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Below-the-Ankle Angioplasty in Patients with Critical Limb Ischemia: A Systematic Review and Meta-Analysis

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ABSTRACT

Purpose: To evaluate the safety and effectiveness of below-the-ankle (BTA) angioplasty and to assess whether additional BTA angioplasty after below-the-knee (BTK) angioplasty would improve clinical outcomes in patients with critical limb ischemia.

Materials and Methods: Two authors independently performed the search, study selection, assessment of methodological quality, and data extraction for this systematic review and meta-analysis. MEDLINE, Embase, and the Cochrane Database of Systematic Reviews were searched. Articles were eligible if it was reported that BTA angioplasty was performed and if the articles were published in English and had the full text available. Methodological quality was assessed using the Methodological Index for Non-Randomized Studies (MINORS) score. The primary outcome was 12-month limb salvage rate. Secondary outcomes were 12-month amputation-free survival, technical success, complications, survival, and freedom from reintervention.

Results: Ten articles met the inclusion criteria, reporting a total of 478 patients with BTA angioplasty performed in 524 legs. Three of the 10 included studies compared BTK angioplasty only to BTK angioplasty and additional BTA angioplasty. The pooled 12-month limb salvage rate was 92% (95% confidence interval [CI], 0.88–0.96). No statistically significant difference was found in limb salvage when additional BTA angioplasty was compared to BTK angioplasty only (odds ratio [OR], 1.23; 95% CI, 0.61–2.49). The pooled 12-month amputation-free survival was 78% (95% CI, 0.69–0.87). No statistically significant difference was found in amputation-free survival rate when additional BTA angioplasty was compared to BTK angioplasty only (OR, 1.58; 95% CI, 0.95–2.64). The methodological quality of the studies included was moderate, according to the MINORS score.

Conclusions: This systematic review and meta-analysis showed that additional BTA angioplasty is a safe and feasible procedure, with a 92% pooled proportion of limb salvage at 12 months.

ABBREVIATIONS

BTA = below-the-ankle, BTK = below-the-knee, CI = confidence interval, CLI = critical limb ischemia, MINORS = Methodological Index for Non-Randomized Studies, OR = odds ratio, PAD = peripheral artery disease

Critical limb ischemia (CLI) is the end stage of peripheral artery disease (PAD), leading to rest pain or tissue loss (1). The TransAtlantic Inter-Society Consensus Working Group II reported an incidence of major amputation due to PAD of 120–500 per million people per year (2). PAD, CLI, and amputation are major contributors in reducing quality of life (3,4). This raises the need for developing new interventions to prevent amputation in CLI patients.

Arterial revascularization is the first-line treatment to restore blood flow into the foot and thus prevent amputation (2). Robust evidence is missing that allows a preference for one treatment modality over the other (endovascular vs open) (5). Over the past few years, new procedures and materials have been introduced in endovascular and surgical techniques (6,7) that improved technical success of below-the-knee (BTK) angioplasty (8,9).

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Tables E1–E3 can be found by accessing the online version of this article on *www.jvir.org* and clicking on the Supplemental Material tab.

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Below-the-ankle (BTA) lesions are the remaining obstacle for an uninterrupted blood flow to the tissue of the foot. The safety and effectiveness of endovascular revascularization in BTA lesions is unclear; whether additional BTA angioplasty after BTK angioplasty will improve the clinical outcomes is also uncertain.

The aim of this study was to evaluate the safety and effectiveness of BTA angioplasty and to assess whether additional BTA angioplasty after BTK angioplasty would improve clinical outcomes in patients with CLI.

MATERIALS AND METHODS

Literature Search

Two authors (E.H. and M.S.) independently searched MEDLINE, Embase, and the Cochrane Database of Systematic Reviews to identify studies reporting clinical outcomes of BTA angioplasty published between June 1964 and March 2018. The following keywords were used: below the ankle, inframalleolar, below the knee, infrapopliteal, tibial arteries, balloon angioplasty, percutaneous transluminal angioplasty, endovascular procedure, endovascular treatment, angioplasty, peripheral artery disease, foot, critical limb ischemia, and arterial occlusive disease. The final search was performed on May 11, 2018.

The "related articles" function in PubMed and reference lists of retrieved articles were also used to identify articles not found in the original search. The search was not restricted to any language. The details of the search strategy are listed in **Table E1** and **Table E2** (available online on the article's Supplemental Material page at *www.jvir.org*).

Validity Assessment

After duplicates were removed, 2 authors (E.H. and M.S.) screened the titles and abstracts of the identified studies for relevance. Full texts were obtained of the remaining relevant studies, and 2 authors (E.H. and M.S.) read the full-text articles and made a final selection of relevant studies. Two authors (E.H. and M.S.) independently assessed the methodological quality of the retrospective articles using the Methodological Index for Non-Randomized Studies (MINORS) score, with a global ideal score of 16 for noncomparative studies and 24 for comparative studies (10). The MINORS score was reported as a percentage of the global ideal score. For this review, a score of ≤8 was considered poor quality, 9–14 moderate quality, and ≥15 good quality for noncomparative studies. For comparative studies, a score of ≤15 was considered poor quality, 16–22 moderate quality, and ≥23 good quality. Discrepancies between the authors during the search, selection, and quality assessment were resolved by discussion. If agreement was not reached, a third author (C.U.) was consulted.

Inclusion and Exclusion Criteria

Studies. Articles were eligible if they reported clinical results of BTA angioplasty (defined as percutaneous transluminal angioplasty of inframalleolar arterial lesions), were published in English, were human studies, and had the full text available. Any type of balloon and stent used for angioplasty was eligible (eg, drug-eluting stent, bare-metal stent, plain balloon, and drug-eluting balloon). Finally, the same criteria were used to screen all cross-references for potentially relevant studies not identified by the initial literature search.

Participants. Studies were included that reported clinical outcomes of patients undergoing BTA angioplasty for limb salvage.

Outcome measures and definitions. The primary outcome was limb salvage at 12 months. Secondary outcomes were amputation-free survival at 12 months, technical success, complications, survival, and freedom from reintervention. Limb salvage was defined as freedom from major amputation (above the ankle). Amputation-free survival was defined as avoidance of major amputation or mortality. Freedom from reintervention was defined as avoidance of any endovascular procedure or bypass surgery.

Data Extraction

Two authors (E.H. and M.S.) independently performed data extraction. Data extracted included study design, study period, inclusion and exclusion criteria, age, sex, comorbidities (eg, diabetes mellitus, hyperlipidemia, hypertension, smoking history or current smoker, and end-stage renal disease), ankle brachial index before and after revascularization, technical approach used, revascularization type, BTA arteries treated, stent used, outcome measures, as described above, and follow-up duration.

Data Analysis

MetaAnalysist 3.1 software was used for the meta-analysis. Kaplan-Meier estimates were converted to proportions using the number enrolled and the survival estimate at 12 months. If Kaplan-Meier estimates were not presented, the amputation numbers and mortality numbers from the text were used to calculate the proportions, only when no patients were lost to follow-up. Rates were pooled using the DerSimonian-Laird random-effects model because of the differences in study designs among the studies. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using binary random-effects model for comparative data. The presence of heterogeneity between the studies was determined by using a Forest plot and by performing a χ^2 heterogeneity test. The I^2 index was also calculated. Data are reported as mean and standard deviation as appropriate.

RESULTS

Description of Studies

The initial search identified 3182 studies. After duplicates were removed and the titles and abstracts were screened

Table 1. Included Studies

Study	Study design	Study period	Inclusion criteria	Exclusion criteria	Pt, n	legs, n	Age, y, mean	M, n (%)	DM, n (%)	HL, n (%)	HT, n (%)	Smoking, n (%)	RD, n (%)	ABI before (mmHg)	ABI after (mmHg)	FU, mean (mo)	MINORS
Abdelhamid 2010	Retrospective	2004-2008	stenosis (>70%) occlusion of the target vessel	-	39	42	72.4	26 (67)	26 (67)	34 (87)	27 (69)	31 (80)	6 (15)	-	-	15	10
Katsanos 2013	Retrospective	2007-2011	CLI and previous PTA of infrapopliteal lesions (Rutherford ≥ 4)	-	37	40	73.5	29 (78)	27 (73)	25 (68)	29 (78)	16 (43)	8 (22)	-	-	20	9
Kawarada 2011	Retrospective	2006-2009	CLI (Rutherford ≥ 4)	-	31	40	67	22 (71)	23 (74)	8 (26)	25 (81)	18 (58)	24 (77)	-	-	19	9
Manzi 2009	Prospective	2007-2008	CLI (Rutherford ≥ 4)	-	114	115	70	86 (75)	109 (95)	34 (30)	95 (83)	37 (32)	-	-	-	10	11
Nakama 2016	Retrospective	2012-2013	CLI with pedal artery occlusion and insufficient WB after conventional above-the-ankle PTA (Rutherford 5–6)	Kawarada type 1	14	14	77.0	11 (79)	10 (71)	5 (36)	11 (79)	6 (43)	5 (36)	0.74	0.94	-	17
Nakama 2017	Retrospective	2012-2014	CLI presenting with de novo infrapopliteal lesions, poor pedal runoff, widespread wounds or severe infection (Rutherford 5-6)	Kawarada type 1	140	140	72.2	96 (69)	101 (72)	44 (31)	96 (69)	67 (48)	89 (64)	0.67	0.88	-	16
Palena 2014	Retrospective	2011-2012	CLI (Rutherford 5–6) requiring metatarsal artery access	-	38	38	73.2	28 (74)	38 (100)	12 (32)	30 (79)	-	8 (21)	-	-	7	10
Teymen 2018	Retrospective	2012-2016	CLI (Rutherford ≥ 4) stenosis or occlusion 1 BTK vessel with incomplete or no pedal loop.	-	48	48	63	33 (73)	48 (100)	34 (76)	38 (84)	31 (69)	8 (18)	0.43	0.88	-	17
Zhu 2009	Retrospective	2007-2009	CLI, occluded DPA or PA, no option for conventional PTA or bypass surgery, no lateral branches (Rutherford ≥ 4)	-	37	57	70.9	24 (65)	37 (100)	-	29 (78)	21 (57)	8 (22)	0.44	0.87	9	9
Zhu 2011	Retrospective	2009-2010	CLI, failure of standard PTA to DPA or PA, angiographic patency DPA or PA, no collateral branches (Rutherford ≥ 4)	-	8	8	74.5	5 (63)	8 (100)	-	-	-	-	0.32	0.75	6	9

Note–Data is presented as counts (percentage).

- = not reported; ABI = ankle brachial index; BTK = below-the-knee; CLI = critical limb ischemia; DM = diabetes mellitus; DPA = dorsalis pedis artery; FU = follow-up; HL = hyperlipidemia; HT = hypertension; M = male; mo = months; PA = pedal artery; Pt = patients; PTA = percutaneous transluminal angioplasty; RD = renal disease; SM = smoking; y = years.

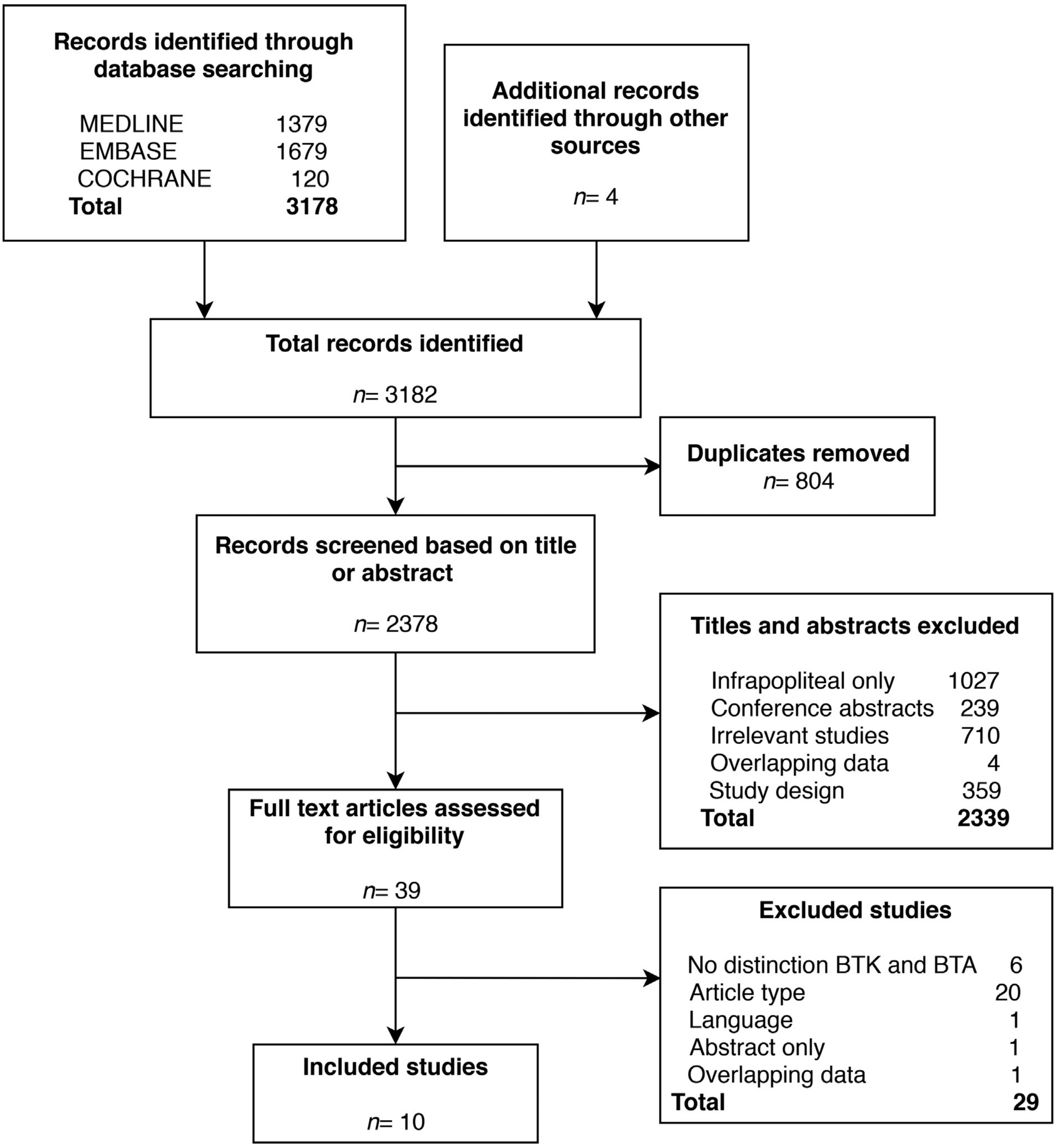

Figure 1. Flow chart of study selection.

for relevance, 39 full-text articles were assessed for eligibility. Applying the inclusion and exclusion criteria resulted in 10 articles (11–20) being finally included in this systematic review. A flow chart of the selection procedure is shown in **Figure 1**. Twenty-nine studies were excluded for the following reasons: no distinction made between patients with and without BTA revascularization (n = 6); written in Chinese language only (n = 1); case reports, editorial comments, or reviews (n = 20); publication with overlapping data (n = 1); and full text not available (n = 1). The excluded studies are listed in **Table E3** (available online on the article's Supplemental Material page at *www.jvir.org*).

The characteristics of included studies are listed in **Table 1**. In 7 of the 10 studies, the purpose was to investigate the feasibility and to report clinical outcomes of BTA angioplasty. In the other 3 studies, the purpose was to compare the results of BTK angioplasty only to BTK angioplasty and additional BTA angioplasty. All 10 studies were included in the meta-analysis for calculating the proportion of 12-month limb salvage and amputation-free survival (when reported in the studies). A separate meta-analysis was performed of the 3 comparative studies to calculate the OR for limb salvage and amputation-free survival in BTK angioplasty only versus BTK angioplasty and additional BTA.

	Abdelhamid 2010	Katsanos 2013	Kawarada 2011	Manzi 2009	Nakama 2016	Nakama 2017	Palena 2014	Teymen 2017	Zhu 2009	Zhu 2011
1. A clearly stated aim	2	2	2	2	2	2	2	2	2	2
2. Inclusion of consecutive patients	2	2	2	2	1	1	2	2	2	2
3. Prospective collection of data	2	1	1	2	2	1	1	1	1	1
4. Endpoint appropriate to the aim of the study	2	2	2	2	2	2	2	2	2	2
5. Unbiased assessment of the study endpoint	0	0	0	0	0	0	0	0	0	0
6. Follow-up period appropriate to the aim of the study	2	2	2	2	2	2	2	2	2	2
7. Loss to follow-up less then 5%	0	0	0	1	0	0	1	0	0	0
8. Prospective calculation of the study size	0	0	0	0	0	0	0	0	0	0
Item 9-12 only for comparative studies										
9. An adequate controle group					2	2		2		
10. Contemporary groups					2	2		2		
11. Baseline equivalence of groups					2	2		2		
12. Adequate statistical analysis					2	2		2		
Total MINORS score	**10**	**9**	**9**	**11**	**17**	**16**	**10**	**17**	**9**	**9**
Maximum possible score	16	16	16	16	24	24	16	24	16	16

moderate quality; poor quality

Figure 2. Study quality assessment (MINORS score).

All included studies were of moderate quality according to the MINORS score (**Fig 2**). None of the included studies reported a prospective calculation of the study size. Three studies (11,14,16) had a prospective collection of data.

The 10 included studies described a total of 478 patients with BTA angioplasty performed in 524 critical ischemic limbs. The study period of the included articles ranged from 2004 to 2016. All included patients had CLI and were classified as Rutherford category 4 (44 legs) or 5 or 6 (420 legs). Two studies (11,18) included patients with Rutherford category ≥4 but did not specify the number of legs per Rutherford category (60 legs). Two studies (15,16) excluded patients with patent dorsal and lateral plantar arteries (Kawarada classification type 1 pedal artery disease) (21).The other studies did not report exclusion criteria (11–14,17–20).

The lesions treated were located in the plantar artery, dorsalis pedis artery, or distal (inframalleolar) posterior tibial artery. If inflow lesions were present, these were treated in the same procedure as the BTA lesions in almost all studies (11,12,14–20). In 1 study, the BTK lesions were treated before the BTA intervention took place (13). The target artery in 2 studies (15,17) was based on the angiosome concept (22). In 1 study (14), the target arteries were both pedal and plantar arteries and their anatomical anastomosis. The target artery in the other studies (11–13,16,18–20) was based on the arterial lesion location.

All studies reported technical success, which ranged from 63% to 95%. Complications were reported in 6 studies (11,13,15,18–20) and included vessel perforation (n = 7), subacute occlusion (n = 12), balloon rupture (n = 3), puncture hematoma (n = 7), retroperitoneal hematoma caused by puncture (n = 1), heart failure (n = 1), and stroke (n = 1).

Plain balloons were used for recanalization in 9 studies (11–7,19,20), and drug-eluting balloons were used in 1 study (18). Stents were used after failed or suboptimal angioplasty in 2 studies (12,13); coronary bare-metal stents were used in 1 study (13); and drug-eluting stents and bare-metal stents were both used in the other study (12).

In 3 studies (14,17,19), a special technique was used to access the arteries and lesions. One of these studies (14) used a pedal-plantar loop technique in which pedal and plantar arteries and their anatomical anastomosis were both recanalized. In the study by Palena et al (17), transmetatarsal artery access was used. The 2011 study by Zhu et al (19) used a retrograde transdorsal-to-plantar or transplantar-to-dorsal intraluminal reentry technique. The last 2 studies (17,19) included only patients in whom standard revascularization failed.

Three of the included studies compared additional BTA angioplasty to BTK revascularization only (15,16,18). In the 2017 study by Nakama et al (15), absence of flow after target artery revascularization, poor pedal artery runoff, and widespread wound or limb-threatening infection were indications for additional BTA revascularization. In the 2016 study by Nakama et al (16), the indication for additional BTA revascularization was based on the wound blush concept (23). Patients underwent BTA if the wound blush was insufficient after BTK angioplasty. One study (18) reported that the reason for additional BTA revascularization was at the operator's discretion. The characteristics and outcomes of the 3 studies comparing BTK angioplasty only to BTK angioplasty and additional BTA angioplasty are listed in **Table 2**.

Twelve-Month Outcomes

The 12-month limb salvage rate was 92% (95% CI, 0.88–0.96) (**Fig 3**). The difference in the limb salvage rate between additional BTA angioplasty and BTK-treated arteries only was not statistically significant (OR, 1.23; 95% CI, 0.61-2.49)

Table 2. Characteristics of Studies Comparing Additional BTA with BTK Only

	Nakama 2016		Nakama 2017		Teymen 2018	
	BTA	BTK	BTA	BTK	BTA	BTK
Pt, n	14	15	140	117	20	25
legs, n	14	15	140	117	20	25
Age, y, mean	77	79	72	74	62	64
Male, n (%)	11 (79)	10 (67)	96 (69)	79 (68)	14 (70)	19 (76)
DM, n (%)	10 (71)	10 (67)	101 (72)	86 (74)	20 (100)	25 (100)
HL, n (%)	5 (36)	3 (20)	44 (31)	32 (27)	15 (75)	19 (76)
HT, n (%)	11 (79)	11 (73)	96 (69)	90 (77)	17 (85)	21 (84)
Smoking, n (%)	6 (43)	7 (47)	67 (48)	44 (38)	18 (90)	22 (88)
ESRD, n (%)	5 (36)	6 (40)	89 (64)	71 (61)	3 (15)	5 (20)
Pedal artery type 3[†]	11 (79)	6 (40)	74 (53)	39 (33)	4 (20)	7 (28)
ABI before	0.74	0.52	0.67	0.66	0.43	0.43
ABI after	0.94	0.86	0.88	0.81	0.88	0.87
Revascularization type	Indirect		Direct		Indirect	
Special technique used	None		None		None	
Reason additional BTA	Wound blush concept		Absence of flow after target artery, poor pedal artery runoff, wound, or limb-threatening infection		Operator's choice	
Technical success, n (%)	93	-	89	-	85	-
Complications	0 (0.0)	-	9 (6.4)	8 (6.8)	4 (20)	3 (12)
Overall survival	86	73	85	80	95	92
Limb salvage	93	83	89	88	84*	73*
AFS	79	53	76	70	-	-
Wound healing	93	60	59	38	-	-

Note–The 12-months outcomes of overall survival, limb salvage, AFS, and wound healing are reported. Data are presented as counts (percentage).
- = not reported; ABI = ankle brachial index; AFS = amputation-free survival; BTA = below-the-ankle; BTK = below-the-knee; DM = diabetes mellitus; ESRD = end-stage renal disease; HL = hyperlipidemia; HT = hypertension; Pt = patients; SM = smoking; y = years.
*Minor amputations are included.
[†]The pedal artery type is based on the Kawarada classification system.

(Fig 4). The amputation-free survival was 78% (95% CI, 0.69–0.87) (Fig 5). No statistically significant difference was found in the amputation-free survival rate when additional BTA angioplasty and BTK angioplasty only was compared (OR, 1.58; 95% CI, 0.95–2.64) (Fig 6). Freedom from BTA reintervention was reported in 4 studies and ranged from 40% to 94%. Survival rates were reported in 7 studies and ranged from 71% to 100%.

DISCUSSION

In this systematic review and meta-analysis of BTA revascularization, the pooled proportion of limb salvage and amputation-free survival at 12 months was 0.92 and 0.78. No statistically significant difference was found in the amputation-free survival rate or limb salvage rate when additional BTA angioplasty-treated patients were compared to BTK angioplasty only.

The quality of the included studies was moderate. This was due to unreported loss to follow-up and no prospective calculation of the study size. In the comparative studies, no randomization was made. One study (18) reported that the choice for additional BTA angioplasty was made by the operator but was not specified.

Although no significant difference was found in limb salvage rates or amputation-free survival rates when BTK angioplasty only was compared to BTK angioplasty and additional BTA angioplasty, the wound healing rates were more promising in the additional BTA angioplasty group. Table 2 shows wound healing rates of 93% versus 60% in Nakama (2016) (16) and 59% versus 38% in Nakama (2017) (15) in favor of the additional BTA angioplasty group. Interestingly, more severe pedal artery disease was seen in the additional BTA group comparing the BTK angioplasty group only (79% type 3 Kawarada (21) artery disease vs 40% in Nakama [2016] (16) and 53% vs 33% in Nakama [2017] (15)). With even more severe pedal artery disease, wound healing results were better in the additional BTA angioplasty group compared to the BTK angioplasty-only group. According to these numbers, additional BTA angioplasty could be beneficial for wound healing. However, stronger evidence is needed to substantiate this benefit.

Clinical heterogeneity was observed in the included studies. Two studies used stents (12,13); 1 study used a

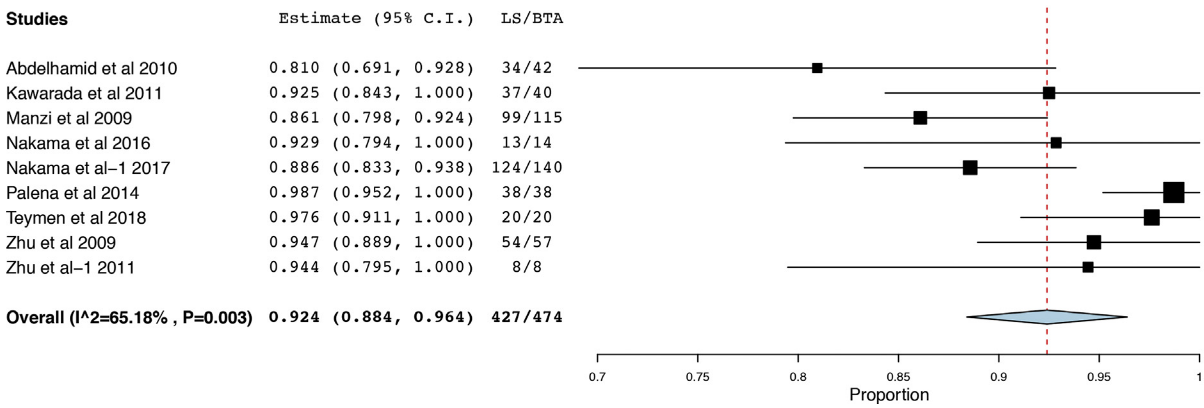

Figure 3. Pooled analysis of limb salvage.

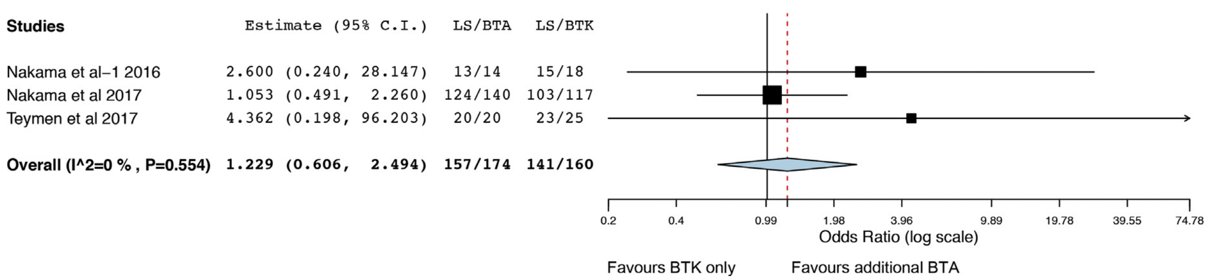

Figure 4. Limb salvage rate of additional BTA angioplasty compared to BTK angioplasty only.

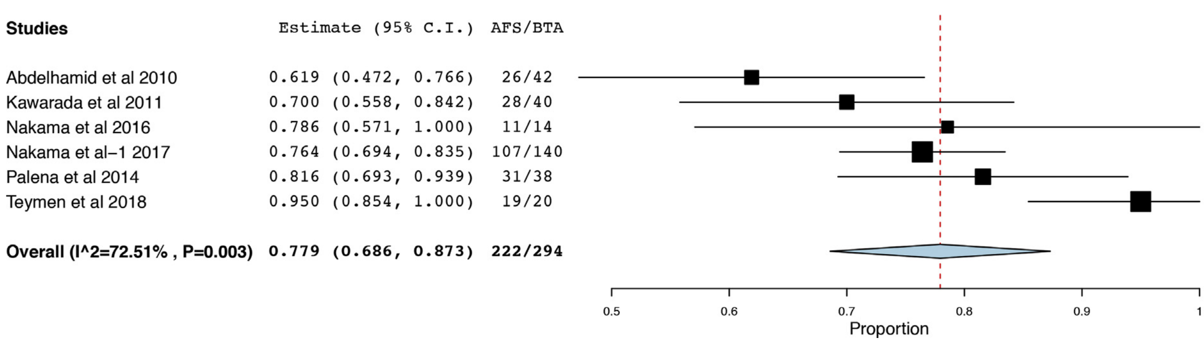

Figure 5. Pooled analysis of amputation-free survival.

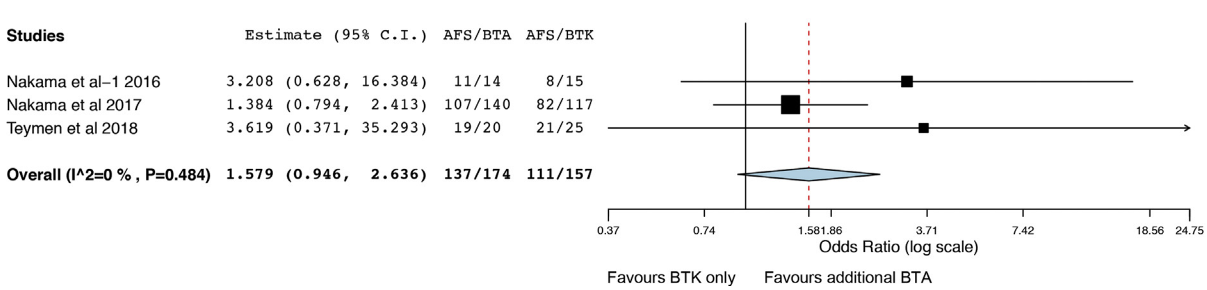

Figure 6. Amputation-free survival rate of additional BTA angioplasty compared to BTK angioplasty only.

drug-eluting balloon (18); 3 studies used a special technique (14,17,19); 1 study used a wound blush as a criterion for additional BTA angioplasty (16); and 2 studies used the angiosome concept (15,17). Also, more pedal arteries were occluded in the additional BTA group compared to the BTK-only group in the studies by Nakama (2016) and Nakama (2017). To deal with these differences, a random-effects model was used for the meta-analysis. Besides that, 2 meta-analyses (24,25) compared major amputation rates after infrapopliteal percutaneous transluminal angioplasty with different methods and different patient characteristics. No statistically difference was found when percutaneous transluminal angioplasty with a plain balloon was compared to a drug-eluting balloon or to a bare metal stent (24). Also, no significant differences were found when different lesions lengths, vessel diameters, and percentage of calcified lesions were compared (25). The presence of clinical heterogeneity must accounted for when interpreting the outcomes. However, the effect of clinical heterogeneity on major amputation is unclear.

This study had several limitations. First, the methodological quality of the included studies was moderate, according to the MINORS score. Nine of the 10 included studies were retrospective cohort studies (11–13,15–20) with a relatively small sample size (mean sample size of 48 patients). The reported loss to follow-up was often inadequate or absent. Furthermore, there was a considerable clinical heterogeneity among studies.

In addition, the focus of this study was the safety, effectiveness, and clinical outcomes defined as limb salvage, technical success, and amputation-free survival rate. However, outcomes such as wound healing, quality of life, and tissue perfusion are of increasing value in CLI patients and should be studied as well.

In conclusion, the currently available evidence suggests that additional BTA angioplasty is a safe and feasible procedure. No statistically significant limb salvage rates or amputation-free survival rates were found when additional BTA angioplasty was compared to BTK angioplasty alone. However, there is a potential benefit in wound healing for additional BTA angioplasty. High-quality research is needed to clarify the benefits of additional BTA angioplasty.

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Table E1. Search Strategy (MEDLINE)

Component of search	Search terms
1. Below the ankle	((((((below the ankle) OR below the knee) OR infrapopliteal) OR inframalleolar) OR tibial arteries[MeSH Terms]) OR tibial artery[MeSH Terms]) OR tibial artery OR foot arteries
AND	
2. Angioplasty	(((((((((((balloon angioplasty[MeSH Terms]) OR balloon angioplasty) OR revascularization) OR PTA) OR angioplasty, percutaneous transluminal [MeSH Terms]) OR percutaneous transluminal angioplasty) OR technique, endovascular[MeSH Terms]) OR endovascular procedure[MeSH Terms]) OR endovascular treatment) OR endovascular interventions) OR angioplasty[MeSH Terms]) OR angioplasty, balloon[MeSH Terms]
AND	
3. Peripheral arterial disease	(((((((((((peripheral artery disease[MeSH Terms]) OR peripheral arterial disease [MeSH Terms]) OR arterial disease, peripheral[MeSH Terms]) OR PAD) OR peripheral artery disease) OR peripheral arterial disease) OR critical limb ischemia) OR arterial occlusive disease[MeSH Terms]) OR disease, arterial occlusive[MeSH Terms]) OR arterial occlusive disease) OR critical limb ischemia) OR CLI

CLI = critical limb ischemia; MeSH = Medical Subject Headings; PAD = peripheral artery disease; PTA = percutaneous transluminal angioplasty.

Table E2. Search Strategy (Embase)

Component of search	Search terms
1. Below the ankle	('infrapopliteal angioplasty'/exp OR 'infrapopliteal artery'/exp OR 'infrapopliteal artery disease'/exp OR 'tibial artery'/exp OR 'below the knee' OR 'below the ankle' OR 'inframalleolar' OR 'infrapopliteal' OR 'infrapopliteal artery' OR ‘foot artery’)
AND	
2. Angioplasty	('percutaneous transluminal angioplasty'/exp OR 'balloon catheter'/exp OR 'balloon dilatation'/exp OR 'leg revascularization'/exp OR 'revascularization'/exp OR 'angioplasty'/exp OR 'PTA' OR 'balloon angioplasty' OR 'endovascular intervention' OR 'endovascular treatment')
AND	
3. Peripheral arterial disease	('peripheral vascular disease·/exp OR 'peripheral occlusive artery disease'/exp OR 'critical limb ischemia'/exp OR 'pad')

PTA = percutaneous transluminal angioplasty.

Table E3. Excluded Studies

First author	Study design	Reason for exclusion
Alexandrescu 2009	Commentary	Study design
Alexandrescu 2011	Retrospective study	No distinction BTK with and without BTA revascularization
Ballotta 2010	Retrospective study	No distinction BTK with and without BTA revascularization
Ferraresi 2015	Retrospective study	No distinction BTK with and without BTA revascularization
Fusaro 2007	Case report	Study design
Fusaro 2007	Case report	Study design
George 2014	Case report	Study design
Hansen 2009	Case report	Study design
Kawarada 2008	Case report	Study design
Kawarada 2012	Retrospective study	No distinction BTK with and without BTA revascularization
Kim 2013	Case report	Study design
Kret 2014	Retrospective study	No distinction BTK with and without BTA revascularization
Manzi 2011	Review	Study design
Manzi 2013	Case report	Study design
Mustapha 2014	Case series	Study design
Mustapha 2017	Editorial comment	Study design
Nakama 2014	Case report	Study design
Palena 2012	Retrospective study	Overlapping data
Palena 2014	Review	Study design
Palena 2014	Review	Study design
Palena 2014	Review	Study design
Prasad 2014	Editorial comment	Study design
Rastan 2010	Prospective study	No distinction BTK with and without BTA revascularization
Safian 2014	Editorial comment	Study design
Shimada 2014	Commentary	Study design
Valle 2017	Review	Study design
Venturini 2013	Case report	Study design
Wu 2012	Prospective study	Only abstract available
Xu 2011	Retrospective study	Full text available only in Chinese

BTK = below-the-knee; BTA = below-the-ankle.