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Drug-Eluting Versus Bare Metal Stents in Saphenous Vein Graft Intervention: An Updated Comprehensive Meta-Analysis of Randomized Trials☆

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ABSTRACT

Background: Drug eluting stents (DES) are preferred over bare metal stents (BMS) for native coronary artery revascularization unless contraindicated. However, the preferred stent choice for saphenous venous graft (SVG) percutaneous coronary interventions (PCI) is unclear due to conflicting results.
Methods: PubMed, Clinical trials registry and the Cochrane Center Register of Controlled Trials were searched through June 2018. Seven studies ($n = 1639$) comparing DES versus BMS in SVG-PCI were included. Endpoints were major adverse cardiac events (MACE), cardiovascular mortality, all-cause mortality, myocardial infarction (MI), target vessel revascularization (TVR), target lesion revascularization (TLR), in-stent thrombosis, binary in-stent restenosis, and late lumen loss (LLL).
Results: Overall, during a mean follow up of 32.1 months, there was no significant difference in the risk of MACE, cardiovascular mortality, all-cause mortality, MI, stent thrombosis, TVR and TLR between DES and BMS. However, short-term follow up (mean 11 months) showed lower rate of MACE (OR 0.66 [0.51, 0.85]; $p = 0.002$), TVR (OR 0.47 [0.23, 0.97]; $p = 0.04$) and binary in-stent restenosis (OR 0.14 [0.06, 0.37]; $p < 0.0001$) in DES as compared with BMS. This benefit was lost on long-term follow up with a mean follow up 35.5 months.
Conclusion: In this meta-analysis of SVG-PCI, DES use was associated with similar MACE, cardiovascular mortality, all-cause mortality, MI, in-stent thrombosis, TVR and TLR compared with BMS during long-term follow up. There was high incidence of MACE noted in both DES and BMS suggesting a need for exploring novel strategies to treat SVG disease to improve clinical outcomes.

1. Introduction

Percutaneous coronary intervention (PCI) is first line therapy for obstructive saphenous vein graft (SVG) disease since repeat coronary artery bypass graft (CABG) carries a higher risk of complications. However, PCI of SVG lesions carries a high risk of in-stent restenosis, peri-procedural myocardial infarction (MI) and no-reflow [1,2]. SVG-PCI is independently associated with higher procedural complications and in-hospital mortality compared with native vessel PCI [3]. Moreover, the optimal treatment using either drug eluting stent (DES) or bare metal stent (BMS) for SVG lesions has not been established. There has been conflicting evidence regarding the efficacy and safety of DES compared with BMS based on the number of observational and randomized controlled trials (RCTs). Three previously conducted RCTs demonstrated reduction in target vessel (TVR) and target lesion revascularization (TLR) with the use of DES [4–6]. In contrast, two recent trials [7,8], including the one that used mostly newer generation DES, showed no difference in outcomes between DES and BMS. The differences in findings between the trials are possibly due to different durations of follow up. Since SVG disease is progressive, the importance of late outcomes following PCI has been clinically more important than the short-term outcomes. A meta-analysis reported lower MACE, all-cause mortality and TLR with DES compared with BMS [9].

☆ Disclosures: none

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However, it predominantly included observational studies which can potentially lead to selection bias and confounding. Furthermore, the results of prior meta-analyses have been conflicting. Two meta-analyses demonstrated a reduction in TVR rate with DES [10,11], whereas the most recent meta-analysis showed no difference in outcomes between DES and BMS [12]. Considering the conflicting results, we performed a comprehensive meta-analysis including a new RCT and long-term data of ISAR-CABG [18], both published in 2018, comparing the efficacy and safety of DES versus BMS for SVG-PCI with the longest follow up. Additionally, we assessed the short-term versus long-term outcomes as well as overall outcomes.

2. Methods

This meta-analysis was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statements for reporting systematic reviews [13]. National Library of Medicine PubMed, Clinicaltrials.gov and the Cochrane Central Register of Controlled Trials were searched through June 2018 to include studies comparing DES with BMS in SVG-PCI. The key words used for searching studies were "saphenous venous graft", "percutaneous coronary intervention", "drug eluting stents", "bare metal stents", "randomized controlled trials", "SVG", "PCI", "DES" and "BMS". In addition to computerized search, we manually reviewed the reference lists and related articles of all retrieved studies for completeness of the searching process. Two independent authors (SB and HBP) reviewed all titles from the search results, and articles were selected for final data extraction. The study selection process is outlined in Fig. 1. RCTs comparing DES with BMS in SVG-PCI were included in this meta-analysis. Endpoints were major adverse cardiac events (MACE), target vessel failure (TVF), cardiovascular mortality, all-cause mortality, myocardial infarction (MI), TVR, TLR and late lumen loss (LLL). The definitions of primary and secondary outcomes were summarized in Table 1. TVF was used as MACE outcome for DIVA trial due to the similarity of MACE definition in other trials with the TVF in DIVA (primary outcome of DIVA was TVF)

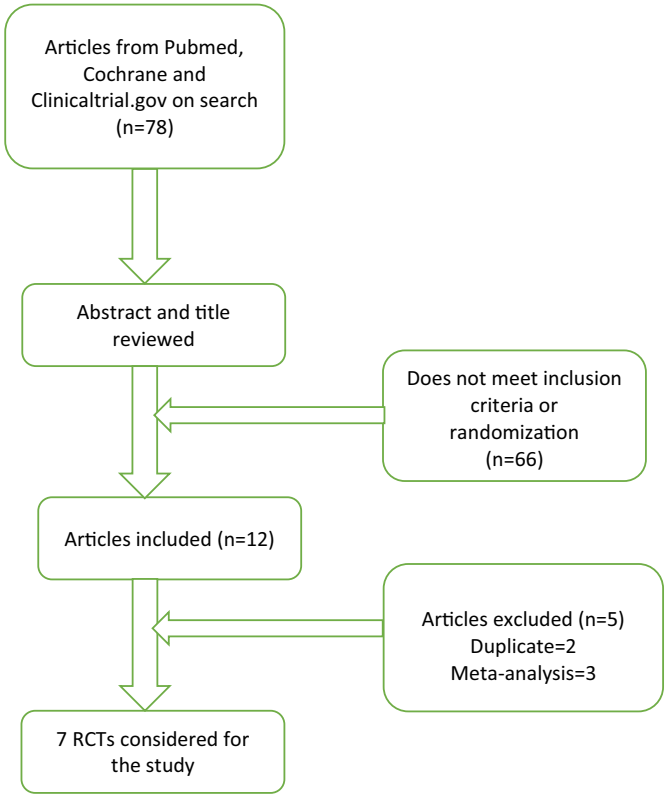


Fig. 1. Study selection flow chart.

Table 1
Study characteristics of included trials.

Trial	DIVA	ADEPT	BASKET-SAVAGE	ISAR-CABG	SOS (long-term follow up)	DELAYED RRISC	BASKET
Number of patients	597 (DES 292, BMS 305)	57 (DES 30, BMS 27)	173 (DES 89, BMS 84)	610 (DES 303, BMS 307)	80 (DES 41, BMS 39)	75 (DES 38, BMS 37)	47 (DES 34, BMS 13)
Publication/reporting year	2017	2018	2016	2018	2011	2006	2009
Follow up length (months)	32	12	36	60	35	32	18
Primary outcomes	TVF (cardiac death, target vessel MI, TVR)	In-stent LLL at 6 months	MACE (cardiac death, non-fatal MI, TVR)	MACE (death, MI, ischemia driven TLR)	TVF (cardiac death, MI, TVR)	All-cause mortality	MACE (cardiac death, non-fatal MI, non-MI-related TVR)
Differences in outcomes between BMS and DES	No difference in TVF at 32-month 34% (BMS) vs. 37% (DES) ($p = 0.46$)	No difference in LLL at 6 months No difference in 12-month MACE (cardiac death, MI, emergent CABG, clinically driven TVR)-22.2% (BMS) vs. 26.6% (DES) ($p = 0.70$)	3-year MACE- 29.8% (BMS) vs. 12.4% (DES) ($p = 0.0012$) 3-year TVR significantly lower with DES ($p < 0.001$)	60-month MACE 53.6% (BMS) vs. 55.5% (DES) ($p = 0.89$)	35-month TVF 72% (BMS) vs. 34% (DES), ($p = 0.001$) 35-month MI, TVR, TLR significantly lower with DES	32-month all-cause mortality 0% (BMS) vs. 29% (DES) ($p < 0.001$) No difference in 32-month TVR	18-month MACE 62% (BMS) vs. 21% (DES), ($p = 0.007$) TVR 46% (BMS) vs. 18% (BMS) ($p = 0.045$)
Follow up completion rate %	99 (at 12 months)	70	100 (at 12 months)	91.9	99	100	99.6

DES: drug eluting stent; BMS: bare metal stent; TVF: target vessel failure; TVR: target vessel revascularization; TLR: target lesion revascularization; MACE: major adverse cardiac events; MI: myocardial infarction; LLL: late lumen loss.

Table 2
Baseline patient characteristics of the individual trial.

DES vs BMS	DIVA	ADEPT	BASKET-SAVAGE	ISAR-CABG	SOS (long-term follow up)	DELAYED RRISC	BASKET
Sample size	292/305	30/27	89/84	303/307	41/39	38/37	34/13
Age (years) mean	69/68	73/73	71/71	71/72	66/67	73/72	71/71
Male %	99/100	83/93	90/89	87/84	100/100	82/89	79/100
Hypertension %	95/97	67/56	91/89	71/73	93/95	58/57	88/83
Hyperlipidemia %	98/96	63/56	85/87	88/86	98/95	87/84	79/92
Diabetes Mellitus %	59/61	33/33	46/41	37/35	44/44	16/14	29/17
Smoker %	21/24	17/11	–	8/6	29/23	5/11	18/0
Previous MI %	56/50	50/44	66/60	56/55	56/59	45/41	59/46
BMI (mean)	31/30	–	–	28/27	30/29	26/26	–
Stable angina %	40/34	47/41	51/55	62/60	29/33	40/49	65/31
ACS %	53/55	37/44	37/39	38/40	63/57	60/51	35/69
DAPT duration (months)	12/1	–	–	6/6	6/1	At least 2 months/12	6/6
Graft age (years)	13.9/12.8	16.5/15.9	12/14	13.4/13.7	11/12	12.4/12.6	–
Target graft (%)		–					–
LAD	21/24		15/17	32/31	29	19/12	
LCx/OM	41/41		45/50	35/36	38	32/53	
RCA	38/35		40/33	33/33	34	49/35	

MI: myocardial infarction; BMI: body mass index; ACS: acute coronary syndrome; DAPT: dual antiplatelet therapy; LAD: left anterior descending artery; LCx: left circumflex artery; OM: obtuse marginal artery; RCA: right coronary artery.

and the term MACE was not used in the DIVA trial. To be selected for this meta-analysis, a study had to meet all the following inclusion criteria: (1) study comparing outcomes of DES with BMS for SVG-PCI and (2) study reporting either clinical or angiographic outcomes. After identifying the relevant articles, data from the trials including authors, publication year, design, sample size, follow up duration, patient characteristics and procedural outcomes were extracted. Two reviewers (SB and HBP) independently extracted data and assessed outcomes. The inter-rater agreement was 95%, and disagreements were resolved by consensus.

The Odds ratio (OR), and mean difference with the corresponding 95% confidence interval (CI) was calculated for each endpoint and a p value of ≤0.05 was considered statistically significant. RevMan 5.3 statistical software was used for data analysis (The Cochrane Collaboration, Copenhagen, Denmark). Heterogeneity of the studies was assessed for each endpoint. Studies that were homogeneous for an endpoint were analyzed by the Mantel-Haenszel fixed effect model and heterogeneous endpoints were analyzed by the random effect model. Publication bias was assessed using the Funnel plot method shown in supplementary file 1, without any evidence of publication bias. Outcomes at the longest follow up were considered for the overall analysis. Studies with follow up ≤12 months (except for SOS 2009 trial where 18 months data were included) and >12 months are considered as short and long-term follow up, respectively, and a sensitivity analysis was performed using short and long term follow up data separately.

3. Results

Seven RCTs involving 1639 patients met the inclusion criteria and were analyzed [4–8,14,15]. Study details, baseline patient characteristics, and procedural outcomes of each study are shown in Tables 1, 2 and 3 respectively. Overall, 337/827 (40.7%) patients in the DES group and 346/812 (42.6%) in the BMS group experienced MACE. After a mean follow up of 32.1 months, there was no significant difference in the incidence of MACE (OR 0.85 [0.65, 1.12]; $p = 0.25$), cardiovascular mortality (OR 1.02 [0.77, 1.34]; $p = 0.90$), all-cause mortality (OR 1.09 [0.89, 1.32]; $p = 0.40$), MI (OR 0.81 [0.51, 1.31]; $p = 0.39$), stent thrombosis (OR 1.13 [0.65, 1.96]; $p = 0.67$), TVR (OR 0.73 [0.48, 1.10]; $p = 0.13$) and TLR (OR 0.99 [0.57, 1.73], $p = 0.97$) between DES and BMS groups (Fig. 2A–G). The short-term follow up (mean 11 months) of 1592 patients showed lower rate of MACE (OR 0.66 [0.51, 0.85]; $p = 0.002$), TVR (OR 0.47 [0.23, 0.97]; $p = 0.04$) and binary in-stent re-stenosis (OR 0.14 [0.06, 0.37]; $p < 0.0001$) in DES group as compared with BMS (Fig. 3A–I). However, this benefit was lost at long-term follow up (mean 35.5 months) [MACE (OR 0.71 [0.42, 1.19]; $p = 0.19$), TVR

Table 3
Procedural characteristics and outcomes of the individual study.

	DIVA	ADEPT	BASKET-SAVAGE	ISAR-CABG	SOS (long-term follow up)	DELAYED RRISC	BASKET
Stent type	Second generation (89%) First generation (6%)	First generation	First generation	First generation	First generation	First generation	First generation
DES type	ZES, EES	PES	PES	PES, SES, BP-SES	PES	SES	PES, SES
BMS type	–	STENTYS Self-expandable	Liberté	Vision, Driver, Yukon, 100 μm	Express2, 132 μm	Bx Velocity, 140 μm	–
Stents used per patient DES/BMS	1.3/1.4	–	1.7/1.5	–	–	1.58/1.46	2.1/2.4
Stent length in target lesion per patient (mm) DES/BMS	27/26.6	–	31/30	–	28/29	36.9/33.4	41/46
Embolic protection device % DES/BMS	69/69	20/15	69/63	<5	51/56	79/84	–
Procedural success % DES/BMS	94/95	87/93	–	–	96	94/90	–
Angiographic follow up DES/BMS	Not performed	6 months	Not performed	6–8 months, 72%	12 months, 80%	6 months, 96%	Not performed

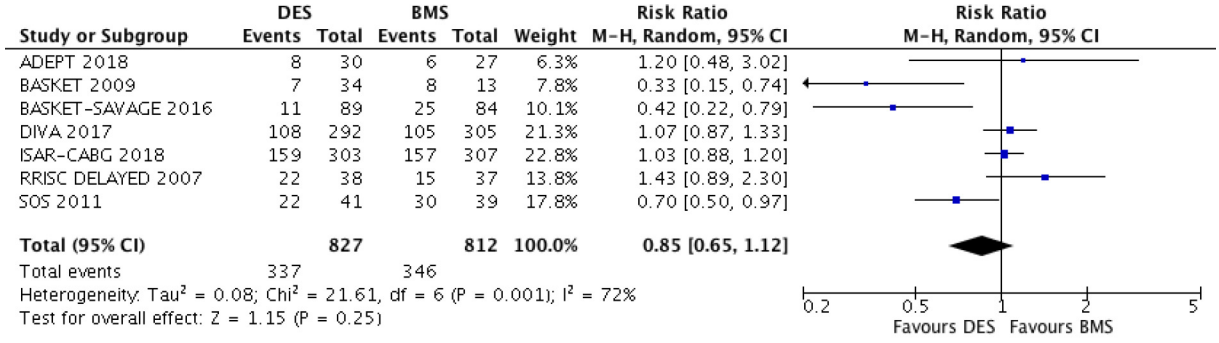
DES: drug eluting stent; BMS: bare metal stent; PES: paclitaxel-eluting stent; BP-SES: biodegradable polymer sirolimus-eluting stent; EES: everolimus-eluting stent; SES: sirolimus-eluting stent; ZES: zotarolimus-eluting stent.

(OR 0.64 [0.36, 1.13]; $p = 0.12$)] among 1582 patients (Fig. 4A–G). Additionally, there was no difference in cardiovascular mortality, all-cause mortality, MI, in-stent thrombosis and TLR in both short-term and long-term follow up (Figs. 3 and 4).

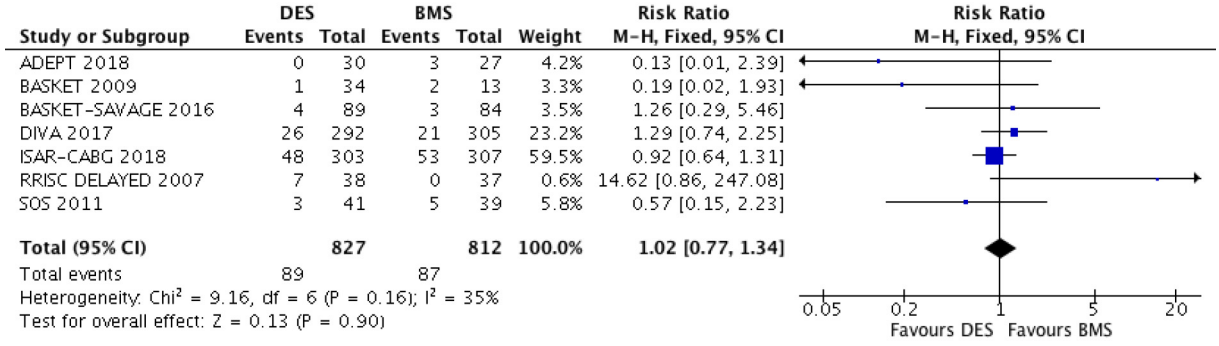
4. Discussion

This comprehensive meta-analysis incorporating data from all seven RCTs comparing DES with BMS in patients undergoing SVG-PCI, shows DES in SVG-PCI is associated with a reduction in MACE, TVR, and binary in-stent restenosis on short-term follow up with no significant difference in the occurrence of MACE, cardiovascular mortality, all-cause mortality, MI, TVR, and TLR on long-term follow up. All the included trials were multi-center, except for the RRISC [14] and BASKET [15] trials which were single center studies. Except for the recent DIVA trial [8] that used mainly second generation stents (everolimus-eluting or zotarolimus-eluting stents), all the other trials used first generation stents either sirolimus-eluting stents (SES) or paclitaxel-eluting stents (PES) or self-expanding stents, which are not clinically available at present in the United States. The duration of dual antiplatelet therapy (DAPT) varied between 1–6 months and 2–12 months after BMS and DES implantation, respectively. Some trials rarely used embolic protection devices [4,15], while other used them to a significant extent (80%) [14].

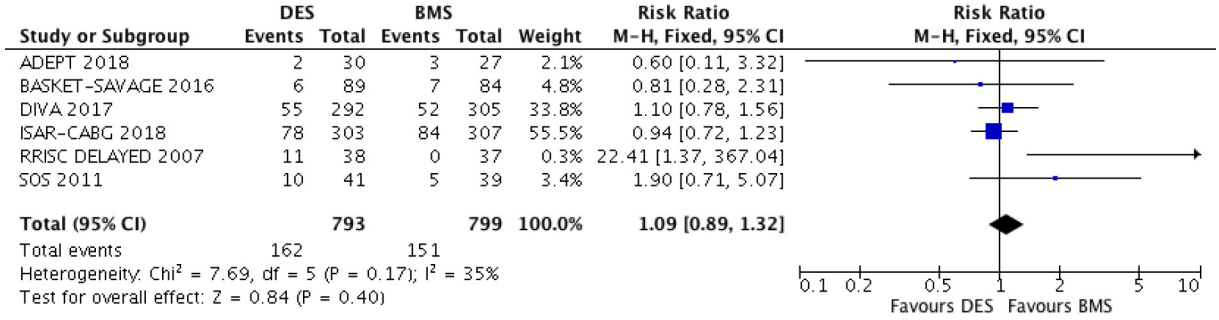
The RRISC and SOS trials were the initially conducted RCTs comparing DES with BMS for SVG-PCI showing reduction in TLR at 6 and 18 months, respectively [16,17]. Both studies had angiographic follow up and the significant reduction in LLL and binary in-stent restenosis provided a biological mechanism to explain the benefits of DES. Subsequent analysis of the same studies at



A- Overall comparison of MACE

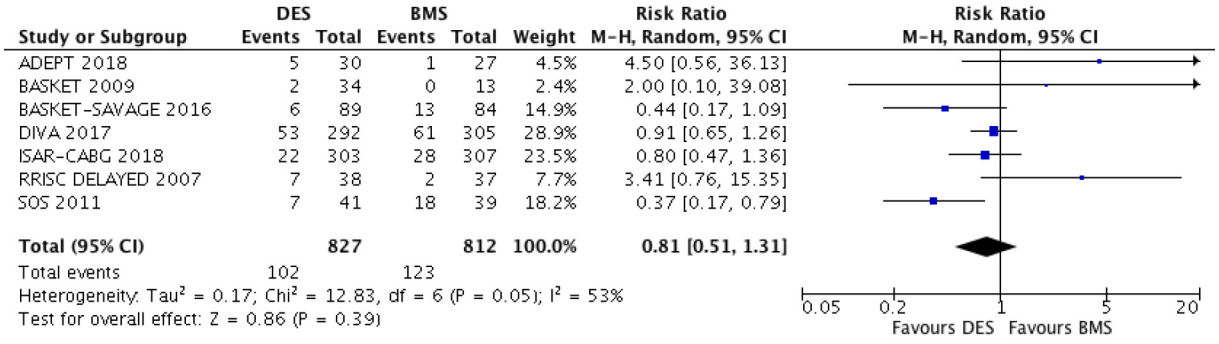


B- Overall comparison of cardiovascular mortality

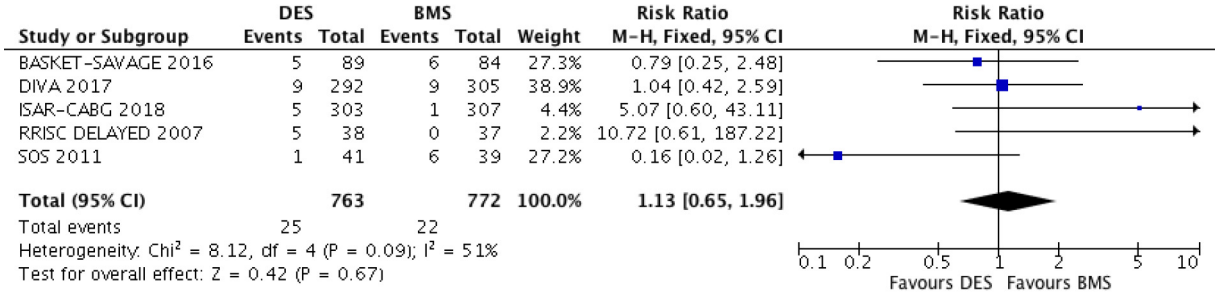


C- Overall comparison of all-cause mortality

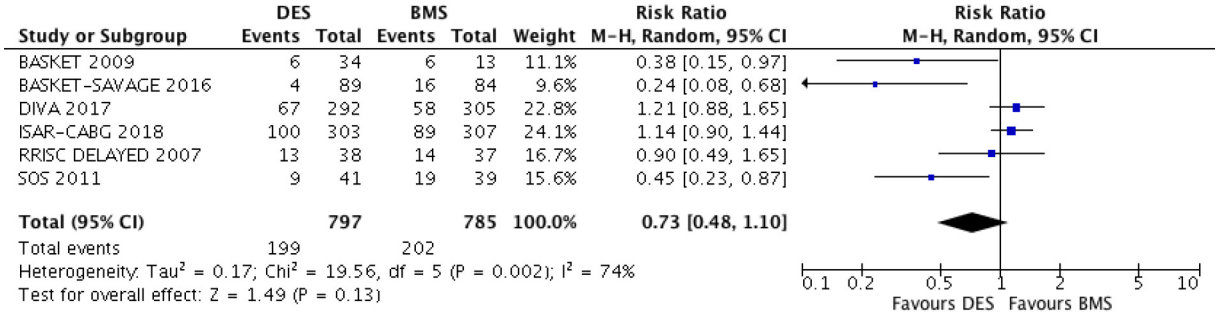
Fig. 2. Overall comparison of MACE (2A), cardiovascular mortality (2B), all-cause mortality (2C), myocardial infarction (2D), in-stent thrombosis (2E), target vessel revascularization (2F) and target lesion revascularization (2G) between DES and BMS. MACE: major adverse cardiac events; DES: drug eluting stents; BMS: bare metal stents.



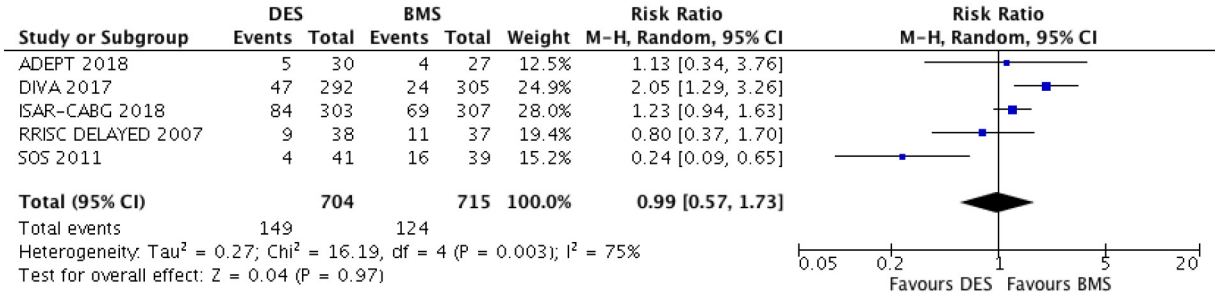
D- Overall comparison of myocardial Infarction



E- Overall comparison of in-stent thrombosis



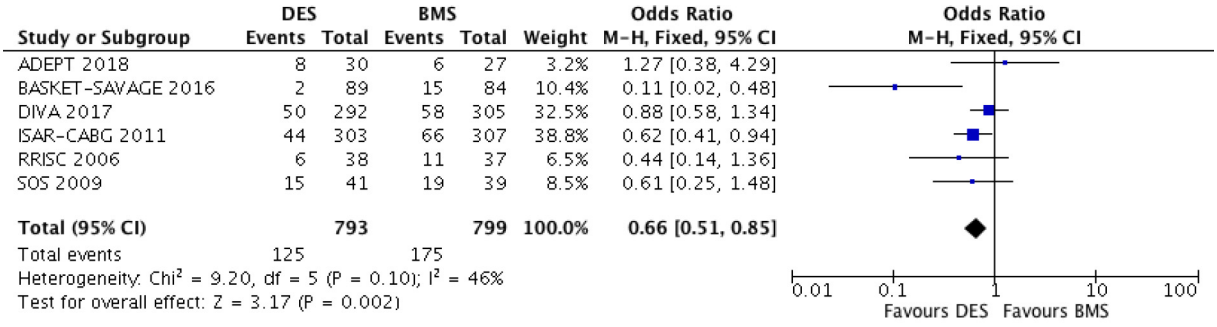
F- Overall comparison of target vessel revascularization



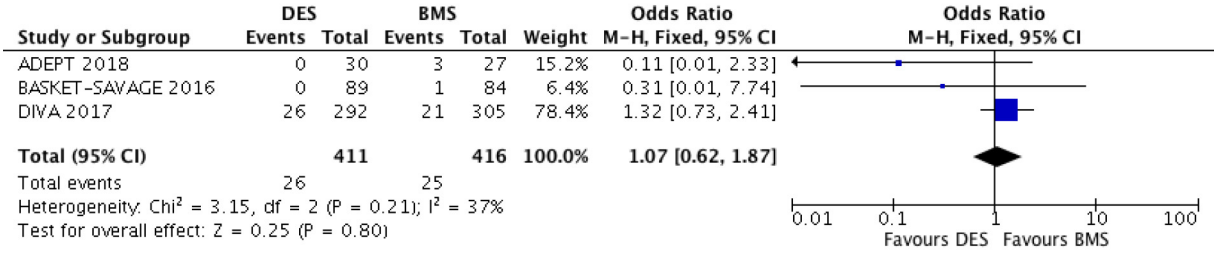
G- Overall comparison of target lesion revascularization

Fig. 2 (*continued*).

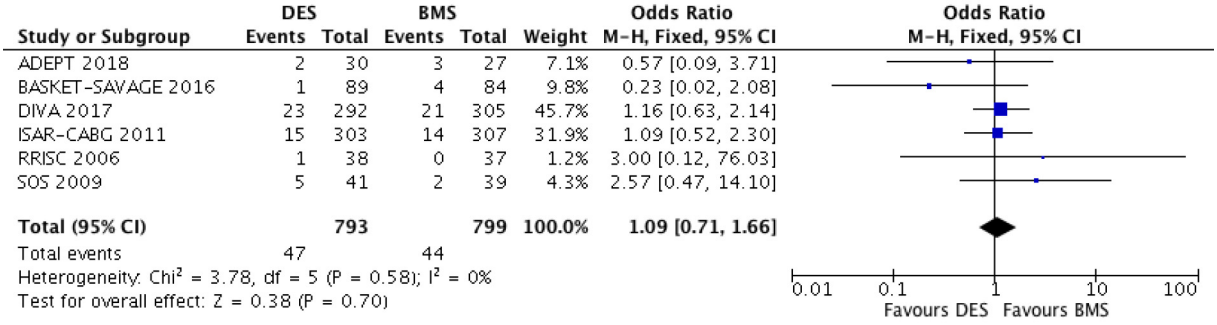
longer term follow up provided conflicting results. The DELAYED RRISC study which reported outcomes of the RRISC trial at 32 months, unexpectedly showed a higher all-cause mortality with DES and loss of the previously noted benefit in reduction in TLR [14]. On the other hand, long-term follow up of the SOS trial showed sustained benefit of antirestenotic efficacy of DES at 35 months [5]. Subsequently, the much larger ISAR-CABG and BASKET-SAVAGE trials demonstrated reduction in MACE and restenosis with DES at 12 months and sustained at 3 years [4,6] without increased mortality [6]. However, very recently published five year follow up of ISAR-CABG trial revealed the loss of benefit of reduction in TLR with DES [18].



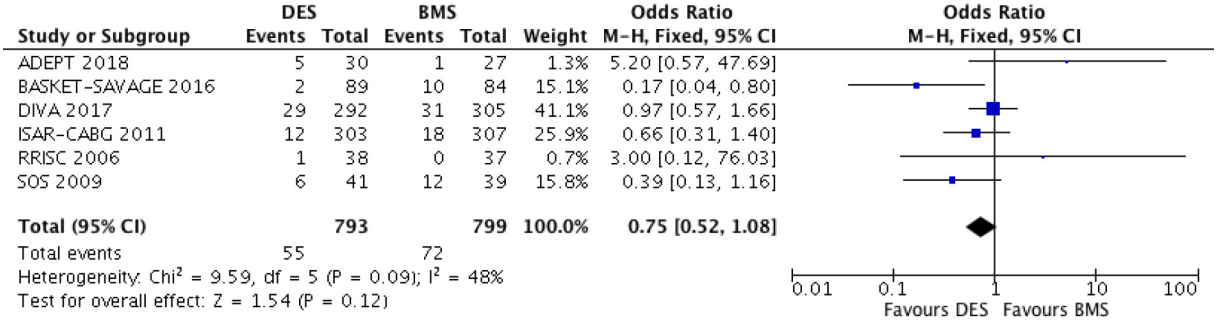
A- Short term follow up comparison of MACE



B- Short term follow up comparison of cardiovascular mortality

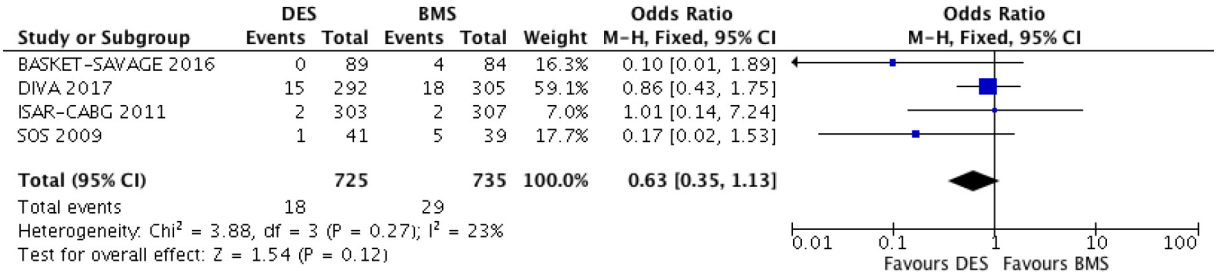


C- Short term follow up comparison of all-cause mortality

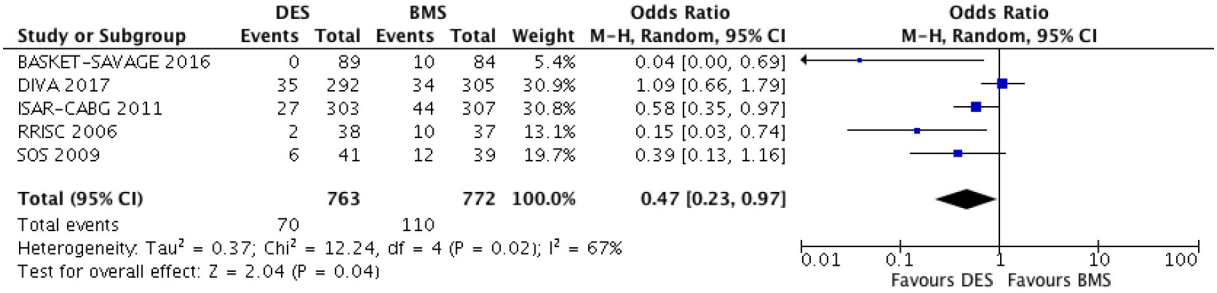


D- Short term follow up comparison of myocardial infarction

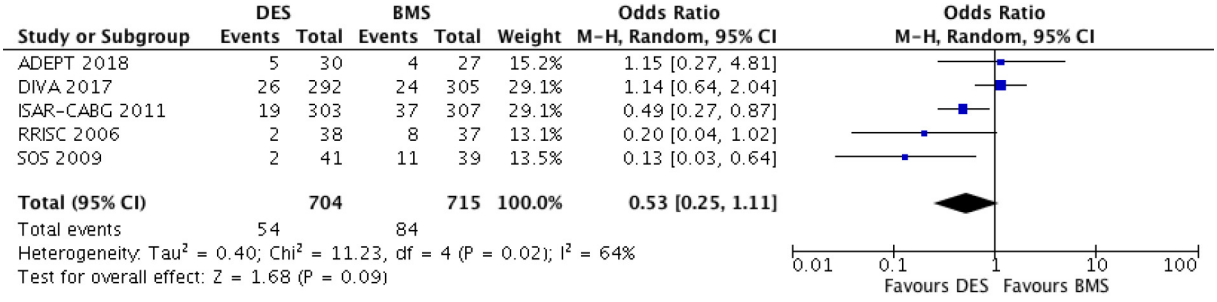
Fig. 3. Short term follow up comparison of MACE (3A), cardiovascular mortality (3B) all-cause mortality (3C), myocardial infarction (3D), in-stent thrombosis (3E), target vessel revascularization (3F), target lesion revascularization (3G), binary in-stent restenosis (3H) and late lumen loss (3I) between DES and BMS. MACE: major adverse cardiac events; DES: drug eluting stents; BMS: bare metal stents.



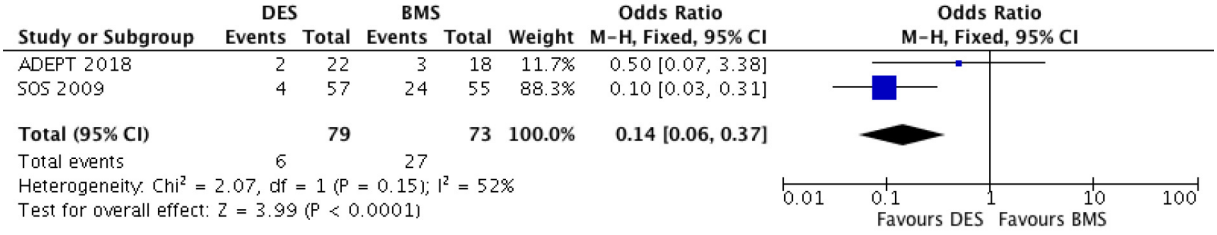
E- Short term follow up comparison of in-stent thrombosis



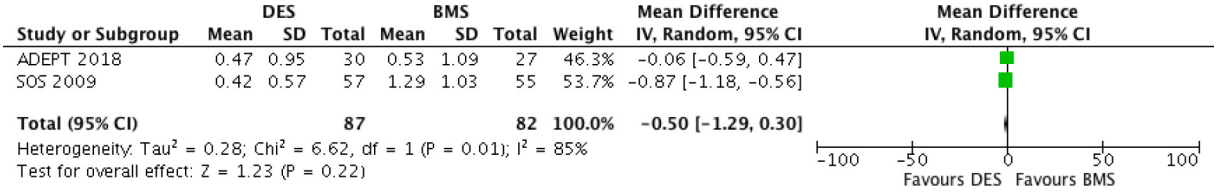
F- Short term follow up comparison of target vessel revascularization



G- Short term follow up comparison of target lesion revascularization

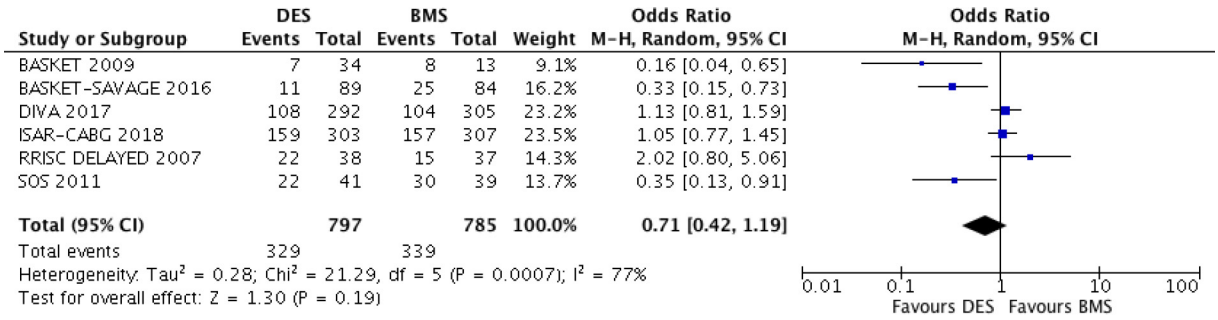


H- Short term follow up comparison of binary in-stentrestenosis

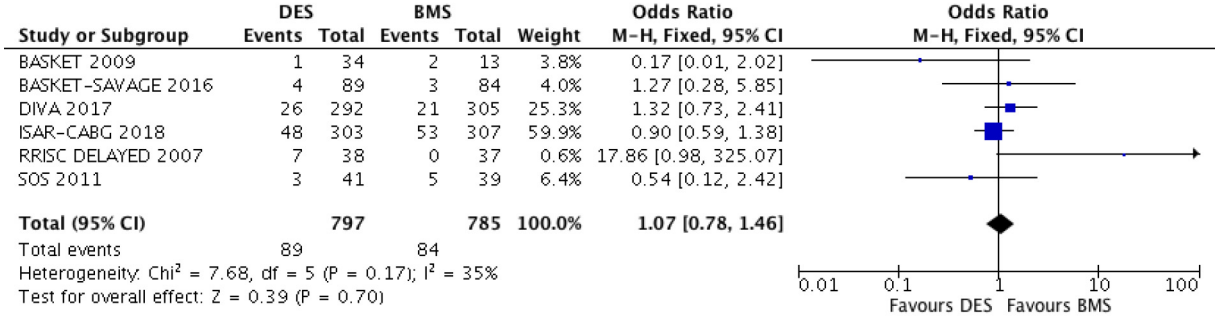


I- Short term follow up comparison of late lumen loss

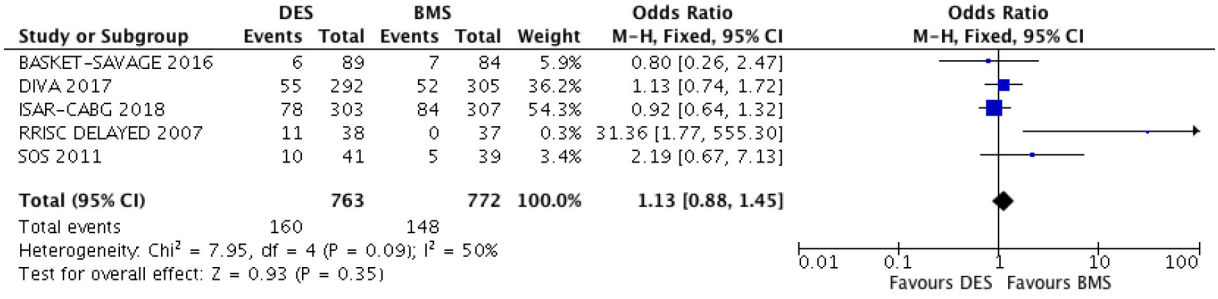
Fig. 3 (*continued*).



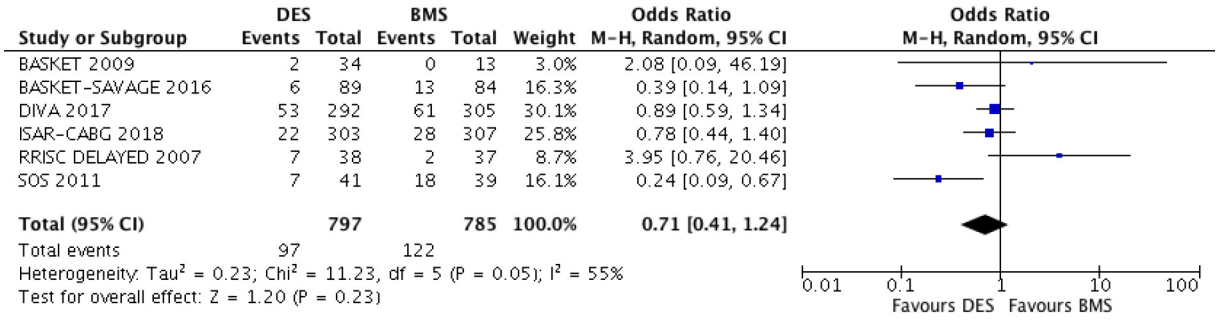
A- Long term comparison of MACE



B- Long term comparison of cardiovascular mortality

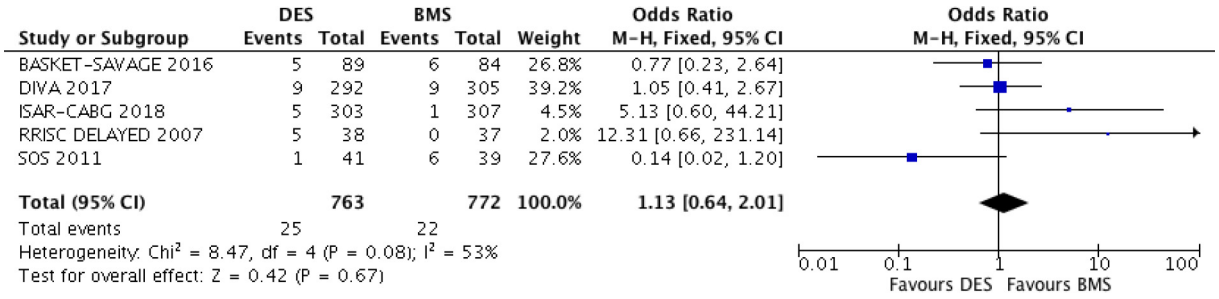


C- Long term comparison of all-cause mortality

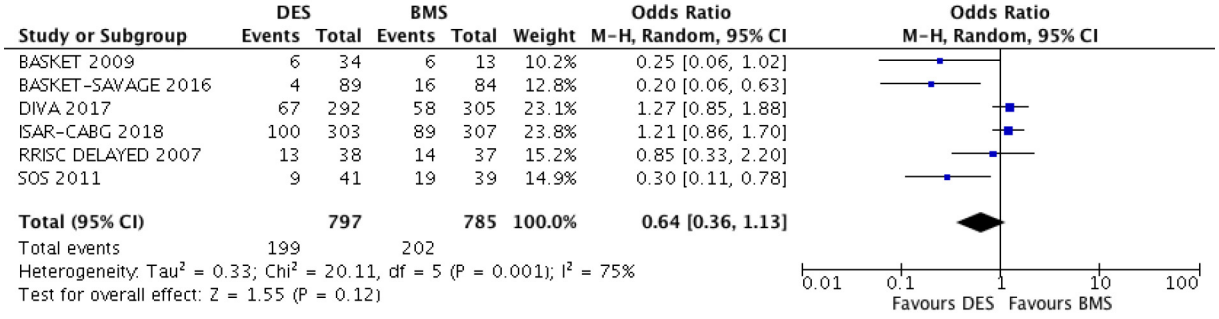


D- Long term comparison of myocardial infarction

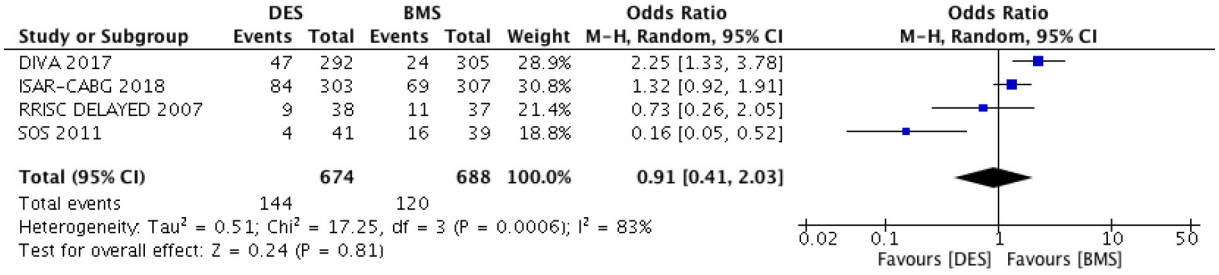
Fig. 4. Long term comparison of MACE (4A), cardiovascular mortality (4B), all-cause mortality (4C), myocardial Infarction (4D), in-stent thrombosis (4E), target vessel revascularization (4F) and target lesion revascularization (4G) between DES and BMS. MACE: major adverse cardiac events; DES: drug eluting stents; BMS: bare metal stents.



E- Long term comparison of in-stent thrombosis



F- Long term comparison of target vessel revascularization



G- Long term comparison of target lesion revascularization

Fig. 4 (*continued*).

The newly reported RCTs are ADEPT and DIVA. ADEPT was a small RCT comparing a novel self-expanding PES with self-expanding BMS (Stentys SA, Paris, France). The study was underpowered to test the study hypothesis. DIVA is the only study to use second-generation DES. DIVA was double-blind, did not have mandatory angiographic follow up, and used mainly second-generation DES and did not show any difference in outcomes between DES and BMS during short- or long-term follow up. There are several differences between the RCTs which may account for the differences in outcomes with DES compared with BMS. Some of these factors include differences in the percentage of diabetics (significantly higher in SOS and DIVA compared with ISAR-CABG), type of BMS (thicker strut BMS in SOS and RRISC compared with ISAR-CABG, which may account for higher ISR and TLR rates in the BMS group in SOS compared with ISAR-CABG), and importantly the type of DES (SES in RRISC compared with PES in SOS, which may have resulted in eventual loss of efficacy during long-term follow up in DELAYED RRISC). The early reduction in TLR at 6 months seen in RRISC, SOS and ISAR-CABG but not in DIVA may have been due to higher percentage of diabetes in DIVA, better performance of BMS and lack of angiographic follow up in DIVA (higher in-stent LLL with BMS may have triggered TLR when angiographic follow up was performed). The TLR rates for DES were high in DIVA (9% and 16% at 1 year and 2.7 years, respectively) compared with ISAR-CABG (6.8% at 1 year) and SOS (5% at 18 months). Conversely the TLR rate for BMS was lower in DIVA (8% at both 1 year and 2.7 years) compared with ISAR-CABG (13.1% at 1 year) and SOS (28% at 18 months).

Due to these conflicting data, several meta-analyses have been conducted. Older meta-analysis which included mainly observational studies showed improved outcomes with DES, with reduction in TVR and in some cases reduction in mortality and TLR [9,19]. The results of this meta-analysis differ from a prior meta-analysis by Mosleh et al. in 2015 [9] which showed a significant reduction in long-term MACE and all-cause mortality with the use of DES compared with BMS. However, this benefit was driven by data from observational studies, and was not found when only RCTs (4 RCTs) were included in the analysis. There was no benefit in reduction in MI or long-term TLR (36 months). Similar findings were noted in a meta-analysis of the same four RCTs by Gao et al. with no long-term benefit in reduction of MACE, MI or mortality [11]. A meta-analysis by Bavishi et al. which

included BASKET-SAVAGE, but did not include longer follow-up data of SOS trial showed a significant reduction in TVR at 18 months with DES without significant difference in mortality, MI or MACE [10]. Another meta-analysis that included five RCTs including the latest DIVA trial (excluded BASKET trial), showed no difference in outcomes between DES and BMS (all-cause mortality, MACE, MI, cardiac mortality and TVR) [12]. Our meta-analysis included all available data from RCTs conducted to date comparing outcomes as overall and stratified by short-term and long-term follow up between BMS and DES in SVG-PCI. The results of this meta-analysis are different from recently performed meta-analysis with respect to TVR [10,20], and show no significant differences in MACE, mortality, MI, TVR, TLR, or stent thrombosis. The lower TVR was seen in both these meta-analysis [10,21] likely due to lack of long term follow up data as longer follow up data of SOS and 5-year data on ISAR-CABG was not included in these analyses.

SVG represents a distinct environment of the venous conduit where it is exposed to arterial pressure rather than inherent lower venous pressure circulation together with thrombosis, intimal hyperplasia and accelerated atherosclerosis leads to graft degeneration and failure [21]. An analysis has shown up to 39% of SVG occluded as compared to 15% of internal mammary artery grafts at 10 year follow up [22]. An alternative approach would be to perform PCI of native vessels including chronic total occlusion (CTO) interventions over SVG intervention. This strategy has shown lower incidence of short and long-term MACE in veteran affairs population with native vessels PCI as compared to SVG intervention [23]. Development of innovative approaches including retrograde CTO intervention should be considered in complexes cases [24]. Further RCTs are required to assess the outcomes of native vessel PCI vs SVG-PCI.

5. Study limitations

This meta-analysis has several limitations. As this is not a patient level meta-analysis, the effects of age, gender, race, and ethnic background on outcomes could not be assessed. Due to inherent limitations of meta-analysis the baseline characteristics between the two groups could not be compared entirely. The individual studies have their own limitations that also reflect on this analysis. Although there is a potential for publication bias as is true for all meta-analyses, this analysis shows that there is no publication bias for any outcome. Four out of seven trials have sample size <100, thus, some of the outcomes may not have enough power to draw a strong conclusion. Only one study used second-generation DES. Studies have variable follow up duration ranging from 6 to 60 months making head to head comparison of duration difficult. Additionally, the duration of DAPT was widely variable. There was heterogeneity noted in several outcomes and random effect models were used to minimize this heterogeneity. The definition of MACE was not similar across the studies.

6. Conclusion

Our meta-analysis shows that DES use is associated with similar incidence of MACE, cardiovascular mortality, all-cause mortality, MI, instent thrombosis, TVR and TLR compared with BMS during long-term follow up in SVG-PCI. RCTs with large sample sizes and long-term follow up are needed to determine if superior outcomes can be achieved with the newer generation DES. There was high incidence of MACE noted in both DES and BMS suggesting a need for novel strategies to treat SVG disease to improve clinical outcomes.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.carrev.2018.11.013.

References

[1] Baim DS, Wahr D, George B, et al. Randomized trial of a distal embolic protection device during percutaneous intervention of saphenous vein aorto-coronary bypass grafts. Circulation Mar 19 2002;105(11):1285–90.
[2] Castagna MT, Mintz GS, Waksman R, et al. Comparative efficacy of gamma-irradiation for treatment of in-stent restenosis in saphenous vein graft versus native coronary artery in-stent restenosis: an intravascular ultrasound study. Circulation Dec 18 2001;104(25):3020–2.
[3] Brilakis ES, Rao SV, Banerjee S, et al. Percutaneous coronary intervention in native arteries versus bypass grafts in prior coronary artery bypass grafting patients: a report from the National Cardiovascular Data Registry. JACC Cardiovasc Interv Aug 2011;4(8):844–50.
[4] Mehilli J, Pache J, Abdel-Wahab M, et al. Drug-eluting versus bare-metal stents in saphenous vein graft lesions (ISAR-CABG): a randomised controlled superiority trial. Lancet Sep 17 2011;378(9796):1071–8.
[5] Brilakis ES, Lichtenwalter C, Abdel-Karim AR, et al. Continued benefit from paclitaxel-eluting compared with bare-metal stent implantation in saphenous vein graft lesions during long-term follow-up of the SOS (Stenting of Saphenous Vein Grafts) trial. JACC Cardiovasc Interv Feb 2011;4(2):176–82.
[6] Jeger RV. Drug-eluting vs. bare metal stents in saphenous vein grafts: the prospective randomized BASKET-SAVAGE trial. European Congress of Cardiology, Rome, Italy; August 2016.
[7] AJJ IJ, Simsek C, van Driel AG, et al. Comparison between the STENTYS self-apposing bare metal and paclitaxel-eluting coronary stents for the treatment of saphenous vein grafts (ADEPT trial). Neth Hear J Feb 2018;26(2):94–101.
[8] Brilakis ES. Drug-eluting stents vs. bare metal stents In saphenous Vein graft Angioplasty (DIVA). European Congress of Cardiology, Barcelona, Spain; August 2017.
[9] Mosleh W, Gandhi S, Elsiddig M, Schwalm JD, Farkouh ME. Comparison of drug-eluting stents with bare-metal stents for PCI of saphenous vein graft lesions: systematic review and meta-analysis. J Invasive Cardiol Dec 2016;28(12):E139–69.
[10] Bavishi C, Chatterjee S, Stone GW. Does current evidence favor drug-eluting stents over bare-metal stents for saphenous venous graft interventions?: insights from an updated meta-analysis of randomized controlled trials. JACC Cardiovasc Interv Dec 12 2016;9(23):2456–8.
[11] Gao J, Ren M, Liu Y, Gao M, Sun B. Drug-eluting versus bare metal stent in treatment of patients with saphenous vein graft disease: a meta-analysis of randomized controlled trials. Int J Cardiol Nov 1 2016;222:95–100.
[12] Elgendy IY, Mahmoud AN, Brilakis ES, et al. Drug-eluting stents versus bare-metal stents for saphenous vein graft revascularisation: a meta-analysis of randomised trials. EuroIntervention 2017. https://doi.org/10.4244/EIJ-D-17-00839 pii: EIJ-D-17-00839, [Epub ahead of print].
[13] Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. Br Med J (Clin Res Ed) Jul 21 2009;339:b2700.
[14] Vermeersch P, Agostoni P, Verheye S, et al. Increased late mortality after sirolimus-eluting stents versus bare-metal stents in diseased saphenous vein grafts: results from the randomized DELAYED RRISC trial. J Am Coll Cardiol Jul 17 2007;50(3):261–7.
[15] Jeger RV, Schneiter S, Kaiser C, et al. Drug-eluting stents compared with bare metal stents improve late outcome after saphenous vein graft but not after large native vessel interventions. Cardiology 2009;112(1):49–55.
[16] Vermeersch P, Agostoni P, Verheye S, et al. Randomized double-blind comparison of sirolimus-eluting stent versus bare-metal stent implantation in diseased saphenous vein grafts: six-month angiographic, intravascular ultrasound, and clinical follow-up of the RRISC trial. J Am Coll Cardiol Dec 19 2006;48(12):2423–31.
[17] Brilakis ES, Lichtenwalter C, de Lemos JA, et al. A randomized controlled trial of a paclitaxel-eluting stent versus a similar bare-metal stent in saphenous vein graft lesions: the SOS (Stenting Of Saphenous Vein Grafts) trial. J Am Coll Cardiol 2009/03/17;53(11):919–28.
[18] Colleran R, Kufner S, Mehilli J, et al. Efficacy over time with drug-eluting stents in saphenous vein graft lesions. J Am Coll Cardiol 1973;71(18):2018.
[19] Paradis JM, Belisle P, Joseph L, et al. Drug-eluting or bare metal stents for the treatment of saphenous vein graft disease: a Bayesian meta-analysis. Circ Cardiovasc Interv Dec 2010;3(6):565–76.
[20] Ha FJ, Nogic J, Montone RA, Cameron JD, Nerlekar N, Brown AJ. Drug eluting versus bare metal stents for percutaneous coronary intervention of saphenous vein graft lesions: An updated meta-analysis of randomized controlled trials. Cardiovasc Revasc Med 2018;19(7 Pt B):837–44.
[21] Motwani JG, Topol EJ. Aortocoronary saphenous vein graft disease. Circulation 1998;97(9):916.
[22] Goldman S, Zadina K, Moritz T, et al. Long-term patency of saphenous vein and left internal mammary artery grafts after coronary artery bypass surgery: results from a Department of Veterans Affairs Cooperative Study. J Am Coll Cardiol 2004/12/07;44(11):2149–56.
[23] Brilakis ES, O'Donnell CI, Penny W, et al. Percutaneous coronary intervention in native coronary arteries versus bypass grafts in patients with prior coronary artery bypass graft surgery: insights from the Veterans Affairs Clinical Assessment, Reporting, and Tracking program. JACC Cardiovasc Interv May 9 2016;9(9):884–93.
[24] Dash D. Retrograde coronary chronic total occlusion intervention. Curr Cardiol Rev 2015;11(4):291–8.