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SYSTEMATIC REVIEW

Restenosis Prevention With Drug Eluting or Covered Stents in Femoropopliteal Arterial Occlusive Disease: Evidence From a Comprehensive Network Meta-analysis

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WHAT THIS PAPER ADDS

This comprehensive network meta-analysis used data from 28 randomised controlled trials of commonly used endovascular treatments for femoropopliteal lesions. It was found that drug eluting stents were significantly more effective than drug coated balloons for the treatment of short lesions. However, the overall analysis did not demonstrate any significant difference in the efficacy of drug eluting stents, covered stents, drug coated balloons, and bare metal stent. Percutaneous transluminal angioplasty alone does not constitute an effective choice. These outcomes may contribute to clinical decision making.

Background/objective: Endovascular interventions for femoropopliteal (FP) arterial diseases are limited by the development of restenosis. Current drug coated devices are capable of preventing restenosis by releasing antiproliferative agents to the vessel wall. However, default strategies for the treatment of FP diseases remain controversial. The aim of this study was to investigate the efficacy differences between drug eluting stents (DES), covered stents (CS), and other commonly used endovascular treatments in FP lesions, including drug coated balloons (DCBs), bare metal stents (BMS), and percutaneous transluminal angioplasty (PTA).

Methods: A comprehensive network meta-analysis was conducted using data from relevant randomised control trials published up to 16 December 2018. Primary patency and target lesion revascularisation (TLR) at 12 months were set as the primary and secondary end points, respectively.

Results: Twenty-eight eligible trials including 4728 patients were selected. DES was ranked as the most effective treatment in the multidimensional analysis of primary patency; however, there was no significant difference in the efficacy of DES and that of CS, DCB, and BMS. However, in short lesions (<10 cm), DES was significantly more effective than DCB (odds ratio 0.35; 95% confidence interval 0.15—0.83). Primary patency at 12 months was significantly lower with PTA. In terms of preventing TLR, DCB was ranked first, followed by DES, CS, BMS, and PTA. TLR was significantly higher with PTA than with other treatment strategies.

Conclusion: The findings of this network meta-analysis suggest that this is not the appropriate time to identify the best endovascular treatment strategy for the FP segment. DES is effective in maintaining mid-term patency, especially in short lesions, whereas DCB seems more suitable for clinical use.

Keywords: Endovascular treatment, Femoropopliteal artery, Network meta-analysis, Peripheral arterial diseases
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INTRODUCTION

Restenosis is recognised as the "Achilles' heel" of the endovascular treatment of peripheral arterial disease (PAD).[1] Interventional treatments such as percutaneous transluminal angioplasty (PTA) and bare metal stent (BMS) implantation have shown a frequent restenosis, nearly 40% and 30%, respectively, in the femoropopliteal (FP) segment.[2,3] The emergence of drug eluting stents (DES) and covered stents (CS) made it possible to prevent restenosis

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through different mechanisms (physical barrier and anti-proliferative agents). These two treatments are now used in clinical practice, as they have been shown to improve significantly vessel patency;[4–6] however, direct comparisons between the two devices are scarce.[7–9] Furthermore, with rapid developments in endovascular techniques, endovascular devices are updated at a fast rate. New devices such as drug coated balloons (DCBs) are also effective.[10,11] The best percutaneous treatment strategy for FP disease remains debated.[12,13] The efficacy differences between DES and CS were estimated and various commonly used endovascular treatment modalities for the FP segment compared.

MATERIALS AND METHOD

This review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Search strategy

Electronic and manual retrieval of data from randomised controlled trials (RCTs) conducted up to 16 December 2018 was performed (Table S1; see Supplementary Material). MEDLINE, the Cochrane Central Register of Controlled Trials, ClinicalTrials.gov, Web of Science, Embase, Scopus, Ovid, Google Scholar, international congresses, and other relevant online sources were all carefully screened. Different search strategies for each database were developed with a combination of relevant terms to ensure identification of all trials. Finally, the reference lists of relevant publications were screened. Two authors (R.H, Y.Y.) independently completed the screening for eligible studies. Differences between investigators were resolved by discussion and then arbitrated by a third and experienced investigator (Z.I. or C.Y.). No language, publication date, or status restrictions were imposed.

Selection criteria

A study that satisfied the criteria below was considered eligible for this review: (i) a RCT that compared endovascular treatments for FP arterial diseases, and included DES, CS, DCB, BMS, and PTA; (ii) a study reporting 12 month data on primary patency and target lesion revascularisation (TLR), which were the outcomes of interest in the present review.

Two authors (R.H. and Y.Y.) independently reviewed the titles and abstracts to check whether they met the inclusion criteria. The quality of the included RCTs was evaluated with the Cochrane Collaboration's tool for assessing risk of bias. Studies that did not provide data on the effectiveness of treatment were excluded.

Data extract

Data extraction was based on an intention to treat strategy. All RCTs that met the eligible criteria were included. For publications of different follow up periods, only the most recent papers providing data on 12 month outcomes were included. Two authors (R.H. and Z.L.) independently reviewed the full texts of the included RCTs, and extracted the outcomes data, patient demographics, and characteristics of lesions, using a predesigned form. Controversies were resolved by discussion and decisions were made by consensus.

Outcome measures

The primary patency at 12 months was set as the primary end point, whereas TLR at 12 months was the secondary end point. Primary patency was defined as a duplex ultrasound derived peak systolic velocity ratio <2.5 or $<50\%$ diameter stenosis from arteriographic core laboratory analysis, when available. Intervention failure and TLR were also considered to indicate loss of primary patency. TLR was defined as any repeat interventions undertaken for treatment of significant target lesion restenosis associated with symptoms of PAD.

Statistical analysis

Traditional meta-analysis methods do not allow adequate assessment of the comparative effectiveness of all treatment strategies. Therefore, a network meta-analysis of all relevant RCT data was done to compare comprehensively and rank percutaneous treatment strategies for the FP segment. A network meta-analysis used direct and indirect data over the entire network, so that estimates of intervention effect are based on all available data for the comparisons. These data may be direct, indirect, or mixed. In other words, Network meta-analysis allows for robust comparisons of multiple treatment modalities that have not been compared directly in an RCT, by using a common reference treatment among similar populations of patients.[14]

This analysis was performed within a frequentist framework. Outcome variables were compared with odds ratios (ORs) and 95% confidence intervals (CIs) by means of network meta-analysis with a random effect model in Stata version 14.0 (StataCorp, College Station, TX, USA) using the mvmeta and network meta-analysis commands, and self programmed Stata.[15–17] BMS served as the reference treatment. Previous meta-analysis set PTA as the reference.[18] However, BMS was used here because CS and DES were compared indirectly. This may be interpreted as (the benefit of A over B) is equal to (the benefit of A over C) minus (the benefit of B over C) such that A—B = (A—C) − (B—C). In practice, this transitivity requires similarity. Actually, the reference C would not considerably influence the comparison outcomes. Outcomes of PTA as a reference were also analysed (Fig. S1; see Supplementary Material), which was the same as that of BMS. First, a network plot was made to demonstrate the comparison relationships between treatments using the "networkplot" command. Network plot is a graphical description of comparisons where each line, or edge, depicts a direct comparison between two intervention nodes, and the nodes are weighted according to the number of studies evaluating each

treatment and the edges according to the precision of the direct estimate for each pairwise comparison. Second, loop specific heterogeneity estimates were used to test the inconsistency of RCTs with corresponding z-tests. Discrepancies between direct and indirect comparisons were recognised as inconsistency. Significant inconsistency threatens the validity of analysis results. An inconsistency plot was generated using the "ifplot" command. An item facility (IF) value close to 0 or Relative Odds Ratio (ROR) value close to 1 indicated a lack of significant inconsistency. Funnel plot is the most commonly used tool to access small study effects in a meta-analysis. The funnel plot was transformed to be "comparison adjusted" to assess the small study effects and publication bias by using the "netfunnel" command. In a funnel plot, the ordinate is the effect size of each study, and the abscissa is the total effect size of control group. A symmetric distribution of this plot indicated a lack of small study effects and publication bias. As the next and the most important steps, network meta-analysis was performed and data synthesised from RCTs. The summary treatment effects in terms of ORs with 95% CIs for each pair of treatments were presented in a predictive interval plot. Compared with conventional meta-analysis, the advantage of network meta-analysis is the precision in the estimates. As network meta-analysis uses direct, indirect, and mixed data throughout the entire network of trials, it has the potential to rank the competing treatments according to the studied outcomes. Multidimensional analysis of meta-analysis outcomes was performed, and a surface under the cumulative ranking curve (SUCRA) plot was generated to present ranking of treatments. The SUCRA value is not probability. It takes the entire distribution of the probabilities into account and expresses the percentage of effectiveness of a treatment that would be ranked always first without any uncertainty.[14] The increased SUCRA value is indicative of a more effective treatment. Finally, a cluster ranking plot was made to demonstrate the ranking of treatments with respect to both end points. The performance of different devices for different lesion lengths was briefly investigated. The included trials were divided into two groups based on mean lesion lengths (>10 cm or < 10 cm). Then, the two sets of data were analysed separately through a network meta-analysis. The glossary and descriptions of network meta-analysis have been published online: http://cmim.cochrane.org/glossary and http://www.mtm.uoi.gr/index.

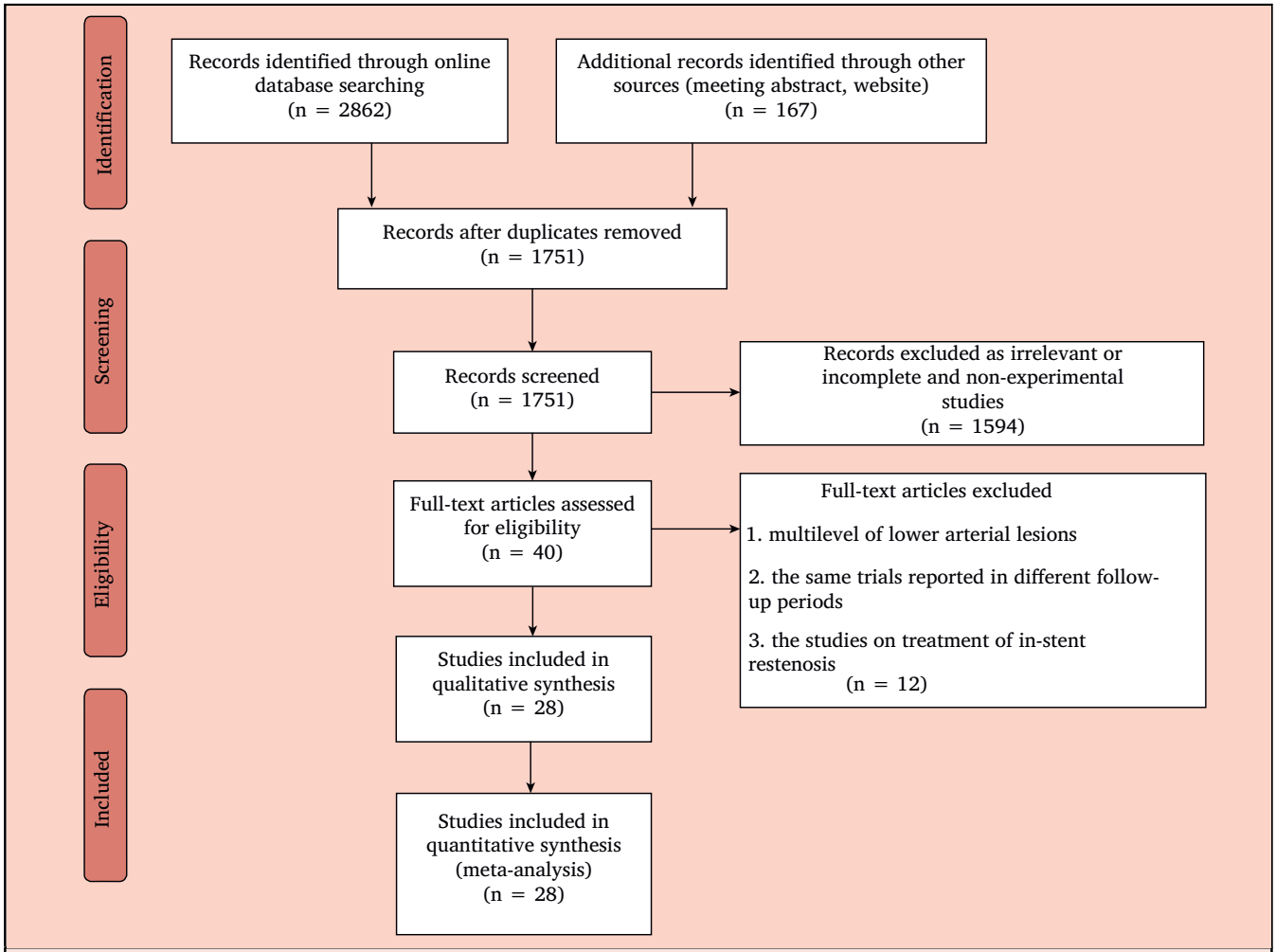

Figure 1. Flow chart of the study search according to the Preferred Reporting for Systematic Reviews and Meta-Analysis (PRISMA) statement.

Table 1. Characteristics of randomised control trials included in the network meta-analysis

Study	Year	Label	Design	Primary patency analysis	Target lesion revascularisation analysis	Sample size (interventions /control)	Follow up (months)	Criteria for > 50% stenosis
Geraghty et al.	2013	VIBRANT	Covered stent (CS) vs. bare metal stent (BMS)	1	1	148 (72/76)	36	Duplex ultrasound (DUS) derived peak systolic velocity ratio (PSVR) > 2.0
Lammer et al.	2013	VIASTAR	CS vs. BMS	1	1	141 (72/69)	12	DUS derived PSVR > 2.5
Saxon et al.	2008	NA	CS vs. percutaneous transluminal angioplasty (PTA)	1	0	197 (97/100)	12	Not available (NA)
Duda et al.	2006	SIROCCO	Sirolimus eluting stents (SES) vs. BMS	0	1	93 (47/46)	24	DUS derived PSVR>2.0
Dake et al.	2011	Zilver PTX	Paclitaxel eluting stents (PES) vs. PTA	1	1	474 (236/238)	12	NA
Takashi et al.	2018	NA	PES vs. BMS	1	1	170 (85/85)	12	DUS derived PSVR > 2.0
Schillinger et al.	2006	NA	BMS vs. PTA	0	1	104 (51/53)	12	12 month arteriography>50%
Krankenberg et al.	2007	FAST	BMS vs. PTA	0	1	244 (123/121)	12	PSVR proximal ≥ 2.4 on DUS
Dick et al.	2009	NA	BMS vs. PTA	0	0	73 (34/39)	12	PSVR > 2.4 (3, 6, and 12 mo)
Laird et al.	2010	RESILENT	BMS vs. PTA	1	1	206 (134/72)	12	PSVR proximal ≥ 2.5 on DUS
Brancaccio et al.	2012	NA	BMS vs. PTA	1	0	50 (25/25)	12	PSVR > 2.4, target lesion
Chalmers et al.	2013	NA	BMS vs. PTA	1	1	150 (74/76)	12	PSVR > 2.5 or absent flow
Rastan et al.	2013	NA	BMS vs. PTA	1	1	246 (119/127)	12	DUS derived PSVR > 2.4
Tepe et al.	2008	THUNDER	Drug-coated balloon (DCB) vs. PTA	0	1	67 (34/33)	60	6 mo arteriography > 50%
Werk et al.	2008	FemPac	DCB vs. PTA	0	1	87 (45/42)	18	6 mo arteriography > 50%
Werk et al.	2012	PACIFIER	DCB vs. PTA	0	1	85 (42/43)	12	6 mo arteriography > 51%
Liistro et al.	2013	DEBATE-SFA	DCB vs. PTA	0	1	104 (53/51)	12	Angiography > 50% or PSVR ≥ 2.5
Scheinert et al.	2014	LEVENT-1	DCB vs. PTA	1	1	87 (45/42)	24	Angiography > 50% or PSVR ≥ 2.5
Rosenfield et al.	2015	LEVENT-2	DCB vs. PTA	1	1	428 (285/143)	12	Angiography > 50% or PSVR ≥ 2.5
Scheinert et al.	2015	BIOLUXP-1	DCB vs. PTA	1	1	49 (25/24)	12	Angiography > 50% at time of follow up
Tepe et al.	2015	IN. PACT-SFA	DCB vs. PTA	1	1	314 (207/107)	12	DUS derived PSVR ≥ 2.4 at the study sites
Xin et al.	2016	ACOART-1	DCB vs. PTA	1	1	193 (97/96)	12	PSVR > 2.4, target lesion
Krishnan et al.	2017	ILLUMENATE	DCB vs. PTA	1	1	300 (200/100)	12	DUS derived PSVR > 2.5, angiography > 50%
Schroeder et al.	2017	ILLUMENATE European	DCB vs. PTA	1	1	294 (222/72)	12	PSVR ≥ 2.5, angiography > 50%
Lida et al.	2017	MDT-2113	DCB vs. PTA	1	1	100 (68/32)	12	DUS derived PSVR > 2.4
Thomas et al.	2018	CONSEQUENT	DCB vs. PTA	1	1	153 (78/75)	24	PSVR > 2.4, angiography > 50%
Sabine et al.	2018	RANGER	DCB vs. PTA	1	1	105 (34/71)	12	DUS derived PSVR ≥ 2.4
Buszman et al.	2018	BIOPAC	DCB vs. PTA	1	1	66 (33/33)	12	PSVR > 2.5, angiography > 50%

CS = covered stents; SES = sirolimus eluting stents; PES = paclitaxel eluting stents; BMS = bare metal stents; DCB = drug coated balloon; PTA = percutaneous transluminal angioplasty (uncoated balloon); NA = not available; DUS = duplex ultrasonography; PSVR = peak systolic velocity ratio; PP analysis = trials involved in the 12 months primary patency analysis; TLR analysis = trials involved in the 12 months target lesion revascularisation (TLR) analysis.

php/tutorial. All procedures followed the hands-on tutorials of Stata.[19–21]

RESULTS

Study selection

In total, 132 potentially eligible studies were identified from 2903 records. For these 132 studies, titles and abstracts were reviewed in detail. A total of 101 studies were excluded for not meeting the inclusion criteria or because of incomplete records; for the remaining 31 studies, the full text or other detailed archived records were assessed. Thereafter, 10 studies were further excluded, one because it dealt with multilevel lower limb arterial lesions, four because they were reports of the same trials at a different follow up period, and five studies were on treatment of in stent restenosis. A second retrieval identified a further seven studies from 126 records. Finally, 28 RCTs were deemed eligible for inclusion (Fig. 1). These 28 studies were two arm RCTs with a total of 4728 patients and a mean follow up of 16.07 $\pm$ 4.01 months (Table 1).

Risk of bias

Twenty-six eligible studies were all prospective RCTs. Risk of bias was assessed with the Cochrane Collaboration's risk of bias tool (Figs. 2 and 3). Random sequence generation was fully described in all trials except one,[22] and allocation concealment was fully described in almost all trials. Most of the trials were single blinded and the methods of blinding were also described in about 75% of the trials, indicating a low risk of bias. The outcomes report of most trials was provided in a predefined way, as described in their Methods sections. Losses to follow up were also reported, and all trials were generally of high quality.

Baseline characteristics

The baseline demographics of all randomised populations are shown in Table S2. The enrolled patients were predominantly male, elderly, and smokers, and had hypertension, dyslipidaemia, and coronary artery diseases. Lesion lengths varied among trials and ranged from 4 to 19 cm; lesions treated with CS were longer than others, and the shortest was in a DCB trial. Within each trial, the baseline demographics were similar between the two groups. A total of 4728 patients were included in the final analysis: 241 patients (5.1%) treated with CS, 368 patients (7.8%) treated with DES, 836 patients (17.7%) treated with BMS, 1815 patients (38.4%) treated with PTA, and 1468 patients (31.1%) treated with DCB. There was no overlapping study population between trials.

Outcomes

Primary patency. Fifteen trials with 3915 patients reported primary patency at 12 months.[4,9,10,22–37] The network plot for these 19 trials is presented in Fig. 4, which indicates that most patients received PTA treatment, and that more trials compared PTA with DCB than with other devices. Two closed loops (CS—BMS—PTA and DES—BMS—PTA) were found in the inconsistency test, with non-significant inconsistency results (IF 0.18 [95% CI 0.00—1.01] and IF 0.79 [95% CI 0.00—1.72], respectively). The outcomes of network meta-analysis are presented in Fig. 5. The 12 month primary patency was significantly lower with PTA. DES was ranked first, with a non-significant OR of 2.26 (95% CI 0.79—6.43) compared with CS. The efficacy discrepancies between DES, DCB, and BMS were also non-significant. The ranking plot and SUCRA values are presented in Fig. 6. DES had the highest SUCRA values (96.6), followed by CS (51.6), BMS (51.0), DCB (50.8), and PTA (0.1). The funnel plot for primary patency at 12 months is presented in Fig. 7. The symmetrical distribution on the graph indicates that this network meta-analysis might not have a small sample effect or publication bias.

Among the trials on $<$ 10 cm lesions, DES was also ranked first (DES $>$ BMS $>$ CS $>$ DCB $>$ PTA), DES was significantly more effective than DCB (OR 0.35, 95% CI 0.15—0.83) and PTA (OR 0.12, 95% CI 0.05—0.25). For trials on lesions $>$10 cm, DCB had the highest SUCRA values and probabilities of being the best treatment (DCB $>$ CS $>$ BMS $>$ PTA).

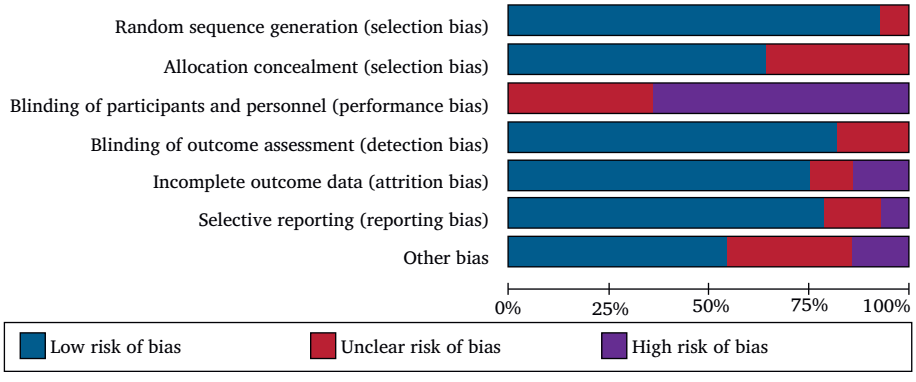

Figure 2. Risk of bias graph: review authors; judgments about each risk of bias item presented as percentages across all included studies.

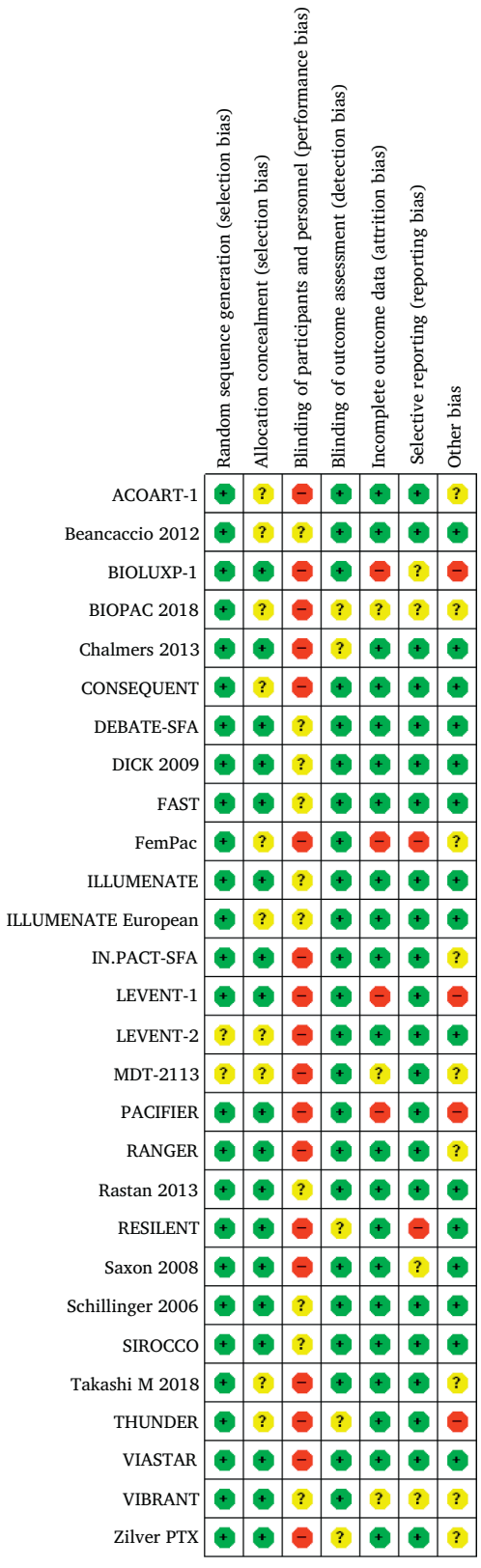

Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

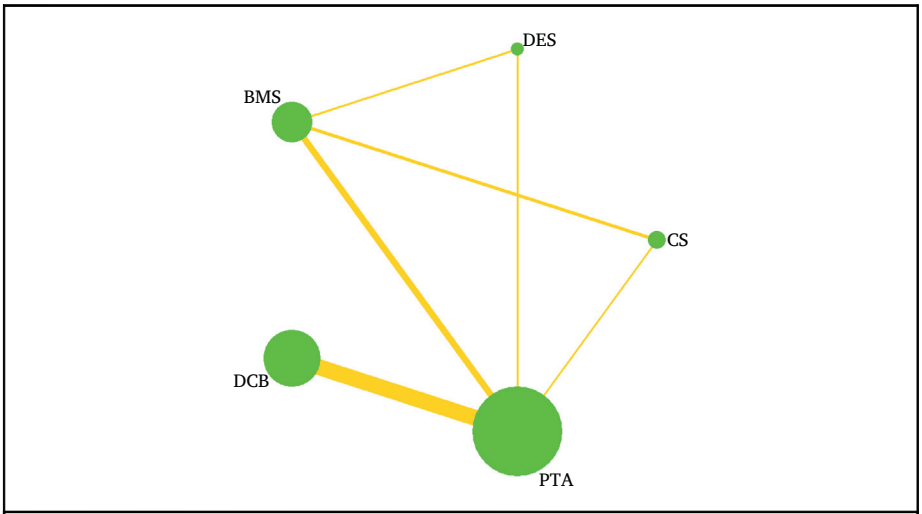

Figure 4. Network plot for primary patency rate. The size of nodes is proportional to the number of patients treated by each intervention and the thickness of lines to the number of direct comparisons in trials (uncoated balloon). BMS = bare metal stent; DES = drug eluting stent; CS = covered stent; DCB = drug coated balloon; PTA = percutaneous transluminal angioplasty.

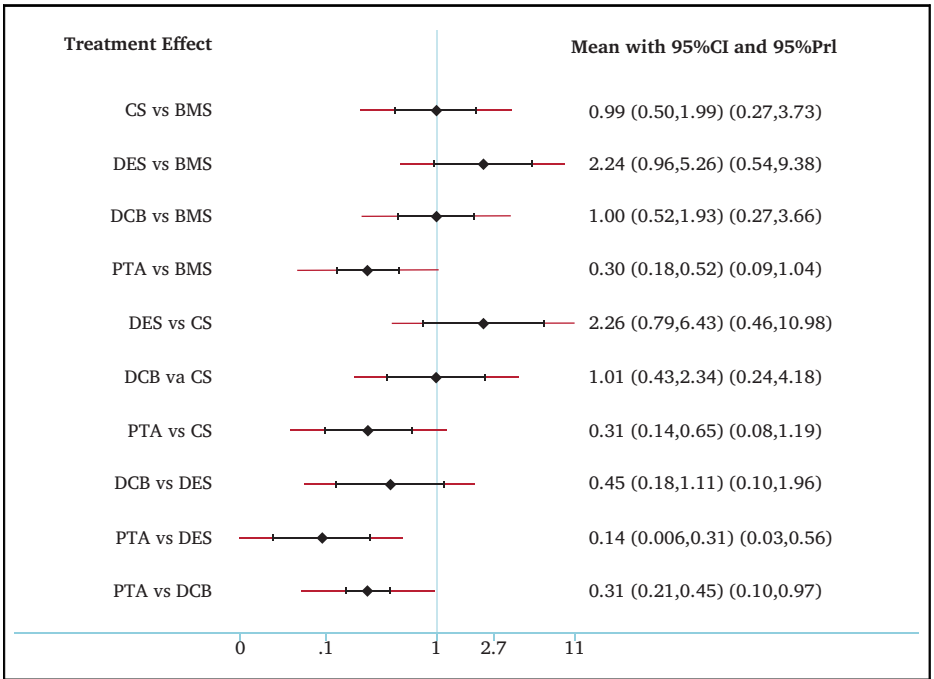

Figure 5. The predictive interval plot for primary patency at 12 months. The black diamonds represent the valve of odds ratios (ORs), the black lines demonstrate the 95% confidence interval (CI) of ORs, and the red lines demonstrate the 95% prediction interval (PrI) of ORs. CS = covered stent; BMS = bare metal stent; DES = drug eluting stent; DCB = drug coated balloon; PTA = percutaneous transluminal angioplasty.

TLR. Data on TLR were available in 25 trials with 4408 patients.[2–4,10,11,22–25,27–42] More connections were seen in the network plot (Fig. 8). One closed loop was found in the inconsistency test (DES—BMS—PTA) with a non-significant inconsistency result (IF 1.173, 95% CI 0.00—3.49). The outcomes of network meta-analysis for TLR are presented in Fig. 9. DCB was ranked first according to the estimated SUCRA values (81.3), followed by DES (67.6), CS (58.4), BMS (40.7), and PTA (2.0). The incidence of TLR was significant higher with PTA than with other treatments, as follows: vs. CS (OR

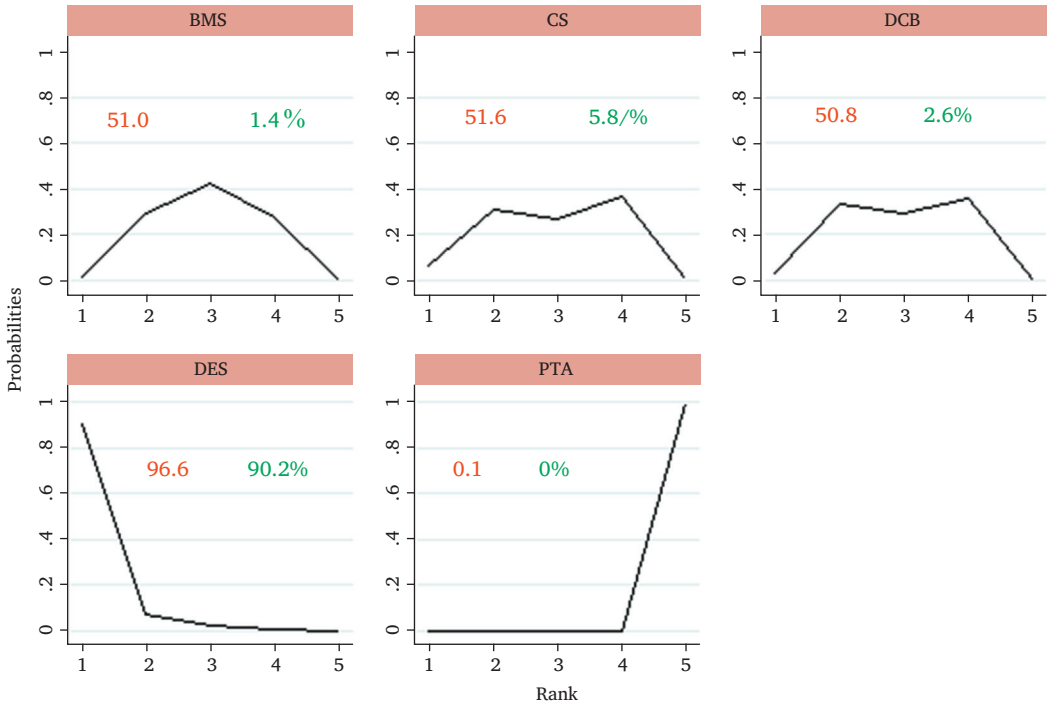

Figure 6. The ranking plot for all treatment modalities in primary patency analysis. The red number represents the surface under the cumulative ranking curve (SUCRA) value of each treatment modality; the green number represents the probability of being the best treatment. BMS = bare metal stent; CS = covered stent; DCB = drug coated balloon; DES = drug eluting stent; PTA = percutaneous transluminal angioplasty.

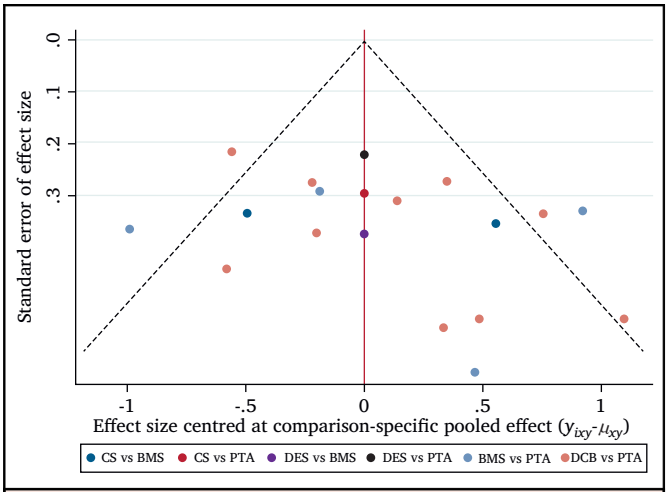

Figure 7. The comparison adjusted funnel plot for primary patency at 12 months, the red line represents the null hypothesis line. Colorful spots represent different comparison pairs. BMS = bare metal stent; CS = covered stent; DCB = drug coated balloon; DES = drug eluting stent; PTA = percutaneous transluminal angioplasty.

2.89, 95% CI 0.79—10.54), vs. BMS (OR 2.28, 95% CI 1.18—4.41), and vs. DCB (OR 4.15, 95% CI 2.68—6.42). The SUCRA values and ranking plot for TLR are shown in Fig. 10. The comparison adjusted funnel plot for TLR is presented in Fig. 11, and small sample effect and publication bias were not found. The cluster plot for SUCRA values of the two end points is shown in Fig. 12. DES was the closest to the apex of the coordinate axis.

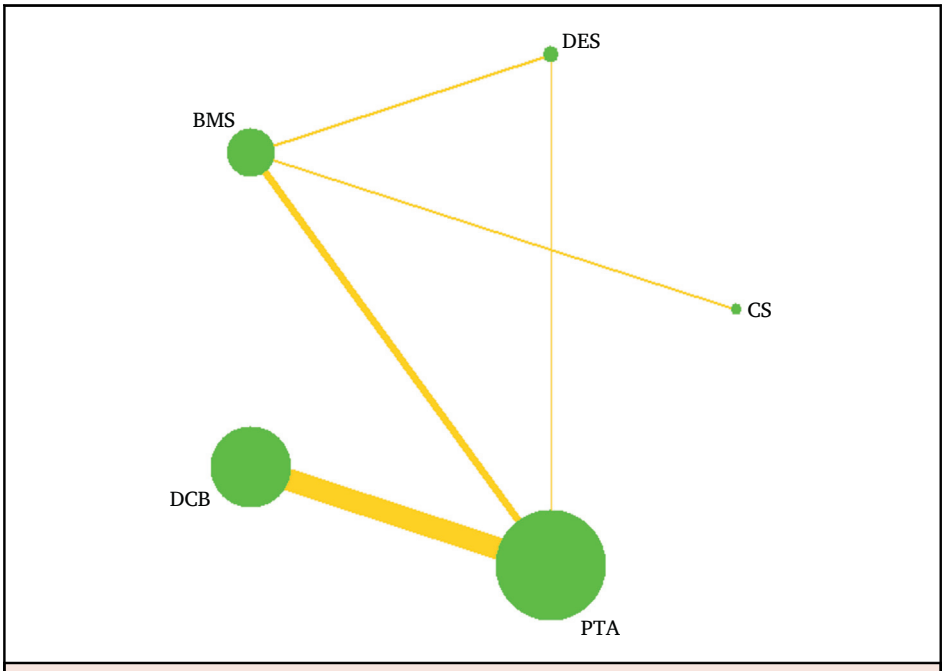

Figure 8. Network plot for target lesion revascularization. The size of nodes is proportional to the number of patients treated by each intervention and the thickness of lines to the number of direct comparisons in trial. BMS = bare metal stent; CS = covered stent; DCB = drug coated balloon; DES = drug eluting stent; PTA = percutaneous transluminal angioplasty.

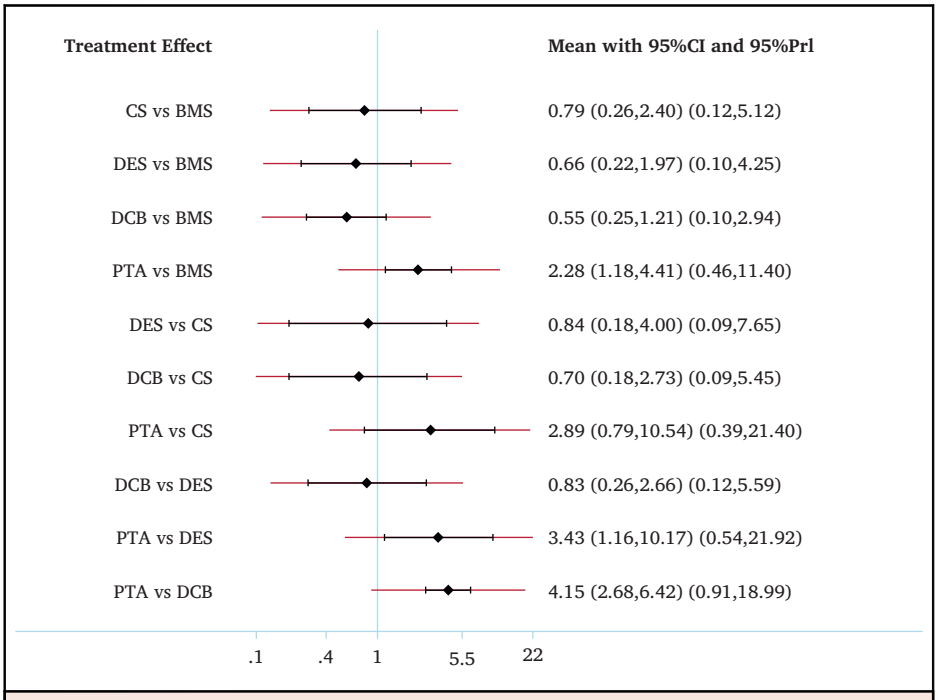

Figure 9. The predictive interval plot for target lesion revascularisation at 12 months. The black diamonds represent the value of odds ratios (ORs), the black lines demonstrate the 95% confidence interval (CI) of ORs, and the red lines demonstrate the 95% prediction interval (PrI) of ORs. BMS = bare metal stent; CS = covered stent; DCB = drug coated balloon; DES = drug eluting stent; PTA = percutaneous transluminal angioplasty.

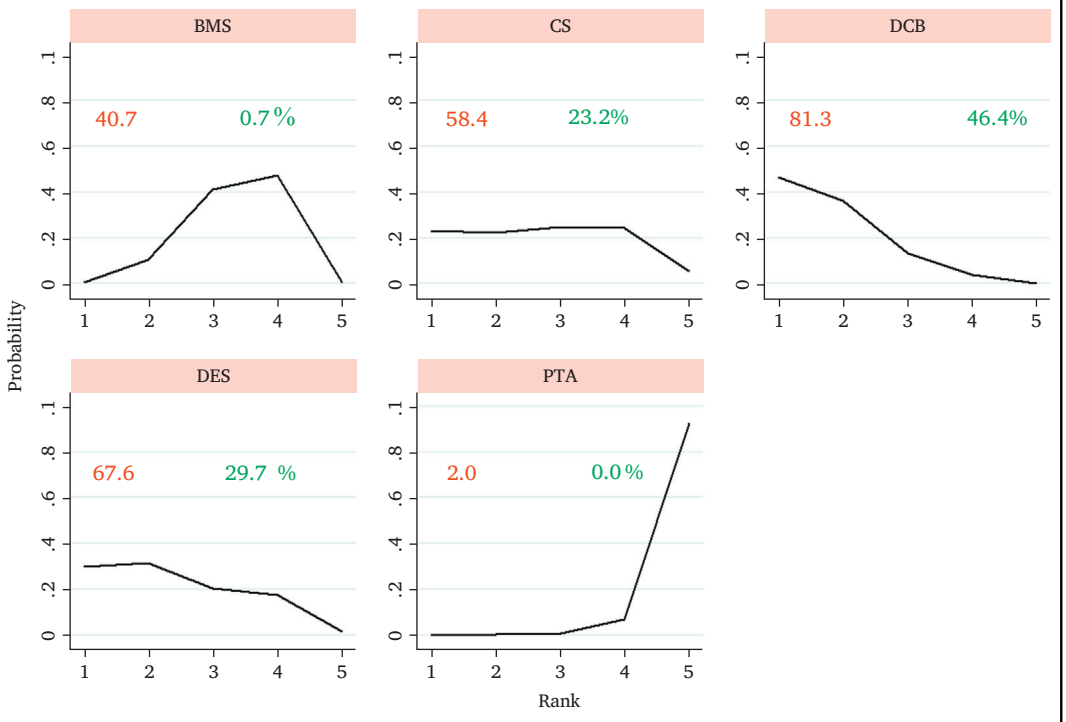

Figure 10. The ranking plot for all treatment modalities in target lesion revascularisation analysis. The red number represents surface under the cumulative ranking curve (SUCRA) value of each treatment modality; the green number represents the probability of being the best treatment. BMS = bare metal stent; CS = covered stent; DCB = drug coated balloon; DES = drug eluting stent; PTA = percutaneous transluminal angioplasty.

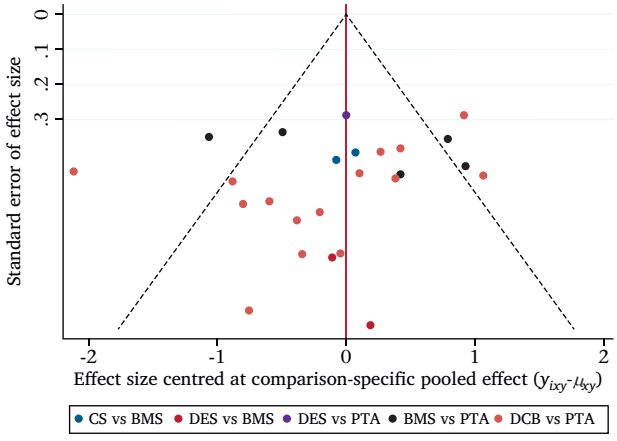

Figure 11. The comparison adjusted funnel plot for target lesion revascularisation at 12 months; the red line represents the null hypothesis line. Colorful spots represent different comparison pairs. BMS = bare metal stent; CS = covered stent; DCB = drug coated balloon; DES = drug eluting stent; PTA = percutaneous transluminal angioplasty.

DISCUSSION

Network meta-analysis is a novel method that enables robust comparisons of multiple treatment modalities by using a common reference treatment. It has been widely used in clinical research.[43–45] This network meta-analysis demonstrates a comprehensive use of data on commonly used endovascular approaches for the FP segment at present. The findings can be summarised as followed: there are no significant differences between DES, CS, DCB, and BMS with regard to primary patency or TLR at 12 months. DES is more

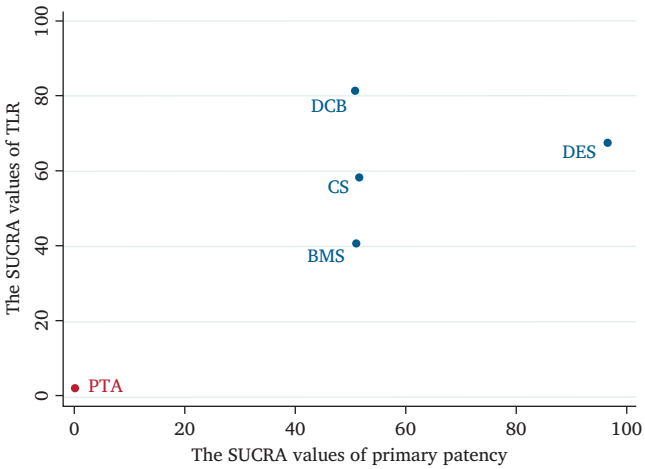

Figure 12. The clusters plot for surface under the cumulative ranking curve (SUCRA) values of primary patency and target lesion revascularisation (TLR) at 12 months. Drug eluting stent (DES) was shown to be closest to the apex of the coordinate axis, with the highest primary patency rates and relatively lower TLR. BMS = bare metal stent; CS = covered stent; DCB = drug coated balloon; PTA = percutaneous transluminal angioplasty.

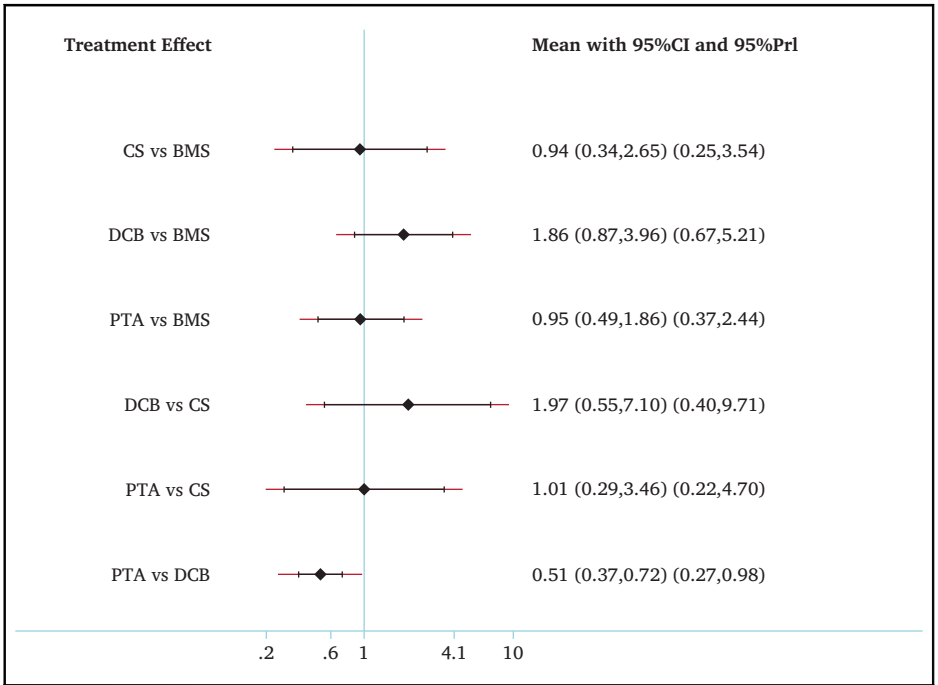

Figure 13. The Rutherford category improvement at 12 months. The black diamonds represent the valve of odds ratios (ORs), the black lines demonstrate the 95% confidence interval (CI) of ORs and the red lines demonstrate the 95%. BMS = bare metal stent; CS = covered stent; DCB = drug coated balloon; PTA = percutaneous transluminal angioplasty.

effective than DCB and PTA for short lesions. Conversely, PTA alone cannot be deemed an effective choice for FP lesions.

Stent application addresses the most striking weakness of PTA. The addition of an antiproliferative coating provides an effect against restenosis. DES was found to be effective in maintaining patency and was ranked first over other devices. Recent trials demonstrated that the paclitaxel eluting stent had a primary patency of 83.1% at 12 months and 74.8% at 24 months for FP lesions vs. PTA (32.8% and 26.5%, respectively). Moreover, the two year freedom from TLR rate

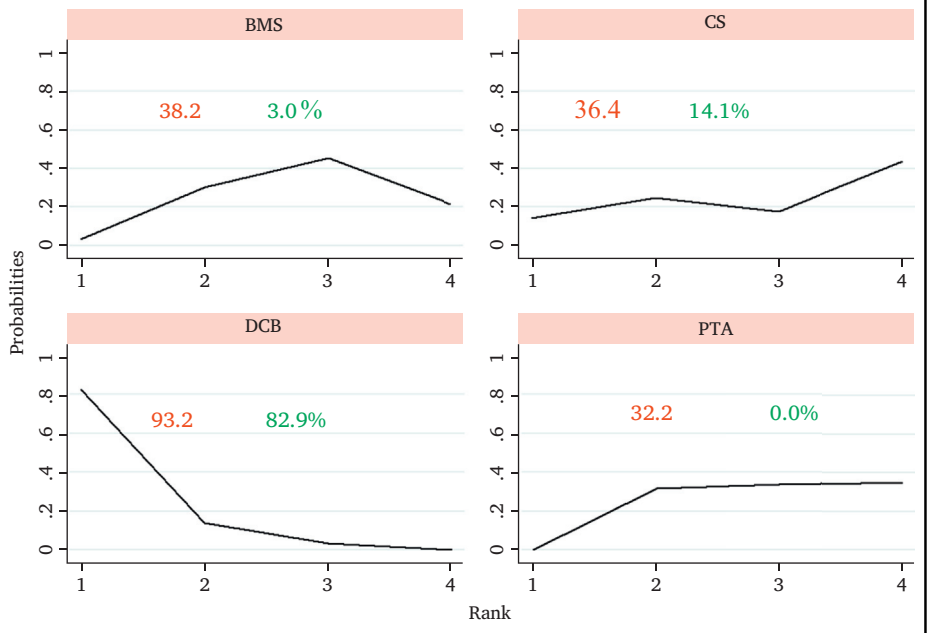

Figure 14. Ranking plots for Rutherford category improvement ≥1 and all treatment modalities. The red number represents the surface under the cumulative ranking curve (SUCRA) value for each treatment modality; the green number represents the probability of being the best treatment. BMS = bare metal stent; CS = covered stent; DCB = drug coated balloon; PTA = percutaneous transluminal angioplasty.

was 86.8% and event free survival was 86.6%.[6,24] CS is currently the most expensive commercially available stent for the FP segment.[12] The deployment of CS may cover the collateral vessels. An optimal outcome was achieved only when stent sizing was done accurately,[12,46] oversizing of stent grafts can cause infolding and subsequent occlusion or turbulent flow at the edge of the devices. These features limited its clinical use and its efficacy is not good as expected.

Notably, DCB was ranked first in the TLR analysis. TLR is related to the recurrence of PAD symptoms. Not all patients who failed to maintain primary patency need to undergo TLR procedures. In the LEVANT-II trial for DCB,[22] primary patency failure occurred in 92 patients, but only 35 of them needed TLR. Freedom from TLR means a continuous remission of symptoms and stable treatment efficacy. Therefore, an attempt was made to investigate the different outcomes of clinical end points between devices. Data on Rutherford category improvement ≥1 at 12 months were collected from the enrolled trials, if available. Detailed information about clinical improvement and the trials included in this analysis are shown in Table S3 (see Supplementary Material). The outcome of this analysis is presented in Fig. 13. DCB was found to be significantly more effective in providing clinical improvement than PTA (OR 0.51, 95% CI 0.37—0.72). DCB was also ranked first according to the SUCRA values and the probabilities of being the best treatment (Fig. 14). Although the anatomical outcomes of DCB may not be as promising as those of DES, DCB improved the mid-term clinical status of patients and decreased the occurrence of TLR. A DCB strategy allows safe and effective treatment with acceptable outcomes, and maintains the possibility of re-intervention. The use of DCB represents a cost effective alternative to PTA with bailout BMS.[47] These advantages are crucial for patients undergoing endovascular treatment.

This is not the first network meta-analysis on the FP segment. A previous meta-analysis collected 16 relevant RCTs and analysed them using a Bayesian model.[18] PTA served as the reference treatment, and the study concluded that DES and DCB offer the best long-term results in FP segment. In the present study, a total of 28 RCTs with 4728 patients were included, and the results confirm those of previous meta-analyses. Nevertheless, the potential limitations of the current study merit discussion. First, the baseline characteristics and inconsistency test did not demonstrate significant heterogeneity among eligible trials that might affect the analysis outcomes. Second, two types of DES were included in the analysis (sirolimus and paclitaxel); paclitaxel stents are significantly more effective in the FP segment than sirolimus stents. Although the current data on treatment modalities show acceptable effectiveness within 12 months, long-term outcomes were insufficient. Further investigations of treatment choices for the FP segment are required.

CONCLUSIONS

The findings of this network meta-analysis suggest that this is not the right time to identify the best endovascular

strategy for FP diseases. For patients with FP disease, treatment with DES or DCB is reasonable. DES shows superior efficacy in short lesions, whereas DCB seems to be more suitable for clinical use. All roads lead to Rome, but the travelling is too slow on the PTA road.

CONFLICT OF INTEREST

None.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2018.12.020.

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