Original research article

JVA The Journal of Vascular Access

A narrative systematic review of randomised controlled trials that compare cannulation techniques for haemodialysis

The Journal of Vascular Access
1–13

DOI: 10.1177/1129729820983174
journals.sagepub.com/home/jva
SAGE

Catherine A Fielding[1,2], Amanda Hadfield[1], Kelly White[1], Dan Waters[1], Cathryn James[1], Heather Buchanan[3], Richard J Fluck[1] and Nicholas M Selby[1,3]

Abstract

Background: Cannulation of arteriovenous access for haemodialysis affects longevity of the access, associates with complications and affects patients' experiences of haemodialysis. Buttonhole and rope ladder techniques were developed to reduce complications. However, studies that compare these two techniques report disparate results. This systematic review performs an in-depth exploration of RCTs, with a specific focus on cannulation as a complex intervention.

Methods: A PICO question and protocol was developed as per PRISMA-P guidance and registered on PROSPERO (CRD42018094656 https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=112895). The systematic review included any RCT performed on adult patients with end-stage kidney disease undergoing cannulation of arteriovenous fistulae or grafts for in-centre haemodialysis, as performed by healthcare staff. Assessment of quality of RCTs and data extraction were performed by two co-authors independently. Data were extracted on the study design, intervention and comparator and outcomes, including patency, infection and patients' experiences.

Results: The literature search identified 241 records. Ten records met inclusion criteria, which described five different RCTs that compared buttonhole to either rope ladder or usual practice. Results were disparate, with patency and infection results varying. Pain Visual Analogue scores were the only measure used to capture patients' experiences and results were inconclusive. All RCTs had differences and limitations in study design that could explain the disparity in results.

Conclusion: Current evidence does not allow definitive conclusions as to whether buttonhole or rope ladder needling technique is superior. Future RCTs should describe interventions and comparators with adequate detail, embed process evaluation, use standardised outcome measures and build on feasibility studies to produce definitive results.

Keywords

Haemodialysis, vascular access, cannulation, arteriovenous fistula, systematic review

Date received: 14 July 2020; accepted: 29 November 2020

Introduction

Vascular access is a critical part of haemodialysis treatments that impacts on patients' experiences,[1] morbidity and mortality.[2] Arteriovenous (AV) fistula or graft are accepted as the optimal form of vascular access for the majority of patients, providing superior haemodialysis, lower rates of complications and better survival when compared with central venous catheters (CVC).[2] Both require repetitive cannulation, which can result in damage

[1]University Hospitals of Derby and Burton NHS Foundation Trust, Derby, UK
[2]UK Renal Registry, Bristol, UK
[3]University of Nottingham, Nottingham, UK

Corresponding author:
Catherine A Fielding, Renal Dialysis Unit, Royal Derby Hospital, University Hospitals of Derby and Burton NHS Foundation Trust, Uttoxeter Road, Derby DE22 3NE, UK.
Email: katie.fielding@nhs.net

to the vessel and can lead to aneurysms and possibly stenoses that predispose to access thrombosis and failure.[3–7] Cannulation can also result in other complications, including infection and life-threatening bleeds, and affects patients' experiences of haemodialysis, associated with fear, pain and anxiety.[8–12] In 2018, a nationwide UK survey of 71 renal centres (responses from 13,770 patients) found cannulation of AV access to be the third lowest rated element of patient satisfaction of renal care (out of 13 themes).[1]

Cannulation techniques have been developed to minimise complications from cannulation,[3,13,14] namely rope ladder (RL) and buttonhole (BH). RL involves progressing cannulation up the vessel in systematic manner, using as much length of the vessel as is possible, whereas BH involves cannulating each site in exactly same manner each time the needles are inserted.[3,15] Area puncture (AP) is a third technique commonly used, often unintentionally. This involves cannulating in the same area, but not the same site, each time, and is often confused with RL. AP increases the risk of stenosis, AV access failure and complications.[5,15] Due to the risks associated with area puncture, the majority of observational studies and randomised controlled trials (RCT) have compared BH with RL, but as of yet there is no consensus whether one technique is best. Previous systematic reviews have included both observational studies and RCTs, reaching different conclusions as to the optimal technique. One review concluded BH is superior in terms of stenosis, aneurysm and thrombosis rates[6] and two others state that BH offers no benefit over RL and may increase infection risk.[16,17]

One critical area that is not previously addressed is that cannulation of AV access fits the Medical Research Council's (MRC) criteria of a complex intervention.[18] Cannulation has multiple interacting components affecting outcomes, is a difficult procedure for the operator to consistently achieve success and there are multiple outcomes of interest. Therefore, how well the cannulation techniques are performed and how outcomes are measured has the potential to affect the results of studies. Failure to regard AV access cannulation as a complex intervention in previous studies may have contributed to the divergent results. The MRC's framework provides guidance on how to conduct RCTs evaluating the effectiveness of a complex intervention, with recommendations for: clear definition of both the intervention and comparator; assessment of consistency of implementation of the intervention and comparator (known as fidelity) through process evaluation; careful consideration of outcomes; and the use of feasibility and pilot trials to determine how to conduct a definitive RCT.[18,19] Lack of consideration of these elements can lead to design flaws and omissions in RCTs that can bias results and interpretation.

Therefore, we aimed to perform an in-depth systematic review including only RCTs that compared cannulation techniques for haemodialysis, with a specific focus on cannulation as a complex intervention. We made the decision to exclude observational studies, to enable in-depth examination of the gold standard of research – RCTs. This focus enables clarification of whether RCTs produce disparate results and if so, why this is the case.

Methods

This systematic review was performed as recommended by the PRISMA statement.[20] The protocol was developed using PRISMA-P[21] and registered on PROSPERO prior to commencement (Registration number CRD42018094656 https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=112895). The research question was structured using PICOS:

'In adults undergoing in-centre haemodialysis for end stage kidney disease (P), does AV fistula cannulation technique (I&C) affect the outcomes of patency, infection and patient experience (O), considering results of RCTs (S)?

Objectives of the systematic review were to identify: results of the included studies; protocols of cannulation techniques used; outcomes used; and, strengths and limitations of studies, in the context of cannulation as a complex intervention.

Eligibility criteria

Studies that compared any type of cannulation technique for adults undergoing in-centre haemodialysis for end-stage kidney disease were included, encompassing AP, RL, or BH. For clarity, usual practice was also included as a comparator. Studies were not excluded based on the outcomes defined in the PICOS, as emerging outcomes were also collected to reflect the objectives of the systematic review. Mixed methods RCTs and grey literature, including trial protocols and conference abstracts, were included, alongside normal quantitative RCTs. Studies were excluded that focussed solely on children 17 years or younger, self or carer cannulation, home haemodialysis, patients with acute kidney injury, or if studies were non-randomised. Home haemodialysis often requires self or carer cannulation, which provides a different context to the cannulation procedure. This was excluded as this context often changes the results of studies, which are less applicable to healthcare cannulation. No date restrictions were applied. Only articles published in the English language were included, as no interpreter services were available to assist with this. Studies that met inclusion criteria, but also met some exclusion criteria (e.g. studies that included both home and in-centre haemodialysis patients), were included in the systematic review for completeness.

Search strategy and screening criteria

A clinical librarian was included in the study team to assist in development and implementation of the search strategy. The search strategy (Supplemental Information 1 and 2) and screening criteria (Supplemental Information 3) were

Table 1. List of clinical databases and clinical trial registries searched.

Clinical databases	Clinical trials registries
Cumulative Index of Nursing and Allied Health Literature (CINAHL)	UK Clinical Trials Gateway
Medline	Clinicaltrial.gov
PubMed	EU clinical trial register
EMBASE	ISRCTN registry
British Nursing Index (BNI)	WHO platform
Cochrane Register of Controlled Trials	Health Canada's Clinical Trials Database
Latin American and Caribbean Health Sciences Literature (LILACS)	Hong Kong Clinical Trials Register
	South African National Clinical Trial Register

created from the eligibility criteria. Databases and clinical trials registries searched are listed in Table 1. Clinical Trial Registries were searched with terms 'Haemodialysis/Hemodialysis' and 'Vascular Access'. Duplicates of individual articles were removed prior to screening, but different articles on the same study were retained. The database search was completed on 07/05/18 and clinical trial database search completed on 30/04/18. The search was updated on 24/09/2020. Screening was performed in two stages by two authors independently, with disagreement adjudicated by the guarantor. Reference lists from any articles identified in the clinical database search, which performed a systematic literature search, were also searched for studies that met the eligibility criteria.

Data extraction and assessment of quality

A bespoke data extraction form was created using templates from 'Centre for Reviews and Dissemination'[22] and 'Joanna Briggs Institute'.[23] This ensured detailed data extraction which incorporated cannulation definition, reporting of cannulation procedures, study design, outcome definition, results and the author's interpretation of results (Supplemental Information 4). Assessment of quality was provided using the 'JBI Checklist for Randomised Controlled Trials'.[24] Data extraction and assessment of quality were performed independently by two authors and differences discussed and agreed in a study group meeting.

Data synthesis

A priori criteria were defined to determine whether to progress to meta-analysis, based on the degree of inter-study clinical heterogeneity in the population, cannulation techniques compared and outcomes measured (including time points of outcome assessment). Data synthesis included a narrative review of the evidence.

Results

Search results

The results of the screening process are summarised in the PRISMA flow diagram (Figure 1). The database search identified nine reviews that included literature searches performed systematically.[6,16,17,25–30] Search of the content and reference lists of these sources identified three trials not identified in the database search.[31–33] None of these trials could be sourced from the references provided and no author contact details were provided. Search of clinical trial registries identified 163 trial protocols related to haemodialysis and vascular access. Only two of these trial protocols compared cannulation techniques and were included. This provided a total of 241 articles for screening.

Four articles could not be sourced in full text, the three trials mentioned above[31–33] plus a conference abstract.[34] A total of 10 articles were identified for inclusion, 8 citations[35–42] and 2 trial registry protocols. Some of the included articles described the same study, which left 10 articles describing five RCTs.

Assessment of quality

The quality assessment identified methodological weaknesses in the design of all RCTs (Table 2). It was noted that blinding was not possible for RCTs, so whilst evaluated within the tool, this was accepted as impossible. Three of the five studies did not recruit study arm populations that were similar at baseline.[36,37,39] Vaux et al.[41] used minimisation to randomise, which did produce similar groups. Two studies were classified as RCTs[38,40] by our eligibility criteria of random allocation of participants and in previous systematic reviews.[6,16,17] However, once examined we judged them not to utilise RCT methodology correctly. The second part of MacRae et al.'s[38] study claims to be a RCT due to follow-up of patients from the previous RCT,[37] but appears to be a follow-up cohort study. Toma et al.[40] describes a study with random allocation, but does not claim to be a RCT. However, even with consideration of this, the study has disparate aims, to evaluate the polycarbonate PEG and to compare BH to normal practice, with the former aim answered through service evaluation. Due to the random allocation in these studies, we continued to include this in the systematic review as a RCT. In all the included RCTs, outcomes were not defined reliably, potentially due to the volume of outcomes measured.

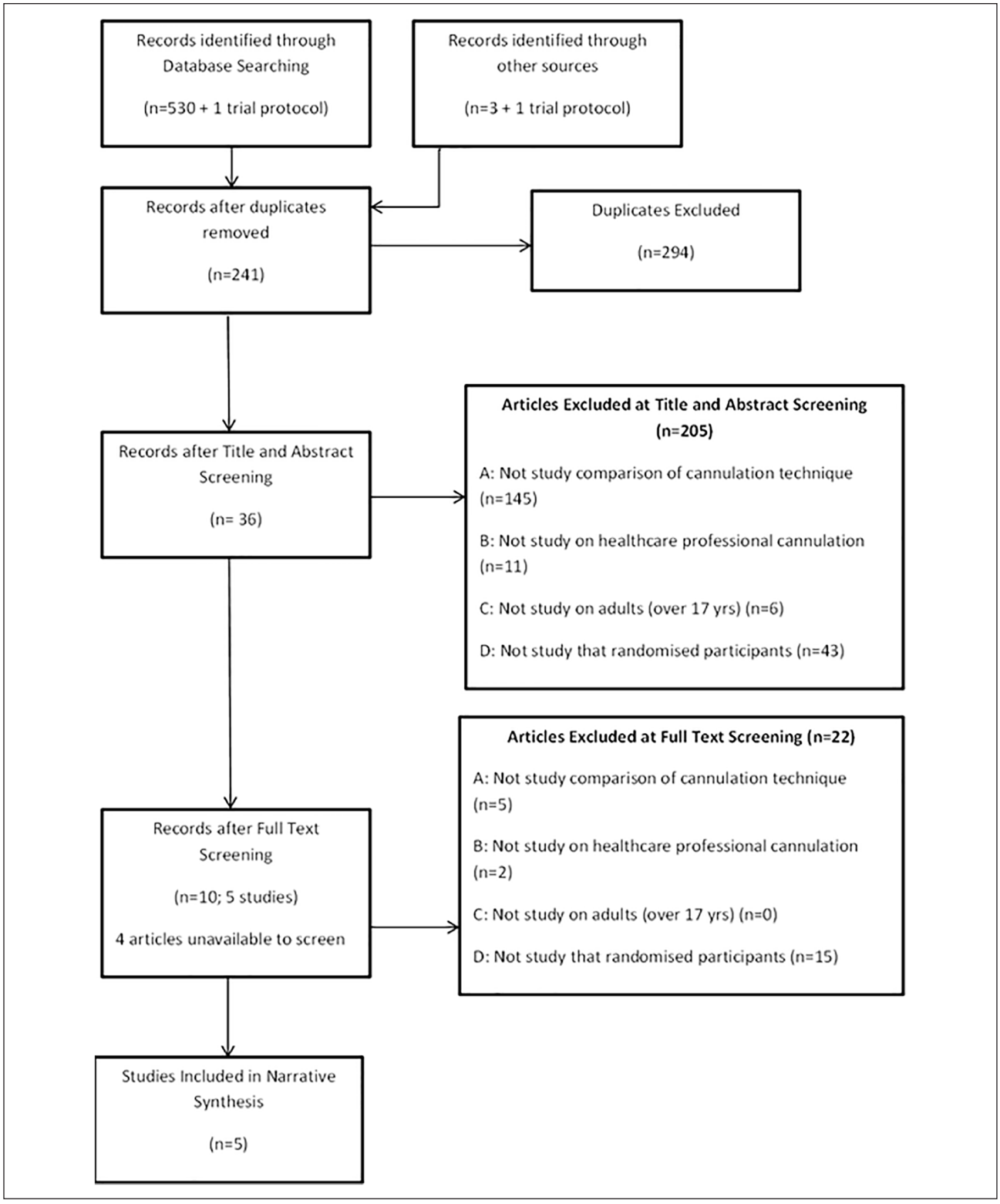

Figure 1. PRISMA flow diagram with reason for exclusion.

Description of studies

A description of all five included RCTs is summarised in Table 3. All studies were parallel group RCTs. All the RCTs used BH as the intervention to be tested and were evaluating BH as a change to normal clinical practice. Struthers et al.[39] and Chow et al.[35,36] compared this to RL whilst the other RCTs compared to usual practice. Vaux

Table 2. Quality assessment using the JBI tool.

	Chow et al.[35,36]	MacRae et al.[37,38]	Struthers et al.[39]	Toma et al.[40]	Vaux et al.[41]
1. Was true randomisation used for assignment of participants to treatment groups?	Yes	Yes	Yes	Unclear	Yes
2. Was allocation to treatment groups concealed?	Yes	Yes	Unclear	Unclear	Yes
3. Were treatment groups similar at baseline?	No	Unclear	No	Yes	Yes
4. Were participants blind to treatment assignment?	No	No	No	No	No
5. Were those delivering treatment blind to treatment assignment?	No	No	No	No	No
6. Were outcomes assessors blind to treatment assignment?	No	No	No	No	Unclear
7. Were treatment groups treated identically other than the intervention of interest?	Unclear	Unclear	Unclear	Unclear	Yes
8. Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analysed?	Yes	2012 – Yes 2014 – No	Yes	Yes	Yes
9. Were participants analysed in the groups to which they were randomised?	Yes	Yes	No	No	Yes
10. Were outcomes measured in the same way for treatment groups?	Yes	Yes	Unclear	No	Yes
11. Were outcomes measured in a reliable way?	Unclear	Unclear	Unclear	No	Yes
12. Was appropriate statistical analysis used?	No	Yes	Yes	No	Yes
13. Was the trial design appropriate, and any deviations from the standard RCT design (individual randomisation, parallel groups) accounted for in the conduct and analysis of the trial?	No	2012 – Yes 2014 – No	Unclear	No	Yes

et al.[41] reported that usual practice was a mixture of RL and AP, whilst MacRae et al.[37,38] used the terms 'standard practice' and RL inter-changeably. The comparator is difficult to determine in Toma et al.'s[40] study, with no definition as to whether this was RL or BH without the polycarbonate PEG used in the intervention arm. The description and content of cannulation protocols varied between RCTs, generally lacking in detailed description (Table 4). None of the papers described how fidelity and consistency of cannulation practices were assured during the study.

The sample sizes varied from 56 patients through to 140 patients. All studies had some element of loss to follow-up in the study period. Outcomes were assessed over time periods that varied from 8 weeks to 12 months. The only outcome measured consistently was pain, reported as a 10-point Visual Analogue Score (VAS) in four RCTs.[36,37,39,41] However, the time point when this was measured varied between studies, making comparison of results difficult. Due to variations in study design, a meta-analysis was not deemed appropriate (Table 5).

Clinical outcomes

Three RCTs reported AV fistula patency as an outcome,[38,39,41] but did so in different ways. Vaux et al.[41] examined access survival at 12 months and MacRae et al.[38] examined median access survival. Vaux et al.[41] reported superiority of BH technique for AV fistula survival, with 100% AV fistula survival at 12 months with BH, compared to 74% with usual practice. Vaux et al. also found fewer interventions to correct stenosis and thrombosis with BH. However, MacRae et al.[38] found no benefit of BH technique over usual practice for AV fistula survival or rate of intervention. Struthers et al. reported Blood Flow Rate and thrombosis rate, and found no difference between the two

Table 3. Descriptions of studies.

Study	Chow et al.[35,36]	MacRae et al.[37,38]	Struthers et al.[39]	Toma et al.[40]	Vaux et al.[41]
Protocol available	Yes – published[32]	Yes – ISRCTN registry (ISRCTN94795553)	No	No	Yes – ISRCTN registry (ISRCTN27841616)
Location	Australia Multi-centre: in-centre and home HD	Canada In-centre HD	Scotland In-centre: 1 main unit and 2 satellite units	Japan Unit type not stated	England In-centre: 1 main unit and 2 satellite units
HCP cannulated only	Health care professionals (HCP) and self-cannunlated.	HCP cannulated only	Not stated	Not stated	Not stated
Intervention	Buttonhole (BH) 'Cannulated in same direction, site and angle.'	Buttonhole (BH) 'Using constant site for both needles.'	Buttonhole (BH) 'Repeated needling at same site with same angle until track has been formed, when less sharp needles are then used.'	Buttonhole technique with polycarbonate peg to form track (BH) 'AV fistula cannulated by same experienced staff until fixed puncture track established.'	Buttonhole with polycarbonate peg to form track 'Constant site technique where needles are inserted at the same angle and depth each time.'
Comparator	Rope Ladder (RL) 'Usual practice of site rotation.'	Standard needling (SN) 'Rotates needling sites at each dialysis and at times, called RL.'	Traditional rope ladder (RL) 'Needles are inserted a short distance above or below the previous needling site and sites progress up and down the vessel.'	Standard practice (SP) Unclear.	Usual practice (UP) 'A combination of RL and AP.'
Study period	6 months	8 weeks (2012) >1 year follow up (2014)	6 months	3 months	12 months
Sample size	70 patients	140 patients	56 patients	76 patients	140 patients
Dropout	BH = 7patients RL = 5 patients	At 8 weeks: BH = 5 patients SN = 4 patients At >1 year: BH = 46 patients SN = 33 patients	BH = 6 patients RL = 3 patients	BH = 6 patients SP = 0 patients	BH = 34 patients UP = 9 patients
Primary outcome	Not stated	Perceived pain post needling, using a 10 cm VAS (2012) AV fistula survival (2014)	Pain score from 10 point VAS	Not stated	AV fistula survival at 1 year

(continued)

Table 3. (continued)

Study	Chow et al.[35,36]	MacRae et al.[37,38]	Struthers et al.[39]	Toma et al.[40]	Vaux et al.[41]
Results for patency outcome	-	Median access survival (in months) BH = 18.4 (10.9–32.7) SN = 16.0 (10.6–29.3) ($p = 0.2$) Number of interventions: BH = 135 PTAs (0.9 (0.66–1.21); SN = 82 PTAs (0.72 (0.48–1.08) ($p = 0.3$) (IRR = 1.28 (0.78–2.10)) 14 surgical (0.09 (0.05–0.16); SN = 14 surgical (0.11 (0.06–0.12) ($p = 0.6$) (IRR 1.79 (1.33–1.89)) Thrombosis rate: BH = 0.04 per pt years at risk (0.02–0.09); SN = 0.05 (0.03–0.11) ($p = 0.6$) (IRR = 0.75 (0.25–2.24))	Mean blood flow rate: BH = 350 mls/min RL = 358 mls/min Thrombosis: BH = 1 event RL = 1 event	-	AV fistula survival at 12 months: BH = 100% survival UP = 86% survival ($p = 0.0005$) Primary patency at 12 months: BH = 74% UP = 49% ($p = 0.01$) Hazard ratio = 0.46 BH to UP (95%CI 0.25–0.87) ($p = 0.02$) Number of access interventions at 12 months: BH = 11 (19%) UP = 27 (39%)
Results for infection outcome	Site infections: BH = 4 RL = 1 ($p = 0.11$)	Localised infection at 8 weeks: BH = 50 per 1000 HD (Median 2 (1–3)) SN = 22.4 per 1000 HD (Median 1(1–1.5)) ($p = 0.003$) Bacteraemia at 8 weeks: BH = 1; SN = 0 ($p = 1.0$) Localised infection (>1 year): BH = 3; SN = 0 Bacteraemia (>1 year): BH = 9; SN = 0 Total infection (>1 year): BH = 12; SN = 0 ($p < 0.001$) in table; $p = 0.003$ in text	BH = 1 BH event RL = 0	Erythema in BH = 1. Signs of infection in SP = 0.	Bacteraemia: BH = 0 UP = 2 (0.09 per 1000 AV fistula days) Exit site: BH = 2 (0.12 per 1000 AV fistula days) UP = 0

(continued)

Table 3. (continued)

Study	Chow et al.[35,36]	MacRae et al.[37,38]	Struthers et al.[39]	Toma et al.[40]	Vaux et al.[41]
Results for pain outcome	Pain 10 cm VAS: BH – Baseline = 0.81 (0.41–1.2); 6 months = 0.56 (0.13–0.99) RL – Baseline = 0.81 (0.48–1.15); 6 months = 0.71 (0.34–1.09) Lignocaine use: 44.4% in BH, 76.7% in RL ($p = 0.013$).	Pain 10 cm VAS at 8 weeks: BH = 1.5 (0.5–3.4) SN = 1.2 (0.4–2.4) ($p = 0.57$)	Pain 10 cm VAS: BH – Baseline = 3.0; 6 months = 2.5 RL – Baseline = 1.0; 6 months = 1.0 Local anaesthetic use: BH – 9 patients reduced use; 6 stopped completely RL – 1 patient stopped use ($p < 0.01$)	No pain with BH but pain with SP = 40.5% Less pain with BH than SP = 40.5% Pain was the same with BH as SP = 18.9% Pain was worse with BH than SP = 0 (Data only collected from BH study arm)	Pain 10 cm VAS at 12 months: BH = 1.3 (1.2–1.9) UP = 1.2 (1–1.5) ($p = 0.05$) Local anaesthetic use: Used at least once: BH = 41%; UP = 37% ($p = 0.7$) More than 50% of needles: BH = 9%; UP = 16% ($p = 0.3$)
Other outcomes measured	Quality of Life Complications Haematological and biochemical analysis Fistula observations (patency, thrombosis, trauma, inflammation, bruising, swelling) Kt/V Cannulation proficiency (number of attempts to insert a functioning arterial and venous needle and by Kt/V of 1.2 or more) Time to hemostasis	2012: Presence and size of haematoma Nursing perceived ease of needling Time to hemostasis (<5 min) AV fistula trauma 2014: Time until BH abandonment Reason for BH abandonment AV fistula complications	Aneurysm size Complications Bleeding time after HD Patient preference Staff preference Time period to form BH track	Bleeding during HD Bleeding time after HD Restrictions on lifestyle whilst PEG in place	Bleeding time at end of HD Time for cannulation New and existing aneurysm enlargement Staff Satisfaction Nurse preference Complications rate Economic analysis Clinical parameters

Table 4. Description of cannulation protocols.

	Chow et al.[35,36]	MacRae et al.[37,38]	Struthers et al.[39]	Toma et al.[40]	Vaux et al.[41]
Pre-cannulation cleaning BH	Washed AV fistula limb with 2% chlorhexidine. Cleaned with 0.5% chlorhexidine before needle insertion and after scab removal.	Cleaned with chlorhexidine before and after scab removal.	Cleaned with povidone-iodine. Used one swab for each BH site.	Not stated	Washed AV fistula arm with antibacterial soap. Cleaned with chlorhexidine 2% before and after scab removal.
Pre-cannulation cleaning – comparator	Washed AV fistula limb with 2% chlorhexidine. Cleaned with 0.5% chlorhexidine before needle insertion.	Cleaned with chlorhexidine.	Not stated	Not stated	Washed hands and AV fistula arm with antibacterial soap. Cleaned with chlorhexidine 2% prior to cannulation.
Track development (BH only)	1 senior nurse performed needle insertions for 2–4 weeks until converted to blunt needles.	The track was developed over 6–9 cannulations, during which the cannulation was performed by the same nurse. The same nurse performed the first 3 occasions of blunt needle insertion.	Created by one principle nurse, using a second nurse if needed who had observed angle and direction of needle insertion from principle nurse.	At the end of HD a peg is inserted into the track along the path of the needle puncture. At next HD the peg is then removed and access punctured with sharp needle. The process is repeated for 2 weeks, except after 2 HD sessions blunt needles are used.	Used polycarbonate peg, placed into needle site after dialysis and left in place until next session. Repeated over 6 haemodialysis sessions/14 days.
Scab removal (BH Only)	Sites soaked with Saline soaked gauze and nurses pinched the gauze to remove the scab	Removed using a sterile dull needle.	Soaked with saline after cleaning and separate needle used to remove scab.	States it is removed but not how.	Scabs were softened with sterile 0.9% Saline soaked gauze and removed using a sharp needle.
Use of mupirocin on cannulation sites	Not stated	None (2012) Introduced in last 6 months of study (2014)	Not stated	Not stated	None
Ensuring fidelity of Intervention	Recorded study procedures, but no results reported.	Recorded angle of insertion and distance from wrist/antecubital fossa	Not stated	Not stated	Not stated
Protocol to trigger blood culture	Not stated	Fever, rigors, malaise or suspected infection generated 2 × blood cultures. IV antibiotics if positive blood culture, fever or abscess/cellulitis.	Not stated	Not stated	Stated response to blood tests would be as standard practice.
Protocol to trigger wound swab	Not stated	If pus or erythema present at AV fistula site, swab taken.	Not stated	Infection at the cannulation site was defined as redness, swelling, tenderness, exudate or pus.	Not stated

Table 5. Assessment of criteria to progress to meta-analysis.

	Achieved	Not achieved
Same cannulation techniques?		X
Same cannulation protocol?		X
Define the outcome in the same manner?	X – pain only	
Measure the outcome using the same method?	X – pain only	
Measure the outcome over the same time period?		X
Is patient demographic data similar?		X

This was developed by the research team as part of the protocol development process, prior to implementing the systematic review.

groups.[39] The other two RCTs did not collect any outcomes related to AV fistula patency.[35,36,40]

All five RCTs reported infection as a secondary outcome (Table 3). Only one RCT found a significantly higher infection rate with BH, but only when bacteraemia and site infections combined) (BH 12 vs RL 0, $p < 0.001$).[38] However, rates of bacteraemia alone were not compared using statistical tests, but there were higher rates of bacteraemia with BH versus RL (9 vs 0, respectively). However, it was difficult to determine the follow up period and whether this was the same for each study arm. Three other RCTs interpreted their results as indicating a higher infection rate with BH, but there were no significant differences in the reported rates of infection between BH and comparator groups.[36,39,40] Comparison of infection rates was confounded in these three studies due to a lack of clarity of what constituted an infection. Toma et al.[40] defined an infection as any erythema at needling sites and did not report bacteraemia rates, Struthers[39] et al. did not define whether site infection or bacteraemia were monitored and Chow et al.[36] only captured site infections. Vaux et al.[41] found the same numbers of total infections in each group, with a low rate of bacteraemia overall (2 usual practice vs 0 BH).

Five RCTs reported pain associated with cannulation, with four using a 10-point VAS,[36–39,41] but at differing time points. Three RCTs found no or minimal difference in pain score,[36,37,41] one found higher pain scores in the BH group but this difference was also present at baseline.[39] Toma et al.[40] found patients experienced less pain with BH. There was only one study that maintained consistent local anaesthetic (LA) use during the study,[37] with three RCTs allowing LA use to be driven by patient choice, reporting less LA use with BH.[36,39,41] Other aspects of patient experience were not explored in-depth within the studies, with no study exploring anxiety. Chow et al.[36] reported results of quality of life questionnaires and the number of attempts to place the needle and found no difference between the two groups. Struthers et al.[39] asked the BH group which technique they preferred, having experienced both techniques, and 95% preferred BH.

Discussion

This systematic review, the first to focus solely on evidence from RCTs, provides an examination of RCTs that compare cannulation techniques. Results show that existing studies have produced opposing results, some favouring RL and others BH, for the outcomes of patency, infection and pain. There remains no clear consensus as to which technique is superior.

All RCTs included in this systematic review compared BH to either RL or usual practice. Whilst individual RCTs make claims of superiority or inferiority of BH in comparison to RL or usual practice, results are inconsistent between RCTs. Vaux et al.[41] reported that BH led to improved preservation of AV fistula function, whilst MacRae et al.[38] found no benefit. Infection rates also differed between studies, leading to inconclusive results. Whilst various claims were made about pain in RCTs, none of the studies reported clinically meaningful differences in scores between cannulation techniques. No other outcomes related to patients' experiences were examined.

Patency of the AV access relates to longevity for haemodialysis use and successful use for haemodialysis. The Standardised Outcomes in NephroloGy (SONG) project identifies access function as an important outcome for both patients and healthcare professionals, which they state should be included in all studies into vascular access for haemodialysis.[43] Wilson and Harwood examined what successful cannulation means for patients, identifying that successful use for haemodialysis is of importance to patients.[44] However, not all RCTs measured this outcome. SONG is currently working on an outcome for patency of vascular access.[45] This outcome needs to be included as an outcome in all future RCTs on cannulation for haemodialysis.

Infection is a potentially serious complication of both vascular access use and haemodialysis.[46] Only one study found a significant difference in infection rates between BH and RL, and only when using a combined endpoint of bacteraemia and exit site infection, over an uncertain follow-up period.[38] Inconsistent reporting of infection across studies made comparison difficult, with differing definitions of what was an infection. Clinical protocols for screening and diagnosis of infection lacked definition and clarity (Table 4), making it unclear if this was performed consistently between study arms. It is important to note that no study was powered to detect a difference in infection. Whilst it would be difficult to perform a study that is large enough to be powered to produce significant results

for infection, study results including statistical inferences need to be reported and interpreted in this context. Infection results should also be interpreted in the context of expertise of the cannulators – in all studies cannulators had experience in the comparator but not in BH. This lack of experience in BH may exaggerate the infection rates related to this technique. One observational study has shown that developing expertise and strict training on asepsis negates the infection risk related to BH.[47] There are other reports that BH may be more vulnerable to infection due to breaches in asepsis,[36,47] with the need for strict training of cannulators and avoidance in patients with a particular infection risk.[48] Therefore, results do not allow definitive conclusions to be drawn about infection, with clinical equipoise still remaining.

Patients' experience of cannulation can affect decisions they make about their choice of vascular access[49] and impacts patients' experiences of haemodialysis.[1] Cannulation experience includes complex concepts including pain, fear and anxiety related to the cannulation procedure, feelings of vulnerability and loss of control, concern about the success of the procedure and worry about the appearance of their AV access.[8–12] This is affected by multiple factors including the relationship with the cannulator, the competence and confidence in the cannulator and the environment.[44,50] However, despite the complexity of cannulation experience, pain was the only outcome used to assess patients' experiences. Four RCTs used a 10 cm pain VAS to provide cannulation pain score.[36,37,39,41] Of these, three demonstrated minimal differences between cannulation techniques (score differences between 0.1 and 0.3), with baseline pain scores low. Whilst there is no universally accepted threshold, the differences found are unlikely to represent a clinically meaningful difference. This indicates insensitivity of the pain VAS to detect cannulation pain in this context. The fourth RCT obtained a larger difference in pain score,[39] with higher pain scores in the BH group at 6 months, but this difference was also present at baseline, indicating the difference was due to differences in the participants in the study arm groups rather than the cannulation technique. Future RCTs should consider how to measure patient-centred outcomes that fully capture patients' experiences of cannulation with sensitivity, whilst ensuring validity and reliability of measures. This may involve: performing a mixed methods RCT, with a qualitative element; development of questionnaires; or recognising that patients' experiences of cannulation, including pain, can only truly be captured by qualitative studies.

As mentioned in the introduction, cannulation is a complex intervention with multiple elements affecting its success. When conducting RCTs in complex interventions, clear description of the intervention and comparator is essential. Implementation can affect the success of complex interventions and standard practice can vary, so there needs to be clarity as to what both are. This is relevant to cannulation of AV access and was lacking in all the RCTs included in this systematic review (Table 4). The intervention was described in more depth than the comparator, providing reassurance that the intervention was BH. Different studies performed BH using different techniques, particularly in pre-cannulation cleaning technique and use of a polycarbonate peg to develop the track (Table 4), which may have influenced the varied results between studies. However, descriptions of the comparator were lacking. RL can be easily confused with AP, with AP occurring when cannulation sites do not cover enough distance on the vessel to become RL.[15] An international survey of 10,807 patients (in 171 centres) identified that 65.8% of haemodialysis patients underwent AP, not RL (or BH), identifying AP as the predominant technique in usual practice.[5] Vaux et al.[41] acknowledges this stating the comparator was a mixture of AP and RL, however the other RCTs do not acknowledge this point. However, in three RCTs[37,39,40] the comparator was defined as usual or standard practice, using this term inter-changeably with RL. Therefore, it is likely there was a proportion of AP in the intervention was unrecognised and unknown. AP is associated with an increase access failure.[5] If BH is compared to AP instead of RL, then BH may generate more favourable results in terms of patency. As the proportion of AP in the comparator is unknown, the effect of this is also unknown, but may explain the inter-study variability in results. The Template for Intervention Description and Replication (TIDieR) checklist recommended by the Equator Network to define interventions and comparators[51] and is suggested for any future RCTs that compare cannulation techniques.

Assessment of fidelity of both intervention and comparator was not present in any of the RCTs. Assessing fidelity involves examining the consistency of the implementation of the intervention and comparator, to ensure this is delivered as defined and not influenced by the effect of variances between individual operators.[19] For example, infection and pain can be moderated by how techniques are performed.[44,47,50] Process evaluation within future RCTs will allow assessment and assurance of fidelity of interventions and comparators and identify how this affects results.[19,52,53]

Three journal articles and one conference abstract were identified as potential studies for inclusion, but could not be sourced.[31–34] These studies do not appear to be reported differently to the RCTs examined, so whilst their results may have added to the clinical outcome results, they are unlikely to have affected the conclusions of this systematic review. Due to the small number of studies included, publication bias was not assessed, however identification of an unpublished RCT,[34] indicates this is a possibility. Following completion of the systematic review, the search was repeated on 24/09/2020 to update this for publication. Only one further feasibility trial protocol was found, which is examining the feasibility randomising participants to a large multi-centre RCT in Canada to compare BH and RL cannulation for haemodialysis. This completed recruitment in March 2019,

but no results are yet available (ClinicalTrials.gov Identifier: NCT01962025). This study has not been included in the systematic review, but once results are published it will contribute to the evidence base in this area.

In conclusion, current RCTs comparing cannulation techniques in patients undergoing in-centre haemodialysis provide disparate results. The quality of studies was poor, making interpretation and application of clinical results from the included studies difficult. Study findings may be attributable to differences in how the cannulation was performed, rather than differences in the actual cannulation techniques. Therefore, we believe that conclusions or recommendations on how cannulation is performed cannot be made. Future RCTs examining cannulation techniques for haemodialysis must be reliable to influence clinical practice, using designs that are mindful of the complexity of the intervention, including:

- A full description and definition of both the interventions and comparator, using the TIDieR checklist as a guide
- Embedded process evaluation to ensure fidelity of intervention and comparator and provide context to study results
- Consideration of outcomes assessed to ensure reliable reporting between study arms and use of standardised outcomes, with particular attention to how patients' experiences are captured

Use of feasibility and pilot studies is recommended to allow further exploration of these elements, ensuring that a large multi-centre RCT produces results that are attributable to true differences in cannulation techniques.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This systematic review was completed as part of a research fellowship from the UK renal registry and Health Education East Midlands Silver Clinical Scholars award.

Ethical statement

This is a systematic review so there are no ethical issues, using only data from previously published research.

ORCID iD

Catherine A Fielding https://orcid.org/0000-0002-2507-9275

Supplemental material

Supplemental material for this article is available online.

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