), (B) target lesion revascularisation (TLR) and (C) in-stent late lumen loss (LLL).

DES may be associated with higher rates of repeat intervention, they are still safe choices and should still be considered in specific patient cohorts. The LEADERS-FREE trial investigated the use of the BioFreedom PF-DES (Biosensors Europe) compared with a BMS in patients with high bleeding risk undergoing PCI utilizing a short one month duration of DAPT [23]. In this randomized controlled trial of 2466 patients, PF-DES was found to be superior to BMS with respect to the primary safety endpoint of a composite of cardiac death, MI and ST. In regard to efficacy outcomes, the PF-DES was superior in the primary endpoint of clinically driven TLR, revealing a clear subset of patients that benefit from this technology.

Interventional cardiologists currently have a multitude of choices when selecting DES for coronary revascularization procedures. Given the extensive clinical experience with current generation everolimus-, biolimus-A9- or zotarolimus-eluting DP-DES, these platforms will likely

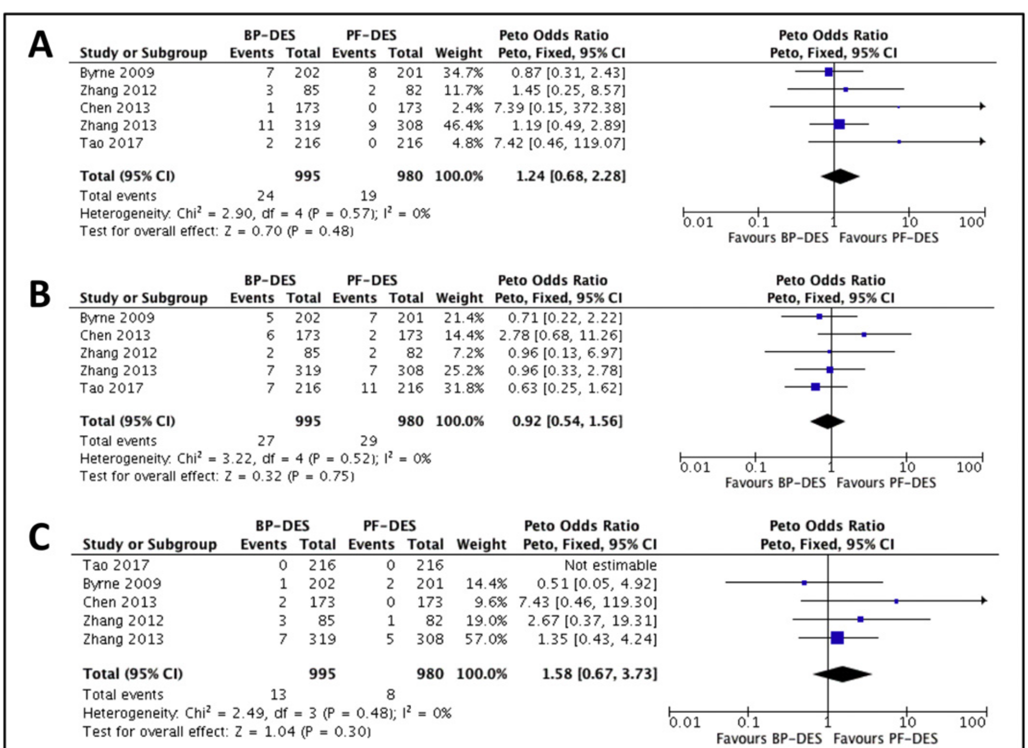

Fig. 3. Safety outcomes. Forest plot displaying summary odds ratio (OR) and 95% confidence intervals (CI) for the occurrence of (A) all-cause death, (B) myocardial infarction and (C) stent thrombosis.

remain the catheterization lab 'workhorse' for the near future. However, there is an increasing presence of BP-DES and PF-DES that are currently (or soon to be) commercially available, with trials showing non-inferiority or even superiority when compared with DP-DES. Our results are important in that although they show both platforms to be as safe as each other, BP-DES may be superior to PF-DES with regard to the efficacy outcomes of TVR, TLR and decreased in-stent LLL. These results suggest that if clinicians have a choice between the two platforms, apart from specific mentioned subgroups, BP-DES should currently be preferred.

5. Limitations

The results of this study should be interpreted in light of some limitations. Firstly, anti-platelet therapy and duration were inconsistently reported between trials. One study did not report DAPT duration or agents used, and one study only utilized 6 months of DAPT, outside of guideline recommendations of 12 months. This inconsistency may have had an impact on clinical events as it is known that shorter duration DAPT increases risk of ischaemic clinical events. Secondly, only a limited number of BP-DES and PF-DES platforms were assessed in the included trials, some of which are not available for use in European and North American markets and these results may not directly apply to other platforms that are not included in the analysis.

6. Conclusion

BP-DES are associated with significantly lower rates of TVR, TLR and angiographic in-stent LLL when compared with PF-DES for the treatment of coronary artery disease. These stent platforms should be preferentially considered by interventional cardiologists in attempts to maximize clinical efficacy without compromising on safety.

Acknowledgements

None.

Funding

AJB is supported by an Early Career Practitioner Fellowship from Monash Health and Monash University.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.carrev.2018.12.010.

References

[1] Nogic J, McCormick LM, Francis R, Nerlekar N, Jaworski C, West NEJ, et al. Novel bioabsorbable polymer and polymer-free metallic drug-eluting stents. J Cardiol 2018;71(5):435–43.
[2] Byrne RA, Joner M, Kastrati A. Stent thrombosis and restenosis: what have we learned and where are we going? The Andreas Gruntzig lecture ESC 2014. Eur Heart J 2015;36(47):3320–31.
[3] John MC, Wessely R, Kastrati A, Schomig A, Joner M, Uchihashi M, et al. Differential healing responses in polymer- and nonpolymer-based sirolimus-eluting stents. JACC Cardiovasc Interv 2008;1(5):535–44.
[4] Finn AV, Nakazawa G, Joner M, Kolodgie FD, Mont EK, Gold HK, et al. Vascular responses to drug eluting stents: importance of delayed healing. Arterioscler Thromb Vasc Biol 2007;27(7):1500–10.
[5] Rizas KD, Mehilli J. Stent polymers: do they make a difference? Circ Cardiovasc Interv 2016;9(6).
[6] Lagerqvist B, James SK, Stenestrand U, Lindbäck J, Nilsson T, Wallentin L. Long-term outcomes with drug-eluting stents versus bare-metal stents in Sweden. N Engl J Med 2007;356(10):1009–19.
[7] El-Hayek G, Bangalore S, Casso Dominguez A, Devireddy C, Jaber W, Kumar G, et al. Meta-analysis of randomized clinical trials comparing biodegradable polymer drug-eluting stent to second-generation durable polymer drug-eluting stents. JACC Cardiovasc Interv 2017;10(5):462–73.
[8] Nogic J, Baey YW, Nerlekar N, Ha FJ, Cameron JD, Nasis A, et al. Polymer-free versus permanent polymer-coated drug eluting stents for the treatment of coronary artery disease: a meta-analysis of randomized trials. J Interv Cardiol 2018;31(5):608–16.
[9] Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ 2009;339:b2700.
[10] Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343:d5928.
[11] Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003;327(7414):557–60.
[12] Byrne RA, Kufner S, Tiroch K, Massberg S, Laugwitz KL, Birkmeier A, et al. Randomised trial of three rapamycin-eluting stents with different coating strategies for the reduction of coronary restenosis: 2-year follow-up results. Heart 2009;95(18):1489–94.
[13] RECOVERY: a randomized trial of bioabsorbable polymer-based metallic DES with a luminal CD34+ antibody coating vs. a polymer-free metallic DES in patients with coronary artery disease. In: Tao LZL, Yenhua L, Hui L, Wei L, Lau H, Xu B, editors. TCT 2017. Denver, Colorado, USA: JACC; 2017.
[14] Zhang L, Yuan J, Liu G, Zhong JP, Yin YH, She Q, et al. One-year clinical outcome of a randomized trial of polymer-free paclitaxel-eluting stents versus biodegradable polymer-based rapamycin-eluting stents in patients with coronary heart disease. J Interv Cardiol 2012;25(6):604–10.
[15] Zhang Y, Shen J, Li Z, Zhu A, Yuan Y, Yue R, et al. Two-year clinical outcomes of different drug-eluting stents with different polymer coating strategies in coronary artery heart disease: a multi-centre, randomised, controlled clinical trial. Int J Cardiol 2013;168(3):2646–52.
[16] Chen SL, Ye F, Zhang JJ, Zou JJ, Qian XS, Li F, et al. Real polymer-free sirolimus- and probucol-eluting versus biodegradable polymer sirolimus-eluting stents for obstructive coronary artery disease: DKPLUS-Wave 1, a multicenter, randomized, prospective trial. Cardiovasc Ther 2013;31(4):193–200.
[17] Stettler C, Wandel S, Allemann S, Kastrati A, Morice MC, Schömig A, et al. Outcomes associated with drug-eluting and bare-metal stents: a collaborative network meta-analysis. Lancet 2007;370(9591):937–48.
[18] Kastrati A, Dibra A, Spaulding C, Laarman GJ, Menichelli M, Valgimigli M, et al. Meta-analysis of randomized trials on drug-eluting stents vs. bare-metal stents in patients with acute myocardial infarction. Eur Heart J 2007;28(22):2706–13.
[19] Serruys PW, Sianos G, Abizaid A, Aoki J, den Heijer P, Bonnier H, et al. The effect of variable dose and release kinetics on neointimal hyperplasia using a novel paclitaxel-eluting stent platform: the Paclitaxel In-Stent Controlled Elution Study (PISCES). J Am Coll Cardiol 2005;46(2):253–60.
[20] Nebeker JR, Virmani R, Bennett CL, Hoffman JM, Samore MH, Alvarez J, et al. Hypersensitivity cases associated with drug-eluting coronary stents: a review of available cases from the Research on Adverse Drug Events and Reports (RADAR) project. J Am Coll Cardiol 2006;47(1):175–81.
[21] Worthley SG, Abizaid A, Kirtane AJ, Simon DI, Windecker S, Brar S, et al. First-in-human evaluation of a novel polymer-free drug-filled stent: angiographic, IVUS, OCT, and clinical outcomes from the RevElution study. JACC Cardiovasc Interv 2017;10(2):147–56.
[22] Wiemer M, Butz T, Schmidt W, Schmitz KP, Horstkotte D, Langer C. Scanning electron microscopic analysis of different drug eluting stents after failed implantation: from nearly undamaged to major damaged polymers. Catheter Cardiovasc Interv 2010;75(6):905–11.
[23] Urban P, Meredith IT, Abizaid A, Pocock SJ, Carrie D, Naber C, et al. Polymer-free drug-coated coronary stents in patients at high bleeding risk. N Engl J Med 2015;373(21):2038–47.