Ultrasound-Guided Subclavian Vein Catheterization: A Systematic Review and Metaanalysis

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Objective: Although ultrasound guidance for subclavian vein catheterization has been well described, evidence for its use has not been comprehensively appraised. Thus, we conducted a systematic review and metaanalysis to determine whether ultrasound guidance of subclavian vein catheterization reduces catheterization failures and adverse events compared to the traditional "blind" landmark method. All forms of ultrasound were included (dynamic 2D ultrasound, static 2D ultrasound, and Doppler).

Data Sources: Medline, Embase, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and CINAHL (from inception to September 2014).

Study Selection: Randomized controlled trials of ultrasound compared to landmark technique for subclavian catheterization in adult populations were considered. Outcomes of interest included safety and failure of catheterization.

Data Extraction: Adverse event data were analyzed according to Peto's method and expressed as odd ratios and 95% CIs. Failure of catheterization was analyzed with inverse variance random effects modeling and expressed as risk ratios and 95% CI.

Data Synthesis: Six hundred and one studies were reviewed and 10 met inclusion criteria (n = 2,168 participants). Six used dynamic 2D ultrasound (n = 719), one used static 2D ultrasound (n = 821), and three used Doppler-guided insertion techniques (n = 628). Overall complication rates were reduced with ultrasound use compared to the landmark group (odd ratio, 0.53; 95% CI, 0.41–0.69). Subgroup analysis demonstrated that dynamic 2D ultrasound reduced inadvertent arterial puncture, pneumothorax, and hematoma formation. No difference in failure of catheterization was noted between the ultrasound group and the landmark method (risk ratio, 0.85; 95% CI, 0.48–1.51). Subgroup analysis of dynamic 2D ultrasound demonstrated a significant decrease in failed catheterization (risk ratio, 0.24; 95% CI, 0.06–0.92).

Conclusions: Ultrasound-guided subclavian catheterization reduced the frequency of adverse events compared with the landmark technique. Our findings support the use of dynamic 2D ultrasound for subclavian catheterization to reduce adverse events and failed catheterization. (*Crit Care Med* 2015; XX:00–00)

Key Words: central catheter; intravenous; metaanalysis; subclavian vein; systematic review; ultrasonography interventional

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It is estimated that approximately 5 million central venous catheters are placed annually in the United States, and this number is rising (1, 2). Central venous catheters are used across a broad range of medical specialties, including critical care, anesthesiology, nephrology, radiology, cardiology, and oncology. Indications for central vein cannulation are varied

and include hemodynamic monitoring, drug administration, dialysis, and parenteral nutrition.

Common sites for insertion of central venous catheters include the internal jugular vein and subclavian vein. Rates of mechanical complications between jugular and subclavian sites of insertion are approximately equal (3–5); however, current guidelines suggest that subclavian vein insertion may benefit from lower infection rates (6). This has led to renewed interest on the best methods of insertion, including whether ultrasound guidance reduces catheterization failures and improves safety over traditional "blind" landmark techniques. Several meta-analyses and recent clinical practice guidelines strongly support ultrasound guidance when inserting through the internal jugular vein (4, 7–12). No systematic review and metaanalysis has comprehensively summarized ultrasound guidance for subclavian vein cannulation. Likely due to this void, recent clinical practice guidelines from a number of different professional societies have had variable suggestions on the use of ultrasound for subclavian vein cannulation (8–10, 13–15).

A comprehensive review of ultrasound-guided subclavian vein catheterization is needed. Thus, we conducted a systematic review and metaanalysis of randomized control trials to answer the question, "In adult patients requiring subclavian cannulation (regardless of clinical setting), does ultrasound guidance decrease catheterization failure and reduce adverse events compared to catheterization with the traditional 'blind' landmark method?" Since central venous catheterization is performed by a variety of specialists and access to technology varies greatly, randomized studies of either sonographic Doppler or 2D ultrasound imaging were considered.

METHODS

Data Sources

We conducted electronic searches of Ovid MEDLINE and MEDLINE In-Process and Other Non-Indexed Citations, Embase and Embase Classic, CINAHL, Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews. All databases were searched from inception to September 2014. Specific strategies were developed for each database with the aid of an information specialist experienced in systematic searches (for complete search strategy, see **Appendix A**, Supplemental Digital Content 1, http://links.lww.com/CCM/B238). Bibliographies of relevant narrative and systematic reviews, clinical practice guidelines, as well as retrieved articles were searched for additional studies. Searches were performed without language restriction. Corresponding authors of included studies were contacted to verify extracted data and provide missing data.

Eligibility Criteria

We included all peer-reviewed, randomized controlled trials of ultrasound-guided subclavian vein catheter insertion compared to the traditional landmark technique. No exclusions were made based on language of publication. No restrictions were placed on clinical setting or operator experience. Both sonographic Doppler and imaging 2D ultrasound were included, as well as dynamic and static use of ultrasound. We excluded studies that involved a pediatric population as our group of investigators has content expertise in adult medicine. Given the differing adverse event profile and technical expertise required, we also excluded studies that involved more invasive procedures (e.g., tunneled catheter placement) or placement of extra devices (e.g., pacemaker placement) compared with a typical percutaneous central catheter.

Study Selection

All titles and abstracts of reports identified by the search were independently assessed by two reviewers (M.M.L., O.A.). Any discrepancies related to eligibility criteria were resolved by discussion with coauthors (A.F., G.L.B.). Overall interrater agreement was calculated with a κ statistic (16).

Risk of Bias Assessment

Risk of bias was assessed in trials that met inclusion criteria according to the Risk of Bias Tool recommended by the Cochrane Collaboration (17). The six criteria in the tool include a description of the random sequence generation, allocation concealment, blinding of personnel, blinding of outcome assessment, completeness of data, and selective reporting. Criteria were individually scored as high, low, or unclear risk of bias.

Data Extraction

Data from each included study were collected independently by two reviewers (M.M.L., O.A.) using a standardized piloted form. Discrepancies were resolved by discussion with coauthors (A.F., G.L.B.). Collected data included the following: 1) author identification, 2) study country of origin, 3) clinical setting, 4) patient demographics, 5) operator experience, 6) type of ultrasound (sonographic Doppler vs imaging 2D ultrasound), 7) ultrasound technique (static vs dynamic and other details), 8) details of landmark comparison technique, 9) a priori listed length of follow-up, and 10) criteria to assess risk of bias.

Outcome Measures: Failure of Catheterization and Safety

Outcomes were determined a priori and included failure of catheterization and safety. Failure of catheterization was dichotomized as "yes/no" for purposes of this review. In crossover trials, only the result from the initial method of cannulation was considered. Time for cannulation and number of attempts were recorded. Safety was defined by the prevalence of adverse events, which included: overall frequency of complications, pneumothorax, arterial bleeding or arterial puncture, infection, thrombus, arrhythmias, malposition, hemothorax, cardiac tamponade, and nerve injuries. Any other reported complications were also recorded. We recorded whether these measures of failure of catheterization and safety were defined a priori in the methods section of each article, as well as any specific definitions for each event, if provided.

Statistical Analysis

We performed metaanalyses for failure of catheterization and adverse event outcomes. Analysis was performed with Comprehensive Metaanalysis (Version 2.2, Biostat, Englewood, NJ). Failure of catheterization was analyzed with Mantel-Haenszel random effects modeling and expressed as risk ratios (RRs) with 95% CIs. Given the rarity of adverse events, pooled adverse events data were analyzed according to Peto's method and expressed as odd ratios (ORs) with 95% CIs (17). For both failure of catheterization and adverse events, a pooled ratio less than 1 favored ultrasound and a ratio greater than 1 favored landmark technique. Heterogeneity between and within trials was evaluated using the I^2 and chi-square tests (18). Subgroup analyses based on ultrasound technique (dynamic 2D ultrasound vs static 2D ultrasound vs Doppler sonography) as well as other data extracted (operator experience, ultrasound details, patient demographics, and clinical setting) were planned. Since dynamic 2D ultrasound reduces adverse events and failed catheterization versus other techniques when cannulating the internal jugular vein (8–10, 13–15), we hypothesized that dynamic 2D ultrasound would have a similar effect when used to cannulate the subclavian vein. Data that could not be pooled by statistical metaanalysis are reported by group according to numbers and proportions. A funnel plot was constructed to inspect for the presence of small study effects.

RESULTS

Study Selection

A total of 601 unique citations were identified through the electronic databases. Ten studies met eligibility criteria following independent screening by title, abstract, and full report along with a manual search of bibliographies (**Fig. 1**). Overall interrater agreement was high ($\kappa = 0.91$). Eight of 10 studies (80%) were full reports and two of 10 studies (20%) were in abstract form. Corresponding authors of all studies were contacted to verify extracted data and provide missing data, with four of 10 responding (3, 19–21).

Study Characteristics and Patient Populations

Baseline study characteristics of included randomized control studies are summarized in **Table 1**. The 10 studies included a total of 2,168 participants. One thousand thirty-five participants were allocated to ultrasound-guided cannulation, and 1,048 were allocated to cannulation with landmark technique. One report provided no details of allocation of its 85 participants, which precluded it from inclusion in our metaanalysis (20). Four of 10 (40%) of the studies were conducted in the United States (3, 5, 20, 22, 23), four of 10 (40%) were conducted in member nations of the European Union (19, 21, 24, 25), one of 10 (10%) was conducted in India (26), and one of 10 (10%) was conducted in South Korea (27). Five of 10 (50%) of the studies were in an ICU setting (19, 21, 23, 25, 26), one of 10 (10%) in an emergency department setting (20), one of 10 (10%) in anesthetized neurosurgical patients (27), and three of 10 (30%) in an outpatient, clinic, or an in-patient setting (3, 22, 24). Operator experience differed between trials, as two of 10 (20%) trials used physicians with limited experience (23, 24), three of 10 (30%) trials used both experienced and inexperienced physicians (3, 20, 26), and four of 10 trials used only experienced physicians (19, 21, 22, 25). Similarly, the number of operators varied in each trial ranging from 1 to 49.

Six of 10 studies (60%) used dynamic 2D ultrasound (19, 20, 23, 25–27), one of 10 (10%) used static 2D ultrasound (3), and three of 10 (30%) used dynamic Doppler-guided ultrasound (21, 22, 24). Three of six dynamic 2D ultrasound studies used longitudinal (in plane) visualization (19, 25, 27) of the subclavian vessel and two of six used transverse (out of plane) visualization (23, 26). Details of the ultrasound and landmark technique used were variably reported (**Table 2**). Similarly, a priori definitions of both efficacy and adverse event outcomes were variable (**Supplemental Table 1**, Supplemental Digital Content 2, http://links.lww.com/CCM/B239; and **Supplemental Table 2**, Supplemental Digital Content 3, http://links.lww.com/CCM/B240).

Risk of Bias Assessment

Risk of bias in the 10 studies is described in **Table 3**. No study fulfilled all six criteria for low risk of bias. Nine of 10 studies (90%) described randomization by a low risk of bias method, with two reporting allocation concealment (24, 27). Due to the nature of these studies, blinding of participants and personnel to the procedure would not be technically feasible. Blinding of outcome assessments was unclear or not reported in six of 10 studies (60%); authors of two studies stated in personal communications that blinding was not performed for any outcome assessments (19, 24), and one study had an unblinded research nurse recording outcomes (3). All studies had low risk of bias for incomplete data reporting. Similarly, all studies fully reported on outcomes prespecified in their methods (i.e., low risk of bias for selective outcome reporting).

Failed Catheterization

All studies (10 of 10) reported on overall failed catheterization. A metaanalysis of overall failed catheterizations revealed no significant difference between ultrasound and landmark technique (RR, 0.672; 95% CI, 0.356–1.268; $I^2 = 75.3\%$) (**Fig. 2*A***). Subgroup analysis of five trials that used 2D dynamic ultrasound demonstrated a significant reduction of failed catheterizations with this ultrasound technique (RR, 0.243; 95% CI, 0.0.064–0.922; $I^2 = 64.4\%$) (**Fig. 2*B***).

Three of 10 studies (30%) reported failure at first attempt (21, 25, 26), with one of these studies (25) providing a definition for this outcome (Supplemental Table 1, Supplemental Digital Content 2, http://links.lww.com/CCM/B239). Metaanalysis demonstrated no significant difference between ultrasound and landmark technique (RR, 1.004; 95% CI, 0.764–1.004; $I^2 = 0.0\%$). Similarly, subgroup analysis of only studies using dynamic 2D ultrasound demonstrated no significant difference between ultrasound and landmark technique for failed catheterizations at first attempt (RR, 0.904; 95% CI, 0.526–1.554; $I^2 = 0.0\%$). Four of 10 studies (40%) reported

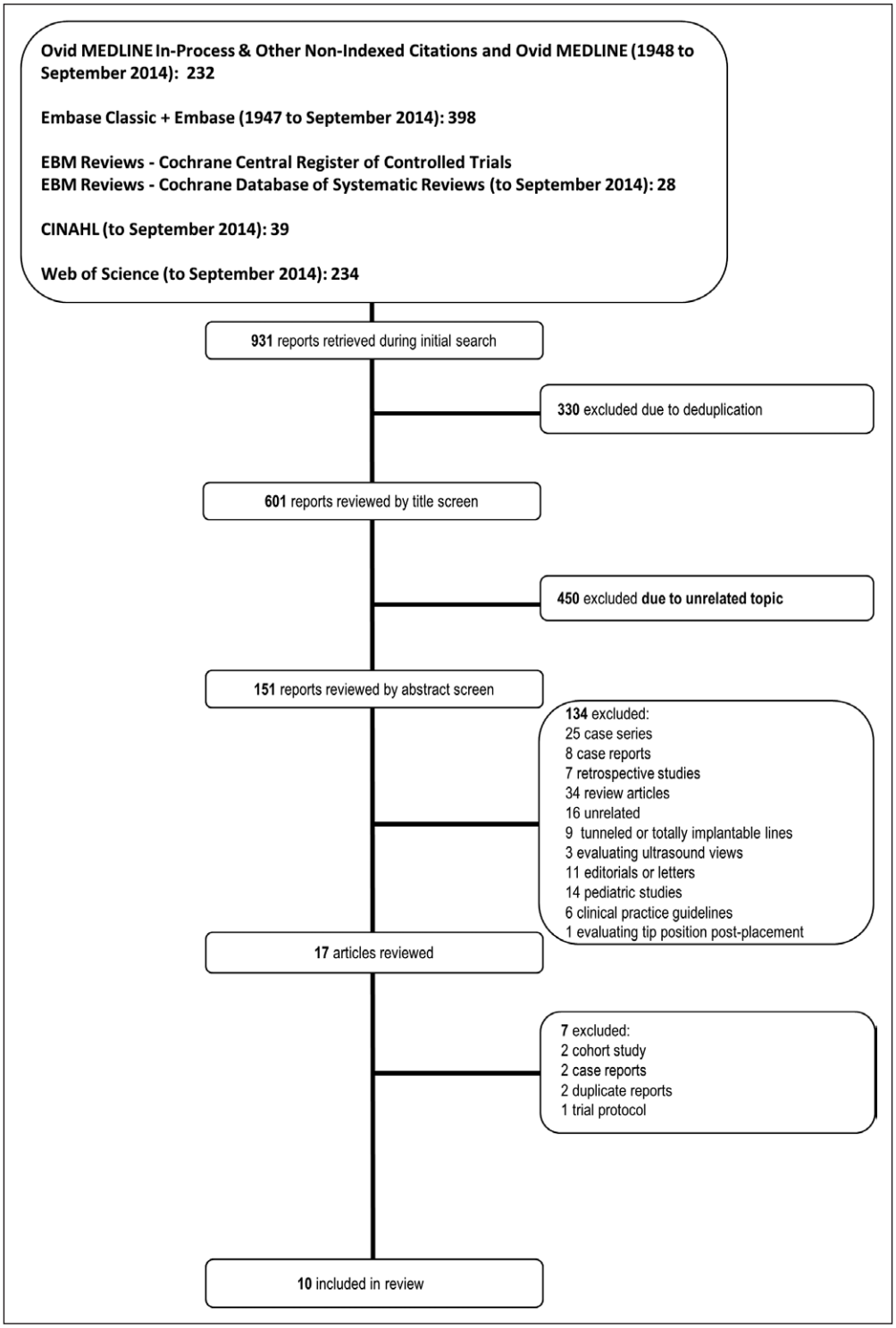

Figure 1. Preferred Reporting Items for Systematic reviews and metaanalysis flow diagram, illustrating search strategy and identification of relevant articles. EBM = Evidence Based Medicine.

time for cannulation (19, 21, 24, 25), with three of four studies (75%) reporting significantly more time being taken for ultrasound-guided cannulation versus the landmark technique (19, 21, 24). Number of attempts was reported by six of 10 studies (67%), with five of six studies (83%) reporting no difference in number of attempts (19, 21, 23, 24, 26), and one study reporting significantly fewer attempts with ultrasound guidance (25). Interstudy variability in the definition of time for attempts and number of attempts precluded pooled analysis.

Safety: Overall Frequency of Adverse Events

Seven of 10 studies (70%) reported on overall frequency of adverse events (3, 19, 21–24, 26), and for two studies the total frequency of complications could be tallied (25, 27). Ultrasound use was associated with a significant decrease in overall complications (OR, 0.531; 95% CI, 0.410–0.688; I^2 = 69.0%) (**Fig. 3*A***). Subgroup analysis of only studies using dynamic 2D ultrasound studies also demonstrated a significant reduction in overall complications (OR, 0.298; 95% CI, 0.202–0.439; I^2 = 52.2%) (**Fig. 3*B***).

Safety: Individual Complications

Six of 10 studies (60%) reported on prevalence of pneumothorax following attempts to cannulate the subclavian vein (19, 21, 23, 25–27). Metaanalysis revealed a significant difference between ultrasound guidance and landmark technique (OR, 0.339; 95% CI, 0.146–0.789; I^2 = 35.5%) (**Fig. 4*A***). Subgroup analysis of the five dynamic 2D ultrasound studies also demonstrated a significant reduction in pneumothorax with ultrasound use versus the landmark technique (OR, 0.277; 95% CI, 0.106–0.726; I^2 = 43.1%) (**Fig. 4*B***).

Six of 10 studies (60%) reported on inadvertent arterial puncture (19, 21, 23, 25–27). Metaanalysis revealed that ultrasound use significantly reduced inadvertent arterial puncture (OR, 0.341; 95% CI, 0.178–0.653; I^2 = 0.0%) (Fig. 4*A*). Subgroup analysis of the five studies that used dynamic 2D ultrasound also revealed a significant decrease in inadvertent arterial puncture (OR, 0.278; 95% CI, 0.119–0.651; I^2 = 0.0%) (Fig. 4*B*). Similarly, five of 10 studies (50%) reported on hematoma formation following subclavian catheterization. Ultrasound use significantly

TABLE 1. Overview of Study, Participants, Setting, Outcomes, and Operator Experience

Study	Year	Country of Origin	Ultrasound Type and Technique	Patient Population	No. of Participants		Outcomes Measured	Operator Experience
					Ultrasound	Landmark		
					Total (% Male)			
Oh et al (27)	2014	South Korea	2D ultrasound dynamic	Neurosurgical patients	33 66 (51%)	33	Success rate, pneumothorax, hemothorax, arterial puncture, malposition	NR
Campbell et al (20)	2011	United States	2D ultrasound dynamic	Emergency setting	NR 85 (NR)	NR	Success rate	Residents and staff physicians
Fragou et al (25)	2011	Greece	2D ultrasound dynamic	ICU	200 401 (52%)	201	Success rate, time to cannulation, number of attempts, pneumothorax, arterial bleeding, hematoma, hemothorax, cardiac tamponade, brachial plexus injury, phrenic nerve injury, malposition	Staff physicians, > 6 yr with central catheter placement
Alic et al (19)	2009	Turkey	2D ultrasound dynamic	ICU	35 70 (NR)	35	Success rate, success rate at 1st attempt, time to cannulation, number of attempts, total complications	One staff physician experienced in both techniques
Palepu et al (26)	2009	India	2D ultrasound dynamic	ICU	17 45 (57.8%)	28	Success rate, number of attempts, total complications, pneumothorax, arterial bleeding, hematoma, arterial puncture, malposition	Both < 6 yr experience and > 6 yr experience in anesthesia and critical care
Gualtieri et al (23)	1995	United States	2D ultrasound dynamic	ICU,	25 52 (NR)	27	Success rate, number of attempts, pneumothorax, arterial bleeding, hematoma, arterial puncture, malposition, air embolism, minor complications	First to second year postgraduate with < 30 central venous catheter placements
Mansfield et al (3)	1994	United States	2D ultrasound static	Oncology patients	411 821 (43%)	410	Success rate, total complications	Forty-nine physicians, ranging from surgical interns to staff
Bold et al (22)	1998	United States	Doppler—dynamic	High-risk oncology patients	121 242 (40.4%)	121	Success rate, total complications, hematoma, hemothorax, malposition	Surgical oncology fellows with 6–10 yr postgraduate experience
Lefrant et al (21)	1998	France	Doppler—dynamic	ICU	143 286 (59.8%)	143	Success rate, success of 1st attempt, time to cannulation, number of attempts, total complications, pneumothorax, arterial bleeding, arterial puncture, malposition	Staff anesthesiologist (not trained in Doppler prior to study)
Branger et al (24)	1995	France	Doppler—dynamic	Medical and surgical patients	50 100 (41%)	50	Success rate, time to cannulation, number of attempts, total complications	Fourteen junior (postgraduate < 5 yr clinical experience) and 8 senior (> 5 yr clinical experience)

NR = not reported.

TABLE 2. Characteristics of Ultrasound Technology and Technique Used in Individual Studies

Study	Ultrasound Technique	Ultrasound Machine	Transducer	Patient Positioning	Approach for Imaging	Axis of Imaging	Approach for Needle	Landmark Technique Approach
Oh et al (27)	Dynamic 2D	SonoSite S-nerve (SonoSite, Bothell, WA)	7.5-MHz high-resolution	Trendelenburg	NR	Longitudinal	NR	Infraclavicular
Campbell et al (20)	Dynamic 2D	NR	NR	NR	Infraclavicular	NR	NR	NR
Fragou et al (25)	Dynamic 2D	HD11 XE ultrasound Machine (Philips, Andover, MA)	7.5-MHz high-resolution	Trendelenburg	Infraclavicular	Longitudinal	In plane	Infraclavicular
Alic et al (19), 2009	Dynamic 2D	GE Logiq Book XP	5–13 MHz transducer	NR	NR	Longitudinal	In plane	NR
Palepu et al (26)	Dynamic 2D	SonoSite (Bothell, WA)	6–13 MHz, 38-mm linear-array transducer	Trendelenburg	Infraclavicular—middle third of the clavicle	Transverse	NR	Infraclavicular
Gualtieri et al (23)	Dynamic 2D	Site Rite (Dymax Corporation, Pittsburgh, PA)	7.5 MHz	Trendelenburg	Infraclavicular—lateral aspect of clavicle	Transverse	NR	Infraclavicular
Mansfield et al (3)	Static 2D	Model 633(Hitachi Aloka, Wallingford, CT)	7.5-MHz linear array	Trendelenburg	Infraclavicular	NR	NR	Infraclavicular
Bold et al (22)	Dynamic Doppler	Smart Needle (Peripheral Systems Group, Mountain View, CA)	14-MHz continuous-wave	NR	NR	NA	NR	Infraclavicular
Lefrant et al (21)	Dynamic Doppler	Pulsed Doppler system (Medical Biophysics Laboratory, Faculty of Medicine, Tours, France)	4-MHz pulsed single, circular	Trendelenburg	Infraclavicular	NA	Through probe indentation	Infraclavicular
Branger et al (24)	Dynamic Doppler	Pulsed Doppler system (Medical Biophysics Laboratory, Faculty of Medicine, Tours, France)	4 MHz pulsed, circular	Trendelenburg	Infraclavicular	NA	30° angulation to body of probe	Infraclavicular

NR = not reported, NA = not applicable.

TABLE 3. Risk of Bias Assessment of Included Studies

Study	Random Sequence Generation	Allocation Concealment	Blinding of Participant and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting
Oh et al (27)	Low	Low	NA	Unclear/NR	Low	Low
Campbell et al (20)	Unclear/NR	Unclear/NR	NA	Unclear/NR	Unclear/ NR	Low
Fragou et al (25)	Low	Unclear/NR	NA	Unclear/NR	Low	Low
Alic et al (19)	Low	Unclear/NR	NA	High	Low	Low
Palepu et al (26)	Low	Unclear/NR	NA	Unclear/NR	Low	Low
Gualtieri et al (23)	Low	Unclear/NR	NA	Unclear/NR	Low	Low
Mansfield et al (3)	Low	Unclear/NR	NA	High	Low	Low
Bold et al (22)	Low	Unclear/NR	NA	Unclear/NR	Low	Low
Lefrant et al (21)	Low	Unclear/NR	NA	Unclear/NR	Low	Low
Branger et al (24)	Low	Low	NA	High	Low	Low

NA = not applicable, NR = not reported.

reduced hematoma formation (OR, 0.351; 95% CI, 0.157–0.782; I^2 = 16.3%) (Fig. 4*A*). Subgroup analysis of the four studies that used dynamic 2D also demonstrated a significant decrease in hematoma with ultrasound use (OR, 0.307; 95% CI, 0.135–0.696; I^2 = 0.0%) (Fig. 4*B*).

Four of 10 studies (40%) reported on hemothorax, one used Doppler ultrasound (22), and three used dynamic 2D ultrasound (19, 25, 27). Metaanalysis demonstrated that ultrasound use significantly reduced hemothorax (OR, 0.235; 95% CI, 0.082–0.676; I^2 = 0.0%; dynamic ultrasound: OR, 0.245; 95% CI, 0.082–0.734; I^2 = 29.1%) (Fig. 4, *A* and *B*). One study described cardiac tamponade with a prevalence of one of 201 using the landmark technique and 0 of 200 using dynamic 2D ultrasound (25).

One study reported phrenic nerve injuries in three of 201 participants when the landmark technique was used compared with 0 of 200 when dynamic 2D ultrasound was used (25). In the same study, six of 201 participants experienced brachial plexus injuries with the landmark technique compared with 0 of 200 participants with dynamic 2D ultrasound (25). Long-term outcomes of these nerve injuries were not described.

Seven of 10 studies (70%) detailed catheter malposition following cannulation (19, 21–23, 25–27). Five of these reports used dynamic 2D ultrasound and two reports used Doppler ultrasound. Metaanalysis of these seven

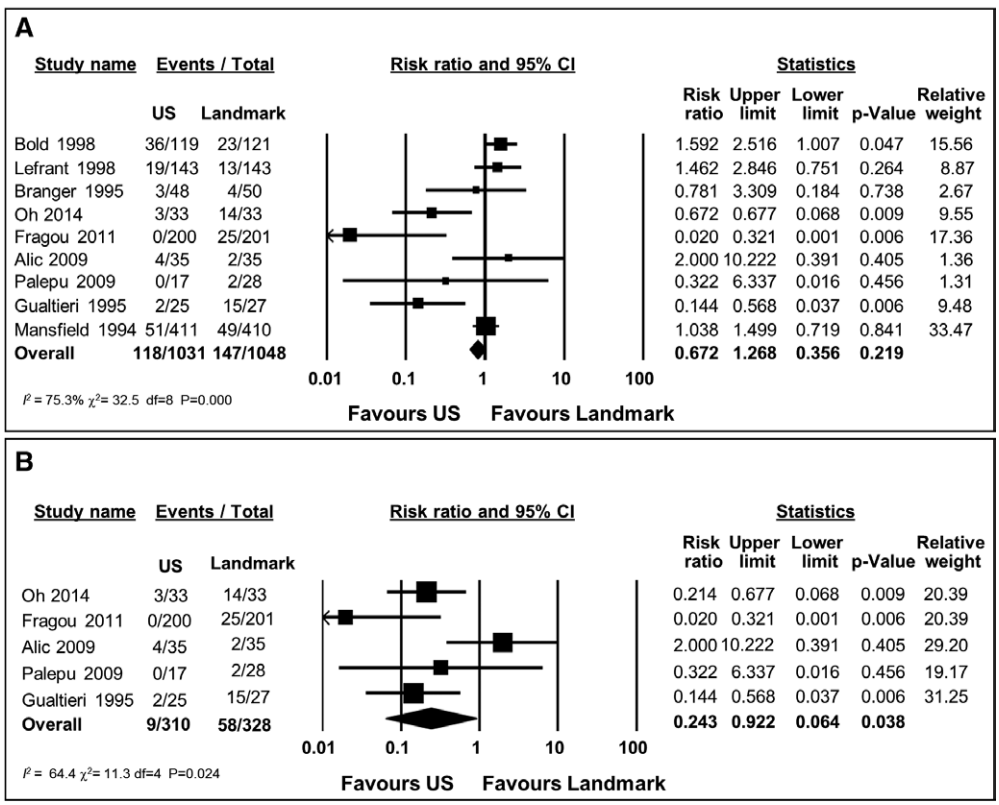

Figure 2. Forest plot of failed catheterization and method of subclavian vein catheterization. **A**, All studies that compared any method of ultrasound (US) vs. landmark technique. **B**, Subgroup analysis of studies that compared dynamic two-dimensional US vs. landmark technique. *Solid lines* denote 95% confidence intervals (CIs) of estimates for individual studies, *box sizes* denote the study weighting, and the *diamond* denotes the CI for the pooled analysis.

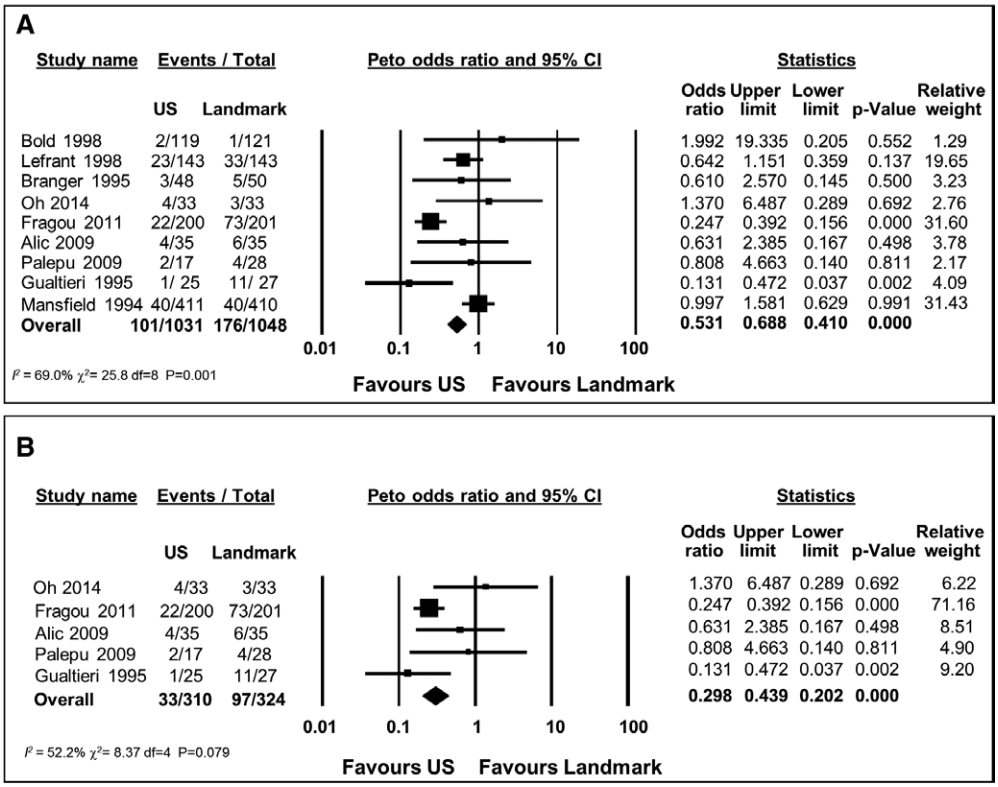

Figure 3. Forest plot of overall adverse events and method of subclavian vein catheterization. **A**, All studies that compared any method of ultrasound (US) vs. landmark technique. **B**, Subgroup analysis of studies that compared dynamic two-dimensional US vs. landmark technique. *Solid lines* denote 95% confidence intervals (CIs) of estimates for individual studies, *box sizes* denote the study weighting, and the *diamond* denotes the CI for the pooled analysis.

studies demonstrated no reduction in catheter malposition with ultrasound guidance (23, 25, 26) (OR, 0.651; 95% CI, 0.394–1.077; I^2 = 50.2%; dynamic ultrasound: OR, 0.846; 95% CI, 0.481–1.487; I^2 = 17.3%) (Fig. 4, *A* and *B*).

No studies reported on infection, thrombus, or arrhythmias. One study monitored for air embolism (23), an adverse event that we had not defined a priori in our review protocol. There were no air embolism events in either arm of this study. Long-term data were presented in one study with follow-up to 3 months following catheterization (25). No studies explicitly defined follow-up frequency for adverse events.

Small Study Effects

Inspection of a funnel plot constructed for the outcome of overall frequency of adverse events did not demonstrate small study effects (**Supplementary** Fig. 1, Supplemental Digital Content 4, http://links.lww.com/CCM/B241). There appeared to be no systematic underreporting of negative trials.

DISCUSSION

Our analysis including all forms of ultrasound (sonographic Doppler and 2D imaging, dynamic and static use) demonstrated that ultrasound significantly reduced overall adverse events associated with subclavian catheterization; however, the number of failed catheterizations compared to the landmark technique remained similar. Subgroup analysis of studies that used only dynamic 2D ultrasound demonstrated both a significant reduction in failed catheterizations and adverse events.

Our systematic review provides the first comprehensive analysis of ultrasound use for subclavian catheterization. We systematically searched a number of databases and focused on the best evidence available (randomized controlled trials). Ultrasound guidance is the standard of care for internal jugular vein catheterization in many centers, and its use is strongly recommended by clinical practice guidelines (8–10, 14, 25). Several metaanalyses have demonstrated that ultrasound use for internal jugular vein catheterization significantly decreased failed catheterization and reduced time for the procedure (4, 7, 12). Individual studies and clinical practice guidelines have suggested that ultrasound guidance may be beneficial for subclavian vein cannulation (9, 10). Our analysis demonstrated no difference in failed catheterization rates between landmark and ultrasound use; however, subgroup of analysis of dynamic 2D ultrasound guidance did demonstrate a significant reduction in failed catheterizations with ultrasound use.

Although this is the first synthesized evidence of a significant decrease in failed catheterizations with dynamic 2D ultrasound guidance, these results should be interpreted with caution. There was an overall low event rate in studies using dynamic 2D ultrasound (67 failed catheterizations, of which nine occurred in participants allocated to 2D ultrasound). As well, heterogeneity existed in patient populations and clinical settings studied. Variations also existed in operator experience and ultrasound approach. Finally, definitions for failed catheterizations were variably defined. We attempted to circumvent this issue by reporting only on complete failure to catheterize, regardless of number of attempts or number of operators.

Our analysis revealed that dynamic ultrasound for subclavian cannulation decreased adverse events including, inadvertent arterial puncture, pneumothorax, hematoma, and overall complications. Although these adverse events are relatively rare, they are clinically significant and some are potentially life-threatening. Since these adverse events are all related to inadvertent placement of the needle into surrounding structures, it is likely that ultrasound helps clarify the position of the needle relative to these structures (22). Although there are barriers to uniformly

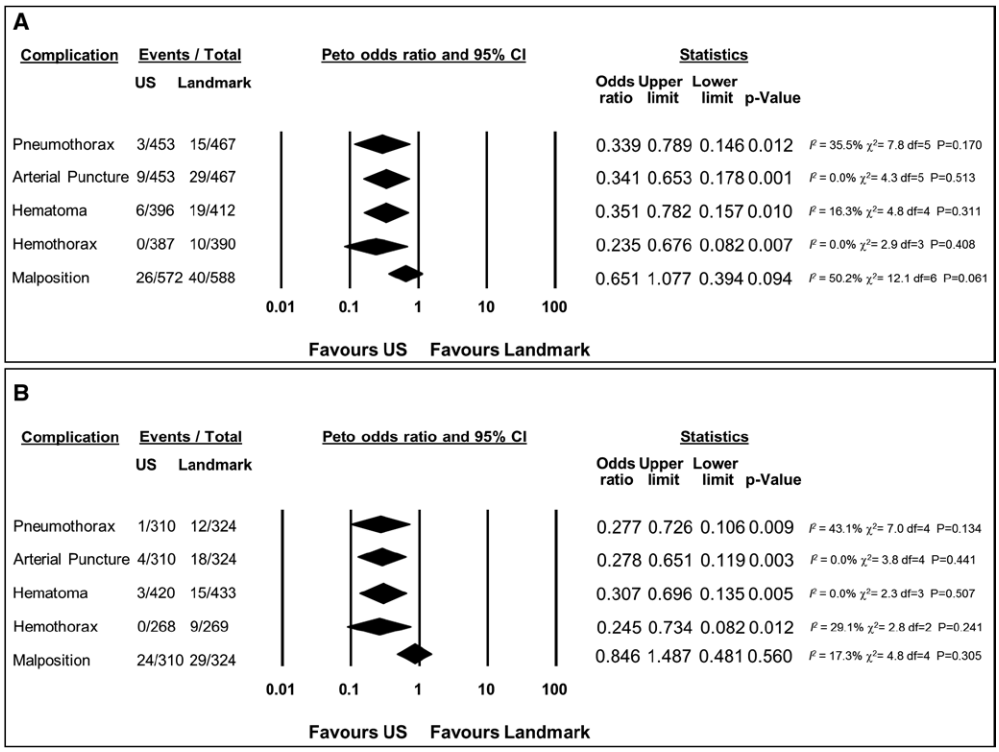

Figure 4. Forest plot of individual complications and method of subclavian vein catheterization. **A**, All studies that compared any method of ultrasound (US) vs. landmark technique. **B**, Subgroup analysis of studies that compared dynamic two-dimensional US vs. landmark technique. *Diamonds* denote the confidence interval (CI) for the pooled analysis of each adverse event.

implementing ultrasound use (e.g., funding to purchase the technology and training to increase proficiency and decrease time for cannulation), given the rates of mechanical complications associated with subclavian cannulation (3), our data suggesting a 50% reduction in overall adverse events would support the routine use of dynamic 2D ultrasound for this procedure.

Limitations

The primary limitation of our analysis is the small number of studies that met eligibility criteria. There have been a limited number of randomized controlled trials of variable methodological quality that have addressed ultrasound use for subclavian catheterization. As such our findings should be interpreted with caution.

Our analysis of adverse events was also limited by variable reporting. No studies reported on infection, thrombus, or arrhythmias; only one study reported on air embolism, cardiac tamponade, and nerve injuries. This was somewhat surprising given that many of these adverse events could be expected from subclavian catheterization; this could represent selective reporting or a failure to screen for these outcomes (28). Alternatively, these particular adverse events may be independent of the insertion technique; however, future studies will need to investigate this. For adverse events that were reported, there were inconsistent a priori definitions, variable grading of events (i.e., no distinction between serious vs nonserious), no formal categorization of events (i.e., expected vs unexpected), and variable duration of follow-up. As well, it was unclear in many studies whether more than one adverse event was included per patient; this may have led to an analysis of nonindependent events. Future studies of ultrasound-guided subclavian catheterization should consider incorporating guidelines for better reporting of adverse events (25).

The patient populations and clinical settings varied in the included studies from stable patients seen in clinics (21) to critically ill patients in the ICU (25). Similarly, experience of the operators varied significantly from inexperienced resident physicians (23) to experienced senior staff physicians (25). Given the small number of studies, further subgroup analyses were not performed. Of note, the largest included dynamic 2D ultrasound was one of the most recent published and demonstrated the largest effect sizes (25). These outcomes may reflect the more recent ultrasound technology being used as well as the use of senior ICU physicians as operators. Future studies will need to identify which patient populations and operators benefit the greatest from ultrasound use for subclavian catheterization.

CONCLUSIONS

Our systematic review provides the largest synthesized dataset for patients undergoing ultrasound-guided subclavian cannulation. Our results suggest that dynamic 2D ultrasound use may reduce failed catheterizations and adverse events associated with subclavian catheterization. Given the heterogeneity of the data, there is a need for more well-designed randomized controlled trials to provide a solid evidence base for future updates of clinical practice guidelines (9, 14, 15).

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