ULTRASOUND-GUIDED ARTERIAL CANNULATION IN ADULT: A SYSTEMATIC REVIEW AND META-ANALYSIS

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I also would like to express my gratitude to my lecturers and colleagues in the Department of Emergency Medicine, Universiti Sains Malaysia for their kindness and support.

Special dedication to my spouse, parents, family and all my colleague who gave their support and ideas for me to make this study a success.

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LIST OF ABBREVIATIONS

BMI	Body Mass Index
ICU	Intensive Care Unit
RCT	Randomized Controlled Trial
MEDLINE	Medical Literature Analysis And Retrieval System Online
EMBASE	Excerpta Medica Database
WHO	World Health Organisation
ICTRP	International Clinical Trials Registry
GRADE	Grading Of Recommendations, Assessment, Development And Evaluation
REVMAN	Review Manager
RR	Risk Ratio
MD	Mean Differences
SD	Standard Deviation
CI	Confidence Interval
US	Ultrasound
SAOOP	Short Axis- Out Of Plane
LAIP	Long Axis- In Plane
ED	Emergency Department
CFA	Common Femoral Artery
MHz	Megahertz
EM	Emergency Medicine

ABSTRACT

Background:

Arterial cannulation is one of the most common procedures done in an acute care setting. However, the usage of ultrasound for artery cannulation has been controversial. This systematic review and meta-analysis were performed to assess the effectiveness of ultrasound in improving first attempt success rate, overall success rate, time to cannulation, number of attempts, and complications rate arterial cannulation in the adult population other techniques at all arterial cannulation sites.

Methods:

We included a randomized control trial in participants above 18 years old, undergoing arterial line placement or puncture in the emergency department, operating room, intensive care unit, and a cardiac catheterization lab. The primary outcomes of this meta-analysis are success rate upon the first puncture and overall success rate. Secondary outcomes are the time to successful cannulation, number of attempts to successful cannulation, and reported complications, including hematoma, bleeding, venipuncture, pseudoaneurysm, dissection, arteriovenous fistula, thrombosis, and retroperitoneal bleeding.

Results:

Total of 38 studies were included. We found that ultrasound substantially improved cannulation or puncture success rate, compare to palpation (RR 1.40, 95% CI 1.27 to 1.55; I^2 statistic= 82%; $P < 0.001$), fluoroscopy (RR 1.47, 95% CI 1.17 to 1.85; I^2 statistic= 95%; $P < 0.001$), Doppler (RR 1.35, 95% CI 1.11 to 1.64; P value 0.003) or vascular device (RR 0.76, 95% CI 0.48 to 1.2; P value 0.003) guided arterial cannulation at the first attempt. Upon comparing ultrasound with palpation group, ultrasound-guided significantly improved overall arterial cannulation success rate (RR 1.13, 95% CI 1.07 to 1.19; I^2 statistic= 87%; $P < 0.001$).

Conclusions:

This meta-analysis provides the most comprehensive analysis of ultrasound-guided arterial cannulation in adults for all the arteries. The data supports the usage of ultrasound in arterial cannulation and should be used as the standard of practice in all clinical settings.

ABSTRAK

Latar Belakang:

Kanulasi arteri adalah salah satu prosedur yang paling biasa dilakukan dalam keadaan penjagaan akut. Walau bagaimanapun, penggunaan ultrasound untuk kanulasi arteri telah menjadi kontroversi. Kajian sistematik dan meta-analisis ini dilakukan untuk menilai keberkesanan ultrasound dalam meningkatkan kadar kejayaan percubaan pertama, kadar kejayaan keseluruhan, masa untuk kanulasi, bilangan percubaan, dan kadar komplikasi kanulasi arteri dalam populasi dewasa.

Kaedah:

Kami memasukkan pesakit berumur 18 tahun ke atas, menjalani penempatan saluran arteri atau tusukan di jabatan kecemasan, bilik operasi, unit rawatan rapi, dan makmal kateterisasi jantung. Hasil utama meta-analisis ini ialah kadar kejayaan pada tusukan pertama dan kadar kejayaan keseluruhan. Hasil sekunder ialah masa untuk kanulasi yang berjaya, bilangan percubaan untuk kanulasi yang berjaya, dan komplikasi yang dilaporkan, termasuk hematoma, pendarahan, venipuncture, pseudoaneurysm, pembedahan, fistula arteriovenous, trombosis, dan pendarahan retroperitoneal.

Keputusan:

Sebanyak 38 kajian telah dimasukkan. Kami mendapati bahawa ultrasound telah meningkatkan kadar kejayaan kanulasi atau tusukan, berbanding dengan palpasi (RR 1.40, 95% CI 1.27 hingga 1.55; statistik I2 = 82%; P <0.001), fluoroskopi (RR 1.47, 95% CI 1.17 hingga I21.85; statistik= 95%; P <0.001), Doppler (RR 1.35, 95% CI 1.11 hingga 1.64; nilai P 0.003) atau peranti vaskular (RR 0.76, 95% CI 0.48 hingga 1.2; nilai P 0.003) berpandukan kalen arteri pertama percubaan. Selepas membandingkan ultrasound dengan kumpulan palpasi, berpandukan ultrasound meningkatkan kadar kejayaan keseluruhan kanulasi arteri (RR 1.13, 95% CI 1.07 hingga 1.19; I2 statistik = 87%; P <0.001).

Kesimpulan:

Meta-analisis ini menyediakan analisis paling komprehensif mengenai kanulasi arteri berpandukan ultrasound pada orang dewasa untuk semua arteri. Data menyokong penggunaan ultrasound dalam kanulasi arteri dan harus digunakan sebagai standard amalan dalam semua tetapan klinikal.

1.0 INTRODUCTION

1.1 BACKGROUND

Description of the condition

It is rated as the second most common procedure done in the intensive care unit [1]. Arterial cannulation is defined as a tube inserted in an artery [2]. In comparison to other procedures such as central venous cannulation, arterial line cannulation, or puncture has not been given high priority [3]. It is especially suitable for monitoring not only shock, extreme peripheral vasoconstriction, or early stages of diseases but also pre- and post-operative surveillance of patient undergoing major or life-threatening surgery. Measurement of intra-arterial blood pressure has been proven to be more effective than measurement of blood pressure by non-invasive means, particularly in critically ill patient [4]. Intra- arterial blood pressure monitoring allowed rapid identification of blood pressure changes, that are essential for patient on vasopressors. Arterial cannulation also enables repeated samples of arterial blood gas to be withdrawn from them, without causing further injuries.

An arterial line can be placed in many arteries, including radial artery, brachial artery, femoral artery, dorsalis pedis artery, posterior tibia artery, ulna artery and axillary artery. In both adult and children, the most common site of arterial cannulation is radial artery [5], followed by the femoral artery. Radial arteries are more shallow and easily compressible, making them the access of choice for most diagnostic and percutaneous procedures, which ensure less vascular access site complications and bleeding [6]. On the other hand, some of the advantages of femoral artery cannulation, are arteries are larger, stronger pulsation, less incident of thrombosis and catheter removal [7]. Arterial cannulation has been noted to be a safe procedure with the rate of major complication of less than 1% [8]. Nonetheless, it is not completely without risks and required enough knowledge of the anatomy that is involved and procedure competencies.

Description of the intervention

The insertion of arterial catheterization traditionally has been performed by using anatomical landmark and by palpating the pulse. The palpation technique has long been the procedure for radial artery placement; however this technique may be difficult in an obese, edematous, and in hypotensive patients [9]. As of, anatomical landmark, up to 30% of the patients may not be helpful in especially in locating radial artery [10]. Both anatomical landmark and palpation technique leads to an increase number of failed attempts that causes patient discomfort, arterial spasm and formation of a hematoma [11]. It is becoming more difficult for emergency physicians and anesthesiologist to locate site to puncture, as each patient having variable artery caliber and alignment. Besides that, controlling the needle and seizing the timing to cannulate an artery is becoming difficult as well.

The use of ultrasound-guided technique perfectly solves these problems. By using ultrasound, artery alignment and needle position can be clearly shown in the longitudinal or transverse section, so that the puncture site and cannulation time can be chosen precisely. Ultrasound-guided arterial cannulation has been proven to increase in first pass success rate and reduced complications rate [12]. As for patient undergoing coronary angiography, it has been proven patient who undergoes ultrasound-guided femoral catheter insertion experience lower vascular complications, including bleeding and hematoma [13].

How the intervention might work

Intervention

Ultrasound guided technique

Arteries were identified using an ultrasound probe and place at the centre of the screen, through short-axis out of plane approach or long-axis in plane approach, perpendicular to the skin. In short-axis out of plane approach, the probe orientated transversely to the artery, and appear as a circular anechoic pulsating image. While in long-axis in plane approach, after localizing the artery via the short axis approach, the ultrasound probe is rotated to 90 degrees, in parallel with the artery and the artery appear as an anechoic tubular pulsating image. An appropriate size cannula inserted perpendicular to the probe, at 30 – 45-degree angle into the skin below the ultrasound probe at its centre under direct ultrasound vision. Once there is a backflow of bright red colour blood, the angle of the cannula is lower to 15 degrees. The cannula redirected or the process repeated until the adequate flow is achieved, for the insertion of a guidewire or the cannula itself.

Comparator

Palpation technique / anatomical landmark technique

The non-dominant hand palpate for the pulse with index and middle finger, by using the anatomical landmark. The strongest pulsation is identified as the puncture site. The dominant hand would insert the cannula at 30 – 45-degree angle. Once bright red blood appears, the angle is reduced, guidewire or cannula itself is inserted.

Doppler probe for auditory assistance

The non-dominant hand holds the doppler probe, to identify the artery by detecting the loudest pulsation signal, while the dominant hand is used to insert the cannula. An increase in pitch or loss of sound, indicates the cannula compressing the artery. The cannula is then advance until the doppler tone returned to normal, signalling re-expansion of the artery, or bright red blood appears, before inserting the guidewire or the cannula.

Fluoroscopy technique

The artery is identified using fluoroscopy, which uses x-ray, to generate still images of the arteries involved. Once been identified, the area for cannula insertion were marked. Subsequently, the non-dominant hand would palpate the artery, and a cannula inserted through the skin over the marked area.

Vascular visualization device technique (Mill Suss)

The artery is identified using near-infrared laser light, which appears as a dark black pulsating structure. A cannula is inserted at 30-45-degree angle and appears as a dark line on the monitor.

Why it is important to do this review

The use of ultrasound for artery cannulation has been controversial over the years. So far, there was no clear evidence or protocol published on the benefit of using ultrasound guidance in arterial puncture or catheterization. Cochrane review protocol that was published previously looked into the usage of ultrasound-guided arterial cannulation in the pediatric population [14], however, there was no any protocol published in the adult population. In an adult, it is traditionally done by digital palpation or by using anatomical landmark. However, sometimes it can be difficult in a patient who is hemodynamically unstable, an obese patient, patient with oedema or patient with small arterial calibre. The traditional method has been widely used in ICU, emergency department, in the cardiac catheterization lab and operating room.

There were multiple systemic review and meta-analysis done on ultrasound-guided radial artery cannulation; however in those reviews, they have included pediatric population as well [15-20]. Thus, it is unclear whether the result was driven by the pediatric population.

As for femoral artery catheterization, several updated reviews investigates the benefits of ultrasound, especially in cardiac catheterization lab [13,21-24] but none included radial artery cannulation as a comparison, as recent literature showed trans radial approach in cardiac catheterization, is safer, cost-effective and provide similar results as in transfemoral approach [25].

Moreover, there were no published reviews that combine or investigate the benefits of ultrasound usage in arterial catheterization or puncture in all the arteries. Thus, we aim to perform a comprehensive systemic review of the randomized controlled trial with meta-analysis, to find out whether ultrasound provides any benefits or advantages compared to the traditional technique in the adult population.

1.2 OBJECTIVE

To determine the primary and secondary outcomes when ultrasound is being used as a guidance for arterial cannulation in the adult population, compared to other techniques (palpation/anatomical landmark/doppler/fluoroscopy/vascular visualization device) at all arterial cannulation sites (radial, dorsalis pedis, axillary and femoral artery).

2.0 STUDY PROTOCOL

2.1 METHODS

Eligibility criteria

Types of studies

We included randomized control trials (RCTs) comparing ultrasound-guided arterial cannulation versus other techniques (palpation, anatomical landmark, fluoroscopy, doppler, and vascular visualization device)

Types of participants

We included all patient >18 years old undergoing arterial line placement or puncture, in the emergency department, operating room, intensive care unit and a cardiac catheterization lab. We excluded trials conducted in paediatric population.

Types of interventions

Ultrasound-guided arterial cannulation with short-axis out of planed or long-axis in planed technique

Comparator:

1. Standard digital palpation/ anatomical landmark technique
2. Doppler probe for auditory assistance
3. Fluoroscopy technique
4. Vascular visualization device technique (Mill Suss)

Types of outcome

Primary outcomes

1. Success rate upon first puncture
2. Overall success rate

Secondary outcomes

1. Time to successful cannulation
2. Number of attempts to successful cannulation
3. Rate of complications

- Hematoma
- Venipuncture
- Retroperitoneal hematoma
- Bleeding
- Pseudoaneurysm
- Arteriovenous fistula
- Thrombosis

Search strategies

Electronic searches

We will search the Cochrane Central Register of Controlled Trials CENTRAL (latest Issue) MEDLINE (1966 to present) and EMBASE. We will use the search strategy in Appendix 1 to search MEDLINE, CENTRAL and EMBASE. We will adapt the search strategy from other databases. We will not impose any language or publication restrictions.

Searching other resources

We will check the reference list of identified RCTs and review articles in order to find unpublished trials or trials not identified by electronic searches. We will search for ongoing trials through the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) http://www.who.int/ictrp/en/ and www.clinicaltrials.gov**.**

Trial selection

We will scan the titles and abstracts from the searches and obtain full-text articles when they appear to meet the eligibility criteria, or when there is insufficient information to assess the eligibility. We will assess the eligibility of the trials independently and document the reasons for exclusion. We will resolve any disagreements between the review authors by discussion. We will contact the authors if clarification is needed. We will translate papers in languages other than English.

Data extraction

Using data extraction form, from each of the selected trials, we will extract:

- Authors/ year of publication / study design
- study setting (ICU / emergency department / operating theater / cardiac catheterization lab)
- participant characteristics (age, sex, ethnicity, height. BMI, comorbid, medication history(anti-coagulant/antiplatelet)
- methodology (number of participants randomized and analyzed/exclusion and inclusion criteria/ definition of cannulation failure)
- ultrasound type / device / approach

- number and experience operator's experience
- details of the outcome
  - Success rate upon first puncture
  - Overall success rate
  - Time to successful cannulation
  - Number of attempts to successful cannulation
  - Rate of complications
    - Hematoma
    - Venipuncture
    - Retroperitoneal hematoma
    - Bleeding
    - Pseudoaneurysm
    - Arteriovenous fistula
    - Thrombosis
- Conclusions of study authors

Risk of bias assessment

We will assess the risk of bias based on random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, completeness of outcome data, the selectivity of outcome reporting and other bias [26], as listed below. Random sequence generation

- Allocation concealment (selection bias)
- Participants blinding
- Attrition bias
- Outcome reporting bias
- Other sources of bias

We will review the assessment and resolve any disagreements by discussion.

Grading quality of evidence

We assessed the quality of evidence for primary and secondary outcomes according to GRADE methodology [27] for risk of bias, inconsistency, indirectness, imprecision, and publication bias; classified as very low, low, moderate, or high.

Statistical analyses

Data synthesis

We plan to undertake meta-analyses using Review Manager 5.3 software [28] if appropriate and will use random-effects model to pool data. We plan to use the guide to the interpretation of heterogeneity as outlined: 0% to 40% might not be important; 30% to 60% may represent moderate heterogeneity; 50% to 90% may represent substantial heterogeneity, and 75% to 100% would be considerable heterogeneity .

Assessment of heterogeneity

We will assess the presence of heterogeneity in two steps. First, we will assess obvious heterogeneity at face value by comparing populations, settings, interventions and outcomes. Second, we will assess statistical heterogeneity using the I^2 statistic [26,29].

Measures of treatment effect

We will measure the treatment effect for dichotomous outcomes using risk ratios (RRs) and absolute risk reduction, and for continuous outcomes, we will use mean differences (MDs) and standard deviation (SD); both with 95% confidence intervals (CIs).

Subgroup analysis and investigation of heterogeneity

If possible, we will conduct subgroup analyses on:

1. Site of cannulation- radial artery, femoral artery, axillary artery and dorsalis pedis artery.

2. Patient population

-critically ill patient versus non-critically ill patients

-cardiac catheterization femoral versus radial

-radial artery puncture for arterial blood gas

3. Expertise in ultrasound usage- trained user versus untrained user

4. Ultrasound technique- short-axis out of planed technique versus long-axis in planed in radial and femoral artery

We will explore the potential sources of heterogeneity when important heterogeneity is present [30].

Unit of analysis issues

We will check included trials for unit of analysis errors. Unit of analysis errors can occur when trials randomize participants to intervention or control groups in clusters, but analyze the results using the total number of individual participants. We will adjust results from trials showing a unit of analysis errors based on the mean cluster size and intracluster correlation coefficient [26,31].

Dealing with missing data

We will contact the original trial authors to request missing or inadequately reported data. We will perform analyses on the available data if missing data are not available.

Sensitivity analysis

We will perform a sensitivity analysis to investigate the impact of risk of bias for sequence generation and allocation concealment of included studies.

Reporting biases

If there are sufficient studies, we will use funnel plots to assess the possibility of reporting biases or small study biases, or both.

2.2 CONTRIBUTIONS OF AUTHORS

Designing the review: Shamini Sangasamy (SS), Norhayati Mohd Noor (NMN), Mohd Boniami Yazid (MBY)

Co-ordinating the review: NMN, MBY

Literature search: SS, MBY.

Quality assessment: SS, NMN, MBY.

Entering data into RevMan: SS, MBY.

Data analysis: SS, NMN, MBY.

Data interpretation: SS, NMN, MBY.

Writing the review: SS.

CHAPTER 3: MANUSCRIPT

3.1 TITLE PAGE

ULTRASOUND-GUIDED ARTERIAL CANNULATION IN ADULT: A SYSTEMATIC REVIEW AND META-ANALYSIS

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3.2 ABSTRACT

Background:

Arterial cannulation is one of the most common procedures done in an acute care setting. However, the usage of ultrasound for artery cannulation has been controversial. This systematic review and meta-analysis were performed to assess the effectiveness of ultrasound in improving first attempt success rate, overall success rate, time to cannulation, number of attempts, and complications rate of arterial cannulation in the adult population compared to other techniques at all arterial cannulation sites.

Methods:

We included a randomized control trial among participants above 18 years old, undergoing arterial line placement or puncture in the emergency department, operating room, intensive care unit, and a cardiac catheterization lab. The primary outcomes of this meta-analysis are success rate upon the first puncture and overall success rate. Secondary outcomes are the time to successful cannulation, number of attempts to successful cannulation, and reported complications, including hematoma, bleeding, venipuncture, pseudoaneurysm, dissection, arteriovenous fistula, thrombosis, and retroperitoneal bleeding.

Results:

Total of 38 studies were included. We found that ultrasound substantially improved cannulation or puncture success rate, compare to palpation (RR 1.40, 95% CI 1.27 to 1.55; I2 statistic= 82%; P < 0.001), fluoroscopy (RR 1.47, 95% CI 1.17 to 1.85; I2 statistic= 95%; P < 0.001), Doppler (RR 1.35, 95% CI 1.11 to 1.64; P value 0.003) or vascular device (RR 0.76, 95% CI 0.48 to 1.2; P value 0.003) guided arterial cannulation at the first attempt. Upon comparing ultrasound with palpation group, ultrasound-guided significantly improved overall arterial cannulation success rate (RR 1.13, 95% CI 1.07 to 1.19; I2 statistic= 87%; P < 0.001).

Conclusions:

This meta-analysis provides the most comprehensive analysis of ultrasound-guided arterial cannulation in adults for all the arteries. The data supports the usage of ultrasound in arterial cannulation and should be used as the standard of practice in all clinical settings.

3.3 INTRODUCTION

Arterial cannulation is defined as a tube inserted in an artery [2]. Measurement of intra-arterial blood pressure has been proven to be more effective than measuring blood pressure by non-invasive means, particularly in critically ill patients [4]. Arterial cannulation also enables repeated samples of arterial blood gas to be withdrawn from them without causing further injuries.

An arterial line can be placed in many arteries, including radial artery, brachial artery, femoral artery, dorsalis pedis artery, posterior tibia artery, ulna artery, and axillary artery. In both adults and children, the most common arterial cannulation site is radial arteries [5], followed by the femoral artery. Arterial cannulation has been noted to be a safe procedure with the rate of major complications of less than 1% [8].

In an adult, it is traditionally done by digital palpation or by using an anatomical landmark. Other techniques being used in arterial cannulation including fluoroscopy, Doppler and vascular visualization device. However, sometimes it can be difficult in a patient who is hemodynamically unstable, an obese patient, a patient with edema, or patient with small arterial caliber. The traditional method has been widely used in ICU, emergency department, in the cardiac catheterization lab, and operating room.

We aim to perform a comprehensive systemic review of the randomized controlled trial with meta-analysis to determine whether ultrasound provides any benefits or advantages compared to the traditional technique in the adult population.

The objective is to assess the effectiveness of ultrasound in improving first attempt success rate, overall success rate, time to cannulation, number of attempts, and complications rate arterial cannulation in the adult population, compared to other techniques at all arterial cannulation sites.

3.4 METHODS

We searched the Cochrane Central Register of Controlled Trials CENTRAL (latest Issue) MEDLINE (1966 to present) and EMBASE. We had used the search strategy in Appendix (Supplementary data, search strategy). We also have adapted the search strategy from other databases. We did not impose any language or publication restrictions.

In our study, we included randomized control trials that was done in participants above 18 years old, undergoing arterial line placement or puncture in the emergency department, operating room, intensive care unit, and a cardiac catheterization lab.

The primary outcomes of this meta-analysis are success rate upon the first puncture and overall success rate. Secondary outcomes are the time to successful cannulation, number of attempts to successful cannulation, and reported complications, including hematoma, bleeding, venipuncture, pseudoaneurysm, dissection, arteriovenous fistula, thrombosis, and retroperitoneal bleeding.

We screened the titles and abstracts from the searches and obtained full-text articles when they appear to meet the eligibility criteria or when there is insufficient information to assess the eligibility. We assessed the eligibility of the trials independently and documented the reasons for exclusion. We also resolved any disagreements between the review authors by discussion. We did contact the authors if clarification is needed.

We assessed the risk of bias based on random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, completeness of outcome data, the selectivity of outcome reporting, and other bias [26]. We had review the assessment and resolved any disagreements by discussion.

We assessed the quality of evidence for primary and secondary outcomes according to GRADE methodology [27] for risk of bias, inconsistency, indirectness, imprecision, and publication bias; classified as very low, low, moderate, or high.

We had undertaken meta-analyses using Review Manager 5.3 software (RevMan, 2014) and used a random-effects model to pool data. We assessed the heterogeneity by using interpretation as outlined: 0% to 40% might not be important; 30% to 60% may represent moderate heterogeneity; 50% to 90% may represent substantial heterogeneity, and 75% to 100% would be considerable heterogeneity.

We assessed the presence of heterogeneity in two steps. First, we assessed obvious heterogeneity at face value by comparing populations, settings, interventions, and outcomes. Second, we assessed statistical heterogeneity using the I2 statistic [26,29].

We measured the treatment effect for dichotomous outcomes using risk ratios (RRs) and absolute risk reduction. For continuous outcomes, we used mean differences (MDs) and standard deviation (SD), both with 95% confidence intervals (CIs).). Continuous outcomes that were reported in the median with low and high-end ranges/interquartile range were converted to mean and SD by using (Luo et al., 2018) and (Wan et al., 2014) method.

We had conducted subgroup analyses on-site of cannulation or puncture (radial artery, femoral artery, axillary artery, dorsalis pedis artery, clinical setting (ICU, emergency department, operating theater, cardiac catheterization lab), ultrasound technique used (short-axis out of planed approach with or without dynamic needle tip position, long-axis in planed), and operator experience in ultrasound usage. We explored the potential sources of heterogeneity when important heterogeneity was present [30].

We had check included trials for the unit of analysis errors. Unit of analysis errors can occur when trials randomize participants to intervention or control groups in clusters but analyze the results using the total number of individual participants. We had adjusted the results from trials showing a unit of analysis errors based on the mean cluster size and intracluster correlation coefficient [26,31]. We had contacted the original trial authors to request missing or inadequately reported data. We had performed a sensitivity analysis to investigate the impact of the risk of bias for sequence generation and allocation concealment of included studies.

3.5 RESULTS

Based on our search strategy, we had screened through 1765 records, and after excluding duplicates, 1654 records were screened. We selected 49 abstracts and titles from those records as potentially applicable articles for our analysis. After independently screening those abstracts and titles, 11 studies were excluded. One study was published as a congress poster, with no qualitative or quantitative data available to analyze [32]. Another ten studies were excluded, as it was randomized only into ultrasound group [33-42]. Finally, 38 articles were eligible to be included in this review (Figure 1). The kappa statistic for full-text article screening was one in view with no dispute among the authors regarding the included studies.

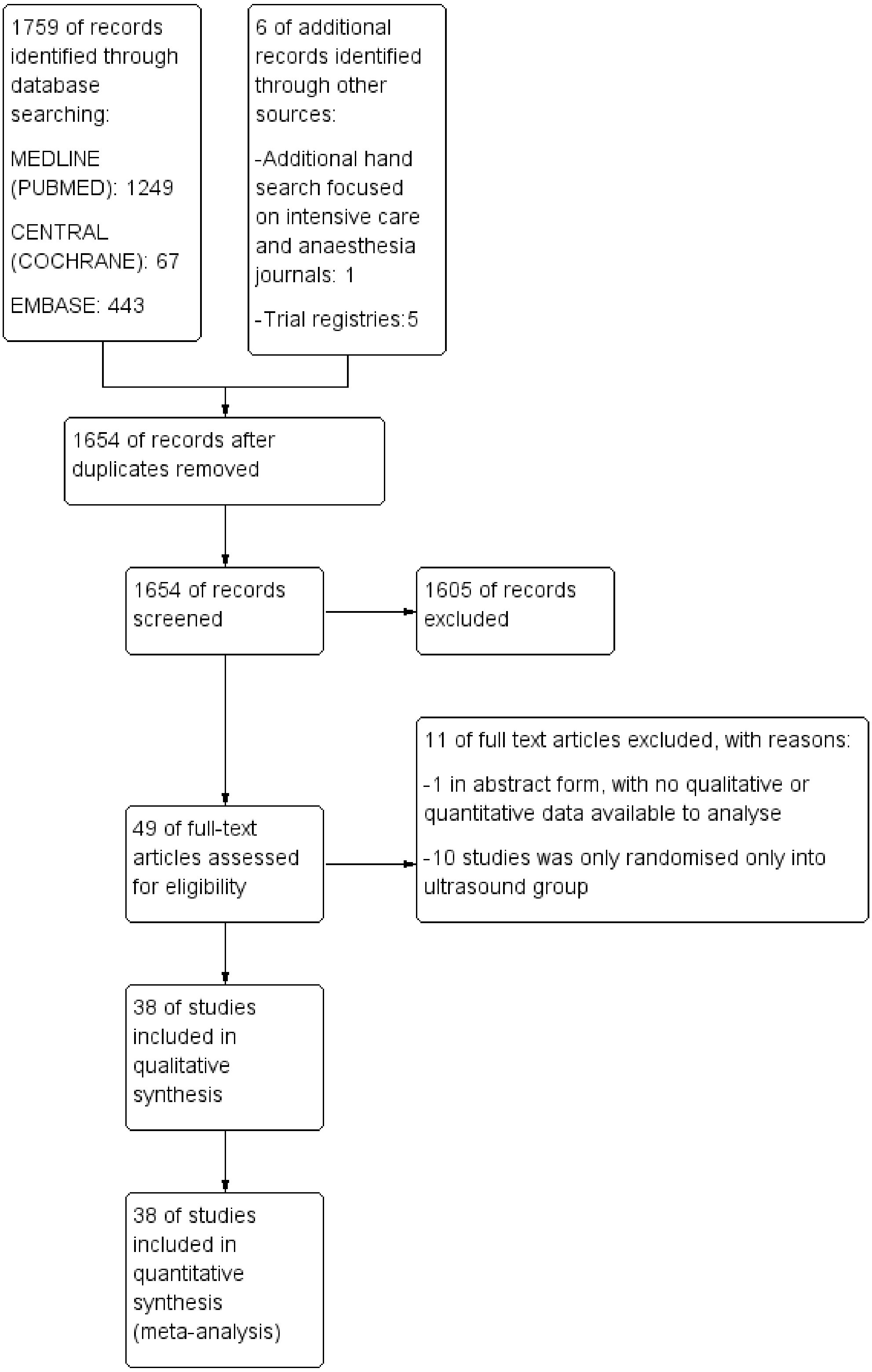

Figure 1. Study flow diagram.

We included 38 studies (Supplementary data, Table 1) published between the year 2003 to 2020, enrolling total of 8826 participants, including 4451 in ultrasound group, 2641 palpation group, 1454 fluoroscopy group, 244 Doppler group, and 36 vascular devices group.

The participants in the included studies were randomized into intervention and control group. All included studies used ultrasound in the intervention group. There were four comparators available in the control group: palpation technique, fluoroscopy, Doppler, and vascular device.

The assessment of risk of bias is shown in Figure 2 and Figure 3. Figure 2 shows the proportion of studies assessed as low, high, or unclear risk of bias for each 'Risk of bias' indicator, presented as percentages across all included studies. Figure 3 shows the 'Risk of bias' based on our judgments about each risk of bias item for each included study.

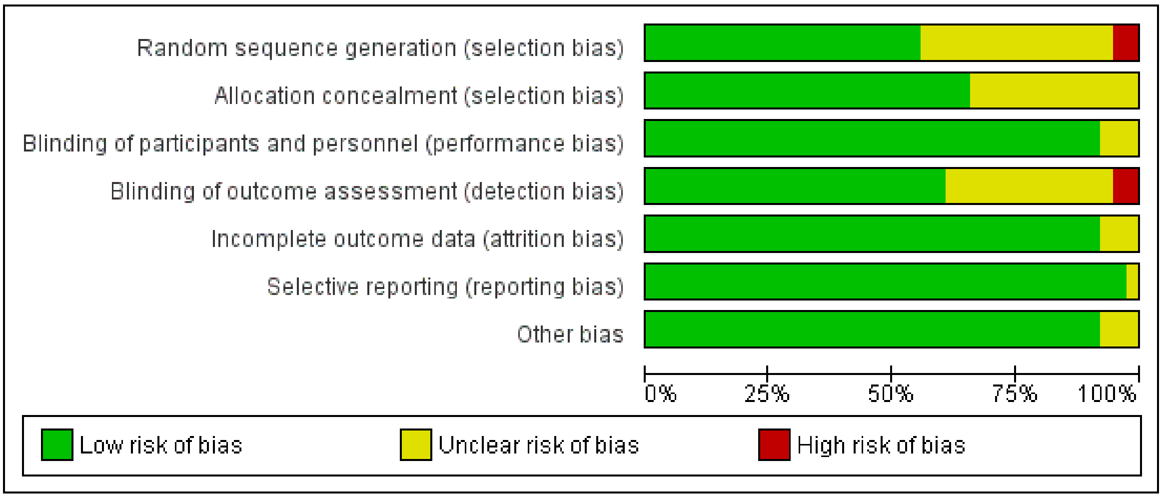

Figure 2.'Risk of bias's graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

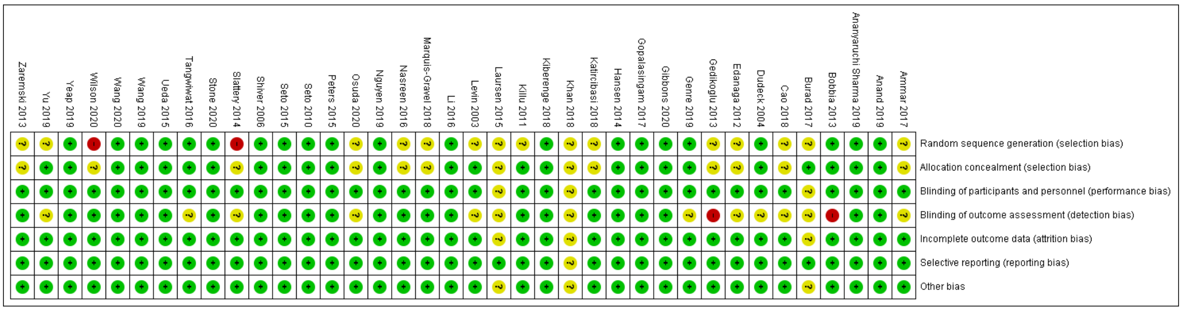

Figure 3. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.

Primary Outcomes

1. Success Rate Upon First Puncture

From the pooled data, we found that ultrasound substantially improved cannulation or puncture success rate, compare to palpation (RR 1.40, 95% CI 1.27 to 1.55; I2 statistic= 82%; P < 0.001; 25 trials, 4919 participants; moderate quality evidence)(Figure 4), fluoroscopy (RR 1.47, 95% CI 1.17 to 1.85; I2 statistic= 95%; P < 0.001; 4 trials, 2836 participants; moderate quality evidence)(Figure 4), Doppler (RR 1.35, 95% CI 1.11 to 1.64; P value 0.003; 1 trial, 493 participants; moderate quality evidence)(Figure 4) or vascular device (RR 0.76, 95% CI 0.48 to 1.2; P value 0.003; 1 trial, 72 participants; moderate quality evidence)(Figure 4) guided arterial cannulation at the first attempt. The quality of evidence was moderate for all the comparisons, owing to the presence of high heterogenicity. To address this, we did subgroup analysis for each comparison.

Subgroup Analysis Based On Site Of Cannulation Or Puncture

Ultrasound, when compared to palpation, significantly increased the success rate of radial artery cannulation at the first attempt (RR 1.42, 95% CI 1.30 to 1.55; I2 statistic= 62%; P < 0.001; 20 trials, 3635 participants; high quality evidence) (Figure 4), and femoral artery cannulation at the first attempt (RR 1.31, 95% CI 1.19 to 1.44; I2 statistic= 0%; P < 0.001; 3 trials, 927 participants; high quality evidence) (Figure 4). Although ultrasound in comparison to palpation technique increases success rate upon the first puncture for dorsalis pedis artery (RR 1.28, 95% CI 0.90 to 1.82; P value 0.17; 1 trials, 60 participants; moderate quality evidence) (Figure 4) and radial artery puncture (RR 1.57, 95% CI 0.38 to 6.49; I2 statistic= 93%; P value 0.53; 2 trials, 297 participants; moderate quality evidence)(Figure 4), however, it is not statistically significant . The test for subgroup differences was not statistically significant (P= 0.64); thus, the heterogeneity is not explained by the site of cannulation or puncture, so other factors likely cause it.

Ultrasound compared to fluoroscopy significantly increased the success rate of femoral artery cannulation at the first attempt (RR 1.47, 95% CI 1.17 to 1.85; I2 statistic= 95%; $P < 0.001$; 20 trials, 3635 participants; moderate quality evidence) (Figure 4).

Ultrasound Versus Palpation

Study or Subgroup	Ultrasound Events	Ultrasound Total	Palpation Events	Palpation Total	Weight	Risk Ratio M-H, Random, 95% CI
1.2.1 Radial Artery Cannulation						
Ammar 2017	44	50	35	50	4.5%	1.26 [1.02, 1.55]
Burad 2017	44	49	31	51	4.3%	1.48 [1.16, 1.88]
Cao 2018	54	60	44	60	4.8%	1.23 [1.03, 1.46]
Gibbons 2020	15	20	0	20	0.1%	31.00 [1.98, 485.13]
Gopalasingam 2017	36	40	28	40	4.4%	1.29 [1.02, 1.61]
Hansen 2014	38	40	23	40	4.0%	1.65 [1.25, 2.18]
Khan 2018	41	49	21	51	3.3%	2.03 [1.43, 2.89]
Kiberenge 2018	109	132	62	128	4.6%	1.70 [1.40, 2.07]
Levin 2003	21	34	12	35	2.2%	1.80 [1.06, 3.06]
Li 2016	32	40	17	40	3.0%	1.88 [1.27, 2.79]
Nasreen 2016	36	50	32	50	4.0%	1.13 [0.86, 1.47]
Nguyen 2019	249	359	207	343	5.3%	1.15 [1.03, 1.28]
Peters 2015	45	63	35	62	4.0%	1.27 [0.97, 1.66]
Seto 2015	153	236	104	237	4.8%	1.48 [1.24, 1.75]
Shiver 2006	26	30	15	30	3.1%	1.73 [1.18, 2.55]
Tangwiwat 2016	35	50	33	50	4.0%	1.06 [0.81, 1.39]
Ueda 2015	132	249	101	256	4.7%	1.34 [1.11, 1.63]
Wang 2019	88	131	22	65	3.3%	1.98 [1.38, 2.85]
Wang 2020	131	143	82	142	5.0%	1.59 [1.37, 1.84]
Yu 2019	29	30	22	30	4.4%	1.32 [1.05, 1.65]
Subtotal (95% CI)		**1855**		**1780**	**77.9%**	**1.42 [1.30, 1.55]**
Total events	1358		926			
Heterogeneity: Tau² = 0.02; Chi² = 50.17, df = 19 (P = 0.0001); I² = 62%						
Test for overall effect: Z = 7.91 (P < 0.00001)						
1.2.2 Femoral Artery Cannulation						
Dudeck 2004	30	56	23	56	3.0%	1.30 [0.88, 1.94]
Marquis-Gravel 2018	40	64	31	65	3.6%	1.31 [0.95, 1.80]
Nguyen 2019	254	329	210	357	5.3%	1.31 [1.18, 1.46]
Subtotal (95% CI)		**449**		**478**	**11.9%**	**1.31 [1.19, 1.44]**
Total events	324		264			
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 2 (P = 1.00); I² = 0%						
Test for overall effect: Z = 5.51 (P < 0.00001)						
1.2.3 Dorsalis Pedis Artery Cannulation						
Anand 2019	23	30	18	30	3.3%	1.28 [0.90, 1.82]
Subtotal (95% CI)		**30**		**30**	**3.3%**	**1.28 [0.90, 1.82]**
Total events	23		18			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.36 (P = 0.17)						
1.2.4 Radial Artery Puncture						
Genre 2019	19	36	7	37	1.4%	2.79 [1.34, 5.82]
Laursen 2015	103	115	103	109	5.4%	0.95 [0.88, 1.02]
Subtotal (95% CI)		**151**		**146**	**6.9%**	**1.57 [0.38, 6.49]**
Total events	122		110			
Heterogeneity: Tau² = 0.98; Chi² = 14.83, df = 1 (P = 0.0001); I² = 93%						
Test for overall effect: Z = 0.62 (P = 0.53)						
Total (95% CI)		**2485**		**2434**	**100.0%**	**1.40 [1.27, 1.55]**
Total events	1827		1318			
Heterogeneity: Tau² = 0.05; Chi² = 137.87, df = 25 (P < 0.00001); I² = 82%						
Test for overall effect: Z = 6.54 (P < 0.00001)						
Test for subgroup differences: Chi² = 1.67, df = 3 (P = 0.64), I² = 0%