Ultrasonographically Guided Peripheral Intravenous Cannulation of Children and Adults: A Systematic Review and Meta-analysis

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Study objective: Peripheral intravenous cannulation is procedurally challenging and painful. We perform a systematic review to evaluate ultrasonographic guidance as an aid to peripheral intravenous cannulation.

Methods: We searched MEDLINE, Cochrane Central Register of Controlled Trials, EMBASE, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Web of Science, ClinicalTrials.gov, and Google.ca. We included randomized trials evaluating ultrasonographically guided peripheral intravenous cannulation and reporting risk of peripheral intravenous cannulation failure, number of attempts, procedure time, or time from randomization to peripheral intravenous cannulation. We separately analyzed pediatric and adult data and emergency department (ED), ICU, and operating room data. Quality assessment used the Cochrane Risk of Bias Tool.

Results: We identified 4,664 citations, assessed 403 full texts for eligibility, and included 9 trials. Five had low risk, 1 high risk, and 3 unclear risk of bias. A pediatric ED trial found that ultrasonography decreased mean difference (MD) in the number of attempts (MD −2.00; 95% confidence interval [CI] −2.73 to −1.27) and procedure time (MD −8.10 minutes; 95% CI −12.48 to −3.72 minutes). In an operating room pediatric trial, ultrasonography decreased risk of first-attempt failure (risk ratio 0.23; 95% CI 0.08 to 0.69), number of attempts (MD −1.50; 95% CI −2.52 to −0.48), and procedure time (MD −5.95; 95% CI −10.21 to −1.69). Meta-analysis of adult ED trials suggests that ultrasonography decreases the number of attempts (MD −0.43; 95% CI −0.81 to −0.05). Ultrasonography decreased risk of failure (risk ratio 0.47; 95% CI 0.26 to 0.87) in an adult ICU trial.

Conclusion: Ultrasonography may decrease peripheral intravenous cannulation attempts and procedure time in children in ED and operating room settings. Few outcomes reached statistical significance. Larger well-controlled trials are needed. [Ann Emerg Med. 2013;61:444-454.]

Please see page 455 for the Editor's Capsule Summary of this article.

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INTRODUCTION

Peripheral intravenous cannulation is one of the most frequently performed inhospital medical procedures. Obtaining peripheral intravenous access is crucial for administering fluids and medications, as well as convenient for obtaining blood samples. The conventional peripheral intravenous cannulation method involves localizing the target vessel through palpation and identification of nearby anatomic landmarks. This procedure is often difficult for the health care provider and painful for the patient. First-attempt success rates for peripheral intravenous cannulation of adults range from 76%[1] to 91%[2]; in pediatric populations, from 53%[3] to 75.6%.[4] Placing an intravenous cannula can be especially difficult in patients who are in shock, are chronically ill, are obese, use intravenous drugs, have a low volume status, or are young infants. When multiple cannulation attempts are required, patients

experience increased pain and anxiety. The additional time spent trying to secure intravenous access increases the demands placed on health care providers, increases costs, and may lengthen a patient's emergency department (ED) stay. When peripheral intravenous cannulation attempts with the conventional method fail altogether, central venous cannulation, venous cutdown, or intraosseous needle placement is often required. These procedures are more painful and time consuming and have a higher risk of complications.[5] Identifying methods or devices that improve peripheral intravenous cannulation is important to patients, health care workers, and hospital administrators.

Many devices have been incorporated as aids to peripheral intravenous cannulation. These include transilluminators, infrared lights, pressure sensors, temperature sensors, constricting bands, povidone-iodine swabs, topical glyceryl

Editor's Capsule Summary

What is already known on this topic

Use of ultrasonography to facilitate placement of peripheral intravenous lines has been encouraged by emergency medicine specialty societies in the United States and Canada.

What question this study addressed

The authors performed a systematic review and meta-analysis to determine the level of evidence supporting use of ultrasonography in securing peripheral intravenous access in children and adults in different care settings.

What this study adds to our knowledge

Nine small trials reflected a variety of techniques and practitioner specialty and discipline. Results varied widely across settings, age, and outcomes but were somewhat more favorable in pediatric patients.

How this is relevant to clinical practice

Larger trials reflecting standardized methods and operators are needed before training and practice recommendations can be justified.

trinitrate ointments, vacuum dressings, warming wraps, and bedside ultrasound machines. Of all these devices, the use of ultrasonography as an aid to peripheral intravenous cannulation is the best documented in the literature.

Ultrasonography was first used for central venous cannulation and was described by Ullman and Stoelting in 1978.[6] It has since been the focus of many randomized controlled trials, systematic reviews, and meta-analyses.[7,8] The procedure is well established and has been endorsed by the Agency for Healthcare Research and Quality in the United States.[9]

The use of ultrasonography for cannulation of peripheral veins has not been as well established. The first study of ultrasonographically guided peripheral intravenous cannulation was a prospective observational study of 101 ED patients published by Keyes et al[10] in 1999. Since then, many case reports and observational studies and several trials have been published. However, most trials have small sample sizes and have produced results of low statistical significance. A systematic review and meta-analysis can overcome some of the limitations of individual trials and may help to determine whether ultrasonography is an effective aid to peripheral intravenous cannulation.

Goals of This Investigation

We determine whether the use of ultrasonography decreases peripheral intravenous cannulation failure, procedure times, and the number of attempts required for successful peripheral intravenous cannulation in individuals requiring intravenous access.

MATERIALS AND METHODS

Study Design

Search methods, study eligibility criteria, outcomes to be reported, and methods of data collection and analysis were specified in advance and documented in a protocol. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were used.[11]

A librarian developed a search string for MEDLINE and adapted it for Cochrane Central Register of Controlled Trials, EMBASE, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Web of Science (see Appendix E1, available online at http://www.annemergmed.com, for search strategy). We searched for published and unpublished articles and abstracts in any language, with no restrictions on publication date.

The search was conducted on June 22, 2012. Titles and abstracts of articles identified by the literature search were screened for eligibility by 2 independent reviewers (J.H. and Z.F.). Articles deemed potentially relevant were obtained and the full articles were reviewed by the same 2 independent reviewers. Any uncertainties surrounding inclusion of articles were resolved through discussion with an additional reviewer (S.C.). After study selection was completed, the reference lists of studies included for meta-analysis were hand searched for additional articles. We also searched for systematic reviews related to ultrasonographically guided peripheral intravenous cannulation and screened their bibliographies for relevant trials. Known names of devices and device manufacturers were entered into Google.ca, and Web sites were searched for references to any unpublished trials. Ongoing trials and trials that had been completed but were not yet published were sought by searching clinicaltrials.gov and by contacting authors. When methods or results were unclear or information was missing, we contacted the study authors. References from the studies obtained and reviews relating to the topic were hand searched for additional studies of relevance.

Studies that compared ultrasonographically guided peripheral intravenous cannulation with the traditional method were included for meta-analysis if they had a randomized design and reported on at least 1 primary outcome measure listed below.

Risk of bias was assessed with the Cochrane Risk of Bias Tool, which assesses studies for validity according to sequence generation; allocation concealment; blinding of participants, personnel, and outcome assessors; incomplete outcome data; and selective outcome reporting.[12] All studies were evaluated independently by 2 blinded reviewers (J.H. and Z.F.). Disagreements between the 2 reviewers were settled by consensus and by consulting a third reviewer (S.C.). Overall risk of bias was considered to be high in trials that were assessed as having a high risk of bias in any domain other than adequate

blinding. We considered overall risk of bias unclear in trials that were not at high risk of bias but had an unclear risk of bias in any domain other than adequate blinding. Our outcome measures were not highly subjective and blinding would have been impossible; therefore, we did not consider the adequate blinding domain when drawing conclusions about the overall risk of bias for a trial.

Data Collection and Processing

A data extraction form was developed, pretested, and applied to all studies included for meta-analysis. Each of 2 reviewers (J.H. and Z.F.) independently extracted data from half of the studies and checked the data extracted by the other reviewer for errors. All disagreements were resolved between the 2 reviewers, with a third reviewer (S.C.) available to provide an additional opinion. To avoid counting any study twice, we compared author names, sample sizes, and outcome data between articles to identify studies that were reported on multiple times.

Data extracted from the articles included author and citation, area cannulated, technique used, the number of operators, study setting, age of participants, study design, sample sizes for treatment and control groups, completion status of study, outcomes reported, and outcome data. We also noted the intervention provider type (eg, nurse, physician, technologist) and whether patients needed a history of difficult intravenous access to be eligible for the study and how this was defined.

Outcome Measures

Four primary outcomes and 4 secondary outcome measures were considered: Primary outcomes were (1) peripheral intravenous cannulation success rate, (2) number of attempts to successful peripheral intravenous cannulation, (3) procedure time for peripheral intravenous cannulation, and (4) time from patient randomization to experimental or control study arms to successful peripheral intravenous cannulation. Secondary outcomes were (1) patient satisfaction, (2) health care worker qualitative rating of effectiveness, (3) health care worker qualitative rating of visibility of peripheral veins before and after technological assistance, and (4) parent or family satisfaction. Studies were also reviewed for any reports of adverse effects such as burns or local reactions.

Primary Data Analysis

Data from individual studies were combined with Review Manager (version 5.1; The Cochrane Collaboration, Copenhagen, Denmark), using a random-effects model. If means were not available in an article, they were imputed from a median. When SDs were not reported for a median, they were imputed from an interquartile range or *P* value. When SDs were not reported for a mean, they were computed from its confidence interval (CI) or *P* value. Relative risk ratios were used to measure intervention effect for peripheral intravenous cannulation success rate. Mean difference was used to measure intervention effect for number of attempts to successful

peripheral intravenous cannulation and time to successful placement of intravenous cannulation; 95% CIs were calculated for all outcome measures.

We took several measures to ensure that there was sufficient homogeneity among studies pooled in our meta-analysis to produce clinically useful point estimates.

Meta-analysis point estimate heterogeneity was assessed statistically for each outcome with the I^2 statistic.[13] We also assessed heterogeneity qualitatively by examining each forest plot for point estimate conformity and CI overlap.[14]

We analyzed data from pediatric and adult trials separately. Smaller veins and more subcutaneous fat make palpation and landmarking of target vessels much more difficult in the pediatric population. There is also increased anxiety for both patient and health care worker during pediatric peripheral intravenous cannulation. These clinically important differences precluded synthesis of adult and pediatric data.

We also decided that differences in study settings were significant enough to obviate the utility of combining data from across them. The operating room is a more controlled setting in which the limitations of the traditional method are not as discernible. Another factor to consider is that many patients in the ED and ICU are dehydrated, hypovolemic, or otherwise acutely unwell, whereas this is not as common in preoperative patients. Because dehydrated or hypovolemic patients are known to have difficult intravenous access, the assistance of ultrasonography may be more beneficial in this population. Data were pooled separately by setting in our meta-analysis.

Data were pooled only for outcomes that would not be significantly affected by protocol variation. We tried to capture data on the preparation time associated with using ultrasonography by including time from randomization to peripheral intravenous cannulation arm to successful peripheral intravenous cannulation as an outcome. A few studies reported this outcome, and we made note of this, but we believed that these data were potentially too dependent on individual study protocols to pool in a meta-analysis.

Finally, to limit heterogeneity caused by study design and ensure the highest available quality of evidence in our synthesis, we only included randomized controlled trials.

RESULTS

Figure 1 outlines the study selection process. All disagreements between the 2 reviewers were resolved by consensus.

We included 9 trials of ultrasonographically guided peripheral intravenous cannulation for meta-analysis. Full, unpublished articles were obtained from 2 abstract authors.[15,16] Six authors[5,15-19] were contacted to clarify aspects of their study methodology.

Two nonrandomized controlled trials,[20,21] 7 observational studies,[1-3,4,9,22,23] and 2 meta-analyses[7,8] did not meet the inclusion criteria for our review but were used to inform our discussion.
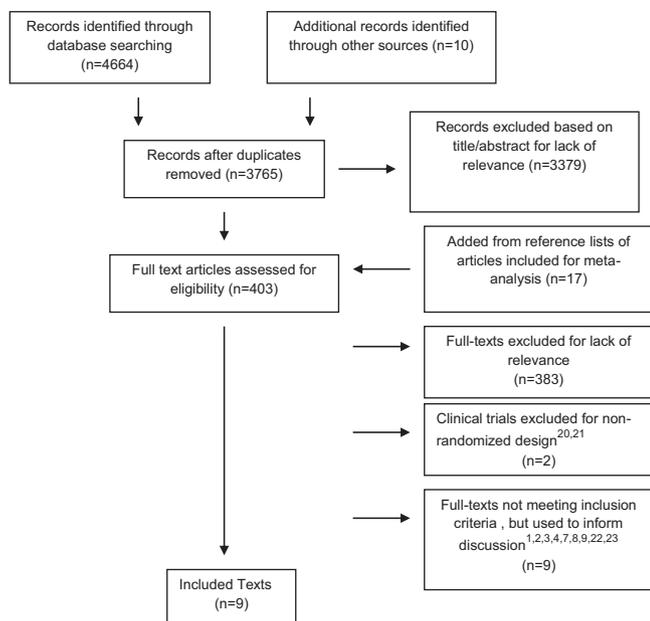
Figure 1. Study selection flow diagram.

Characteristics of the included studies are described in Table 1. All 9 studies included for meta-analysis were randomized controlled trials.[5,15-19,24-26]

Five studies were published as articles in peer-reviewed journals. Three studies were published as conference abstracts.[15-17] One study was published as a letter to the editor.[19]

In 6 studies, the eligible participants were adults (aged 18 years or older). Three of the studies included children only, in one case the patients were younger than 10 years,[5] in another they were younger than 7 years,[24] and in a third they were younger than 3 years.[18]

In 4 studies, previous failed peripheral intravenous cannulation attempts using the traditional method were required for eligibility. In 2 studies, patients were eligible if they reported past difficulty with intravenous access or after 2 cannulation attempts failed.[5,16] One study included patients who were identified by the anesthesia provider as having potential for difficult intravenous access or if they reported past difficulties with peripheral intravenous access in the preoperative interview.[25] Another study included patients if they were identified as having difficult intravenous access by an attending nurse.[19] Finally, 1 study included patients who had at least 1 limb in which no vein was visible or palpable.[18]

The studies included for meta-analysis involved a total of 376 participants. The smallest study included 18 participants,[15] whereas the largest included 60.[19] The mean study size was 41 patients. Of the 9 studies, 5 took place in EDs, 3 took place in the operating room, and 1 took place in an ICU.

The comparator was the traditional "blind method" in 6 studies and the traditional method with optional transillumination in 1.[5] It was not clear what percentage of control arm patients were cannulated with transillumination in

this study. Therefore, we did not pool data from this study in our meta-analysis. One study crossed patients over to the ultrasonographic arm after 2 attempts with the traditional method.[19] Another study allowed nurses to repeat attempts with the traditional method or obtain help from a nurse intravenous team or a physician using ultrasonographic guidance.[16] None of the studies included in our synthesis were ongoing at analysis.

Peripheral intravenous cannulation was considered successful if the line could be used for fluid administration or a blood draw. It was considered a failure after 1,[24,25] 2,[19] or 4 attempts.[5] One trial reported on both failure after 1 unsuccessful attempt and failure after 15 minutes (overall failure).[18] One trial did not specify how many attempts were allowed before peripheral intravenous cannulation was considered a failure.[17]

A peripheral intravenous cannulation attempt was defined as 1 percutaneous needle puncture. Procedure time started when skin was punctured and was stopped after successful peripheral intravenous cannulation. Time from randomization to peripheral intravenous cannulation began when individuals were randomized to either ultrasonography or traditional method study arms and ended after successful peripheral intravenous cannulation.

Data on risk of bias within each study as assessed with the Cochrane Risk of Bias Tool are presented in Table 2. Five studies had a low risk of bias, 1 study had a high risk of bias, and 3 had an unclear risk of bias. Studies with an unclear risk of bias did not explicitly describe their method of sequence generation and allocation concealment.[17,19,25] The study with a high risk of bias did not address incomplete outcome data.[15]

Main Results

Results of the individual studies included in the review, as well as the meta-analysis results, are presented in Figures 2 and 3.

Two pediatric trials that took place in the ED found that the use of ultrasonography did not affect the risk of peripheral intravenous cannulation failure (Figure 2). A single pediatric trial reported that ultrasonographic guidance reduced attempts (mean difference -2.00; 95% CI -2.73 to -1.27) and procedure time in the ED (mean difference -8.10 minutes; 95% CI -12.48 to -3.72 minutes).

One pediatric trial run in the operating room found that the use of ultrasonography decreased the risk of first-attempt peripheral intravenous cannulation failure but did not affect overall failure (first-attempt failure risk ratio 0.23; 95% CI 0.08 to 0.69). The same trial reported that ultrasonographic guidance reduced peripheral intravenous cannulation attempts (mean difference -1.50; 95% CI -2.52 to -0.48) and procedure time (mean difference -5.95 minutes; 95% CI -10.21 to -1.69 minutes).

A single adult trial found that ultrasonographic guidance did not affect risk of peripheral intravenous cannulation failure in the ED (Figure 3). Meta-analysis of 3 adult ED trials showed that ultrasonographic guidance reduced the number of attempts required before successful peripheral intravenous cannulation in the ED (mean difference -0.43; 95% CI -0.81 to -0.05; $I^2=0\%$). Three ED trials reported on time from randomization

Table 1. Descriptive characteristics of studies included in the review.

Author, Year	Report Type	Size	Comparison	Provider	Population	Setting	Area Cannulated	Technique	Operators
Bair,[24] 2008	Journal article	44	Traditional method	Physician-operated ultrasonography, nurse-placed catheter	Children (<7 y)	ED	No restrictions	Static	2
Doniger,[5] 2009	Journal article	50	Traditional method with option of transillumination	Physician-operated ultrasonography, nurse-placed catheter	Children (<10 y)	ED	No restrictions	Dynamic	2
Benkhadra,[18] 2012	Journal article	40	Traditional method	Anesthesiologists and nurse anesthetists	Children (<3 y)	OR	Upper or lower limb for ultrasonography group, lower limb for blind group	Dynamic	1
Darvish,[16] 2011	Conference abstract	25	Traditional method with option to call for help from nurse IV team or physician	ED nurses	Adults (>18 y)	ED	No restrictions	Dynamic	1
River,[17] 2009	Conference abstract	47	Traditional method	ED nurses	Adults (>18 y)	ED	Unknown	Unknown	Unknown
Stein,[26] 2009	Journal article	57	Traditional method	Emergency physician+nurse or resident if 2 operators preferred by physician	Adults (>18 y)	ED	Leg veins not allowed, external jugular vein allowed	Dynamic	1 or 2 (choice of operator)
Kerforne,[19] 2012	Journal letter	60	2 attempts at traditional method and then ultrasonographic rescue	ICU nurses	Adults (>18 y)	ICU	Unknown	Dynamic	Unknown
Aponte,[25] 2007	Journal article	35	Traditional method	Nurse anesthetist	Adults (>18 y)	OR	Hand, wrist, forearm, antecubital fossa	Dynamic	1
Pappas,[15] 2006	Conference abstract and internal report	18	Traditional method	Nurse anesthetist	Adults (>18 y)	OR	Antecubital fossa, wrist	Dynamic	1

OR, operating room; *IV*, intravenous.

Table 2. Risk of bias assessments.*

Author, Year	Adequate Sequence Generation	Allocation Concealment	Adequate Blinding	Incomplete Outcome Data Addressed	Free of Selective Outcome Reporting	Free of Other Bias	Overall Risk of Bias
Bair, 2008[24][†]	Yes	Yes	No	Yes	Yes	Yes	Low
Doniger, 2009[5][†]	Yes	Yes	No	Yes	Yes	Yes	Low
Benkhadra, 2012[18][†]	Yes	Yes	No	Yes	Yes	Yes	Low
Darvish, 2011[16]	Yes	Yes	No	Yes	Yes	Yes	Low
River, 2009[17]	Unclear	Unclear	No	Yes	Yes	Yes	Unclear
Stein, 2009[26]	Yes	Yes	No	Yes	Yes	Yes	Low
Kerforne, 2012[19]	Unclear	Unclear	No	Yes	Yes	Yes	Unclear
Aponte, 2007[25]	Unclear	Unclear	No	Yes	Yes	Yes	Unclear
Pappas, 2006[15]	Yes	Unclear	No	No	Yes	Yes	High

*Risk of bias was assessed by 2 blinded reviewers using the Cochrane Risk of Bias Tool. Disagreements between the 2 reviewers were settled by consensus and by consulting a third reviewer.
[†]Pediatric trial.

to successful peripheral intravenous cannulation. These studies started timing when patients were randomized to treatment groups and stopped the clock when blood was drawn or intravenous fluids were administered through the line. None of these trials found that ultrasonographic guidance affected time from randomization to successful cannulation (Figure 3).

One adult trial conducted in the ICU reported that ultrasonographic guidance decreased risk of peripheral intravenous cannulation failure (risk ratio 0.47; 95% CI 0.26 to 0.87) but did not affect procedure time (Figure 3).

An adult operating room trial found that ultrasonographic guidance does not affect risk of failure (Figure 3). Meta-analysis of 2 adult operating room trials found that ultrasonography does not affect the number of attempts before successful peripheral intravenous cannulation or procedure time (Figure 3).

One trial reported a single arterial puncture during ultrasonographically guided peripheral intravenous cannulation, resulting in a 4% complication rate for the procedure.[5] No other trials reported any complications in either study arm.

In our sensitivity analysis, meta-analyses were limited to include only studies with a low risk of bias (Table 2). When the results of one study with an unclear risk of bias[17] were left out of the data pool for number of attempts to successful peripheral intravenous cannulation of adults in the ED, there was no significant change to the point estimate (mean difference −0.37 minutes; 95% CI −0.89 to 0.15 minutes). Sensitivity analysis was not possible for number of attempts to adult peripheral intravenous cannulation in the operating room and adult procedure time in the operating room because none of the included studies had a low risk of bias.

There was little evidence of statistical heterogeneity for point estimates of number of attempts to successful peripheral intravenous cannulation of adults in the ED (I^2=0%) or adult procedure time in the operating room (I^2=0%). A high degree of point estimate conformity and CI overlap is appreciable in the forest plots for each of these point estimates, supporting their homogeneity.
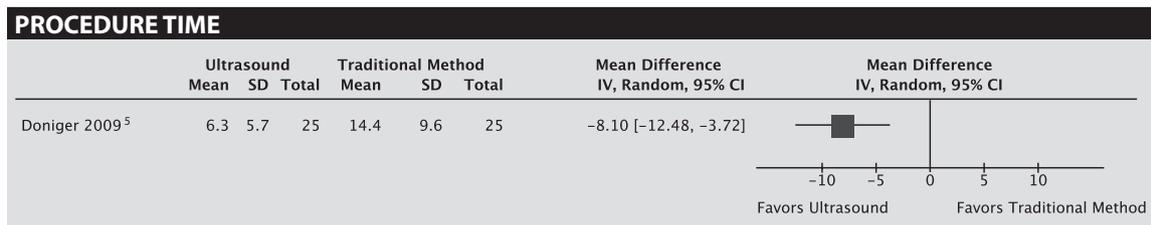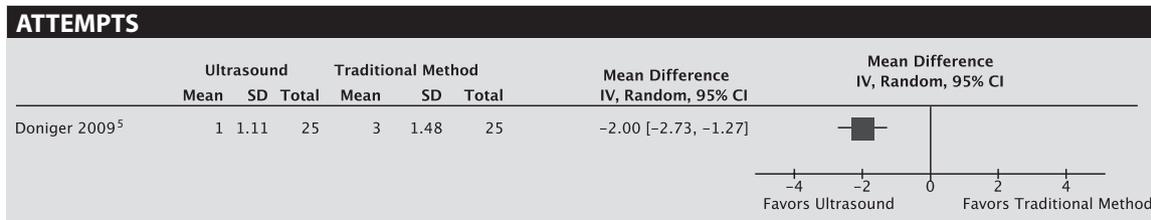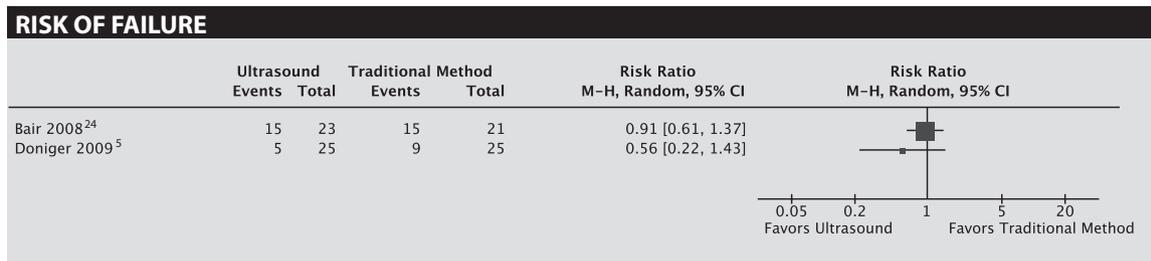
There was evidence of substantial statistical heterogeneity (I^2=56%) in our meta-analysis point estimate for number of attempts to successful peripheral intravenous cannulation of adults in the operating room. However, an exploration of the features of the 2 studies likely to have a great influence on heterogeneity reveals that they are clinically very similar[15,25] (Table 1). In both studies, cannulation was performed preoperatively by a nurse anesthetist who used the dynamic technique, independent of another operator. The 2 studies allowed for cannulation of the wrist and antecubital fossa, but one also allowed for cannulation of the hand and forearm.[25] Finally, both studies focused on peripheral intravenous cannulation of adult surgical patients and compared ultrasonographic guidance with the traditional method. The clinical homogeneity of these 2 studies supports pooling of their data in the face of statistical heterogeneity. Additionally, the CI around the mean number of attempts reported by Pappas et al[15] is large and almost completely covers the CI around the mean number of attempts reported by Aponte et al.[25]

Patient satisfaction with ultrasonographically guided peripheral intravenous cannulation and the traditional method was compared in 3 of the trials included in our meta-analysis. In all 3 trials, satisfaction with the ultrasonographically guided procedure was higher but not statistically significant.[16,17,26] Some of this difference may be due to a "wow factor,"[26] or a perception that any use of technology represents an improvement in care.[20] One study reported that nurses were significantly more satisfied with the ultrasonographically guided method than with the traditional method.[17] No studies reported on health care worker qualitative ratings of peripheral vein visibility or parent and family satisfaction.

LIMITATIONS

One limitation of our review is that we were unable to investigate publication bias. There were too few studies that reported on each outcome in our meta-analysis to make interpretation of a funnel plot possible. We are reassured by our

EMERGENCY DEPARTMENT

RISK OF FAILURE

	Ultrasound Events	Total	Traditional Method Events	Total	Risk Ratio M–H, Random, 95% CI	Risk Ratio M–H, Random, 95% CI
Bair 2008[24]	15	23	15	21	0.91 [0.61, 1.37]	
Doniger 2009[5]	5	25	9	25	0.56 [0.22, 1.43]	

0.05 0.2 1 5 20
Favors Ultrasound   Favors Traditional Method

ATTEMPTS

	Ultrasound Mean	SD	Total	Traditional Method Mean	SD	Total	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Doniger 2009[5]	1	1.11	25	3	1.48	25	−2.00 [−2.73, −1.27]	

−4 −2 0 2 4
Favors Ultrasound   Favors Traditional Method

PROCEDURE TIME

	Ultrasound Mean	SD	Total	Traditional Method Mean	SD	Total	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Doniger 2009[5]	6.3	5.7	25	14.4	9.6	25	−8.10 [−12.48, −3.72]	

−10 −5 0 5 10
Favors Ultrasound   Favors Traditional Method

OPERATING ROOM

RISK OF FAILURE

	Ultrasound Events	Total	Traditional Method Events	Total	Risk Ratio M–H, Random, 95% CI	Risk Ratio M–H, Random, 95% CI
Benkhadra 2012,[18] 1 attempt	3	20	13	20	0.23 [0.08, 0.69]	
Benkhadra 2012,[18] Overall	2	20	3	20	0.67 [0.12, 3.57]	

0.05 0.2 1 5 20
Favors Ultrasound   Favors Traditional Method

ATTEMPTS

	Ultrasound Mean	SD	Total	Traditional Method Mean	SD	Total	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Benkhadra 2012[18]	1	1.65	20	2.5	1.65	20	−1.50 [−2.52, −0.48]	

−4 −2 0 2 4
Favors Ultrasound   Favors Traditional Method

PROCEDURE TIME

	Ultrasound Mean	SD	Total	Traditional Method Mean	SD	Total	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Benkhadra 2012[18]	1.06	1.3	20	7.01	9.63	20	−5.95 [−10.21, −1.69]	

−10 −5 0 5 10
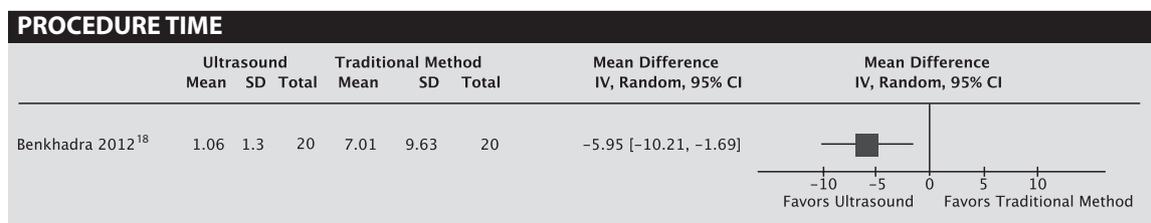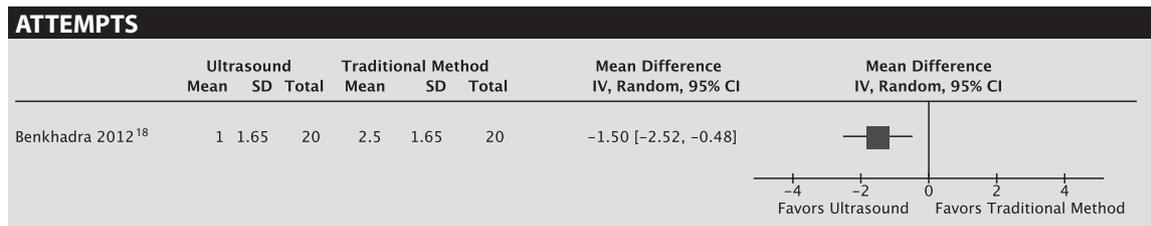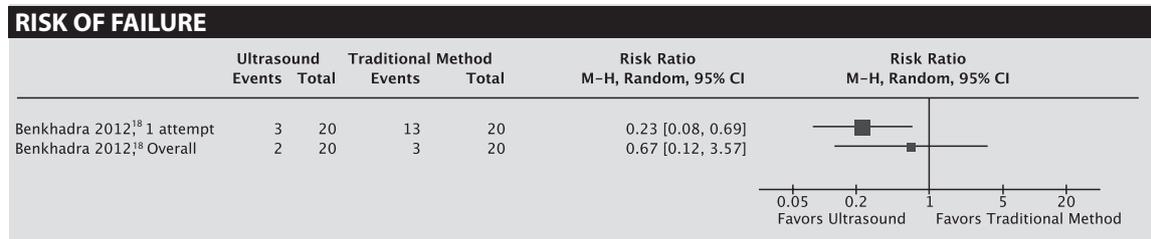Favors Ultrasound   Favors Traditional Method

Figure 2. Forest plot, pediatric trials. All trials compared ultrasonographically guided peripheral intravenous cannulation to the traditional method. Doniger et al[5] allowed for optional use of transillumination in its control group. Data are ordered first by setting and then outcome. Risk of failure is expressed as individual risk ratios for each trial. Attempts and procedure time are expressed as the mean difference between intervention groups for each trial.

extensive search of the gray literature for unpublished trials. Because of lack of resources, we were also unable to hand search target journals and conference proceedings.

DISCUSSION

There were few statistically significant results reported by the trials included in this review. Early results are more promising in the pediatric population, in which ultrasonographic guidance was shown to be associated with a significant reduction in attempts and procedure times in both the ED and operating room. Ultrasonographically guided peripheral intravenous cannulation may perform better in the pediatric population because failure rates with the traditional method are much higher in children than adults. Ultrasonography may not be as beneficial in adults, in whom target vessels are easier to locate. However, the adults included in the studies we reviewed were identified as having difficult intravenous access before being randomized to a study arm, which may explain why there was a trend toward reduced risk of peripheral intravenous cannulation failure and fewer attempts before successful peripheral intravenous cannulation when ultrasonography was used.

As hypothesized, there was a trend toward ultrasonographic guidance affording a greater benefit in the ED and ICU than the operating room. We suspect that this is because patients in the ED and ICU are more likely to be hypovolemic and acutely ill, factors known to be associated with difficult intravenous access. It stands to reason that the benefit of ultrasonographic guidance would be better discerned in populations in whom intravenous access is more difficult to obtain at baseline.

There are a number of important differences between the studies included in this review that deserve consideration (Table 1). One is protocol differences between the included studies. Ultrasonographically guided peripheral intravenous cannulation can be performed with either 1 or 2 operators. In the 1-operator technique, a single health care worker uses the probe to locate the vessel with one hand while placing the intravenous cannula with the other. In the 2-operator technique, one health care worker locates the vessel with the probe while the other places the intravenous cannula. Both pediatric ED trials used the 2-operator technique, with a physician performing the ultrasonography and a nurse placing the intravenous cannula. Another important protocol feature that varied between studies was whether ultrasonographically guided peripheral intravenous cannulation was performed with a static or dynamic approach. In the static approach, ultrasonography is used only to localize and mark the vessel, whereas the dynamic approach uses real-time ultrasonographic guidance to navigate the needle. These

variations could have contributed heterogeneity to our meta-analysis point estimates.

The expertise of the intervention providers performing peripheral intravenous cannulation also varied between studies. Providers ranged from ED nurses, to nurse anesthetists, to physicians. Each study used a different training protocol to familiarize intervention providers with the ultrasonographically guided peripheral intravenous cannulation procedure. In all 6 studies, the providers had more experience with the traditional method of peripheral intravenous cannulation placement than the ultrasonographically guided method. There was also potential for varying proficiency among intervention providers within each study. This is an important source of potential bias and could also add to meta-analysis heterogeneity.[27]

A number of studies have examined failure rates, infections, and other complications of ultrasonographically guided peripheral intravenous cannulation. It has been reported that intravenous cannulae placed with the assistance of ultrasonography dislodge, infiltrate, or stop working sooner than their counterparts placed with the traditional method.[22] There was only 1 reported complication in the 9 trials included in our review: ultrasonographically guided peripheral intravenous cannulation resulted in a single arterial puncture.[5] A prospective observational study of 151 peripheral intravenous cannulations placed with ultrasonography found that 11% of the cannulations failed after 4 hours and 14% failed after 12 hours.[22] The authors also observed that peripheral intravenous cannulation failure independently correlated with placement in deep and proximal vessels. A retrospective review compared infection rates in 402 patients with peripheral intravenous cannulae placed with ultrasonography to 402 matched patients with cannulae placed with the traditional method. Infection rates were low for cannulae placed with both methods, and there was no statistically significant difference between them.[23] Two quasi-randomized controlled trials have reported on complication rates as an outcome. One study found no significant difference in the number of complications between the ultrasonography and traditionally placed peripheral intravenous cannulation groups,[21] whereas another found no significant complications in either group.[20] Hematomas were the most commonly reported complication.[21]

To the best of our knowledge, this is the first systematic review of ultrasonographically guided peripheral intravenous cannulation. There are 2 systematic reviews of ultrasonographically guided central venous cannulation.[7,8] Both reviews found that ultrasonographic guidance decreased failure rates and the number of complications associated with the

Figure 3. Forest plot, adult trials. All trials compared ultrasonographically guided peripheral intravenous cannulation (PIVC) to the traditional method. Data are ordered first by setting and then outcome. Risk of failure is expressed as individual risk ratios for each trial. Attempts, procedure time, and time from randomization to peripheral intravenous cannulation are expressed as the mean difference between intervention groups. Meta-analysis point estimates were calculated by pooling outcome data by setting.

procedure. The Agency for Healthcare Research and Quality also advocates ultrasonographic guidance during central venous cannulation and considers it among the top 11 ways patient safety can be improved in the United States.[9]

Despite the absence of definitive evidence supporting ultrasonographically guided peripheral intravenous cannulation, the procedure is endorsed throughout the literature and has been encouraged by 2 important emergency medicine bodies. The American Association of Emergency Physicians lists procedural guidance as one of the core emergency medicine ultrasonographic applications and cites a trial of ultrasonographically guided peripheral intravenous cannulation as part of the body of evidence in support of ultrasonographically guided vascular access.[20,28] The Canadian Association of Emergency Physicians has included peripheral vascular access as part of the emergency physician's scope of practice in their 2012 position statement on point-of-care sonography.[29] The summary of evidence provided by our review may help illuminate questions that need further attention.

Future studies should explicitly measure ultrasonographic transport and setup times and report their methods of doing so in a way that can easily be reproduced. A standardized approach to training of personnel in use of new equipment before trial commencement would help reduce this variable as a source of heterogeneity for future systematic reviews. Standardization of protocols with respect to details of equipment use would also help reduce heterogeneity. This standardization will help improve certainty around the efficacy of ultrasonographically guided peripheral intravenous cannulation, but this may not reflect the "real-world" effectiveness of the procedure. Accordingly, future trialists may instead choose to take a pragmatic approach to assessment of ultrasonographically guided peripheral intravenous cannulation and allow for sources of variation that exist in typical practice settings.[30]

Ultrasonographically guided peripheral intravenous cannulation appears to be most promising in the pediatric population. However, there have been only 3 published pediatric randomized controlled trials, preventing any definitive conclusions. More pediatric trials across ED, ICU, and operating room settings are needed.

Early evidence suggests that ultrasonographically guided peripheral intravenous cannulation of children significantly decreases attempts and procedure times in both ED and operating room settings. Given the distress that this procedure causes in the pediatric population, this result has considerable clinical significance. Ultrasonographically guided peripheral intravenous cannulation of adults in the ED results in a statistically significant reduction in attempts, with marginal clinical significance. Evidence from one trial suggests that ultrasonographic guidance may decrease risk of failure among adults in the ICU. Generally, heterogeneity with mixed setting and type of health care providers leave strong conclusions uncertain. More trials with larger numbers and low risk of bias

design would help to further clarify the utility of ultrasonography as an adjunct to the peripheral intravenous cannulation procedure.

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APPENDIX E1.

Search

The following search terms were used to search MEDLINE and were adapted to search the other trials registers and databases:

1. Catheterization, Peripheral/
2. Catheterization/
3. limit 2 to yr="1860 - 1987"
4. (peripheral or intravenous).mp.
5. 3 and 4
6. ((cannulation or catheterization) adj5 (peripheral or intravenous)).ti,ab.
7. ((intravenous adj5 line*) or (intravenous adj5 place*) or (intravenous adj5 position*) or (intravenous adj5 access*)).ti,ab.
8. blood specimen collection/or phlebotomy/
9. (venipuncture* or venesection* or phlebotomy or (blood adj2 draw*)).ti.
10. 1 or 5 or 6 or 7 or 8 or 9
11. ultrasonography/or ultrasonography, interventional/
12. exp Light/
13. exp Infrared Rays/
14. (ultrasonography or infrared or veinviewer or cold light).ti,ab.
15. (ultrasonography or ultrasonograph* or infrared or veinviewer or cold light).ti,ab.
16. light*.ti.
17. (Betadine or alcohol swab*).ti,ab.
18. Accuvein.ti,ab.
19. LumenVu.ti,ab.
20. SmartNeedle.mp.
21. smartneedle.mp.
22. (Accuvein or LumenVu or SmartNeedle or Vacuderm or NanoMaxx or iLook or sonosite or Olberon).mp.
23. (Otoscope or Landry Vein Light or Venocscope or transilluminat* or trans illuminat*).mp.
24. nitroglycerin.mp.
25. guide* wire.mp.
26. Rapid Intravascular Start.mp.
27. (device* or technolog* or machine*).ti.
28. instrument*.ti.
29. or/11-28
30. 10 and 29
31. (cardiac catheter* or heart catheter* or urinary catheter*).mp.
32. 30 not 31