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Effectiveness of Ultrasound-Guided Arteriovenous Fistulas Cannulation in Difficult Hemodialysis Arteriovenous Access: A Meta-Analysis of Randomised Controlled Trials

Alison Hiu Ming Chan, Angie Ho Yan Lam*

School of Nursing, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China
Email: u3596468@connect.hku.hk, *angielam@hku.hk

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Abstract

Aim(s): Complex Arteriovenous fistula (AVF) poses challenges to cannulation. Ultrasound (US)-guided cannulation may promote successful cannulation and prevent AVF-related complications. Renal nurses performing US-guided cannulation may improve successful cannulation and reduce complications associated with unnecessary punctures. The study aims to conduct the meta-analyze to examine the effectiveness of renal nurse-performed US-guided cannulation to improve successful cannulation and reduce AVF-related complications in difficult AVF access. **Design:** A meta-analysis of randomised controlled trials. **Methods:** A systemic search was performed on electronic databases including CINAHL Plus, Web of Science, and PubMed from inception to October 2023. Risk ratios (RR) and standardized mean differences (SMD) were estimated using random-effect models for considerable homogeneity, and the Scottish Intercollegiate Guidelines Network (SIGN) methodology was adopted for critical appraisal. **Results:** Four RCTs were included. The results showed US-guided AVF cannulation had a significant effect in improving successful cannulation (RR: 0.19, 95% CI: 0.06 to 0.63, p = 0.007), and was favorable in reducing cannulation-associated complications (RR: 0.44, 95% CI: 0.10 to 1.93, p = 0.28), compared with blind needle cannulation. **Conclusion:** US-guided cannulation performed by renal nurses has the potential to improve successful cannulation, and fewer complications in hemodialysis patients with difficult arteriovenous access. **Relevance to Clinical Practice:** The results suggest the value of further training for renal nurses in US-guided cannulation, and broader implementation of US-guided cannulation to improve patient outcomes. Future studies could explore the optimal nursing training and longer-term benefits of US-guided cannulation by renal nurses in difficult AVF access. **Patient or Public Contribution:** No Patient or Public Contribution as this is a meta-analysis using the secondary data published in the RCTs.

Keywords

Arteriovenous Fistula, Cannulation, Dialysis Access, Hemodialysis, Renal Nurse, Ultrasound Guidance, Vascular Access

1. Introduction

End-stage renal disease (ESRD) is a debilitating disease which is not inferior to mainstream diseases [1]. In America, approximately two in one thousand people are living with ESRD [2]. In Shanghai, the prevalence and incidence of dialysis were 544.7 per million people and 82.9 per million people in 2011, with an increasing trend [3]. Dialysis, including hemodialysis (HD), peritoneal dialysis (PD) and kidney transplant, are the treatments for ESRD (National Institute of Diabetes and Digestive and Kidney Disease, 2023), where dialysis is the mainstay of renal replacement therapy Indeed [4].

In hemodialysis, arteriovenous fistula (AVF) is the preferred form of vascular access [5] as it exhibits the lowest risk of complications, lowest needs for treatments and superior long-term patency compared to alternate access methods [6]. The ideal site of AVF is in the forearm (radio-cephalic or distal AVF) according to National Kidney Foundation [7]. AVF requires 6 to 8 weeks of maturation to develop the turbulent flow for cannulation [6]. An optimal AVF access has flow of more than 600 mL/min, minimum 0.6 cm vein diameter and maximum 0.6 cm depth with clear margins. Otherwise, AVF will count as difficult access [7]. Moreover, various biological and non-biological factors, including new or immature AVF, deeper and upper extremity AVF, brachiobasilic fistula without transposition, limited length of the blood vessel within a confined region, aging, obese and frail vein and skin are contributing AVF to difficult arteriovenous access [8]-[11].

The above-contributing factors of difficult AVF access pose a challenge in cannulation. The access may be difficult to cannulate and require multiple attempts, leading to iatrogenic complications [12]. In the hemodialysis quality aspect, repeated unsuccessful cannulation in difficult access may result in high venous pressure, inadequate dialysis, and poor blood flow rate. In the AVF access aspect, fail cannulation may cause fistula thrombosis, direct trauma, access stenosis, infection, extra vascular hematoma, aneurysm and oozing at the cannulation site [11] [13]. Those complications will further exacerbate the difficulty in cannulation and create a vicious circle [14]. In the worst case, it may lead to a transient or permanent loss of access. Repeated fail cannulation may also relate to lower quality of life, associated hospitalization, feeling of pain, fear and anxiety and increasing dependency on CVC [11] [13] [15].

Currently, traditional blind needling technique is adopted in most hemodialysis centres. Renal nurses guide the needle placement by listening to the bruits and palpating the thrill of AVF [9]. However, it is found that the current blind cannulation is not reliable for difficult AVF access cannulation. A higher rate of failure cannulation is rendered, and its failure cannulations diminish AVF survival [15]. In blind cannulation, less than 10% of AVF are successfully cannulated, and there is 2.98 times higher infiltration risk in difficult and new AVF [8]. Dua Niyyar *et al.* (2023) reported that mild infiltration occurs frequently over 50% of all AVFs, and major infiltrations are 5% - 7% that are cannulated by blind needling technique [16]. Lee, Baker and Allon (2006) reported that a mean of 2.4 additional diagnostic tests, interventions and surgery appointments are caused by AVF needling infiltration [12]. Therefore, there is an eagerness to innovate cannulation technique, using ultrasound (US) guided cannulation technique instead of blind cannulation.

There is an emerging trend in utilizing ultrasound guidance for cannulation to increase the success rate of first-attempt cannulations and minimize fail needling. The recently updated AIUM Practice Parameter stated that the use of ultrasound guidance has been successfully applied in difficult peripheral vein access, such as peripheral venous cannulation and insertion of central venous access in order to reduce iatrogenic injury [17]. Nonetheless, US-guided AVF cannulation is not widely adopted in clinical nursing practice in hemodialysis centres [9], even though studies have shown the promising effects of US-guided AVF cannulation, including increased accuracy of cannulation, decreased adverse events in difficulty AVF and improved nurses' confidence in AVF cannulation [5] [8] [9] [14] [18]. This review, thus, aims to conduct a systematic review and meta-analysis, including critical appraisal of the results and effects of nurse-performed ultrasound-guided cannulation in hemodialysis patients with difficult AVF access.

2. Methods

2.1. Eligibility Criteria

2.1.1. Participants

The review considered studies that patients were diagnosed with ESRD undergoing hemodialysis regularly at least two times per week; and patients have difficult AVF access, which is determined based on the anticipation of difficulty, taking into consideration a combination of factors. These factors include, but are not limited to, the timing of AVF creation, AVF morphology, history of complications and difficult cannulation, patient tolerance level, and predictive parameters of AVF maturation.

2.1.2. Interventions

This review included studies that used US-guided cannulation techniques as the only intervention. The cannulation should be conducted by renal nurses. Study designs included full-text, peer-reviewed studies, English-language, randomized control studies or a pilot randomized trial.

2.1.3. Comparator

Studies compared usual cannulation techniques (blind needling) in the control groups.

2.1.4. Outcomes

The primary outcome of interest is successful AVF cannulation, defined as renal nurses inserting two needles for arterial and venous connection without missed cannulation or extra attempts. The secondary outcomes of interests were pain associated with cannulation, and puncture-related complications such as infiltration, hematoma formation or thrombosis events.

2.2. Exclusion Criteria

Studies were excluded if the US-guided interventions targeted CVC insertion or AVF creation or different vein or artery procedures instead of targeting difficult AVF cannulation, and Ultrasound-guided cannulations were conducted by nephrologists instead of renal nurses.

2.3. Searching Strategy

The research was searched through three electronic databases, including CINAHL Plus, Web of Science and PubMed. Moreover, Google Scholar was used as an adjunct tool to identify additional studies. According to PICO, patient/problem and intervention were the two main groups of keywords to search for with connecting wording "and". For patient or problem keywords searching, "ESRD patient", "hemodialysis patient", "Difficult AVF access", and "New AVF access" were used. For another intervention group, keywords searching, "cannulation", "Ultrasound-guided cannulation" and "ultrasound-guided needling" were applied. All searched results were imported to EndNote 21 software with different database subgroups labelling and helped to extract and screen out duplicated research by the same title. The remaining studies' abstracts were screened by two independent reviewers according to the inclusion and exclusion criteria. Then, studies were further assessed for eligibility, and the remaining full-text studies would be extracted for analysis and review. The final studies' content and references were screened to explore any additional eligible studies being available. Disagreements between reviewers on the articles with unclear eligibilities were resolved by discussion and consensus.

2.4. Quality Assessment

All eligible studies went through an appraisal process. Scottish Intercollegiate Guideline Network (SIGN) Critical Appraisal Checklists for RCT study were used to critically assess the study's risk of bias within and across studies [19]. The selected studies will be appraised according to the clarity of the research question, the method of randomization and concealment, the blinding strategy, the similarity of participant characteristics, additional treatment components beyond the protocol, reliable and validated outcome measurements, dropout rate, the application of intention-to-treat analysis and whether the data are comparable for multi-site studies. For the overall quality of the study, the SIGN checklist had a grading system for criticizing the levels of evidence of the studies into four grades: high quality (++), acceptable (+), low quality (−) and unacceptable-reject (0).

2.5. Data Extraction

Information was extracted from the trials based on the characteristics of the study (author, publication year, country), participants (setting, age, gender, primary disease, sample size) intervention and comparator (design, component of intervention, frequency, duration, follow-up period), and study results and outcomes significance to the review question.

2.6. Statistical Analysis

Review Manager (RevMan) software version 5 was used to analyse the data extracted from studies. Risk ratios with 95% confidence intervals (CI) were estimated for dichotomous variables, and standardized mean differences (SMD) with 95% confidence intervals (CI) were estimated for continuous variables. I^2 statistics and with a chi-square test were used to assess statistical heterogeneity [20]. The fixed-effect model was used for low statistical heterogeneity across studies, as indicated by $I^2 < 50\%$ and $p \geq 0.10$. The random-effect model was adopted for high heterogeneity, as indicated by $I^2 \geq 50\%$ and $p < 0.10$.

3. Results

3.1. Search Result

The literature review was done on 6th November 2023. A total of 122 studies were enlisted from 3 electronic databases. One study that was found to be duplicated and was removed. Then, 121 studies were screened for titles and abstracts, and 112 studies relating to inappropriate and irrelevant interventions and outcomes were excluded. After the title screening, nine studies remained and were eligible for full-text screening and review. It resulted in leaving only four studies. Five more studies were further excluded for the reasons that one study was a study protocol, two studies were cohort study and observational study, one study showed that diverse interventions in cannulating difficult AVF and the US-guided cannulation were one of the given interventions, and one study showed that cannulation was conducted by nephrologist instead of nurses. Furthermore, other methods from Google Scholar helped in searching studies and resulted in four eligible studies. However, those were all duplicate studies and were excluded. Therefore, a total of four studies were left in the end, and their reference lists were screened for additional study, but no additional study fit the criteria. The literature searching flow is briefly shown in the PRISMA flow diagram attached in **Figure 1**.

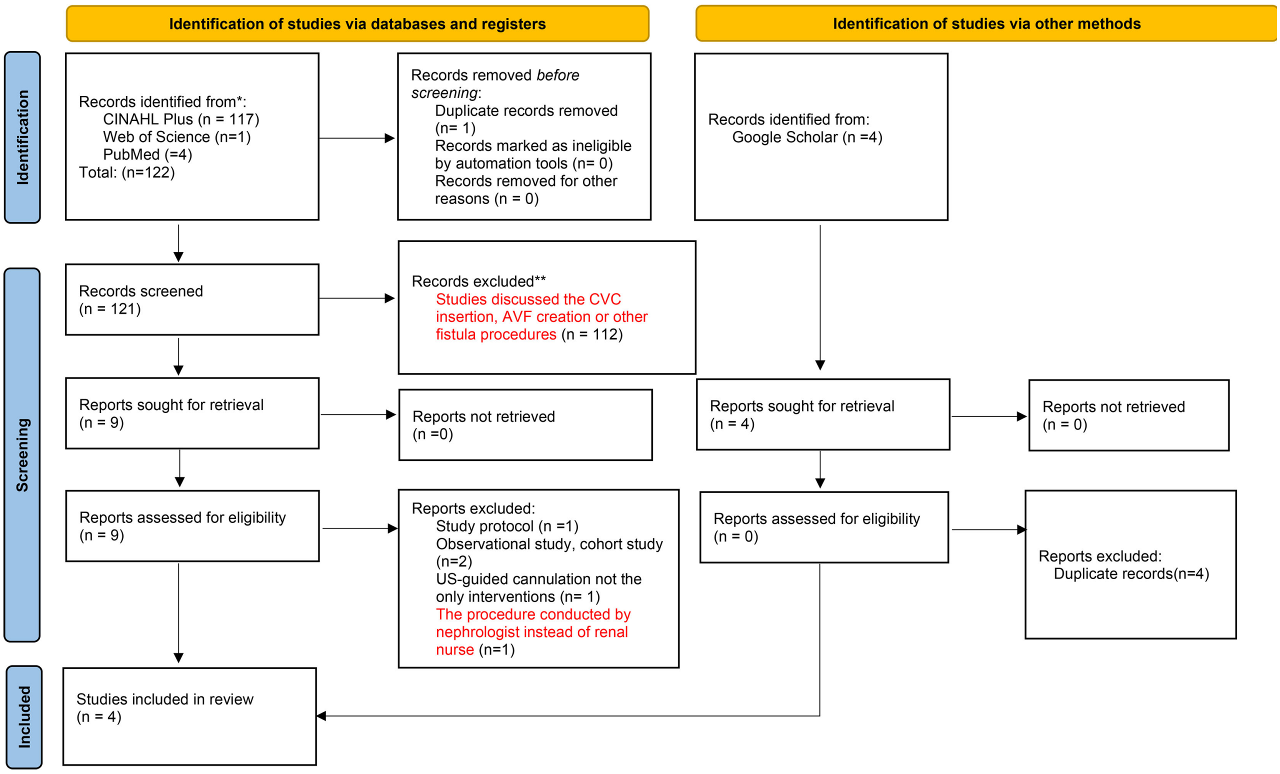

Figure 1. PRISMA flow diagram.

3.2. Study Characteristics

The four selected studies are all RCT studies published between 2018 and 2022. Four different places were conducted by the four studies: Singapore [9], the United Kingdom [18], China [14], and the United States of America [8]. All four studies were single-centre trials in dialysis units [8] [9] [14] [18]. Three of the studies were conducted in the dialysis department inside the hospital [9] [14] [18]. One of the studies was conducted in a community-based dialysis centre [8]. Table 1 illustrates the evidence of the four selected studies.

Table 1. Table of evidence.

Reference, Country, Quality	Participant's characteristics	Intervention (sample size)	Control (sample size)	Outcomes
Chen *et al.* (2022) Singapore RCT (+)	Difficult AVF: 1. First cannulation: 24% 2. After angioplasty/ thrombectomy: 42% 3. Stenosis: 18% 4. Multiple cannulation history: 60% 5. Deep vein: 14% 6. Bruise/hematoma: 54% 7. Clot: 8%	Point-of-care ultrasound guided AVF cannulation technique (n = 25) 1. Renal nurses were first being trained by accredited interventional nephrologists and assessed for competency. 2. The procedure was performed under aseptic technique. 3. Place the sterile drape underneath fistula arm.	Conventional cannulation technique (routine protocol) (n = 25) 1. Preformed physical assessment to assess for the presence of thrills (palpation) and bruit (auscultation by stethoscope). 2. Observed for signs of	Successful cannulation rate (%) Immediate complications that limited the use of AVF/AVG for the same dialysis session (e.g. the need for a temporary central venous catheter, single-needle dialysis,

	Gender: Male: 56% Female: 44% Mean age: IG = 58.3 (SD: 2.0) CG = 64.9 (SD: 1.9) Premorbid diseases: 1. Diabetes: 76% 2. Hypertension: 84% 3. CHD: 48% 4. PVD: 22% Fistula type: 1. Radio-cephalic: 38% 2. Brachiocephalic: 54% 3. Brachiobasilar: 8%	4. Use nondominant hand to hold the sterile sleeves covered US probe and found the target vein showing at the screen. 5. Use dominant hand to held fistula needle and inserted to the point of entry corresponding to the center of the probe. 6. At least 3 cm proximate to the identified sit when fistular needling was inserted and 3 cm away from anastomosis site. 7. Under US-vision-guided in real-time, the needle was advanced slowly. 8. When the screen shoed the needle shadow was inside the blood vessel, further advanced the needle downstream and move the US along with the tip of the needle to the ideal position. 9. Blood was aspirated to confirm the patency and position. 10. Obverse any swelling or pain around site of cannulation when flushing.	infection, poor circulation, pain, tenderness, oedema, bruise, and hematoma. 3. Started cannulation as routine practice when sterile set was prepared.	or infiltration (e.g., hematoma). Immediate Pain score (numeric rating scale).
Eves *et al.* (2021) United Kingdom RCT (+)	Gender: Male: 65.6% Female: 34.4% Age median: 68 Co-morbidities: 1. Diabetes mellitus: 50.0% 2. Hypertension: 68.8% 3. Smoker:40.6% 4. PVD: 28.1% 5. CHD: 31.3% Fistula type: 1. Brachiocephalic: 53.1% 2. Radio-cephalic: 34.4% 3. Basilic vein transposition: 12.5% Dialysis three times weekly via two needle	USG cannulation: an aseptic transverse ultrasound technique, Sonosite Edge II ultrasound system withHFL50X Sonosite straight probe (n = 170) 1. Staff training package: two theory sessions and two practical teaching sessions in transverse imaging cannulation technique with assessment by a senior vascular surgeon and 2 investigators. 2. Equipment: sterile gel, sterile probe covers, standard drape covers. 3. Time recording: starting when US probe placing on fistula and stopping when blood "flash back" was checked in both needles.	Standard Ropeladder cannulation technique (n = 176) Equipment: standard drape covers. Performed vision and palpation to guide placement of needle. Using "wet" cannulation.	Number of additional needle passes Absolute number of needle passes Additional skin punctures Absolute number of skin puncture Immediate Pain associate with cannulation (Visual Analogue Scale) Immediate Local Complications • Bleeding events • Infiltration events • Vessel thrombosis events • Needle thrombosis events
Wu, Huang, Zhang & Li. (2022)	Mean age: IG: 56.19 years (SD: 9.95) CG: 55.4 years (SD: 9.49)	Ultrasound in-plane guided cannulation technique with Mindray M7 Super portable L12-4s probe was installed in color Doppler US-guided	Canonical blind cannulation (n = 20) 1. AVF was observed and	One-time success rate of internal fistula cannulation:

China RCT (+)	Gender: Male: 67.5% Female: 32.5% Primary disease: 1. Hypertension: 42.5% 2. Chronic nephritis: 50% 3. Others: 7.5% Blood vessel parameters 1. Time cannulation time (week): IG: 6.72 (SD: 0.56) CG: 6.75 (SD: 0.61) 2. Fistula depth(mm): IG: 5.56 (SD: 0.69) CG: 5.52 (SD: 0.52) 3. Fistula diameter (mm): IG: 4.81 (SD: 0.51) CG: 4.79 (SD: 0.35) 4. Fistula blood flow (mL/min): IG: 730.29 (SD: 73.49) CG: 729.85 (SD: 7.85) Regular hemodialysis (3 times/week) (4 hours/time)	equipment (n = 20) 1. Disinfected the drape and using 0.2% active iodine for disinfect patient's entire upper arm. 2. Nurse wore sterile groves and color US probe was covered sterile cover. 3. Disinfected the probe by the disinfectant coupling reagent. 4. Used of upper extremity vein mode to develop the longitudinal section of AVF. 5. Used left hand to fix US probe and cannulation site was marked by the probe. 6. Right hand handled the needle to insert at the cannulation site which was the distal end of US probe. 7. Screen displayed the cannulation needle's running track under the skin. 8. Adjusted the cannulation angle until the needle fully entered with an optimal site.	palpated to determine the cannulation point. 2. Placed a therapeutic towel. 3. To tie a tourniquet therefore to dilate the blood vessel. 4. Disinfection with 2% active iodine.	Immediate Incidences of adverse events: • Oozing • Subcutaneous hematoma Immediate pain score (Visual Analogue Scale)
Kumbar *et al.* (2017) United States RCT (−)	Mean age (years): IG: 66 CG: 52.5 Gender (Male): IG: 60% CG: 50% Co-morbidities: 1. DM: 55.56% 2. HT: 100% 3. CAD: 33.34% Left AVF: IG: 80% CG: 75% Fistula age before use (days & SD) IG: 114.4 (49.7) CG: 64.5 (31)	The real time ultra-sound-guided cannulation with a novel C mode handheld ultrasound device (n = 5) 1. Simulated training on the operation of US machine was provided by competency with evaluation for dialysis staffs. 2. Titration of needle sizes over three-weeks period. 3. Pre-clearance US evaluation of AVF was done. 4. Site of cannulation was identified by US device. 5. Showing real-time guidance by US device of needle gauge or needle tracking. 6. Hydrogen peroxide disinfectant wipes was used for device disinfection and transparent adhesive film was covered to avoid the direct contact with patient and device. 7. Special sterile US gel was used for real-time guided cannulation.	Standard cannulation practices (n = 5) 1. Using 17 G needle for first 3 times, then changed to 16 G for 3 times and followed by 15 G for 3 times. 2. The direction of the needle could be antegrade or retrograde.	Successful cannulation rate Immediate Pain score Immediate Infiltration • Major infiltration • Minor infiltration • fistula rest • catheter usage due to infiltration • Fistula still in use 3 months follow up (after infiltration): • Fistula still in use • Repeated treatment • Hospitalization or catheter related complications • Access abandon

Footnote: G, gauge; AVF, arteriovenous fistular; IG, Intervention group; CG, Control group; USG, Ultrasound-guided; US, Ultrasound; SD, Standard deviation; MD, mean difference; DM, Diabetes mellitus; HT, Hypertension; CAD, Coronary artery disease; CHD, Coronary heart disease; PVD, Peripheral vascular disease.

3.3. Participant's Characteristics

The sample size of the four selected studies was small, ranging from 10 participants (Kumbar *et al.*, 2018) to 50 participants [9]. The mean age of participants was 61.61, ranged 52.5 [8] to 68 [18]. Three of the studies recruited more male participants, which accounted for 65.6% [18], 67.5% [14] and 56% [9] of all the samples being recruited. A pilot study recruited equal male and female participants, which accounted for 50% male and 50% female [8] of the sample recruited.

Patients recruited in four eligible studies were all having ESRD with regular hemodialysis three times per week via difficult AVF access. Apart from ESRD, patients have other comorbid disease. In three of the studies recruited, the majority of co-morbidity was hypertension, which accounted for 68.8% [18], 84% [9] and 90% [8]. The second most common co-morbidity was diabetes mellitus, which accounted for 50% [8] [18] and 76% [9] of the participants, respectively. Kumbar *et al.*'s (2018), Eves *et al.*'s (2021) and Chen *et al.*'s (2023) studies also recruited patients suffering from coronary artery disease as co-morbidity [8] [9] [18]. At the same time, Wu *et al.* (2022) recruited chronic nephritis as the major comorbid disease, which accounted for 50% and hypertension as the second most common comorbid disease, which accounted for 42.5% of the participants, respectively [14]. The most common type of AVF access in two eligible studies was brachiocephalic [9] [18] while Kumbar *et al.* (2018) and Wu *et al.* (2022) did not provide any data on fistula type [8] [14], however, Wu *et al.* (2022) had mentioned the blood vessel parameters for cannulation sites of participants including the fistular depth, diameter, and bold flow [14].

For the difficult AVF access's characteristics, four of the selected studies referred to difficult AVF access as newly established AVF fistular less than three months or first cannulation AVF [8] [9] [14] [18]. Chen *et al.* (2023) also referred to difficult AVF access as postangioplasty or thrombectomy AVF, with less than 30% residual stenosis, imaging confirmed partial AVF stenosis with no functional compromise, history of failed cannulation, bruises, or hematoma around AVF and over 0.8 cm depth in skin AVF [9]. Eves *et al.* (2021) referred to difficult AVF access as a history of difficult in cannulation, less than six weeks of recent complications from cannulation and regular complications of cannulation [18]. This study also considered personal factors such as patients with high levels of anxiety and invisible cannulation site as difficult AVF access. Wu *et al.* (2022) referred to difficult AVF access as newly established AVF fistular within 6 to 26 weeks, upper extremity AVF and the internal fistula diameter, which was determined by ultrasonography, being equal to or greater than 4 mm with a depth of 4 to 7 mm from the skin and a blood flow rate of over 600 mL/min [14]. Kumbar *et al.* (2018) identified new AVF as difficult access due to its increased susceptibility to needle infiltration, which can result in significant morbidity [8].

The reviewed studies excluded the participants who had active AVF complications [18], non-high autologous AVF as access [14], cannulation by physicians [9] and not new AVF access [8].

3.4. Intervention

All four of the eligible studies adopted US-guided cannulation in the intervention group and the standard blind needling technique in the control group [8] [9] [14] [18].

All four selected studies chose a portable US machine which showed real-time vessel track under the skin to guide needling [8] [9] [14] [18]. However, Chen *et al.* (2023) reported the use of handheld US device without reporting the machine brand, the machine setting and the selection of probe [9]. Eves *et al.* (2021) used the brand Fujifilm Sonosite from Washington with the Sonosite Edge II ultrasound system being loaded [18]. Moreover, the HFL50X Sonosite straight probe with a simple US straight probe was applied in the intervention with no preset. Wu *et al.* (2022) was the only study using colour Doppler ultrasound equipment and installed a Mindray M7 Super portable L12-4s probe [14]. Kumbar *et al.*'s (2018) US machine was sponsored by Analogic Ultrasounds [8].

All four studies used an aseptic technique with sterile gloves when handling US-guided cannulation. Different sanitizers were used in four studies. Three studies mentioned the use of sterile US probe covers or sleeves, sterile gel, and sterile drape to place underneath the AVF arm to maintain aseptic environment for cannulation [9] [14] [18]. Kumbar *et al.* (2018) used transparent adhesive film covering the US machine to avoid direct contact with the patient and special sterile US gel packs when cannulation [8]. Chen *et al.* (2023) used 2% chlorhexidine for patient's AVF arm skin disinfection [9]. Eves *et al.* (2021) and Kumbar *et al.* (2018) did not mention any sanitizer for skin disinfection [8] [14]. But Kumbar *et al.* (2018) used hydrogen peroxide disinfectant wipes for device disinfection between uses [8]. Wu *et al.* (2022) mentioned using 0.2% active iodine for disinfection, including the entire upper arm [14]. Also, Chongqing Anbijie disinfectant medical ultrasonic couplant (the disinfectant coupling reagent) was applied to the probe before being used [14].

Two selected studies used the "Wet" cannulation method (using normal saline to pre-flushed the fistula needling) as a standard practice in AVF needling [9] [18], and others did not mention it [8] [14].

For US probe direction, Chen *et al.* (2023) and Eves *et al.* (2021) used a transverse section on AVF access [9] [18]. Wu *et al.* (2022) used upper extremity venin mode to develop a longitudinal section of AVF access [14], and Kumbar *et al.* (2018) did not mention any probe direction [8].

For cannulation site locating when using the US, the US probe was held by the non-dominant hand, and fistula needling was held by the dominant hand [9] [14]. The Fistula needle entry point corresponding to the center of the probe was inserted. Fistula needling was advanced slowly along with US vision guidance [9]. The study of Wu *et al.* (2022) marked the cannulation site by the probe (the distal end of the US probe) [14]. The running tracking of the needle was displaced on the US screen in order to adjust the cannulation angle. Kumbar *et al.* (2018) mentioned a pre-cannulation evaluation of AVF, including suggested needle size and vessel luminal diameter, was done by a US machine [8]. The cannulation site and real-time needle track were guided by a US device. Finally, blood was aspirated to confirm needle position and pain, or swelling was observed for patency when flushing [9] [18]. Wu *et al.* (2022) and Kumbar *et al.* (2018) did not mention the way to confirm needling placement, but only confirmed by US guidance [8] [14].

Three of the selected studies had provided training for nursing staff before performing the US-guided AVF cannulation [8] [9] [18], while one of the studies did not mention pre-ultrasound-guided cannulation technique training [14]. Kumbar *et al.* (2018) provided three hours of simulated training in the operation of a US device [8]. Chen *et al.* (2023) trained renal nurses by accredited interventional nephrologists and provided a competency assessment to assess renal nurses with US-guided cannulation technique [9]. Eves *et al.* (2021) provided a training package that developed by a senior vascular surgeon. The training included two theory sessions covering the use of portable US machines and two practical teaching sessions with low-fidelity models [18]. Then, following with an assessment of the US-guided cannulation technique. Each nursing staff member had to cannulate low-fidelity model vessels accurately and independently at least three times before performing alone [18].

3.5. Comparator

All selected studies performed AVF cannulation in blind cannulation technique and started with assessing the presence of thrills and bruit. Also, nurses observed for any signs of infection of AVF, including discharge, pain, redness, or warmth and poor circulation of AVF such as coolness, pallor, or cyanosis [8] [9] [14] [18]. "Wet" cannulation and rope-ladder cannulation techniques were used in Eves *et al.*'s (2021) control group [18]. Wu *et al.* (2022) mentioned that a tourniquet was tied to help dilate the AVF blood vessel in the blind cannulation technique [14]. Lastly, Kumbar *et al.* (2018) started using a smaller gauge for needling for the first three times and changed to a larger gauge for the next three times and subsequent sessions (from needle 17 G to 16 G and finally to 15 G) [8]. Needling placement could be antegrade or retrograde, which was decided by nurses.

3.6. Outcome Measures

All selected studies counted the successful cannulation rate as their primary outcome. Successful cannulation procedure refers to renal nurses inserting two needles for arterial and venous connection without missed cannulation or extra attempts. The need to insert more than one needle per arterial or venous connection was defined as missed cannulation [8] [9] [14] [18]. Wu *et al.* (2022) also criteria successful one-time cannulation as the needle tip travelled in a straight line from the skin to the AVF blood vessel without detours and with a one-time attempt [14]. Moreover, Eves *et al.* (2021) reflected the successful needling placement form by counting the number of needle passes required [18]. Needle passes were counted for successful placement as there was no withdrawal of the needle from the skin, only a pullback and change in needle direction [18]. Evidence was found that increased needle passes were correlated and created superior AVF complications, including increased risk of AVF repairment, AVF loss, and associated hospitalization [13].

The rate of complications was counted as the secondary outcome of four selected studies. Chen *et al.* (2023) only counted for the incidence rate of complication [9], while the other three studies defined and counted the incidence ratio for complications such as bleeding events, infiltration events, vessel thrombosis events, needle thrombosis events [18], oozing, subcutaneous hematoma [14], majority of infiltration and catheter usage [8].

Moreover, pain sensation was counted as one of the outcomes from four of the selected studies. Chen *et al.* (2023) used a numeric rating scale [9], Eves *et al.* (2021) and Wu *et al.* (2022) used a Visual Analogue scale to assess pain scores [14] [18], while Kumbar *et al.* (2018), apart from using pain score topical anaesthetic cream usage were also used to reflect pain [8].

All outcomes, including one-time successful cannulation rate, rate of complications and pain scores, were measured immediately after US-guided cannulation technique or blinded needling technique [8] [9] [14] [18]. Kumbar *et al.* (2018), apart from measuring outcomes immediately after needling, also conducted a three-month follow-up period to track repeated or further fistula infiltration episodes [8].

3.7. Effect of Intervention

Three studies examined successful cannulation with a total 2337 cannulation attempts [8] [9] [14]. Moderate heterogeneity was found in the included studies ($I^2 = 59\%$, $p < 0.09$) and random-effect model was adopted. The results showed US-guided AVF cannulation had a significant effect in improving successful cannulation (Risk ratio (RR): 0.19, 95% CI: 0.06 to 0.63, p = 0.007) (**Figure 2**). In addition, the study by Eves *et al.* (2021) demonstrated that US-guided cannulation resulted in a significant reduction in the incidence of additional puncture (p = 0.016) and additional needle passes (p = 0.007), which is defined as needle pull back and change in direction of the needle following skin puncture.

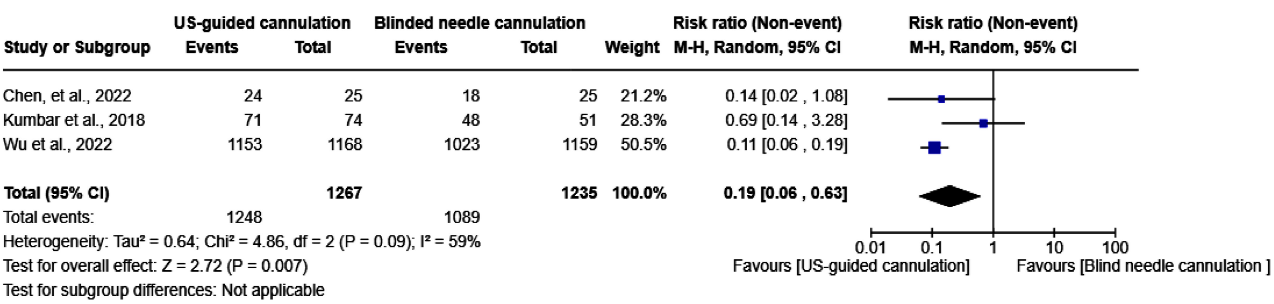

Figure 2. Meta-analysis for Successful cannulation between US-guided AVF cannulation and blind needle cannulation.

Three studies examined pain associated with cannulation [8] [9] [18]. Considerable heterogeneity was found in the included studies ($I^2 = 59\%$, $p < 0.09$) and random-effect model was adopted. Even though two studies demonstrated significantly lower pain scores in US-guided cannulation compared to the blind needling method [9] [14], the meta-analysis showed US-guided AVF cannulation had insignificant effects in improving procedural-associated pain (Mean difference (MD): −0.25, 95% CI: −0.74 to 0.24, p = 0.31) (**Figure 3**).

All included studies examined cannulation-associated complications [8] [9] [14] [18]. Considerable heterogeneity was found in the included studies ($I^2 = 92\%$, $p < 0.00001$) and random-effect model was adopted. The forest plot showed US-guided AVF cannulation was favorable compared with blind needle cannulation in reducing cannulation-associated complications, including bleeding events, infiltration, haematoma formation, oozing blood, missed cannulation and thrombosis events (RR: 0.44, 95% CI: 0.10 to 1.93, p = 0.28) (**Figure 4**). Specifically, the incidence rates of hematoma and oozing were significantly reduced in the ultrasound-guided cannulation group in Wu *et al.*'s study (0.34% vs. 8.11% for hematoma, and 0.59% vs. 2.24% for oozing, all p < 0.001) [14]. However, Eves *et al.* (2021) did not detect any significant differences between groups regarding local complications, including bleeding events, infiltration, and thrombosis [18]. Chen *et al.*, (2023) and Kumbar *et al.*, (2018) further defined the complication related to the limited use of fistula or the need of fistula rest due to infiltration, and both studies found no significant difference in this complication when comparing the intervention and control groups [8] [9].

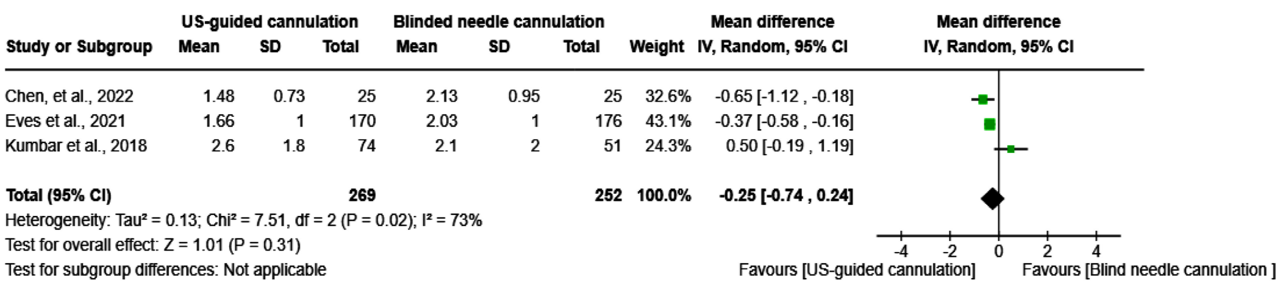

Figure 3. Meta-analysis for pain associated with cannulation between US-guided AVF cannulation and blind needle cannulation.

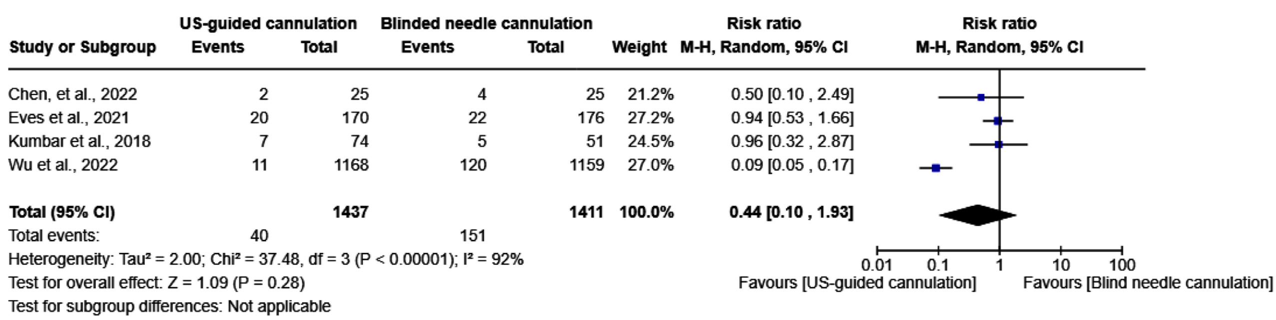

Figure 4. Meta-analysis for cannulation-associated complications with cannulation between US-guided AVF cannulation and blind needle cannulation.

3.8. Appraisal Results

The Scottish Intercollegiate Guidelines Network (SIGN) methodology checklist for RCT was used to critically appraise four eligible studies.

3.8.1. Research Question

The research question of the four selected studies was clear and focused on the PICO format. The population was patients with difficult AVF access who underwent regular hemodialysis. The intervention was a US-guided cannulation technique. The comparison was the conventional blind needling technique. The primary outcome was the rate of successful needling, and the secondary outcomes were the rate of complications and pain score.

3.8.2. Randomization, Concealment, and Blinding

All four eligible studies adopted randomization to minimize the selection bias. Three of the studies confirmed that randomization was done using computer-generated codes and software [9] [14] [18]. However, the pilot study did not clearly mention the method of randomization [8].

The allocation concealment, Wu *et al.* (2022), Eves *et al.* (2021) and Chen *et al.* (2023) were generated by a computerized allocation system and the studies mentioned the use of sequentially numbered, opaque and concealed envelopes [14] [18]. However, the pilot study did not mention the concealment method [8].

For the blinding aspect, all the selected studies were non-blind studies. Because of the nature of the study, there was no possible blinding for subjects and investigators due to the huge difference in the cannulation method of US-guided and conventional blind needling. Moreover, all the studies did not mention any compensated method to minimize the detection bias [8] [9] [14] [18].

3.8.3. Similarity of Participants

The participants in four eligible studies were stated to have similar and comparable baseline characteristics, including gender, age, type of difficult AVF access, type of fistula and co-morbidities. Subjects were randomly allocated to treatment and control groups in a 1:1 ratio. Furthermore, the baseline demographics of the recruited patients exhibited similar characteristics, with no significant difference observed between the intervention and the control group with a p-value > 0.05 [8] [9] [14] [18].

3.8.4. Outcome Measurement

All selected studies' treatment was according to protocol and were treated equally within the same group. The US-guided cannulation was the only treatment in the intervention group. Also, all studies had clear primary and secondary outcomes, and all the outcome measure methods and tools were stated clearly in standard, valid, and reliable ways, including the rate of successful cannulation and complication and pain score applied.

3.8.5. Dropout Rate and Intention-to-Treat

Chen *et al.* (2023) and Wu *et al.* (2022) had a 0% dropout rate and no risk of attribution bias [9] [14]. Moreover, intention-to-treat was used, and all the data were included for analysis. One of the studies had 12.5% in which four participants dropped out as one withdrew and three transferred to other units; Intention-to-treat was applied in this study [18]. The pilot study had a 10% dropout rate but did not apply intention-to-treat. This study used the per-protocol method to analyze the data as this pilot study only analyzed the data based on participants who completed the study and their allocated intervention. It did not deal with missing data [8].

3.8.6. Comparability of Multi-Site Results

There was no comparison of multi-site could be made as all of the four selected studies were single-centre studies [8] [9] [14] [18].

3.8.7. Level of Evidence

SIGN checklist was used to appraise the quality of all selected studies. There were three acceptable-quality studies and one low-quality pilot study. The studies of Chen *et al.* (2023), Eves *et al.* (2021) and Wu *et al.* (2022) were RCT (+) and rated as acceptable quality with clear research questions [9] [14] [18]. Computerized randomization and concealment were properly performed to minimize the bias. Moreover, the dropout rate ranges from 0% [9] [14] (Chen *et al.*, 2023; Wu *et al.*, 2022) to 12.5% [18] of the study, which was within the acceptable range, being lower than 20%. Intention to treat analysis was applied. There was no blinding to subjects and investigators, although it was explained based on the nature of the study. Also, there was a small sample size with no mention of statistical power. Nevertheless, those studies used valid and reliable tools to access the outcomes. In conclusion, most criteria were met, although some criteria in those studies did not fulfil and might be associated with risk of bias. Therefore, those studies' conclusions might change in further studies.

The study of Kumbar *et al.* (2018) was a pilot RCT (−) and rated as low quality [8]. The study did not mention the method of randomization, concealment and no blinding to the subject and investigators. Those lead to bias. Although there was only a 10% dropout rate, which was acceptable, there was no intention to treat. Also, a small sample size with no mention of statistical power will affect the quality of this study. Therefore, with overall missing critical criteria, the overall effect is uncertain and might need further RCT study.

4. Discussion

This is the first review to examine the current research evidence on ultrasound-guided arteriovenous fistula (AVF) cannulation in hemodialysis patients with difficult vascular access, with a specific focus on the role of renal nurses in performing the procedure. The findings of this review suggest that US-guided AVF cannulation, when performed by renal nurses, may result in a higher successful cannulation rate and reduced complications such as hematoma, oozing blood, and infiltration compared to the conventional blind needling method.

Certified renal nurses play a crucial role as the primary providers of AVF treatment and access care. However, it is important to acknowledge that cannulation skill may vary among nurses due to differences in expertise, including factors such as cannulation assessment and techniques. The accuracy and skill level of nurses are critical for the successful implementation of US-guided cannulation in difficult AVF access. Failure to achieve proper cannulation can result in complications and have a negative impact on AVF survival [5] The reviewed studies provided training for nursing staff before performing the US-guided AVF cannulation [8] [9] [18], including simulated US device operation training [8], theory sessions and practical sessions provided by nephrologists and senior vascular surgeons [9] [18]. Nurses' competence was also assessed by requiring at least three successful cannulations using ultrasound (US) devices before performing US-guided cannulation on patients [9] [18]. The results provided insight into the staff training required before renal nurses can effectively implement US-guided cannulation. However, the optimal training elements for quality improvement warrant further investigation.

While difficult AVF access can lead to severe complications which require close attention, the current literatures fail to provide a clear and universally accepted definition. This lack of a standardized definition can lead to inconsistencies in clinical practice, suggesting the need for further research and consensus on defining difficult AVF access. Meanwhile, the selected studies included diverse characteristics of AVF as difficult access, including new AVF fistular that less than three months or first cannulation AVF as difficult AVF access [8] [9] [14] [18], failure or difficulty in cannulation's AVF with complications (bruises or hematoma) [9] [18], stenosis AVF [9], postangioplasty/thrombectomy AVF [9], upper extremity AVF [14] and deep-seated AVF access (4 - 7 mm from skin) [9] [14]. This synthesis provides insights into the characteristics of difficult AVF that may benefit from US-guided cannulation. These identified characteristics should be considered and further investigated when assessing the potential for successful implementation and transferability of US-guided cannulation performed by renal nurses.

The use of a handheld US device was recommended by all studies [8] [9] [14] [18]. Based on the notable improvement in clinical outcomes and the acceptable quality study conducted by Wu *et al.* (2022), it is recommended to utilize color Doppler ultrasound specifically in the longitudinal section view, for assessing AVF access [14].

Infection control during cannulation procedures is critical in minimizing the risk of complications. Using sterile gloves was considered a standard aseptic technique during ultrasound-guided cannulation to reduce the risk of needling-induced infections [8] [9] [14] [18]. Sterile US probe covers/sleeves, sterile gel, and sterile drape were also used to facilitate sterile US-guided cannulation [8] [9] [14] [18]. However, the reviewed studies adopted diverse aseptic technique for skin preparation and devise disinfection. Chen *et al.* (2023) and Wu *et al.* (2022) used 2% chlorhexidine and 0.2% active iodine respectively for skin disinfection [9] [14].

Kumbar *et al.* (2018) disinfected the ultrasound-guided device using hydrogen peroxide disinfectant wipes [8], while Wu *et al.* (2022) applied a disinfectant medical ultrasonic couplant to the probe before use [14]. Kumbar *et al.* (2018) further used transparent adhesive film covering the US machine during the procedure [8]. This disparity in study design underscores the necessity for further research with robust methodologies to definitively establish effective infection control protocols in cannulation practices.

For the cannulation technique, it is recommended to use the non-dominant hand (left hand) to hold the US probe and the dominant hand (right hand) to insert the needling, as suggested by Chen *et al.* (2023) and Wu *et al.* (2022) [9] [14]. Followed by marking the cannulation site using the distal end of the US probe [9] [14] (Chen *et al.*, 2023; Wu *et al.*, 2022). To adjust the cannulation angle, the US screen should be used to show the running track of the needle, as advised by Chen *et al.* (2023), Wu *et al.* (2022), and Kumbar *et al.* (2018). Finally, to confirm the needle position and patency, the blood flushed back into the fistular needle tubing should be observed, as suggested by Chen *et al.* (2023), Wu *et al.* (2022), and Eves *et al.* (2021) [9] [14] [18].

5. Limitations

This study has several limitations. Firstly, only four randomized controlled trials (RCTs) were included in the analysis. Secondly, the outcome measures and intervention implementations, including the use of ultrasonic devices, cannulation techniques, and infection control measures, were highly varied. This variability could limit the generalizability of the findings. Thirdly, the study only included research published in English-language peer-reviewed journals. Any unpublished research and relevant literature in other languages or other forms of publications were excluded, potentially omitting valuable data. Finally, the results of the risk of bias assessment showed various types of biases according to the SIGN assessment tool. This could potentially over- or under-estimating the effects of nurse-performed US-guided cannulation. These limitations suggest a need for caution in interpreting and generalizing the study's findings. All studies focused on the immediate effects without examining the longer-term benefits. Further research with longer-term follow-up is needed to evaluate the potential advantages of US-guided AVF cannulation by renal nurses in difficult AVF access.

6. Conclusions

This meta-analysis of four studies has shown that, as compared to blind needle cannulation, US-guided cannulation performed by renal nurses has demonstrated higher successful cannulation, and fewer complications. Meanwhile, the selected studies showed risk of bias across studies, which would affect the reliability and generalization of this meta-analysis.

Despite the limitations, renal nurses have shown competency in utilizing US-guided cannulation for difficult AVF access in improving clinical outcomes after receiving training. The results suggest the value of further training for renal nurses in US-guided cannulation, which may lead to broader implementation of US-guided cannulation and, consequently, improved patient outcomes. Future studies could explore the optimal nursing training and longer-term benefits of US-guided cannulation in difficult AVF access.

Declaration of Generative AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work, the author(s) used ChatGPT 3.5 for English editing. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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