Comparative efficacy and safety of four common balloon angioplasty techniques for an arteriovenous fistula or graft stenosis: a systematic review and network meta-analysis of randomized controlled trials

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Background: Balloon angioplasty could decrease restenosis of hemodialysis vascular access. The present study investigated the comparative effects and safety of commonly available balloon angioplasty techniques for treating patients with failing autogenous arteriovenous fistulas (AVFs) and grafts (AVGs) stenosis.

Methods: A comprehensive literature search, including an updated search of PubMed and Embase (via Ovid) and screening of published meta-analyses, was conducted. Primary patency at 6 and 12 months was the primary outcome, and the incidence of complications was the secondary outcome. The random-effects model was used to conduct all statistical analyses, which were performed using RevMan 5.3 and ADDIS 1.16.8.

Results: A total of 20 eligible studies involving four balloon angioplasty techniques were entered into the final analysis. Although the direct meta-analysis indicated that cutting balloon angioplasty (CtBA) significantly improved primary patency at 6 [odds ratio (OR), 1.91; 95% confidence interval (CI): 1.27 to 2.86] and 12 (OR, 1.56; 95% CI: 1.13 to 2.15) months compared with conventional balloon angioplasty (CBA), this was not supported by network meta-analysis, which suggested that CtBA was associated with a higher risk of complications compared with drug-coated balloon angioplasty (DcBA) [OR, 0.05; 95% credible interval (CrI): 0.00 to 0.83], high-pressure balloon angioplasty (HBA) (OR, 0.04; 95% CrI: 0.00 to 0.69), and CBA (OR, 0.11; 95% CrI: 0.02 to 0.59). Subgroup analysis of AVFs did not detect any significant differences.

Conclusions: In failing AVF and AVG stenosis, HBA might be a preferential option as it is related to a lower risk of complications and has numerically higher primary patency than DcBA and CBA. Further studies are needed to confirm these findings.

Keywords: Arteriovenous fistula (AVF); balloon angioplasty; drug-coated balloon; cutting balloon; high-pressure balloon

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Introduction

Currently, several different guidelines recommend arteriovenous fistula (AVF) or arteriovenous graft (AVG) as the preferred vascular access for patients with kidney failure requiring hemodialysis; however, vascular access dysfunction remains a major cause of morbidity and hospitalization in patients with end-stage renal disease (ESRD) (1,2). The most common cause of vascular access dysfunction is venous stenosis caused by neointimal hyperplasia (3-5), which results from the response to vascular trauma initiated by angioplasty used to repair the injured vessel walls (6).

Updated Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines (2) suggest percutaneous transluminal angioplasty (PTA) as the first choice for the treatment of vascular access dysfunction. Although it is fast and convenient, the primary patency rate of this technique at 12 months is relatively low, ranging from 26% to 62% (7-10). In order to further enhance the durability of therapy, a variety of balloon angioplasty strategies have been explored, such as cutting balloon angioplasty (CtBA), high-pressure balloon angioplasty (HBA), and drug-coated balloon angioplasty (DcBA) (11,12). Currently, there is no consensus on the comparative safety and efficacy of existing balloon angioplasty techniques.

Even though some head-to-head meta-analyses for AVF/AVG treatment have been published (13-18), they were not designed to identify the optimal treatment among various treatment options. A recent network meta-analysis has investigated the comparative therapeutic effects of different endovascular accesses in treating patients suffering from failing autogenous AVFs with outflow vein stenosis (19). Unfortunately, that network meta-analysis incorrectly incorporated standard- and high-pressure balloons into an individual intervention and enrolled a cohort (20) study into the final analysis. It also missed an eligible study (21) that compared CtBA with conventional balloon angioplasty (CBA).

Highlight box

Key findings

- High-pressure balloon angioplasty may be the preferred therapeutic option for failing autogenous arteriovenous fistulas and grafts stenosis.

What is known and what is new?

- Balloon angioplasty is effective in decreasing restenosis of hemodialysis vascular access.
- Compared with drug-coated balloon angioplasty and conventional balloon angioplasty, high-pressure balloon angioplasty is associated with a lower risk of complications and a numerically higher primary patency rate.

What is the implication, and what should change now?

- Drug-coated balloon angioplasty should not be preferentially used in patients with failing autogenous arteriovenous fistulas and grafts stenosis to improve primary patency, instead, high-pressure balloon angioplasty should be prioritized in these patients to achieve higher primary patency rate while reducing complications.

In addition, several eligible studies (22-24) have also been recently published following the previous network meta-analysis. It is therefore essential to perform a more comprehensive network meta-analysis to ascertain the best treatment option. Therefore, we present the following article in accordance with the PRISMA NMA reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-381/rc) (25,26).

Methods

Study registry

This updated network meta-analysis complied with the Cochrane handbook for reviewer of systematic review (27); however, its protocol has not been publicly registered. No institutional ethical approval or patients' informed consent was required as this was a network meta-analysis of published data.

Literature search

A recent network meta-analysis was identified after initially searching PubMed; therefore, an updated literature search strategy was developed. Two independent reviewers conducted an updated electronic search of PubMed and Embase (via Ovid) for potentially eligible studies published between January 2020 and July 2021. The strategies used for PubMed and Embase are summarized in Table S1. Eligible studies from published meta-analyses were also detected. Moreover, two independent reviewers manually checked the reference lists of the included studies. Finally, the same reviewers double-checked all the results. Conflicts between two reviewers were solved by consulting a third reviewer.

Selection criteria

The following selection criteria, which refer to patients, intervention, control, outcome, and study design, were developed according to the previous network meta-analysis with the PICOS methodology: (I) patients with stenotic AVF or AVG for hemodialysis, regardless of *de novo* or recurrent condition; (II) common balloon angioplasty techniques, including CBA, HBA, CtBA, and DcBA, were compared with each other in a randomized controlled trial (RCT); (III) reported at least one of the following outcomes, including target lesion primary patency (TLPP) at 6 and

12 months of follow-up and the rate of complications; (IV) full-text could be accessed.

The study was excluded if at least one of the following criteria was met: (I) patients were confirmed with central vein stenosis; (II) repeated study with poor methodological quality and relatively fewer data; (III) abstract without sufficient information; or (IV) studies with ineligible design such as observational studies, animal studies, and letters to the editor.

Study selection

Following the requirements proposed by the Cochrane Handbook, study selection was independently conducted by two reviewers. The whole progress included five following steps: (I) records first identified from the target databases were imported into the EndNote software, after which the repeated records were removed; (II) ineligible records were initially excluded through screening of the titles and abstracts; (III) the full-texts of the potentially eligible studies were accessed to confirm their eligibility; (IV) full-texts of the studies that have been included in previous meta-analyses were also accessed and checked for eligibility; (V) the reference lists of all included studies were manually checked to identify additional eligible studies. Discrepancies between the two reviewers were solved through a consultation with a third reviewer.

Definition of outcomes

Three outcomes were evaluated in this network meta-analysis to determine the comparative effectiveness and safety of common balloon angioplasty techniques. TLPP at 6 and 12 months of follow-up were regarded as primary outcomes, and the incidence of complications was considered the secondary outcome. TLPP had to be defined using recognized criteria and clearly reported in the eligible studies.

Data extraction

Two reviewers independently extracted data. The sample size was extracted after randomization as the intention-to-treat analysis was preferable to a full-analysis-set analysis and per-protocol analysis.

The following data were extracted: reference identifiers including the first author's name and publication year; characteristics of the patients including sample size, the proportion of male patients, mean age of the patient, type of target lesion, the definition of the primary outcome; characteristics of the intervention regimens, including the type of balloon, paclitaxel dose, and follow-up duration. The corresponding authors were also contacted when additional data were needed. Conflicts between two reviewers were solved by consulting a third reviewer.

Construction of the evidence network

The current status of the available evidence in terms of all outcomes was displayed by constructing an evidence network using Stata 14.0 (Stata Corp LP, College Station, Texas, USA). The circle size was weighted according to the accumulated sample size, and the width of the line directly connecting two interventions was weighted using accumulated numbers of eligible studies.

Methodological quality assessment

The risk of bias in the included studies was assessed using the Cochrane risk of bias assessment tool (28) from the following seven items: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and selective reporting. Each item was labeled with a "high", "unclear", or "low" risk of bias depending on the criteria. Moreover, the overall level of methodological quality was determined according to the proportion of "unclear" and "high" risk of bias.

Statistical analysis

A direct random-effects meta-analysis was first performed by using RevMan version 5.3 (Copenhagen: The Nordic Cochrane Centre, the Cochrane Collaboration, 2014). All outcomes were dichotomous variables; thus, the odds ratio (OR) with a 95% confidence interval (CI) was used to express the pooled results. Before performing quantitative synthesis, statistical heterogeneity was evaluated across studies using the chi-square test (29) and I^2 statistics to quantify heterogeneity (30).

Next, the aggregate data drug information system (ADDIS) 1.16.8 software (Groningen, the Netherlands, https://www.drugis.org/) was used to perform a network meta-analysis, which was based on the Markov Chain Monte Carlo (MCMC) simulation. Results from the network meta-analysis were expressed as OR, accompanied by a

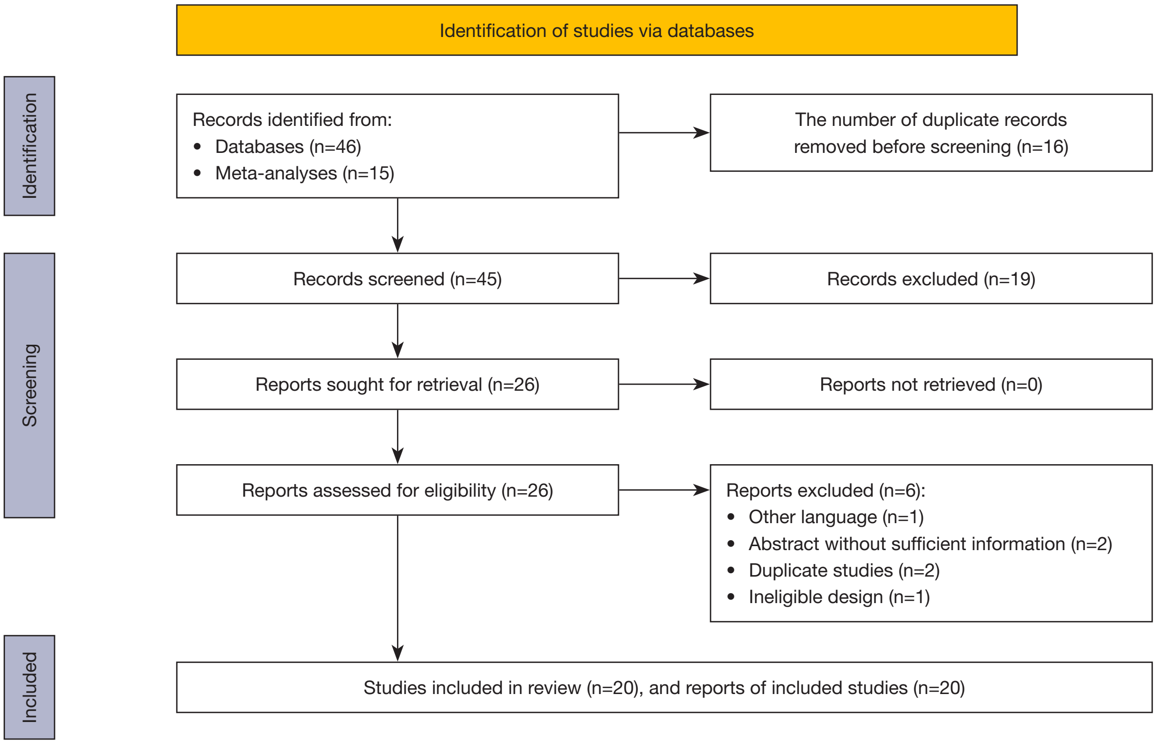

Figure 1 PRISMA flow chart of identification and selection of studies.

95% credible interval (CrI). Before conducting quantitative synthesis, the split node method was first used to explore the possibility of inconsistency between direct and indirect effects (31,32), which was performed using Stata 14.0 (Stata Corp LP, College Station, Texas, USA). Direct and indirect effects were considered consistent if the 95% CI contained 0, with a P value >0.05. A number of chains was set to 4, tuning iterations to 2,000, simulation iterations to 50,000, thinning interval to 10, inference samples to 10,000, and variance scaling factor to 2.5 in order to achieve good convergence (33), which was evaluated by using potential proportional reduction factor (PRF) (34,35). We also separately investigated the comparative effectiveness and safety of four available balloon angioplasty techniques in patients with AVFs.

After completing the network meta-analysis, Stata 14.0 (Stata Corp LP, College Station, Texas, USA) was used to draw a comparison-adjusted funnel plot to evaluate the robustness of pooled results when the accumulated numbers of eligible studies were >10 (36).

Finally, the surface under the cumulative ranking curve (SUCRA) values were calculated to rank all targeted balloon angioplasty techniques by estimating the possibility of a certain ranking (37).

Results

Identification and selection of study

Among 46 records that were identified from the updated search, 16 repeated records were removed. After checking out the titles and abstracts, 19 ineligible records were excluded. After checking the full texts of 11 unique records, 8 studies met our selection criteria, and 3 ineligible studies were excluded due to language (n=1) and abstract with insufficient information (n=2). Moreover, 15 potentially eligible studies were initially identified from published meta-analyses. Then, 12 eligible studies were judged to meet the selection criteria after excluding 3 ineligible studies from repeated studies (n=2) and ineligible design (n=1). Finally, 20 eligible studies (21-24,38-53) were included in this network meta-analysis. There was no conflict regarding study selection between the two independent reviewers. The PRISMA flow chart of the literature search is shown in *Figure 1*.

Studies' characteristics

Table 1 summarizes the characteristics of the eligible studies. Among the 20 studies, 2 (21,50) compared CtBA with CBA; 2 (38,48) compared CtBA with HBA; 8 (39,41,44,45,47,49,51,53) compared DcBA with CBA; and 8 (22-24,40,42,43,46,52) compared DcBA with HBA. There were 12 studies (22-24,38,39,41,43,45,48,50,51,53) that enrolled patients with target lesion of AVF; 2 (21,44) enrolled patients with AVG, and 6 (40,42,46,47,49,52) enrolled patients with mixed target lesions including AVF and AVG. The follow-up duration of the studies ranged from 6 to 42 months.

Assessment of study quality

Except for one study (41), all the others used appropriate methods to produce the random sequence. Meanwhile, all but two (46,49) of the 18 studies (21-24,38-45,47,48,50-53) concealed allocation. Only 7 studies (22,23,39,41,44,47,49) stated to avoid performance bias; however, 12 studies (22,23,39,40,42,44,45,47,48,51-53) avoided detection bias through blinding outcome assessors. The results in 6 studies could be adversely affected by attrition bias; however, only 2 studies encountered a reporting bias. Moreover, ten studies (38,39,41-45,47-49) were judged with a high risk of bias due to insufficient sample size. There were no conflicts regarding the risk of bias assessment between the two independent reviewers. *Table 2* summarizes the details of the risk of bias in each eligible study.

Evidence structure

All studies reported TLPP at 6 months follow-up and the incidence of complications; however, TLPP at 12 months was missing from 2 studies. Based on these results, the evidence networks of the three outcomes were constructed and displayed in *Figure 2*.

Inconsistency examination

Inconsistency examination suggested that direct and indirect effects were consistent in terms of TLPP at 6 [inconsistent factor (IF), 0.229; 95% CI: 0.00 to 2.98; P=0.797] and 12 (IF, 0.415; 95% CI: 0.00 to 3.02; P=0.463) months; however, the direct and indirect effects were inconsistent in terms of the incidence of complications (IF, 1.288; 95% CI: 0.00 to 6.42; P<0.001).

Meta-analysis of TLPP at 6 months

Two studies compared CtBA with CBA, and a direct meta-analysis indicated that patients receiving CtBA had higher TLPP at 6 months of follow-up compared with patients receiving CBA (OR, 1.91; 95% CI: 1.27 to 2.86; P=0.002); however, remaining comparisons did not reach statistical significance (Figure S1A). Unfortunately, the significant results in the direct meta-analysis were not confirmed in the network meta-analysis (OR, 1.81; 95% CrI: 0.40 to 8.19) (*Figure 3A*). Ranking based on probability suggested that CtBA was the optimal treatment option (55.0%), followed by HBA (36.0%), DcBA (38.0%), and CBA (51.0%) (*Figure 3A*).

Meta-analysis of TLPP at 12 months

Among 2 studies that compared CtBA with CBA, only one reported TLPP at 12 months of follow-up. The direct meta-analysis indicated a higher TLPP at 12 months of follow-up related to the CBA (OR, 1.56; 95% CI: 1.13 to 2.15; P=0.006) (Figure S1B); however, the remaining comparisons did not reach statistical significance (Figure S1B). Unfortunately, the network meta-analysis did not detect all comparisons as statistically significant (*Figure 3B*). Ranking based on probability suggested that CtBA was the optimal treatment option (53.0%), followed by HBA (37.0%), DcBA (37.0%), and CBA (55.0%) (*Figure 3B*).

Meta-analysis of complications

All 20 studies reported the incidence of complications after receiving balloon angioplasty. Direct meta-analysis revealed no significant differences among the available comparisons (Figure S2). Network meta-analysis found that CtBA was associated with increased incidence of complications compared with CBA (OR, 8.95; 95% CrI: 1.77, 64.79), HBA (OR, 27.94; 95% CrI: 1.44, 1,511.80), and DcBA (OR, 0.05; 95% CrI: 0.00, 0.83) (*Figure 3C*). The remaining comparisons, including DcBA versus CBA, DcBA versus HBA, and HBA versus CBA, did not reach significant differences (*Figure 3C*). Ranking based on probability suggested that HBA was the optimal treatment option (70.0%), followed by DcBA (66.0%), CBA (72.0%), and CtBA (99.0%) (*Figure 3B*).

Sensitivity analysis of TLPP

For meta-analysis of TLPP, substantial statistical heterogeneity

Table 1 Characteristics of included studies (n=20)

Study	Comparison	Patients (n)	Male (n)	Mean age (years)	Paclitaxel dose	Target lesion	Antiplatelet therapy	Follow-up (months)	Definition of primary outcome
Saleh 2014	CBA *vs.* CtBA	316 *vs.* 307	185 *vs.* 137	60.4 *vs.* 61.9	n.a.	AVF	Heparin 2,000 IU	15	Maintained patency until access failure due to restenosis
Vesely 2005	CBA *vs.* CtBA	173 *vs.* 167	115 *vs.* 110	61.4 *vs.* 63.4	n.a.	AVG	n.r.	6	Patency until the next intervention performed on the target lesion
Aftab 2014	HBA *vs.* CtBA	35 *vs.* 36	25 *vs.* 24	57.6 *vs.* 62.5	n.a.	AVF	n.r.	24	Uninterrupted patency until next access thrombosis or reintervention
Rasuli 2015	HBA *vs.* CtBA	20 *vs.* 19	11 *vs.* 11	70.0 *vs.* 61.0	n.a.	AVF	n.r.	32	The interval following intervention until the next access thrombosis or repeated intervention
Björkman 2019	CBA *vs.* DcBA	20 *vs.* 19	13 *vs.* 10	67.0 *vs.* 67.4	3.5 μg/m^2	AVF	Aspirin 100 mg/d + clopidogrel 75 mg/d or warfarin	12	Any reintervention due to the same lesion or any loss of the AVF
Kim 2020	CBA *vs.* DcBA	19 *vs.* 20	9 *vs.* 12	63.7 *vs.* 60.7	n.r.	AVF	Heparin 2,500 IU	42	The presence of a functional dialysis circuit with no clinical need for repeat intervention at the TL
Liao 2020	CBA *vs.* DcBA	22 *vs.* 22	9 *vs.* 3	65.9 *vs.* 70.4	n.r.	AVG	n.r.	12	No need for reintervention on the target lesion
Maleux 2018	CBA *vs.* DcBA	31 *vs.* 33	18 *vs.* 24	66.9 *vs.* 69.3	n.r.	AVF	n.r.	12	Patent functional fistula without TLR
Pang 2021	CBA *vs.* DcBA	20 *vs.* 20	17 *vs.* 15	57.4 *vs.* 58.1	n.r.	AVF/AVG	n.r.	12	Patent functional fistula without TLR
Roosen 2017	CBA *vs.* DcBA	18 *vs.* 16	7 *vs.* 14	80.0 *vs.* 83.0	n.r.	AVF/AVG	Heparin 2,500 IU	24	Occlusion or restenosis of >50% on duplex and blood flow measurements lower than 600 mL/min
Swinnen 2019	CBA *vs.* DcBA	60 *vs.* 68	37 *vs.* 42	64.5 *vs.* 65.2	3.0 μg/m^2	AVF	Aspirin 100 mg/d + clopidogrel 75 mg/d or warfarin	12	Reintervention to the index trial area
Trerotola 2020	CBA *vs.* DcBA	144 *vs.* 141	83 *vs.* 75	61.0 *vs.* 64.0	2 μg/mm^2	AVF	n.r.	24	No thrombosis or need for TLR
Irani 2018	HBA *vs.* DcBA	60 *vs.* 59	40 *vs.* 39	59.4 *vs.* 59.0	3.0 μg/m^2	AVF/AVG	100 mg acetylsalicylic acid + 75 mg clopidogrel bisulphate	12	No need for reintervention on the target lesion
Karunanithy 2021	HBA *vs.* DcBA	106 *vs.* 106	61 *vs.* 67	64.1 *vs.* 66.9	n.r.	AVF	n.r.	12	Patency with no reintervention to the area 5 mm proximal to, within, and 5 mm distal to the index treatment segment

Table 1 (*continued*)

Table 1 (*continued*)

Study	Comparison	Patients (n)	Male (n)	Mean age (years)	Paclitaxel dose	Target lesion	Antiplatelet therapy	Follow-up (months)	Definition of primary outcome
Kitrou 2015a	HBA *vs.* DcBA	20 *vs.* 20	14 *vs.* 15	62.5 *vs.* 65.7	3 μg/m^2	AVF/AVG	Aspirin 100 mg/d	12	<50% angiographic restenosis with no TLR
Kitrou 2015b	HBA *vs.* DcBA	20 *vs.* 20	14 *vs.* 12	57.0 *vs.* 64.3	3 μg/m^2	AVF	Aspirin 100 mg/d	12	Functional dialysis circuit with no CD-TLR
Lookstein 2020	HBA *vs.* DcBA	160 *vs.* 170	101 *vs.* 112	65.5 *vs.* 65.8	n.r.	AVF	n.r.	6	Freedom from clinically driven target-lesion. Revascularization or access-circuit thrombosis measured during the 6 months after the index procedure
Moreno-Sánchez 2020	HBA *vs.* DcBA	78 *vs.* 70	52 *vs.* 55	71.0 *vs.* 69.0	n.r.	AVF/AVG	Heparin 80 IU/kg previous angioplasty	12	The time elapsed between the completion of effective. Angioplasty and the appearance of clinical and anatomic restenosis
Therasse 2021	HBA *vs.* DcBA	60 *vs.* 60	50 *vs.* 50	66.6 *vs.* 63.5	n.r.	AVF/AVG	n.r.	12	Adjusted late lumen loss
Yin 2021	HBA *vs.* DcBA	83 *vs.* 78	42 *vs.* 44	54.0 *vs.* 56.0	3.0 μg/m^2	AVF	None	12	Target lesion intervention-free survival in conjunction with a DUS-derived PSVR ≤2.0

CBA, conventional balloon angioplasty; CtBA, cutting balloon angioplasty; HBA, high-pressure balloon angioplasty; DcBA, drug-coated balloon angioplasty; n.a., not applicable; n.r., not reported; IU, international unit; AVF, arteriovenous fistula; AVG, arteriovenous graft; TL, target lesion; TLR, target lesion revascularization; CD-TLR, clinically driven target lesion revascularization; DUS, Doppler ultrasound; PSVR, peak systolic velocity ratio.

Table 2 Summary of risk of bias of all included studies (n=20)

Study/items	Generation of random sequence	Allocation concealment	Performance bias	Detection bias	Attrition bias	Reporting bias	Other bias
Saleh 2014	Low (+)	Low (+)	High (–)	High (–)	Low (+)	High (–)	Low (+)
Vesely 2005	Low (+)	Low (+)	Unclear	Unclear	Low (+)	Low (+)	Unclear (?)
Aftab 2014	Low (+)	Low (+)	High (–)	High (–)	Low (+)	High (–)	High (–)
Rasuli 2015	Low (+)	Low (+)	High (–)	Low (+)	High (–)	Low (+)	High (–)
Björkman 2019	Low (+)	Low (+)	Low (+)	Low (+)	High (–)	Low (+)	High (–)
Kim 2020	Unclear (?)	Low (+)	Low (+)	High (–)	High (–)	Low (+)	High (–)
Liao 2020	Low (+)	Low (+)	Low (+)	Low (+)	Low (+)	Low (+)	High (–)
Maleux 2018	Low (+)	Low (+)	High (–)	Low (+)	Low (+)	Low (+)	High (–)
Pang 2021	Low (+)	Low (+)	Low (+)	Low (+)	Low (+)	Low (+)	High (–)
Roosen 2017	Low (+)	Unclear (?)	Low (+)	High (–)	Low (+)	Low (+)	High (–)
Swinnen 2019	Low (+)	Low (+)	High (–)	Low (+)	Low (+)	Low (+)	Low (+)
Trerotola 2020	Low (+)	Low (+)	High (–)	Low (+)	Low (+)	Low (+)	Low (+)
Irani 2018	Low (+)	Low (+)	High (–)	Low (+)	Low (+)	Low (+)	Low (+)
Karunanithy 2021	Low (+)	Low (+)	Low (+)	Low (+)	High (–)	Low (+)	Low (+)
Kitrou 2015a	Low (+)	Low (+)	High (–)	Low (+)	Low (+)	Low (+)	High (–)
Kitrou 2015b	Low (+)	Low (+)	High (–)	High (–)	Low (+)	Low (+)	High (–)
Lookstein 2020	Low (+)	Low (+)	Low (+)	Low (+)	Low (+)	Low (+)	Low (+)
Moreno-Sánchez 2020	Low (+)	Unclear (?)	High (–)	Unclear (?)	Low (+)	Low (+)	Low (+)
Therasse 2021	Low (+)	Low (+)	High (–)	Low (+)	High (–)	Low (+)	Low (+)
Yin 2021	Low (+)	Low (+)	High (–)	High (–)	High (–)	Low (+)	Low (+)

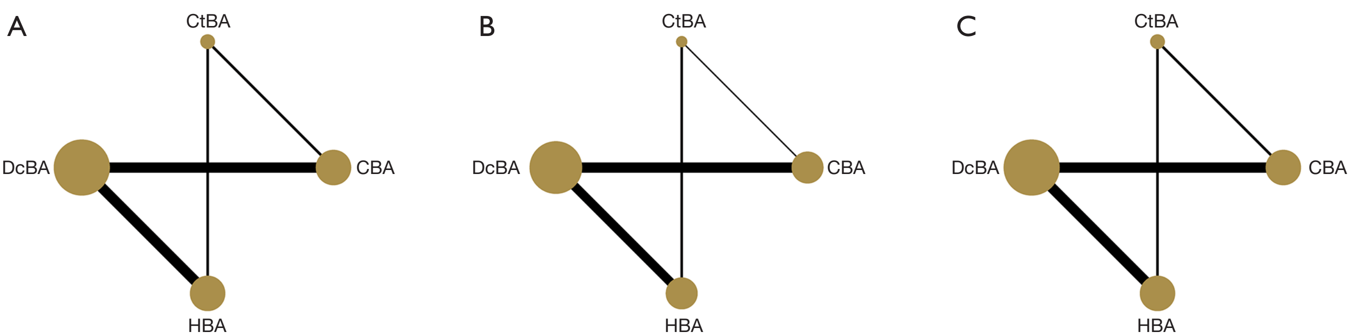

Figure 2 Evidence structure plots of primary patency at 6 (A) and 12 (B) months, and the risk of complications (C). The accumulated sample size weighted the size of the circle size, and the accumulated number of eligible studies weighted the width of the line. CBA, conventional balloon angioplasty; CtBA, cutting balloon angioplasty; HBA, high-pressure balloon angioplasty; DcBA, drug-coated balloon angioplasty.

A. Direct meta-analysis of TLPP at 6 months (upper right)			
DcBA	n.a.	0.97 (0.46, 2.01)	1.20 (0.49, 2.95)
0.70 (0.15, 3.49)	CtBA	1.21 (1.08, 8.01)	**1.91 (1.27, 2.86)**
0.92 (0.35, 2.26)	1.29 (0.27, 5.83)	HBA	n.a.
1.27 (0.48, 3.44)	1.81 (0.40, 8.19)	1.38 (0.41, 5.12)	CBA
Network meta-analysis of TLPP at 6 months (left bottom)			

Ranking: (worst) CBA DcBA HBA CtBA (best)

B. Direct meta-analysis of TLPP at 1 year (upper right)			
DcBA	n.a.	1.10 (0.61, 1.98)	1.30 (0.63, 2.66)
0.77 (0.15, 4.21)	CtBA	1.29 (0.12, 14.17)	**1.56 (1.13, 2.15)**
0.96 (0.37, 2.28)	1.26 (0.24, 5.81)	HBA	n.a.
1.36 (0.58, 3.54)	1.77 (0.35, 10.01)	1.42 (0.44, 5.32)	CBA
Network meta-analysis of TLPP at 1 year (left bottom)			

Ranking: (worst) CBA DcBA HBA CtBA (best)

C. Direct meta-analysis of complications (upper right)			
DcBA	n.a.	1.37 (0.94, 2.01)	0.83 (0.19, 3.56)
0.05 (0.00, 0.83)	CtBA	3.16 (0.32, 31.38)	4.60 (0.30, 69.50)
1.32 (0.63, 2.47)	**27.94 (1.44, 1,511.80)**	HBA	n.a.
0.59 (0.08, 3.20)	**8.95 (1.77, 64.79)**	0.32 (0.01, 5.54)	CBA
Network meta-analysis of complications (left bottom)			

Ranking: (worst) CtBA CBA DcBA HBA (best)

Figure 3 Pooled results and rankings of primary patency at 6 (A) and 12 (B) months, and the risk of complications (C). Data are shown as OR (95% CrI). A bold numerical value indicates statistical significance. TLPP, target lesion primary patency; CBA, conventional balloon angioplasty; CtBA, cutting balloon angioplasty; HBA, high-pressure balloon angioplasty; DcBA, drug-coated balloon angioplasty; n.a., not applicable; OR, odds ratio; CrI, credible interval.

across studies was detected. Therefore, we conducted the sensitivity analysis for comparisons with enough eligible studies by using the leave-one-out method. The results revealed that the pooled estimates of the target comparisons were robust and credible, as presented in Table S2.

Subgroup analysis of AVF

We performed a separate network meta-analysis to determine the comparative effectiveness and safety of the four common balloon angioplasty techniques in patients with AVF. Pooled results did not reveal significant differences in all comparisons regarding all outcomes (Figure S3).

Publication bias examination

The comparison-adjusted funnel plots of TLPP at 6 (Figure S4A) and 12 (Figure S4B) months of follow-up indicated asymmetric outline, suggesting a possibility of publication bias. A symmetric comparison-adjusted funnel plot of complications suggested an absence of publication bias (Figure S4C).

Discussion

Although balloon angioplasty has been regarded as the preferred option for treating venous outflow stenosis by clinical guidelines (1,2,54), it remains unclear which type of balloon angioplasty technique should be selected in routine daily practice. This network meta-analysis aimed to solve this issue. Our results revealed that all available balloon angioplasty techniques were not statistically significant in terms of TLPP at 6 and 12 months; however, CtBA was found to have a higher risk of complications than DcBA, HBA, and CBA. Moreover, the network meta-analysis did not detect significant differences among patients with AVFs.

Three direct meta-analyses (16-18) investigated the comparative effectiveness and safety of DcBA versus CBA in patients with AFVs, AVGs, and CVFs. Among three meta-analyses (16,18), two found that DcBA was superior to CBA in primary patency. However, another meta-analysis of RCTs (17) suggested that DcBA did not have a significant patency benefit for treating hemodialysis vascular access dysfunction compared with CBA, which is consistent with our findings. Interestingly, two meta-analyses that combined RCTs and cohort studies detected statistically significant differences, which might be the major reason for the conflicting results.

Two meta-analyses (13,15) investigated the comparative effectiveness and safety of DcBA versus CBA in patients with AVFs. Abdul Salim *et al.* found that DcBA did not significantly improve over CBA in decreasing fistula stenosis in the RCT (13), which is consistent with our findings. However, Cao *et al.* reported DcBA as an effective procedure associated with lower 6- and 12-month TLPP than CBA in *de novo* or recurrent AVF stenosis (15). DcBA has been found to have greater treatment benefits for restenotic lesions than *de novo* lesions (39,40), which may somewhat explain these inconsistencies. Moreover, the inclusion of cohort studies might contribute to the conflict because statistical significance was identified in cohort studies by Abdul Salim *et al.* (13).

In 2015, Agarwal *et al.* performed the first meta-analysis to compare CtBA with CBA, reporting CtBA as more effective in treating hemodialysis access stenosis, with significantly higher six-month patency than balloon angioplasty (14), which is not in line with our findings. Unfortunately, the authors combined conventional and high-pressure in this meta-analysis as an individual regimen (21,38,50). Meanwhile, another eligible study that compared CtBA with HBA and detected a conflicting result was excluded (48). These two reasons are of critical importance for explaining these conflicting findings.

In 2021, a network meta-analysis was conducted to investigate the comparative effectiveness of different endovascular treatments for patients with failing autogenous AVFs with outflow vein stenosis (19). In this network meta-analysis, the authors found that DcBA was substantially superior to CBA, with improved 6-month failure rates, which is inconsistent with our findings. It must be noted that this network meta-analysis incorrectly included a study with an ineligible design in the final analysis (20). Meanwhile, CBA and HBA were simultaneously combined as an individual regime. However, in the present network meta-analysis, CBA and HBA were separately defined as individual regimens, and eight additional eligible studies were included. More importantly, we also evaluated the safety of four available balloon angioplasty techniques, finding that CtBA was associated with an increased risk of complications. Published evidence suggested that AVFs were associated with the lowest risk of complications, lowest need for intervention, and best long-term patency compared to other access routes (55). It was also found that AVF patency post-angioplasty was usually superior to AVG patency (43,56). Therefore, a separate network meta-analysis in patients with AVFs was performed in the present study; yet, the subgroup analysis with 4 additional studies still did not detect any significant differences in available comparisons.

The present network meta-analysis has several limitations. First, most eligible studies included in our network meta-analysis only enrolled a limited sample size, which might introduce a small sample bias. Second, doses of paclitaxel were different from one to another, and most eligible studies did not provide information on the dose. Therefore, performing subgroup analyses to explore the impact of dose on pooled results was not possible. Third, eligible studies included in this network meta-analysis comprised combinations of various AVF configurations and *de novo* lesions with recurrent ones. However, subgroup analysis could not be designed due to limited data, which may impair the reliability of our pooled results. Forth, the majority of eligible studies were judged with a high risk of bias, which may inevitably impair the robustness and reliability of our findings.

Conclusions

For patients with failing autogenous AVFs and AVGs stenosis, although it might be a preferred option for improving primary patency, CtBA should not be selected as a preferential approach considering it may significantly increase the risk of complications. In contrast, HBA might be a preferred treatment option as it is associated with a lower risk of complications and has numerically higher primary patency than DcBA and CBA. However, our findings should be further verified owing to the several limitations detailed above.

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Footnote

Reporting Checklist: The authors have completed the PRISMA NMA reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-381/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-381/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. No institutional ethical approval and patients' informed consent was required as this is a network meta-analysis of published data.

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Supplementary

Table S1 Search strategies of performing updated literature search in PubMed and Embase

Search number	Query
Strategy of PubMed	
7	#6 Filters: from 2020/1/1 - 2021/7/31
6	#3 and #4 and #5
5	random*[Title/Abstract]
4	(((((((((drug-coated balloon[Title/Abstract]) OR (drug coated balloon[Title/Abstract])) OR (drug-eluting balloon[Title/Abstract])) OR (drug eluting balloon[Title/Abstract])) OR (paclitaxel-coated balloon[Title/Abstract])) OR (paclitaxel coated balloon[Title/Abstract])) OR (paclitaxel-eluting balloon[Title/Abstract])) OR (paclitaxel eluting balloon[Title/Abstract])) OR (cutting balloon[Title/Abstract])) OR (cutting-balloon[Title/Abstract])
3	#1 or #2
2	((((((((((((Arteriovenous Fistula[Title/Abstract]) OR (Arteriovenous Fistulas[Title/Abstract])) OR (Arteriovenous Aneurysm[Title/Abstract])) OR (arteriovenous fistulae[Title/Abstract])) OR (AV fistulas[Title/Abstract])) OR (arteriovenous access[Title/Abstract])) OR (hemodialysis fistulas[Title/Abstract])) OR (hemodialysis access[Title/Abstract])) OR (dialysis fistulas[Title/Abstract])) OR (dialysis access[Title/Abstract])) OR (dialysis fistula[Title/Abstract])) OR (dialysis fistulae[Title/Abstract])) OR (dialysis fistulas[Title/Abstract])
1	"Arteriovenous Fistula"[Mesh]
Strategy of Embase (via Ovid)	
1	(Arteriovenous Fistula or Arteriovenous Fistulas or Arteriovenous Aneurysm or arteriovenous fistulae or AV fistulas or arteriovenous access or hemodialysis fistulas or hemodialysis access or dialysis fistulas or dialysis access or dialysis fistula or dialysis fistulae or dialysis fistulas).af.
2	(drug-coated balloon or drug coated balloon or drug-eluting balloon or drug eluting balloon or paclitaxel-coated balloon or paclitaxel coated balloon or paclitaxel-eluting balloon or paclitaxel eluting balloon or cutting balloon or cutting-balloon).af.
3	random*.af.
4	#1 and #2 and #3
5	limit 4 to (embase and yr="2020 -Current")

and * indicate order and truncation characters in all search strategies, respectively.

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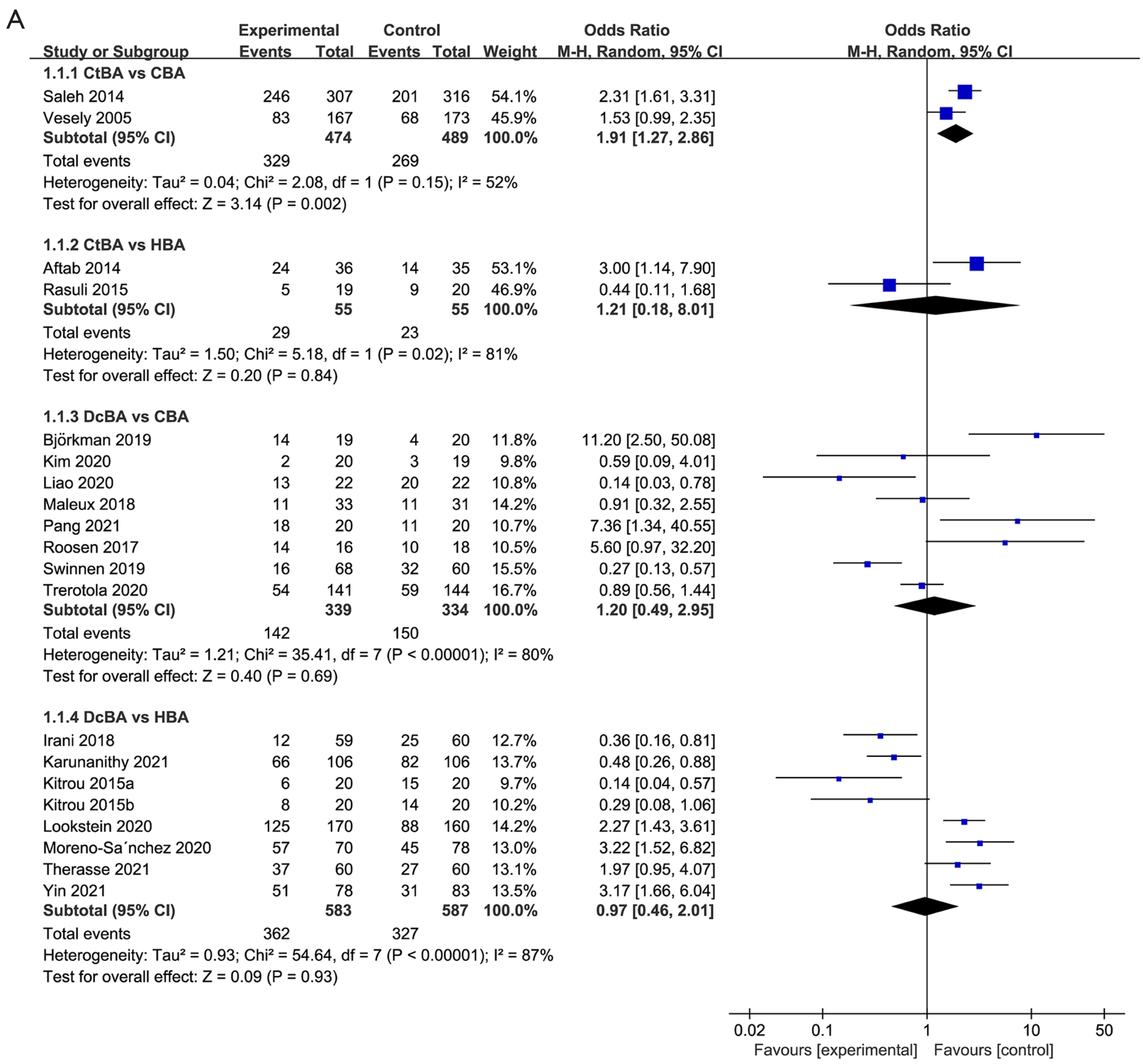

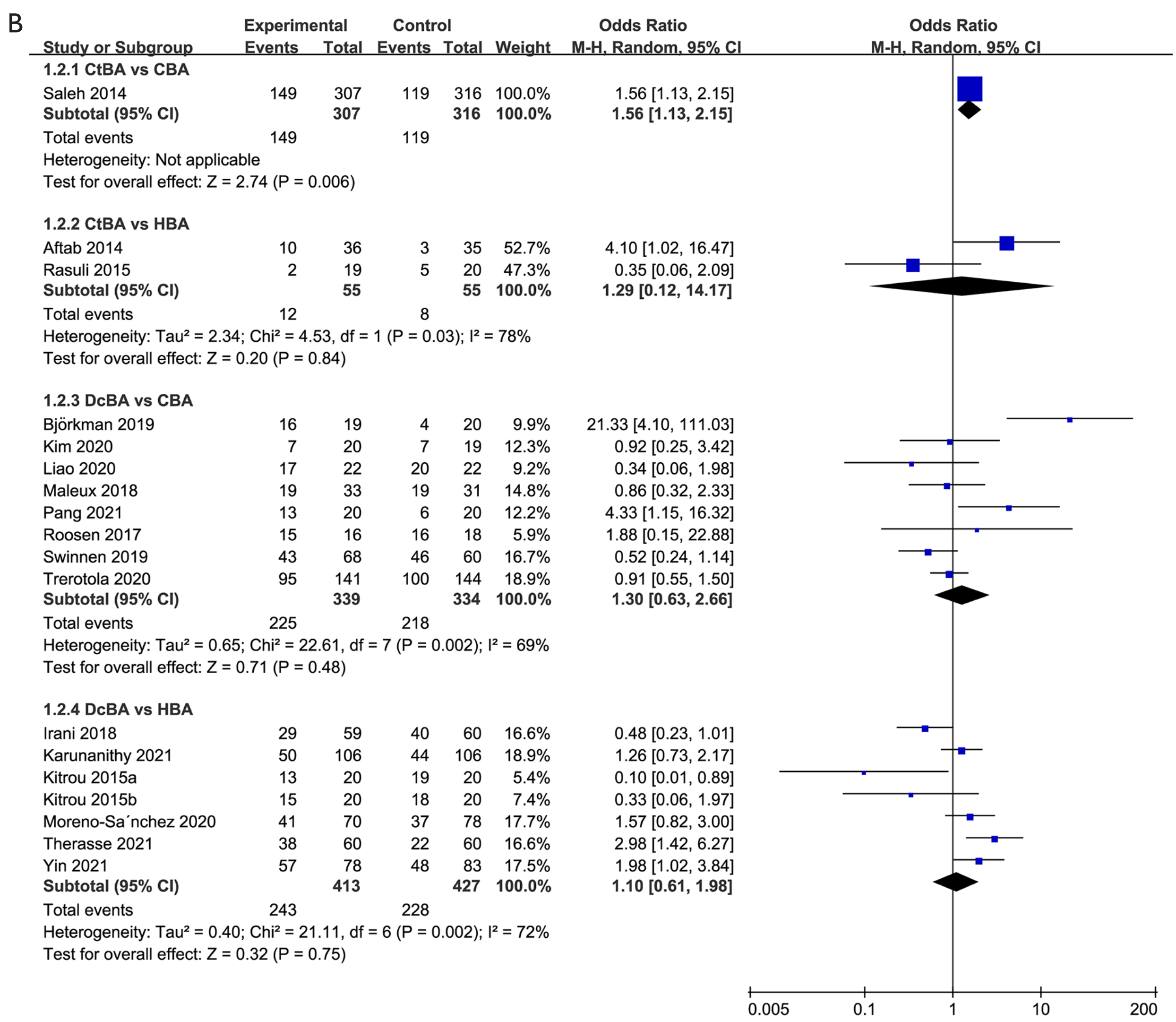

Figure S1 Direct meta-analysis of primary patency at 6 (A) and 12 (B) months. CBA, conventional balloon angioplasty; CtBA, cutting balloon angioplasty; HBA, high-pressure balloon angioplasty; DcBA, drug-coated balloon angioplasty; M-H, Mantel-Haenszel test; CI, confidence interval.

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Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
1.3.1 CtBA vs CBA						
Saleh 2014	3	307	2	316	58.1%	1.55 [0.26, 9.34]
Vesely 2005	9	167	0	173	41.9%	20.80 [1.20, 360.26]
Subtotal (95% CI)		**474**		**489**	**100.0%**	**4.60 [0.30, 69.50]**
Total events	12		2			
Heterogeneity: Tau² = 2.46; Chi² = 2.67, df = 1 (P = 0.10); I² = 62%						
Test for overall effect: Z = 1.10 (P = 0.27)						
1.3.2 CtBA vs HBA						
Aftab 2014	1	36	0	35	50.4%	3.00 [0.12, 76.16]
Rasuli 2015	1	19	0	20	49.6%	3.32 [0.13, 86.75]
Subtotal (95% CI)		**55**		**55**	**100.0%**	**3.16 [0.32, 31.38]**
Total events	2		0			
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.97); I² = 0%						
Test for overall effect: Z = 0.98 (P = 0.33)						
1.3.3 DcBA vs CBA						
Björkman 2019	0	19	0	20		Not estimable
Kim 2020	0	20	0	19		Not estimable
Liao 2020	0	22	0	22		Not estimable
Maleux 2018	0	33	0	31		Not estimable
Pang 2021	0	20	1	20	19.9%	0.32 [0.01, 8.26]
Roosen 2017	1	16	1	18	25.9%	1.13 [0.07, 19.74]
Swinnen 2019	0	68	0	60		Not estimable
Trerotola 2020	2	141	2	144	54.2%	1.02 [0.14, 7.35]
Subtotal (95% CI)		**339**		**334**	**100.0%**	**0.83 [0.19, 3.56]**
Total events	3		4			
Heterogeneity: Tau² = 0.00; Chi² = 0.42, df = 2 (P = 0.81); I² = 0%						
Test for overall effect: Z = 0.25 (P = 0.80)						
1.3.4 DcBA vs HBA						
Irani 2018	1	59	2	60	2.4%	0.50 [0.04, 5.67]
Karunanithy 2021	36	106	23	106	38.2%	1.86 [1.01, 3.42]
Kitrou 2015a	0	20	0	20		Not estimable
Kitrou 2015b	0	20	0	20		Not estimable
Lookstein 2020	7	112	7	101	12.2%	0.90 [0.30, 2.65]
Moreno-Sa´nchez 2020	10	70	6	78	12.6%	2.00 [0.69, 5.82]
Therasse 2021	24	60	21	60	26.2%	1.24 [0.59, 2.60]
Yin 2021	4	78	6	83	8.4%	0.69 [0.19, 2.56]
Subtotal (95% CI)		**525**		**528**	**100.0%**	**1.37 [0.94, 2.01]**
Total events	82		65			
Heterogeneity: Tau² = 0.00; Chi² = 3.80, df = 5 (P = 0.58); I² = 0%						
Test for overall effect: Z = 1.65 (P = 0.10)						

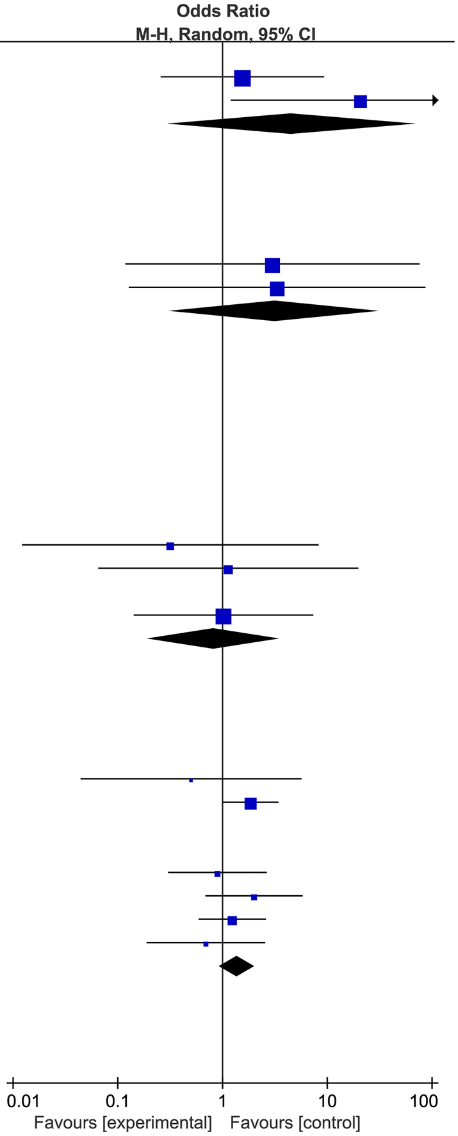

Figure S2 Direct meta-analysis of the risk of complications. CBA, conventional balloon angioplasty; CtBA, cutting balloon angioplasty; HBA, high-pressure balloon angioplasty; DcBA, drug-coated balloon angioplasty; M-H, Mantel-Haenszel test; CI, confidence interval.

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Table S2 Sensitivity analysis for TLPP

Study omitted	Estimate	95% confidence interval	
		Lower limit	Upper limit
DcBA *vs.* CBA at 6 months			
Björkman 2019	0.86912698	0.37871107	1.9946122
Kim 2020	1.3063101	0.49086684	3.476393
Liao 2020	1.5423765	0.60705429	3.9188018
Maleux 2018	1.2796054	0.44235927	3.7014937
Pang 2021	0.95854467	0.38811821	2.3673403
Roosen 2017	0.99810743	0.3950333	2.5218596
Swinnen 2019	1.5773673	0.60431349	4.1172137
Trerotola 2020	1.3194708	0.38023081	4.5788059
Combined	1.2002981	0.48867757	2.9481924
DcBA *vs.* HBA at 6 months			
Irani 2018	1.1267979	0.53241336	2.3847518
Karunanithy 2021	1.085014	0.50376171	2.3369291
Kitrou 2015a	1.196044	0.5838905	2.4499819
Kitrou 2015b	1.1119275	0.52160305	2.3703523
Lookstein 2020	0.82626736	0.34848315	1.9591126
Moreno-Sánchez 2020	0.80419916	0.36116749	1.7906824
Therasse 2021	0.85656273	0.36956403	1.9853116
Yin 2021	0.80011308	0.35871392	1.7846562
Combined	0.96595591	0.46425638	2.009818
DcBA *vs.* CBA at 12 months			
Björkman 2019	0.90605354	0.55998427	1.465993
Kim 2020	1.3840177	0.61242169	3.1277549
Liao 2020	1.4920369	0.69672459	3.1952
Maleux 2018	1.4265829	0.61000663	3.3362572
Pang 2021	1.0816749	0.52561241	2.2260141
Roosen 2017	1.2752627	0.5961675	2.7279165
Swinnen 2019	1.5750393	0.68441933	3.6246033
Trerotola 2020	1.465888	0.55817395	3.8497458
Combined	1.2969767	0.63291672	2.6577723
DcBA *vs.* HBA at 12 months			
Irani 2018	1.3674501	0.78225172	2.3904324
Karunanithy 2021	1.0063983	0.46996474	2.1551354
Kitrou 2015a	1.2824373	0.74747241	2.2002757
Kitrou 2015b	1.2162904	0.66808385	2.2143359
Moreno-Sánchez 2020	0.97911733	0.47352758	2.0245299
Therasse 2021	0.92053491	0.49961829	1.6960638
Yin 2021	0.94708562	0.47157124	1.9020904
Combined	1.101362	0.61166319	1.9831148

TLPP, target lesion primary patency; CBA, conventional balloon angioplasty; CtBA, cutting balloon angioplasty; HBA, high-pressure balloon angioplasty; DcBA, drug-coated balloon angioplasty; TLPP, target lesion primary patency.

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A. TLPP at 6 months			
DcBA			
0.61 (0.09, 3.86)	CtBA		
0.85 (0.25, 2.62)	1.43 (0.22, 7.37)	HBA	
1.08 (0.32, 3.55)	1.76 (0.26, 11.64)	1.25 (0.27, 6.55)	CBA
Ranking: (worst) CBA	DcBA	HBA	CtBA (best)
B. TLPP at 12 months			
DcBA			
0.75 (0.11, 5.10)	CtBA		
0.98 (0.22, 3.55)	1.29 (0.19, 6.91)	HBA	
1.29 (0.42, 4.52)	1.72 (0.27, 13.59)	1.31 (0.29, 9.19)	CBA
Ranking: (worst) CBA	DcBA	HBA	CtBA (best)
C. Complications			
DcBA			
0.21 (0.01, 2.29)	CtBA		
1.38 (0.54, 3.17)	6.33 (0.63, 102.67)	HBA	
0.48 (0.07, 3.87)	2.38 (0.37, 24.60)	0.37 (0.05, 3.24)	CBA
Ranking: (worst) CtBA	CBA	DcBA	HBA (best)

Figure S3 Separate network meta-analysis of AVFs. Data are shown as OR (95% CrI). AVFs, arteriovenous fistulas; TLPP, target lesion primary patency; CBA, conventional balloon angioplasty; CtBA, cutting balloon angioplasty; HBA, high-pressure balloon angioplasty; DcBA, drug-coated balloon angioplasty; OR, odds ratio; CrI, credible interval.

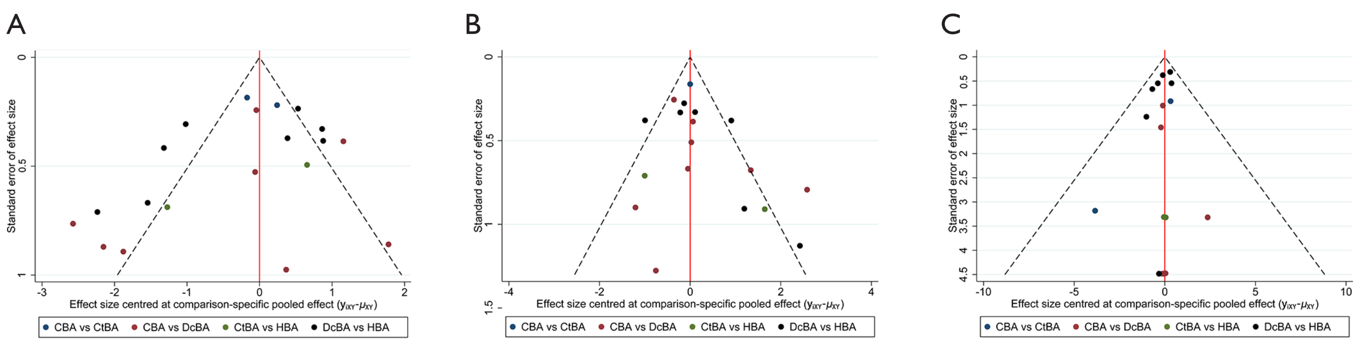

Figure S4 Comparison-adjusted funnel plot of primary patency at 6 (A) and 12 (B) months, and the risk of complications (C). CBA, conventional balloon angioplasty; CtBA, cutting balloon angioplasty; HBA, high-pressure balloon angioplasty; DcBA, drug-coated balloon angioplasty; CI, confidence interval.