


Effect of buttonhole cannulation versus rope-ladder cannulation in hemodialysis patients with vascular access

A systematic review and meta-analysis of randomized/clinical controlled trials

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Abstract

Background: Safe and effective arteriovenous fistula (AVF) puncture techniques must be used to reduce harm to hemodialysis patients. The relative benefits of buttonhole (BH) cannulation over those of rope ladder (RL) cannulation for AVF remain unclear and inconsistent.

Methods: This systematic review and meta-analysis was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. Literature searches were conducted in June 2020 in multiple scientific databases including Cochrane library, CINAHL, PubMed/ Medline, Airiti Library, National Digital Library of Theses and Dissertations in Taiwan, Google scholar, Embase, and ProQuest. We included all randomized controlled trials (RCTs) and clinical controlled trials (CCTs) that explored the efficacy of BH cannulation in hemodialysis patients. These included reports published in either English or Chinese that enrolled adults aged 18 years or older who underwent hemodialysis using an autogenous AVF. Studies that showed poor design, such as use of a self-control group or no control group, were excluded from analysis. *The critical appraisal skills program checklist for RCTs were used to assess the quality of the evidence and RevMan software were used to perform the meta-analysis.*

Results: Fifteen studies (11 RCTs and 4 CCTs) met the inclusion criteria and were used for the meta-analysis. Meta-analysis showed that BH cannulation significantly reduced aneurysm formation (RR = 0.18, 95% confidence interval [CI] [0.1, 0.32]), stenosis (RR = 0.44, 95% CI [0.25, 0.77]), thrombosis formation (RR = 0.4, 95% CI [0.2, 0.8]), and hematoma (RR = 0.63, 95% CI [0.40, 0.99]) and showed no differences in AVR infection (≤ 6 months, RR = 2.17, 95% CI [0.76, 6.23]; >6 months, RR = 2.7, 95% CI [0.92, 7.92]) compared to RL cannulation.

Conclusions: Given the benefits of BH, this meta-analysis found that BH cannulation should be recommended as a routine procedure for hemodialysis but that hospitals and hemodialysis clinics should strengthen staff knowledge and skills of BH cannulation to reduce the risk of AVF infection.

Abbreviations: AVF = arteriovenous fistula, BH = buttonhole cannulation, CASP = critical appraisal skills programs, CCT = controlled clinical trial, CINAHL = cumulative index to nursing and allied health literature, CIs = confidence intervals, FSN = fail-safe number, GRADE = The grading of recommendations, assessment, development and evaluation, ITT = intention to treat, NRS = numerical rating scale, OR = odds ratios, RCT = randomized control trial, RL = rope ladder cannulation, RR = relative risk, PRISMA = reporting items for systematic reviews and meta-analyses, TL = tolerance level, VAS = visual analog scale.

Keywords: aneurysm, buttonhole cannulation, hematoma, meta-analysis, rope ladder cannulation, stenosis

The author(s) of this work have nothing to disclose.

The datasets generated during and/or analyzed during the current study are publicly available.

Ethics Approval: Not required for this study.

Ethical Statement: Ethic approval is not applicable in this study because it is a systematic review and meta-analysis.

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1. Introduction

Vascular access is regarded as a second lifeline for patients with hemodialysis, and arteriovenous fistulas (AVFs) are considered the best access method for long-term dialysis patients. The average life span of an AVF ranges from 3 months to 3 years, and the occlusion rate and infection rate are relatively lower than those associated with other vascular access methods.^[1] The quality of the puncture made by AVF is key in determining the duration of its future lifespan and is therefore considered a major factor in the success of hemodialysis treatment.^[2] Clinically, stenosis or obstruction of the fistula is a common complication that can cause patients to be hospitalized.^[3] Not only does this decrease their quality of life, but it also exerts considerable pressure on nursing staff. Therefore, a less complicated and painless puncture method would benefit all parties involved.

Rope ladder (RL) cannulation is the most commonly used technique for AVF puncture. It uses sharp needles that are fixed in pairs at several points along the fistula. Another AVF puncture technique is buttonhole (BH) cannulation. BH cannulation has been popular in Europe for nearly 30 years and has been gaining attention in U.S. as the recommended cannulation technique.^[4] A BH track is generally formed after 6 to 9 cannulations with a sharp needle, with sites at a 20–30° angle and at least 3 cm from the arterial or venous anastomosis. Most studies indicate that the benefits of BH puncture include increased fistula survival, reduced complications, and reduced puncture pain.^[5–7] while other studies propose that BH puncture increases AVF infection rate.^[8–9] Although there has been some effort to produce systematic reviews and meta-analyses on the topic^[10–14] conclusions based on consistent empirical research are still lacking. More specifically, results used in these reviews were either based on low quality design^[10, 11, 13] or lacked depth, scope, and reach^[11–14] or had a small follow up duration^[10, 14]. Therefore, this study aims to explore and compare the effects of BH puncture with RL puncture on vascular access, infection, and pain by performing a systematic review and meta-analysis of studies with more rigorous design (RCT or CCT) or longer follow up period, and to provide reliable research integration evidence as the basis for future clinical care.

2. Materials and Methods

2.1. Search and screening strategies

This systematic review and meta-analysis was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.^[15] Literature searches were conducted in June 2020 in multiple scientific databases including Cochrane library, Cumulative Index to Nursing and Allied Health Literature (CINAHL), PubMed/ Medline, Airtiti Library, National Digital Library of Theses and Dissertations in Taiwan, Google scholar, Embase, and ProQuest. We conducted searches on the above electronic databases using the following keywords: “arteriovenous fistula”, “A-V shunt”, “vascular access”, “Buttonhole Cannulation”, “Buttonhole needling”, “constant-site cannulation”, “constant site”, “rope ladder cannulation”, “rope ladder”, or “rope-ladder technique”. Two authors (LPW and LHT) independently performed the literature search, along with study identification, screening, and data extraction. Titles and abstracts of all articles were screened and identified in the listed databases and reviewed the full text of the eligible articles. In addition, the references of the included studies were manually checked to identify additional potential studies. All screening processes were discussed by the entire team. Figure 1 presents the flow diagram of this systematic review and meta-analysis.

2.2. Inclusion and exclusion criteria

We included all randomized controlled trials (RCTs) and controlled clinical trials (CCTs) that explored the efficacy of BH cannulation in hemodialysis patients. These included reports published in either English or Chinese that enrolled adults aged 18 years or older who underwent hemodialysis using an autogenous AVF. Studies that showed poor design, such as use of a self-control group or no control group, were excluded from analysis. Other exclusion criteria were opinion pieces, editorials, and conference abstracts. Patients who underwent BH cannulation were considered the experiment group, and patients who underwent RL cannulation were considered the control group. The primary outcome measures were infection, aneurysm formation, fistula survival, and stenosis. Secondary endpoints were pain, hematoma, and thrombosis.

2.3. Data extraction

Information extraction was based on the studies’ full text; including author, year, country, study design, sample size, characteristics of subjects, follow-up length, and outcome measures.

2.4. Quality assessment

Three authors (LPW, LHT, and HYH) independently evaluated the quality of the chosen studies. Disagreements were resolved by a fourth investigator (SEG). The Critical Appraisal Skills Programs (CASP) scale was used to assess the methodological quality of both RCTs and CCTs.^[16, 17] The CASP scale consists of 11 items designed to rate the evaluation quality. Kappa values were used to evaluate the consistency between 2 reviewers. The grading of recommendations, assessment, development and evaluation (GRADE) scoring system was used to evaluate the level of evidence.^[18]

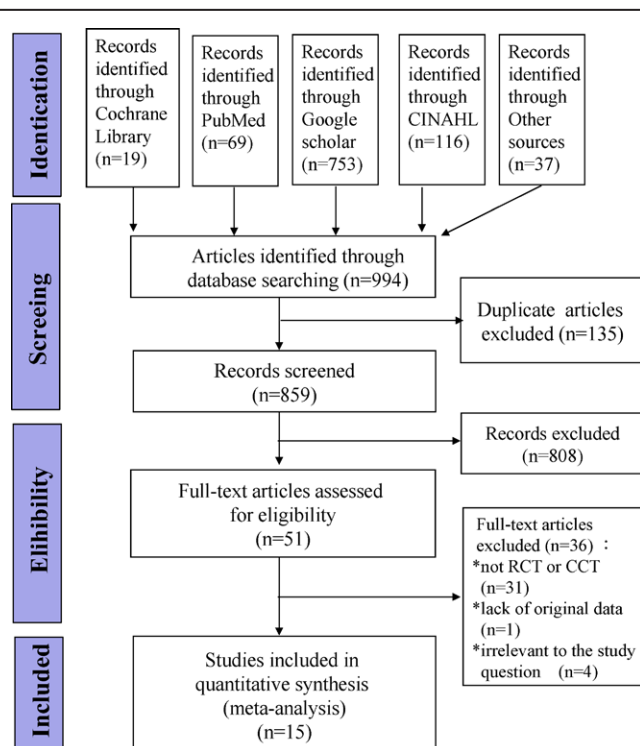


Figure 1. Flowchart of preferred reporting items for systematic reviews and meta-analyses (PRISMA).

2.5. Statistical analysis

After the eligible studies were identified, each study was analyzed using RevMan 5.2 (Review Manager version 5.2, Cochrane). Heterogeneity test was assessed using forest plots that used both Q (a significant result that indicates statistical heterogeneity) and I² (a significant result that indicates methodological heterogeneity) statistics.^[19] A fixed-effects model was adopted for analysis when P > .1 and I² < 50% (because of trial homogeneity), whereas a random-effects model was adopted when P < .1 and I² ≥ 50%^[20]. Descriptive analysis was used in lieu of heterogeneity calculations in cases in which outcome indicators came from an insufficient number of articles. α < 0.05 was considered statistically significant. The magnitude and significance of the effects of outcomes were calculated and are presented as odds ratios (ORs) with 95% confidence intervals (CIs).^[21] The publication bias test of literature is detected by fail-safe number (FSN). A FSN value greater than the tolerance level (TL) means that the publication bias is small, and by consequence, the more credible and stable the results of the meta-analysis.^[22]

3. Results

3.1. Search retrievals

The study selection process, as described above, is illustrated in Figure 1 following PRISMA guidelines. A total of 994 articles were retrieved from the databases, and 135 duplicate articles were deleted; 808 were excluded after reading titles and abstracts; 36 were excluded for ineligible study characteristics, such as different outcome variables, interventions, or populations. Finally, 15 studies that included qualitative and quantitative synthesis were used for meta-analysis.

3.2. Study characteristics

The detailed information of the 15 articles is summarized in Table 1. All of the studies were published between 2003 and

2020. Fifteen studies were conducted 7 in China, 2 in North America, 3 in Europe, 2 in Australia, and 1 in Japan. The study employed 2 outcome categories: primary and secondary. Primary results included 12 infections, 9 aneurysms, 2 fistula survival rates, and 5 stenoses. Secondary results included 13 reports of pain, 8 hematomas, and 6 thromboses.

3.3. Quality assessment

This study included 11 RCTs and 4 CCTs. The results of CASP criteria are listed in Table 2. Of all 15 included studies, 11 RCTs were originally Level II. However, upon further analysis, two of them^[23,24] were found to be unblinded. Additionally, the studies did not conduct Intention to Treat (ITT) or calculate the intervention effect and accuracy. Even in van Loon,^[24] there is no homogeneity analysis of the 2 groups. Consequently, these 2 articles were downgraded to Level III. Although the 2 articles^[23,24] started on a high GRADE score due to their status of RCTs (see Table 3), this was later reduced to moderate level because of some risk of bias, accuracy, and unknown circumstances. In terms of overall study quality, most of the included studies had performance bias and detection bias. Table 3 illustrates the risk of bias of each study. The Kappa value of the consistency between the 2 reviewers is 0.79. The analysis between the reviewers has a certain degree of consistency according to McHugh,^[25] in which a score of 0.60–0.79 is considered moderate.

3.4. Effects for primary outcome of BH and RL on vascular access

3.4.1. Infection. Gram-positive bacteria are the main pathogens of vascular access in dialysis patients. Symptoms of infection include fever, local redness, tenderness, or suppuration.^[26] The summarized effects of 12 studies showed a small effect on infection (Table 4). The statistical heterogeneity was low (homogeneity, I² = 0%; P = .56). However, considering that the definition of infection is heterogeneous between studies, we

Table 1
Systematic review and characteristics of the studies selected for meta-analysis and relevant outcomes (alphabetically).

Study	Origin	Study design	Sample size		Follow up (mo)	Age (years)		participants characteristics (Heterogeneity)	primary results BH:RL	Secondary results BH: RL
			BH	RL		BH (M ± SD)	RL (M ± SD)			
Chan ^[23] 2014	USA	CCT	45	38	12	60.9 ± 16.9	64.1 ± 19.6	diabetic status: BH > RL*	infection: BH > RL survival: BH < RL	–
Chen ^[24] 2012	China	RCT	20	20	12	NA	NA	–	aneurysm: BH < RL*	–
Chen ^[25] 2016	China	RCT	30	29	3	54.3	54.5	–	stenosis: BH < RL† infection: BH > RL	pain: BH < RL* thrombosis: BH < RL† hematoma: BH < RL*
Chow ^[26] 2011	Australia	RCT	34	35	6	<45Y:11 45-59Y:10 > 60Y: 13	<45Y:8 45-59Y:14 > 60Y: 13	–	infection: BH > RL	–
Lai ^[27] 2018	China	RCT	50	50	24	66.1 ± 7.2	65.3 ± 9.7	–	infection: BH > RL† aneurysm: BH < RL stenosis: BH > RL	pain: BH < RL* thrombosis: BH < RL† hematoma: BH < RL
MacRae ^[28] 2012	Canada	RCT	70	70	12	70.3 ± 12.3	66.7 ± 14.4	–	infection: BH > RL*	pain: BH > RL hematoma: BH < RL*
Peng ^[29] 2018	China	RCT	40	40	12	52.4 ± 13.4	51.3 ± 17.4	–	infection: BH > RL*	pain: BH < RL† thrombosis: BH > RL
Qian ^[30] 2014	China	CCT	40	30	12	47 ± 12	51 ± 10	–	infection: BH < RL aneurysm: BH < RL*	pain: BH < RL* thrombosis: BH < RL
Smyth ^[31] 2013	Australia	CCT	41	63	3	60 ± 14	61 ± 14	hospital incentre unit: BH < RL*	infection: BH > RL aneurysm: BH < RL*	pain: BH > RL hematoma: BH < RL

Table 2
Summary of CASP-RCT checklist among included studies.

Study	Study design	Item criteria											Item
		1	2	3	4	5	6	7	8	9	10	11	
Chan ^[23] 2014	CCT	1	0	0	0	1	0	1	0	1	1	0	5
Chen ^[24] 2012	RCT	1	1	0	1	1	0	1	0	1	1	0	7
Chen ^[25] 2016	RCT	1	1	0	1	1	0	1	0	1	1	0	7
Chow ^[26] 2011	RCT	1	1	0	1	1	0	1	0	1	1	0	7
Lai ^[27] 2018	RCT	1	1	0	1	1	0	1	0	1	1	0	7
MacRae ^[28] 2012	RCT	1	1	0	1	1	1	1	1	1	1	0	9
Peng ^[29] 2018	RCT	1	1	0	1	1	0	1	1	1	1	0	8
Qian ^[30] 2014	CCT	1	0	0	1	1	1	0	1	1	0	7	
Smyth ^[31] 2013	CCT	1	0	0	0	1	0	1	0	1	1	0	5
Struthers ^[32] 2010	RCT	1	1	0	1	1	0	0	1	1	1	0	6
Toma ^[33] 2003	RCT	1	1	0	0	1	0	0	0	1	1	0	5
vanLoon ^[34] 2010	CCT	1	0	0	0	1	1	1	0	1	1	0	6
Vaux ^[35] 2013	RCT	1	1	0	1	1	0	1	0	1	1	0	7
Wang ^[36] 2015	RCT	1	1	0	1	1	0	1	1	1	1	0	8
Yin ^[37] 2014	RCT	1	1	0	1	1	1	1	0	1	1	0	8

Note: RCT = randomized control trial; CCT = controlled clinical trial; CASP checklist.

Score (Yes = 1; No = 0): (1) focus? ; (2) Was the assignment of patients to treatments randomized? ; (3) Were measures objective or were the patients and clinicians kept "blind" to which treatment was being received? ; (4) Consistent sample characteristics?; (5) Is treatment of each group consistent?; (6) intention-to-treat analysis?; (7) How large was the treatment effect?; (8) How precise was the estimate of the treatment effect?; (9) Will the results help me in caring for my patient? (Applicability); (10) Contains important results?; (11) harm and costs?

Table 3
Summary of risk of bias for each included study.

Study	Selection bias		Performance bias	Detection bias		Attrition bias	Reporting bias	Level of evidence
	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment (patient reported outcome)	Blinding of outcome assessment (objective outcome)	Incomplete outcome data	Selective reporting	
Chan ^[23] 2014	-	-	-	-	+	-	+	III
Chen ^[24] 2012	+	+	-	-	-	+	+	II
Chen ^[25] 2016	+	+	-	-	-	-	+	II
Chow ^[26] 2011	+	+	-	-	-	+	+	II
Lai ^[27] 2018	+	+	-	-	-	+	+	II
MacRae ^[28] 2012	+	+	-	-	-	+	+	II
Peng ^[29] 2018	+	+	-	-	-	-	+	II
Qian ^[30] 2014	-	-	-	-	-	?	+	III
Smyth ^[31] 2013	-	-	-	-	-	+	+	III
Struthers ^[32] 2010	+	+	-	-	-	+	+	III
Toma ^[33] 2003	+	?	-	-	-	+	+	III
vanLoon ^[34] 2010	-	-	-	-	-	+	+	III
Vaux ^[35] 2013	+	+	-	+	+	+	+	II
Wang ^[36] 2015	+	-	-	-	-	-	+	II
Yin ^[37] 2014	+	-	-	-	-	-	+	II

Note: "+" indicates low risk of bias; "-" stands for high risk of bias; "?" indicates uncertain risk of bias.

opted to perform the meta-analysis with a random-effects model. As time to estimate infection might be an important factor in its development, variation between studies related to this aspect was also taken into consideration. We used 6 months as the cut-off point for evaluating the infection rate. Data from a total of 1113 patients, of whom 39/548 were infected through BH cannulation and 13/565 were infected through RL cannulation, were used. Results showed that within 6 months, the vascular access infection rate of BH cannulation relative to that of RL cannulation was 2.17 ($P = .15$). Over 6 months, the BH infection rate increased to 2.7; however, this was still not yet a statistically significant difference ($OR = 2.7$, 95% CI [0.92, 7.92], $Z = 1.8$, $P = .07$). Results found no publication bias ($FSN > TL$).

3.4.2. Aneurysm formation. Due to the turbulent flow of blood to the local (fistula) blood vessel wall, vertical force is applied, causing the blood vessels to dilate and form an aneurysm.^[26]

The summarized effects of 9 studies showed a small effect on aneurysm formation (Table 4). The statistical heterogeneity was low (homogeneity, $I^2 = 12\%$; $P = .33$). Regardless of whether a fixed- or random-effects model was used, the combined effect shows that using BH cannulation will significantly reduce aneurysm formation ($RR = 0.18$, 95%CI [0.1, 0.32], $Z = 5.67$, $P < .00001$). Since the number of articles is less than ten^[27], the FSN was used ($FSN = 124 > TL = 55$) and showed no publication bias.

3.4.3. Fistula survival. The definition of fistula survival is the period from the start of the puncture to the failure of the fistula function after establishment.^[26] The summarized effects of 2 studies showed a small effect on fistula survival (Table 4). The statistical heterogeneity was moderate (heterogeneity, $I^2 = 78\%$; $P = .03$). Vascular access practiced by the injection staff was heterogeneous among the studies. As a result, meta-analysis with random

Table 4
Effect sizes for studies measuring on primary outcome.

Study (year)	BH		RL		Weight (%)	Odds ratio/ 95%CI
	Events	Total	Events	Total		
1 Infection ≤ 6 months						
Chen ^[25] (2016)	1	30	0	29	4.3	3.0 [0.12, 76.68]
Chow ^[26] (2011)	4	34	1	35	9	4.53 [0.48, 42.82]
Smyth ^[31] (2013)	3	41	4	63	18.8	1.16 [0.25, 5.49]
Struthers ^[32] (2010)	1	28	0	28	4.3	3.11 [0.12, 79.64]
Toma ^[33] (2003)	1	37	0	43	4.3	3.58 [0.14, 90.45]
Total (95%CI)	10	170	5	198	40.8	2.17 [0.76, 6.23]
Heterogeneity: Chi2 = 1.22, df = 4 (P = .88); I2 = 0% Test for overall effect: Z = 1.44 (P = .15)						
2 Infection >6 months						
Chan ^[23] (2014)	5	45	3	38	20.1	1.46 [0.32, 6.55]
Lai ^[27] (2018)	8	50	1	50	10.1	9.33 [1.12, 77.7]
MacRae ^[28] (2012)	2	70	1	70	7.7	2.03 [0.18, 22.91]
Peng ^[29] (2018)	8	40	0	40	5.4	21.18 [1.18, 380.9]
Qian ^[30] (2014)	1	40	1	30	5.7	0.74 [0.04, 12.39]
VanLoon ^[34] (2010)	5	75	0	70	5.3	11 [0.6, 202.7]
Vaux ^[35] (2013)	0	58	2	69	4.8	0.23 [0.01, 4.9]
Total (95%CI)	29	378	8	367	59.2	2.7 [0.92, 7.92]

Heterogeneity: Chi2 = 8.41, df = 6 (P = .21); I2 = 29%.
Test for overall effect: Z = 1.8 (P = .07).

effect model was used. BH and RL cannulation do not show statistically significant differences in fistula survival after analysis (OR = 1.44, 95% CI [0.56, 3.66], Z = 0.7, P = .48). The FSN (FSN = 17 < TL = 30) shows that this result may have a publication bias.

3.4.4. Stenosis. Fistula stenosis can reduce blood flow or weaken thrill in the fistula.^[28] The summarized effects of 5 studies showed a small effect on fistula stenosis (Table 4). The statistical heterogeneity was low (homogeneity, I2 = 21%; P = .28). Both fixed- and random-effects model analysis shows that BH cannulation significantly reduces fistula stenosis compared to RL cannulation (RR = 0.44, 95% CI [0.25, 0.77], Z = 2.85, P = .004). The result of the FSN (FSN = 17 < TL = 30) shows that there may have been a publication bias.

3.5. Effects for secondary outcome of BH and RL on vascular access

3.5.1. Pain. Pain level is based on subjective feelings during puncture. Commonly used assessment tools include the visual analogue scale (VAS) and the numerical rating scale (NRS), both of which range from 1 (no pain) to 10 points (severe pain).^[29] Of the 13 studies recording pain, 8 studies used VAS or NRS assessment tools, and 1 used Wong-Baker Pain Rating Scale (ranging from 0 to 5). Some articles were not included in the meta-analysis. These were articles which could not obtain complete data and articles in which the results were presented using different calculation methods. The summarized effects of 4 studies showed a small effect on pain (Table 5). The statistical heterogeneity was high (heterogeneity, I2 = 96%; P < .00001). After the literature data were carefully checked, heterogeneity could not be ruled out; therefore, a random-effects model was used. Meta-analysis showed no significant difference in the average difference in pain caused by puncture between the 2 groups (SMD = -0.69, 95% CI [-1.78, 0.4], Z = 1.25, P = .21). The FSN (FSN = 34 > TL = 30) shows no

Table 5
Effect sizes for studies measuring on second outcome.

Study (year)	BH			RL			Weight (%)	Odds Ratio/ 95%CI
	Mean	SD	Total	Mean	SD	Total		
1 Pain*								
Chow ^[26] (2011)	0.56	1.23	34	0.71	1.02	35	24.5	-0.15 [-0.68, 0.38]
Lai ^[27] (2018)	2.04	0.94	50	3.34	1	50	25.2	-0.4 [-0.78, -0.02]
Qian ^[30] (2014)	1.06	0.53	40	3.35	1.05	30	25.1	-2.29 [-2.7, -1.88]
Smyth ^[31] (2013)	1.9	1.07	41	1.82	0.93	63	25.2	0.08 [-0.32, 0.48]
Total (95%CI)			165			178	100	-0.69 [-1.78, 0.4]
2 Hematoma†								
Chow ^[26] (2011)	4	34	0	35	2.4	9.26 [0.52, 165.65]		
MacRae ^[28] (2012)	12	70	25	70	23.5	0.48 [0.26, 0.88]		
Smyth ^[31] (2013)	11	41	20	63	22.9	0.85 [0.45, 1.57]		
Struthers ^[32] (2010)	19	28	27	28	35.1	0.7 [0.54, 0.92]		
VanLoon ^[34] (2010)	2	75	14	70	8	0.13 [0.03, 0.57]		
Wang ^[36] (2015)	3	33	4	33	8.2	0.75 [0.18, 3.09]		
Total (95%CI)	51	281	90	299	100	0.63 [0.4, 0.99]		
3 Thrombosis‡								
Chen ^[24] (2012)	1	20	7	20	27.6	0.14 [0.02, 1.06]		
Lai ^[27] (2018)	1	50	2	50	7.9	0.5 [0.05, 5.34]		
Peng ^[29] (2018)	1	40	0	40	2	3.0 [0.13, 71.51]		
Qian ^[30] (2014)	2	40	6	30	27	0.25 [0.05, 1.15]		
Struthers ^[32] (2010)	1	28	1	28	3.9	1.0 [0.07, 15.21]		
Wang ^[36] (2015)	4	33	8	33	31.5	0.5 [0.17, 1.5]		
Total (95%CI)	10	211	24	201	100	0.4 [0.2, 0]		

*Heterogeneity: Tau2 = 1.18; Chi2 = 78.77, df = 3 (P < .00001); I2 = 96%. Test for overall effect: Z = 1.25 (P = .21).

†Heterogeneity: Tau2 = 0.14; Chi2 = 10.3, df = 5 (P = .07); I2 = 51%. Test for overall effect: Z = 2.0 (P = .05).

‡Heterogeneity: Chi2 = 3.55, df = 5 (P = .62); I2 = 0%. Test for overall effect: Z = 2.61 (P = .009).

publication bias. However, this result needs to be considered with caution due to the limited sample size of articles used in its determination.

3.5.2. Hematoma. Hematoma occurs as a result of frequent punctures that make it difficult for the fistula blood vessel wall to stop bleeding.^[26] Two studies^[30, 31] were eliminated for the meta-analysis because the number of punctures used as the calculation unit differed from the other studies. The summarized effects of 6 studies showed a small effect on hematoma (Table 5). The statistical heterogeneity was high (heterogeneity, $I^2 = 51\%$; $P = .07$). The meta-analysis with random-effects model shows that BH cannulation will reduce hematoma occurrence with significant margin (RR = 0.63, 95%CI [0.4, 0.99], $Z = 2.0$, $P = .05$). The result of the FSN (FSN = 70 > TL = 40) shows no publication bias.

3.5.3. Thrombosis. Intimal cell proliferation and thrombosis occur due to long-term urotoxin stimulation and repeated vascular endothelial damage and inflammation.^[32] The summarized effects of 6 studies showed a small effect on thrombosis (Table 5). The statistical heterogeneity was low (homogeneity, $I^2 = 0\%$; $P = .62$). Both fixed- and random-effects models show that BH cannulation will reduce thrombosis significantly (RR = 0.4, 95%CI [0.2, 0.8], $Z = 2.61$, $P = .009$). The result of the FSN (FSN = 32 < TL = 40) shows that there may have been a publication bias.

4. Discussion

4.1. Method quality evaluation of included studies

Overall, the quality of the included studies was moderate to high. The Cochrane Collaboration tool for assessing risk of bias^[33] and CASP-RCT checklist were used to evaluate all studies. This meta-analysis study included 15 original studies. The 4 CCT studies^[24, 34–36] did not report allocation concealment; therefore, there may have been selection bias. BH and RL cannulation are 2 visibly different puncture methods. Therefore, blinding could not be applied to patients, nurses, or researchers. Consequently, all studies may have detection bias. However, studies may not have performance bias because most outcome variables, except pain, could not be controlled by patient themselves. There may have been attrition bias because 2 studies^[37, 38] conducted per-protocol analysis, whereas 4 studies used ITT analysis.^[24, 31, 35, 39] Furthermore, 6 studies^[30, 31, 40–43] did not provide relevant information. The attrition rate of 3 studies^[23, 39, 44] was 6.4%, 16.1%, and 7%, respectively (i.e., all under 20%). Although this indicates a small impact on the population, it also indicates a considerable impact on the effectiveness of intervention.^[45] In 4 of the included studies,^[23, 24, 34, 36] the attributes of the participants between 2 groups were nonhomogeneous. Two of these studies^[34, 36] included control variables, reducing the risk of bias. However, the other 2 had obvious heterogeneous characteristics such as age, fistula duration in Toma,^[23] history of disease, dialysis time, and body mass index in van Loon.^[24] This bias might influence the effectiveness of interventions. However, our meta-analysis showed that this did not affect the significance of results related to infection and aneurysm, even after taking those 2 studies out of the meta-analysis^[23, 24] (OR = 2.05, 95% CI [0.67, 6.24], $Z = 1.26$, $P = .21$ for ≤ 6 months infection; OR = 2.27, 95% CI [0.71, 4.8], $Z = 7.26$, $P = .17$ for > 6 month infection; RR = 0.22, 95% CI [0.12, 0.38], $Z = 5.21$, $P < .00001$ for aneurysm). It did, however, affect results related to hematoma levels. Without one of the studies,^[24] meta-analysis with a fixed-effects model showed that BH cannulation significantly reduced the cases of hematoma development (RR = 0.72, 95% CI [0.55, 0.94], $Z = 2.42$, $P = .02$).

4.2. Efficacy evaluation

This study involved a systematic literature review and subsequent meta-analysis designed to explore the differences between BH and RL cannulation on the quality of vascular access in hemodialysis. The results show that BH cannulation can significantly reduce aneurysms, stenosis, and hematoma and thrombosis formation. These results are similar to those of the comprehensive analysis reports of Ren (2016)^[11] and Yang (2018).^[13] Of the 15 studies included in this meta-analysis, more than half (9) show that BH cannulation can reduce aneurysm, regardless of the observation period.^[36, 41] The results of this meta-analysis indicate that the BH technique employs a blunt needle that is applied to the same site, with minimal damage to blood vessels and surrounding tissues. Therefore, patients with initial or long-term dialysis can significantly reduce aneurysm of the AVF. According to the literature,^[46] AVF outlet stenosis is the most common location.

Based on the results of 5 studies that monitored patients from 12 months to 24 months, the probability of stenosis in the first year is about 20%.^[46] The results of this meta-analysis are consistent with Ren,^[11] Wang,^[12] and Yang,^[13] who show that BH cannulation can significantly reduce fistula stenosis. Regarding thrombosis, Tordoir^[47] proposed that about 85% of fistula thrombosis is caused by vascular stenosis. The results of this meta-analysis indirectly support this proposition as they show that BH cannulation significantly reduces the occurrence of both stenosis ($P = .004$) and thrombosis ($P = .009$). This result is consistent with Ren.^[11] Furthermore, not only does BH cannulation reduce aneurysm and stenosis occurrence for long-term dialysis patients, but it might also reduce hematoma formation. This means that the arm of the patient might maintain its usual appearance, which is the most common perception of negative body image in patients with hemodialysis.

The analysis of hematoma levels in this study showed that BH cannulation reduces hematoma at levels that are almost statistically significant ($P = .05$). If van Loon^[24] is removed because of the heterogeneity between 2 groups, the results are even more significant ($P = .02$). Wang^[12] stated that when BH cannulation is performed using a blunt needle, the lack of a sharp cutting surface and the often inelastic position of the blood vessel will easily lead to a subcutaneous hematoma. However, some researchers presume that there is a lack of consensus on the definition and quantification of hematoma.^[11, 45] Chow^[37] pointed out that BH cannulation is associated with high rates of hematoma formation because of the lack of experience of hemodialysis staff. Therefore, the impact of the formation of hematomas needs to be confirmed by further studies, and research in the future should include the training and work experience of the staff under question.

No differences were found in the risk of infection (both ≤ 6 m and > 6 m) between BH and RL cannulation. The results of this meta-analysis show that BH cannulation has a similar risk of AVF infection as RL cannulation. However, this finding might need to be applied to clinical settings with caution as “infection” was not clearly defined in certain studies. Some studies defined “infection” as redness, fever, and exudate,^[23] whereas other studies estimated “infection” with a bacterial culture,^[42] and others still did not define the symptoms of fistula infection at all.^[44] Furthermore, the result is inconsistent with the analysis of Nadeau-Fredette and Johnson,^[48] Muir,^[49] Wong,^[10] and Wang.^[12] Because of these conflicting findings, further studies that take into consideration the clear definition of infection are warranted. In addition, as time to estimate infection might be an important factor, future studies should also take time into consideration. For example, data from follow-ups conducted every 6 months and for a period of up to 3 years should be analyzed in order to understand both short-term and long-term infections. Moreover, some studies considered that the occurrence of infection due to BH cannulation is related to the scab tissue

of the fistula BH. Skin scab tissue hyperplasia causes a bulging deformity at the BH, which may account for the bacterial infection. Therefore, it is recommended that the nursing staff use a disposable disinfection needle to patiently remove the scab or use a soaked saline gauze to cover the scab for about 30 minutes before removing it. The iodine ointment should be applied at the BH after the dialysis is finished.^[9, 35, 50] It is also recommended to increase the number of BH injection locations and to avoid using the same position within the same week.^[41]

The results regarding fistula survival rates did not reach a statistically significant difference between BH and RL cannulation ($P = .48$). According to the literature^[1], AVF can be used for more than 3 years. Therefore, it is possible that the observation time is too short to yield significant differences in survival rates between BH and RL cannulation. This is especially true since the included studies estimated fistula survival rates over a time-frame that ranged from 12 months to 18 months. Additionally, MacRae^[51] proposed that “time” might not be the only key factor. According to their results from 5-year study, there was no difference between the effect that BH and RL cannulation have on the survival of vascular access. This study also found that BH cannulation can significantly reduce the aneurysm, stenosis, and thrombosis of vascular access, which are important factors affecting the survival rate of fistulas. Based on this, it was expected that BH cannulation also improves fistula survival rates compared RL cannulation. However, no difference was found between the 2 techniques. It is recommended that future studies perform more analysis on this area, with at least 3 years of long-term follow-up. Doppler ultrasound monitoring of fistula blood flow should be included as well, so that fistula survival rates can be more precise.

The analysis of the level of pain caused by fistula puncture showed that BH cannulation could not significantly reduce the pain ($P = .21$). This result is different to the reports of Yang.^[13] It is possible that this is accounted for by the difference in pain level quantification methods (mean \pm standard deviation). Chow^[37] compared only the first and last (after 6 months) BH cannulations, Lai^[41] used the mean value of pain scores during 24 months, Qian^[35] calculated the average pain scores of ten events, and Smyth^[36] calculated the pain mean value after each dialysis punctures in 12 weeks. Furthermore, pain is a subjective and complex experience. The feeling of pain depends on personal perception. Every person has a different sensation, even when the needle is applied at the same location every time. Sensitivity of the local pain nerve and pain intensity are also affected by related factors such as personal, psychological, cultural, and social factors.^[52] Therefore, it is difficult to analyze pain levels objectively.

4.3. Strengths and limitations

Overall, the studies included in this meta-analysis were of moderate-to-high quality. The authors used a rigorous literature search method which employed 7 primary databases and 1 secondary database and included manual research to avoid publication bias. However, some outcome variables were only described by few articles (such as fistula survival, 2 articles; pain, 4 articles). This might still result in publication bias and therefore requires further longitudinal studies with a larger sample size and rigorous design. A cost-effect analysis between BH and RL cannulation also needs to be conducted to further evaluate their exact potential advantages and disadvantages.

5. Conclusions

This meta-analysis demonstrated that BH cannulation significantly reduced aneurysms, stenosis, hematoma, and thrombosis formation. In addition, there were no differences in the risk of infection between BH and RL cannulation. Therefore, BH

should be recommended as the routine cannulation procedure for hemodialysis. Moreover, hospitals and dialysis clinics need to provide staff training and establish a clinical guideline for infection prevention. A blinded RCT study with a large sample size and a long-term follow-up of at least 3 years needs to be conducted in future.

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