## Original Article

# Efficacy of buttonhole cannulation (BH) in hemodialysis patients with arteriovenous fistula: a meta-analysis

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Abstract: Objective: This study is to evaluate the efficacy of buttonhole cannulation (BH) in hemodialysis patients with arteriovenous fistula. Method: Systematic search on Cochrane Library, JBI Evidence-Based Practice Network, PubMed, EMbase, CBMdisc, Wanfang and CNKI database was performed to identify all randomized controlled trials or quasi-randomized controlled trials of BH in hemodialysis patients until May 2015. Three independent investigators evaluated all articles and extracted information. RevMan5.0 was used for meta-analysis of all eligible studies. Results: A total of 8 randomized controlled trials and 2 quasi-randomized controlled trials were included. Meta-analysis showed that compared with rope-ladder cannulation (RL), BH significantly reduced aneurysm formation [RR = 0.17, 95% CI (0.06, 0.48), P < 0.05], thrombus formation [RR = 0.44, 95% CI (0.22, 0.90), P < 0.05], and stricture formation [RR = 0.29, 95% CI (0.12, 0.70), P < 0.05]. However, there were no pain reduction [SMD = -1.48, 95% CI (-4.41, 1.18), P > 0.05] or intervention reductionfor fistula prevention [RR = 0.70, 95% CI (0.35, 1.36), P > 0.05]. Conclusions: Compared with RL, BH can significantly reduce the formation of aneurysm, thrombosis and stenosis, but there were no pain or intervention reduction for fistula prevention in hemodialysis patients with arteriovenous fistula. The efficacy of BH in infection and hematoma control, bleeding time reduction and fistula survival rate needs further study.

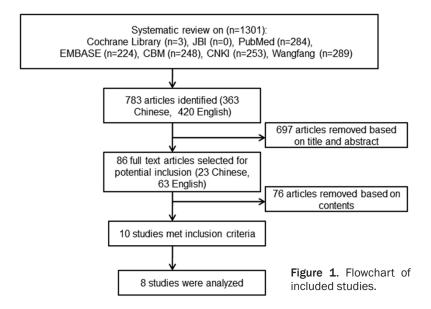
**Keywords:** Buttonhole cannulation, hemodialysis, rope-ladder cannulation, arteriovenous fistula, systematic review

#### Introduction

Hemodialysis is the most common replacement treatment for patients with end-stage renal kidney disease, and vascular access is vital to hemodialysis patients to prolong life and improve quality of life [1]. In 2006, US Kidney Disease Outcomes Quality Initiative proposed that autogenous arteriovenous (AV) fistula was preferred for vascular access, and buttonhole cannulation (BH) was recommended for autogenous AV [2]. China's first expert consensus also suggested autogenous AV for hemodialysis vascular access with the use of BH [3]. Appropriate methods and successful puncture is essential for hemodialysis and fistula maintenance, while inappropriate and unsuccessful puncture would lead to fistula complications, such as thrombus, stenosis, hematoma, pseudoaneurysm [2, 4, 5].

There are 3 ways for autogenous AV fistula, including BH, rope-ladder cannulation (RL) and

regional technique [5-10]. The incidence of pseudoaneurysm, hematoma and pain were significantly higher in regional technique than that of BH and RL, thus, its use has been gradually decreasing [5, 6]. BH has been first proposed as "constant-site technique" by Polish scholar Twardowski [11] in 1977, and renamed BH by Kronung in 1984 [12]. BH can be divided into two stages: the first stage is to establish cannulation, with each puncture entering the same skin and blood vessels point, and cannulation would be established after 6-9 times of puncture over 2-3 weeks (may be prolonged for diabetes patients); the second stage is togently biopsy using blunt needle through the established cannulation to avoid vessel and soft tissue injury [4, 13, 14]. It is shown that [15-19] BH is advantageous over RL due to its less demanding vessel length, shorter bleeding time, less formation rate of pain, aneurysm and hematoma, lower infection incidence and high patient satisfaction, as BH was first applied in patients with limited vascular length. However,



it is shown that [18, 20-22] BH would increase infection incidence and prolong bleeding time. It is also suggested there were no difference of infection and pain between BH and RL [10, 23]. Due to the contradictory results and lack of high quality large sample randomized control trials, we conducted a systematic review on the BH efficacy in autogenous AV fistula aiming to provide evidence for future BH use in China.

#### Materials and methods

#### Search strategy

We reviewed articles in Chinese and English until May 2015 using "dialysis/hemodialysis/haemodialysis/chronic kidney failure/end stage renal disease/end stage kidney disease/renal replacement therapy" and "buttonhole/constant site/rotating-site/rope ladder" and "ateriovenous fistula/AVF" and "cannulation/technique/needling/puncture" as searching words on Cochrane Library, Joanna Briggs Institute Evidence-Based Practice Network, PubMed, EMBASE, Chinese Biomedical Literature Database, Wanfang databases and China National Knowledge Infrastructure.

We first identified clinical guidelines from US National Guideline Clearinghouse and Registered Nurses' Association of Ontario and systematic reviews and meta-analysis from Cochrane Library and Joanna Briggs Institute Library Evidence-Based Practice Network; we then screened titles and abstracts of all articles

identified in the listed above databases and reviewed the full-test of the eligible articles; reference lists of all included reviews and systematic reviews were also reviewed.

# Inclusion and exclusion criteria

We included all randomized controlled trials or quasirandomized controlled trials of BH's efficacy in hemodialysis patients. The inclusion criterion was that patients of 18 years old or above receiving hemodialysis with autogenous AV fis-

tula. The exclusion criteria were that hemodialysis patients combined with other malignant diseases (such as cancer) or with dysfunctional fistula (such as dialysis rate less than 200 ml/min). Poorly designed trials were also excluded, such asself-control or no control group. Patients with BH were considered as experiment group, and scab was cleaned to prevent needle blockage or infection [24, 25]. Patients with RL were considered as control group.

#### Outcome indicators

The primary outcome measures were pain, infection, aneurysm formation, hematoma, bleeding time, fistula survival, thrombosis and stenosis and number of interventions.

#### Quality evaluation

Two JBI trained investigators independently evaluated the quality of included studies. When they disagree with each other, the third investigator joined in and final decision was made among consensus. Cochrane Handbook for Systematic Reviews of Interventions (Version 5.1.0, 2011) was used for quality evaluation [26].

#### Information extraction

Information extraction was based on full-text, including author, year, country, study design, sample size, characteristics of subjects, intervention type, dialysis type, follow-up length and outcome measures.

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Table 1. Characteristics of included studies

Included studies	Origin	Study design	Sample size		A	Interventions				Frankrata d
			Experiment group	Control group	Average age (years)	Experiment group	Control group	Dialysis	Follow up (month)	Evaluated factors
Tomas 2003	Japan	RCT	37	43	60 (BH), 64 (RL)	ВН	RL	Center (3/week)	3	125
Struters 2010	England	RCT	28	28	61 (BH), 60 (RL)	ВН	RL	Center	6	123457
Chow 2011	Australia	RCT	34	35	N/A	BH	RL	Home and center	6	124
MacRae 2012	Canada	RCT	70	70	70.3 (BH) 66.7 (RL)	ВН	RL	Center (3/week)	① 2; ②④⑤ 12	1245
Guixian Chen 2012	China	RCT	20	20	N/A	BH	RL	Center (2-3/week)	12	13457
Vaux 2013	England	RCT	58	69	62 (BH), 64 (RL)	ВН	RL	Center	12	123568
Chan 2014	US	CCT	45	38	60.9 (BH), 64.1 (RL)	ВН	RL	Center	12 (median)	268
MacRae 2014	Canada	RCT	70	69	70.2 (BH), 66.1 (RL)	ВН	RL	Center (3/week)	BH 19.2; RL 17.2 (median)	2678
Wenyan Qian 2014	China	CCT	40	30	47 (BH), 51 (RL)	ВН	RL	Center (2-3/week)	12	12357
Jinmei Yin 2014	China	RCT	28	28	49.62 (BH), 50.70 (RL)	ВН	RL	Center (2-3/week)	18	34

Note: ① pain, ② infection, ③ aneurysm formation, ④ hematoma, ⑤ bleeding time, ⑥ fistula survival, ⑦ thrombosis and stenosis, ⑧ number of interventions.

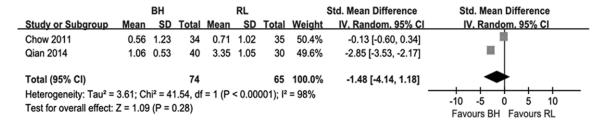


Figure 2. Impact of BH and RL on pain.

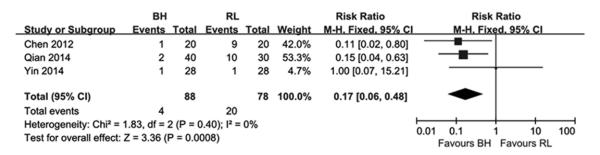


Figure 3. Impact of BH and RL on aneurysm formation.

#### Statistical analysis

RevMan 5.0 (Review Manager version 5.0, Cochrane, Copenhagen, Denmark) was used for meta-analysis. Continuous data measured by the same measurement was analyzed by weighted mean difference (WMD); if measured by different measurements, data was analyzed by standardized mean difference (SMD). Categorical data was analyzed for randomized response. Chi-square test was used for identification of heterogeneity between studies. P > 0.1 and I<sup>2</sup> < 50% were considered as homogeneous among studies, thus, fixed effects model was used; when P < 0.1 and  $I^2 \ge 50\%$  and heterogeneity was considered clinically, random effects model was used; when P < 0.1 and heterogeneity was not determined or outcome indicators were from limited number articles, descriptive analysis was used [27].  $\alpha$  < 0.05 was considered statistically significant.

#### Results

#### Characteristics of included studies

There were 1301 articles identified, including 511 articles in English and 790 articles in Chinese. After exclusion of duplicates, 783 were screened by titles and abstracts. There were 86 articles with well-designed random-

ized or quasi-randomized controlled studies. After review of full-text, 10 studies were finally identified, including 8 studies in English and 2 studies in Chinese, 8 randomized controlled studies [6, 28-34] and 2 quasi-randomized controlled studies [35, 36]. The flow chart was shown in **Figure 1**. Characteristics of included studies were shown in **Table 1**.

#### Method quality evaluation

Cochrane Handbook for Systematic Reviews of Interventions (Version 5.1.0, 2011) was used as quality evaluation criteria [26]. Of all 10 included studies, 2 were in of A level [28, 30], while the rest 8 were of B level. BH and RL are two significantly different puncture methods thus blinding could not be applied to patients or nurses, therefore only evaluation investigator was blinded. The above results indicate that the quality of included studies was medium and only single blinding was achieved.

#### Efficacy evaluation

There were 7 studies [19, 29-35] reported pain after BH, including 3 studies [29, 30, 33] reported as median, 1 [34] lacked data and 1 [31] reported as dichotomous. This data could not be merged. After merging data of the rest 2 studies [32, 35], it showed homogeneity test

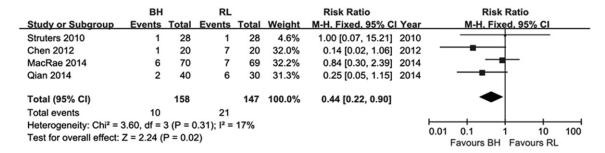


Figure 4. Impact of BH and RL on thrombosis formation.

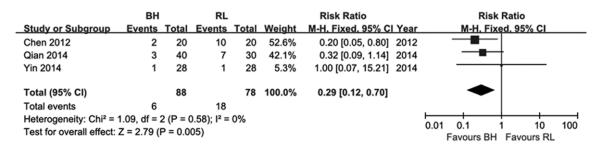


Figure 5. Impact of BH and RL on stenosis formation.

with P < 0.1 and  $I^2$  = 98% > 50% using random effects model (as in **Figure 2**). BH failed to show pain reduction [SMD = -1.48, 95% CI (-4.14, 1.18), P = 0.28 > 0.05]. However, Chow [32] showed 44.4% BH patients and 76.7% RL patients were under local anesthesia. Nonmerge Struters's study [30] showed that 6 patients stopped local anesthesia in BH group while only 1 patient in RL group. It is reported that nearly half patients believed BH could reduce pain [29] but Vaux [29] also showed 8 patients switched BH to RL due to excessive pain. The non-merge studies mostly showed contradictory results thus meta-analysis can only be used as reference.

There were 8 studies [28-30, 32-36] reported infection after BH. However, data could not merge due to various definitions of infection and methodology. For example, Struthers [33] did not define fistula infection, while Toma [34] defined fistula infection as pain, swelling or exudation of puncture site. Three studies [32, 35, 36] showed no difference of infection between BH and RL group, 3 studies [29, 33, 34] did not report whether difference existed, and 2 studies [28, 30] showed BH increased infection. Therefore, no consensus was made whether

BH could reduce infection and future study is needed.

There were 5 studies [6, 29, 31, 33, 35] reported aneurysm formation after BH, and data from 3 studies was merged [6, 31, 35]. Homogeneity test showed P > 0.1 and  $I^2 = 0\% < 50\%$  using fixed effects model (as in **Figure 3**). It showed BH could significantly reduce aneurysm formation [RR = 0.17, 95% CI (0.06, 0.48), P < 0.05]. The non-merge studies showed BH was advantageous over RL in terms of diameter [33] and size [29] of aneurysm. Therefore, from perspective of reducing aneurysm, BH is recommended.

There were 5 studies [6, 30-33] reported hematoma formation after BH. However, data could not merge due to various definitions of hematoma formation and methodology. For example, Chow [32] did not define hematoma formation, while Guixian Chen [31] defined hematoma as swelling, pain or increased venous pressure at puncture site. One study [33] did not show results; 2 studies [30, 31] showed BH could reduce hematoma formation; 1 study [6] showed no difference between BH and RL; 1 study [32] showed RL could reduce hematoma formation. Therefore, no consensus was made

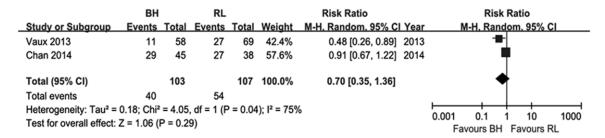


Figure 6. Impact of BH and RL on number of interventions.

whether BH could reduce hematoma formation and future study is needed.

There were 6 studies [29-31, 33-35] reported bleeding time after BH. However data could not merge due to various definitions of bleeding time. Three studies [29, 30, 33] showed no difference between BH and RL; 2 studies [31, 35] showed BH could decrease bleeding time. Toma [34] showed the ratio of bleeding time < 5 min was significantly higher in BH group (54.1%) than RL group (27.9%). There was no study reporting that BH would increase bleeding time. Therefore no consensus was made whether BH could reduce bleeding time and future study of the same definition is needed.

There were 3 studies [28, 29, 36] reported fistula survival after BH. However data could not merge due to various expressions of fistula survival. Vaux [29] showed BH could increase fistula survival, while 2 studies [28, 36] showed no impact of BH on fistula survival. Therefore future study of fistula survival is needed.

There were 4 studies [28, 31, 33, 35] reported thrombosis after BH. Homogeneity test showed P=0.31>0.1 and  $I^2=17\%<50\%$  using fixed effects model (**Figure 4**). It showed that BH statistically significant reduced thrombosis formation [RR = 0.44, 95% CI (0.22, 0.90), P=0.02<0.05]. When one study [28] with large sample was excluded, it still showed reduction of thrombosis for BH with 95% CI (0.09, 0.73), indicating the above results were robust and reliable.

There were 3 studies [6, 31, 35] reported fistula stenosis after BH. Homogeneity test showed P = 0.58 > 0.1 and I<sup>2</sup> = 0% < 50% using fixed effects model (**Figure 5**). It showed BH significantly reduced fistula stenosis [RR = 0.29, 95% CI (0.12, 0.70), P = 0.005 < 0.05].

Therefore, from the prospective of thrombosis and stenosis reduction, BH is recommended.

There were 3 studies [28, 29, 36] reported number of interventions for AV fistula, and data from 2 studies [29, 36] could be merged. Homogeneity test showed P < 0.1 and  $I^2 = 75\%$  > 50% using random effects model (**Figure 6**). There were no differences of BH in intervention reduction [RR = 0.70, 95% CI (0.35, 1.36), P > 0.05]. Therefore, there was no impact of BH in number of intervention for AV fistula.

#### Discussion

Method quality evaluation of included studies

The 10 studies included 8 randomized controlled studies and 2 quasi-randomized controlled studies. Of the 8 randomized controlled studies, there were no detailed illustration of randomization in 5 studies [6, 29, 31, 32, 34]. 4 studies reported allocation concealment [28, 30, 32, 33], and 3 studies reported blinding to evaluation investigators [28, 30, 32]. There were 5 studies [28-30, 32, 33] reported loss of follow-up and their reasons, and 2 studies [29, 30] reported intentional analysis. All studies reported the baseline characteristics of patients, including age, gender, dialysis length, and comorbidities. In most studies, there were no significant difference of baseline characteristics between experiment and control groups, however the number of diabetes patients were more in BH group than that of RL group in Chan's study [36].

#### Efficacy evaluation

In this study, by evaluating 8 outcome measures, we found that BH could reduce aneurysm, thrombosis and stenosis formation. It may be resulted from the same puncture site of

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skin and blood vessel, and blunt needle was used after cannulation in BH. Without sharp cutting surface, blunt needle slowly enters blood vessel with minimal injury on blood vessel and surrounding tissue, thus intimal hyperplasia was reduced. In this study, it showed that BH did not reduce the incidence of pain. but reduced the use of local anesthesia. If local anesthesia were controlled in both groups, BH may be shown to reduce the pain. However, due to various definitions and information formats, data of infection, hematoma and bleeding time could not be merged. Fistula flow and survival are very important outcome indicators, but there were limited research. Future research with Doppler ultrasound flow monitoring and enough follow-up length is needed.

#### Strengths and limitations

Overall, the quality of included studies was medium. Most randomized controlled trials lacked blinding and allocation concealment, and outcome measure definition and data formats were different. The follow-up length varied from 3 to 18 months with significant differences, leading to heterogeneity of study outcomes. Also, we only identified study published in English or Chinese, thus might not cover all studies. This study showed reduction of aneurysm, thrombosis and stenosis formation in BH; therefore BH is recommended as routine procedure for hemodialysis. In the meantime, future research with rigorous design, unified outcome definition, evaluation methods and information formats, larger sample size, longer follow-up is needed to determine BH's impact on infection, hematoma, bleeding time, fistula survival and number of interventions.

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#### Disclosure of conflict of interest

None.

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