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Central venous catheter-related infections: a systematic review, meta-analysis, trial sequential analysis and meta-regression comparing ultrasound guidance and landmark technique for insertion

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Abstract

Background During central venous catheterization (CVC), ultrasound (US) guidance has been shown to reduce mechanical complications and increase success rates compared to the anatomical landmark (AL) technique. However, the impact of US guidance on catheter-related infections remains controversial. This systematic review and meta-analysis aimed to compare the risk of catheter-related infection with US-guided CVC versus AL technique.

Methods A systematic search on MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), and Web of Science databases was conducted until July 31, 2024. Randomized controlled trials (RCTs) and non-randomized studies of intervention (NRSI) comparing US-guided versus AL-guided CVC placement were included. The primary outcome was a composite outcome including all types of catheter-related infection: catheter-related bloodstream infections (CRBSIs), central line-associated bloodstream infections (CLABSIs), catheter colonization, or any other type of reported infection. The secondary outcomes included individual infection types and mortality at day-28. Subgroup analyses based on study type and operator experience were also performed.

Results Pooling twelve studies (8 RCTs and 4 NRSI), with a total of 5,092 CVC procedures (2072 US-guided and 3020 AL-guided), US-guided CVC was associated with a significant reduction in catheter-related infections compared with the AL technique (risk ratio (RR) = 0.68, 95% confidence interval (CI) 0.53–0.88). In the RCT subgroup, the pooled RR was 0.65 (95% CI 0.49–0.87). This effect was more pronounced in procedures performed by experienced operators (RR = 0.60, 95% CI 0.41–0.89). In inexperienced operators, the infection risk reduction was not statistically significant. The pooled analysis of CRBSIs and CLABSIs also favored US guidance (RR = 0.65, 95% CI 0.48–0.87).

Conclusion US-guided CVC placement significantly reduces the risk of catheter-related infections compared to the AL technique, particularly when performed by experienced operators.

Trial registration PROSPERO CRD42022350884. Registered 13 August 2022.

Keywords Central venous catheterization, Ultrasound guidance, Catheter-related bloodstream infection, Meta-analysis

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Introduction

Nearly three-quarters of patients admitted to intensive care units (ICUs) require central venous catheterization (CVC) [1], for various clinical indications, including hemodynamic monitoring, medication administration (vasopressors, venotoxic drugs), fluid resuscitation, repeated blood sampling and parenteral nutrition [2]. Ultrasound (US) guidance for CVC has been extensively studied over the last two decades [3–5], and is now recommended for all puncture sites in numerous international guidelines [1, 6–8]. Indeed, US guidance decreases immediate mechanical complications, puncture attempts, shortens the CVC procedure, and improves both overall and first-time success rates [4, 5, 8], when compared to the traditional anatomical landmark (AL) puncture technique. However, US-guidance remains underutilized, being used in 36–68% of insertions (less than 30% of cases for the subclavian site). [9–11]

While the benefits of US guidance in reducing immediate complications and enhancing puncture quality are well-established, its effect on the incidence of infectious complications remains debated, as conflicting results have been reported. Buetti et al. (2020) [12] conducted a post-hoc analysis of three large French randomized controlled trials (RCTs) and suggested a potentially increased incidence of catheter-related bloodstream infections (CRBSI) with US guidance compared to insertion using AL (hazard ratio (HR) of 2.21 (95% confidence interval (CI), 1.17–4.16, $p=0.01$)). The authors hypothesized that a higher risk of asepsis errors related to the handling of US equipment may increase the risk of infectious complications. However, no definitive conclusion could be drawn as the studies included in this post hoc analysis were not randomized based on the use of US guidance. Conversely, Takeshita et al. (2020) [13] conducted a meta-analysis that found no significant difference in the incidence of CRBSI between AL and US-guided punctures. This analysis included only four RCTs [14–17], extracted from two databases, of which two reported a significant reduction in CRBSI associated with US guidance [15, 17]. Finally, an observational retrospective study (n = 220) found significant less catheter-related infections associated with US-guided CVC (0% versus 19.3%, $p=0.002$). [18]

Given the conflicting evidence, there is a clear need for an updated systematic review and meta-analysis to elucidate the impact of US guidance on the risk of infectious complications in CVC. This systematic review and meta-analysis aims to synthesize data from a broader range of studies, including both RCTs and Non-Randomized Studies of Intervention (NRSI). The objective is to provide more definitive insights into whether US guidance alters the infectious risk compared to the traditional AL technique.

Methods

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines [19]. The meta-analysis protocol was prospectively registered on the PROSPERO register of systematic reviews (CRD42022350884).

Search strategy

Studies were selected from three databases, until July 31, 2024: MEDLINE (via PubMed), the Cochrane Central Register of Controlled Trials (CENTRAL), and Web of Science. The search strategy is described in detail in the supplementary material (Appendix 1).

Selection criteria

We searched for RCTs and prospective NRSI, comparing AL and US-guided techniques for CVC placement, and reporting infectious complications. We included all studies of short-term catheters in adult populations (age ≥ 18 years), with no other restriction regarding population characteristics, study setting (ICU, operating room, emergency department), central venous catheterization site, or inserter experience. We included articles with no restriction on publication date, published and unpublished studies, and restricted to Latin alphabet languages.

The following studies were not included: pediatric population (age < 18 years), long-term catheters (peripherally inserted central catheter, tunneled and/or cuffed CVC, long-term dialysis catheters, and totally implantable devices), and non-prospective interventional studies (e.g., historical control group).

Outcomes

The primary outcome was a composite outcome including all types of catheter-related infection: catheter-related bloodstream infections (CRBSIs), central line-associated bloodstream infections (CLABSIs), catheter colonization, or any other type of reported infection. The CRBSIs, CLABSIs and catheter colonization were defined according to the Centers for Disease Control and Prevention (CDC) [20–22] and the Infectious Diseases Society of

America (IDSA) [23]. Outcomes that did not meet these definitions were classified as "undefined infections".

Secondary outcomes included each component of the composite outcome alone (CRBSIs, CLABSIs, and catheter colonization), and mortality rate at day 28. CRBSIs and CLABSIs were also evaluated together, in a composite secondary endpoint.

Data collection and quality assessment

Two authors (NB, JP) independently screened the titles and abstracts, determined the eligibility of the manuscripts according to the inclusion and exclusion criteria, extracted data, and assessed the risk of bias using the Cochrane Risk of Bias 2 (RoB 2) tool for RCTs [24], and the Cochrane Risk Of Bias In Non-Randomized Studies—of Interventions (ROBINS-I) tool for NRSI [25]. Any disagreements were resolved through discussion until a consensus was reached. The risk-of-bias plots were created with *robvis* tool [26]. Data were entered into an Excel database, specifically designed for this review.

Publication bias

Publication bias was assessed by searching studies that had been registered on ClinicalTrials.gov and World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) but had not been published. Publication bias was also evaluated graphically using a Funnel plot (plot of treatment effect against trial precision).

Data analyses

The percentage of total variation across studies arising from heterogeneity rather than chance (statistical heterogeneity) was estimated by the Q-Cochrane heterogeneity test (Q statistic with degree of freedom (df) and the I [2] statistic [19]. The weighted treatment effect was calculated across trials. The true effect size was estimated calculating risk ratio (RR) and corresponding 95% confidence intervals (CIs). A random-effect model was performed.

Additionally, we performed a leave-one-out analysis where we excluded each study in turn and then performed a pairwise meta-analysis on the remaining studies to detect potential outliers [27].

Then, we conducted a cumulative meta-analysis according to publication year, by updating the pooled risk ratio each time a result of a new trial was published for the primary outcome, as described before [28]. This statistical method is used to detect the dynamic trend of the association result or further stabilize the meta-analysis conclusion. Additionally, we carried out a meta-regression to determine the effect of time (assessed by the year of publication, independent variable) on the primary outcome (dependent variable) [29].

We used trial sequential analysis (TSA) to assess the risk of random errors due to sparse data and to calculate the required information size [28, 30]. The required information size considers the event rate in the control group, the heterogeneity variance (D2), and the assumption of a relative risk reduction (RRR). We selected an alpha risk of 5%, a beta risk of 10%, and a D2 as suggested by the trials. We used a realistic a priori RRR of 10% [30]. A random pooled effect model was performed using DerSimonian-Laird estimator.

We decided a priori to perform subgroup analyses, based on study design (RCT and NRSI), and on inserter experience, divided into three groups, according to the information reported in the studies: experienced, inexperienced and unknown. The "experienced" group had at least 1 year's training in US-guided CVC followed by 3-years of continuous practice, or at least 20 procedures performed, or were defined as experienced in the studies. The "inexperienced" group corresponded to operators who did not meet these criteria. The "unknown" group corresponded to operators for whom no information was available.

All tests were two-sided and p values less than 0.05 were considered statistically significant.

Data were analyzed using R software (version 4.3.1).

Results

Study selection

We identified 5661 articles through the three databases using the search strategy. 414 citations were excluded because of duplications. After assessing the title and abstract, 96 full-text articles were assessed for eligibility, and 12 studies were included in the qualitative

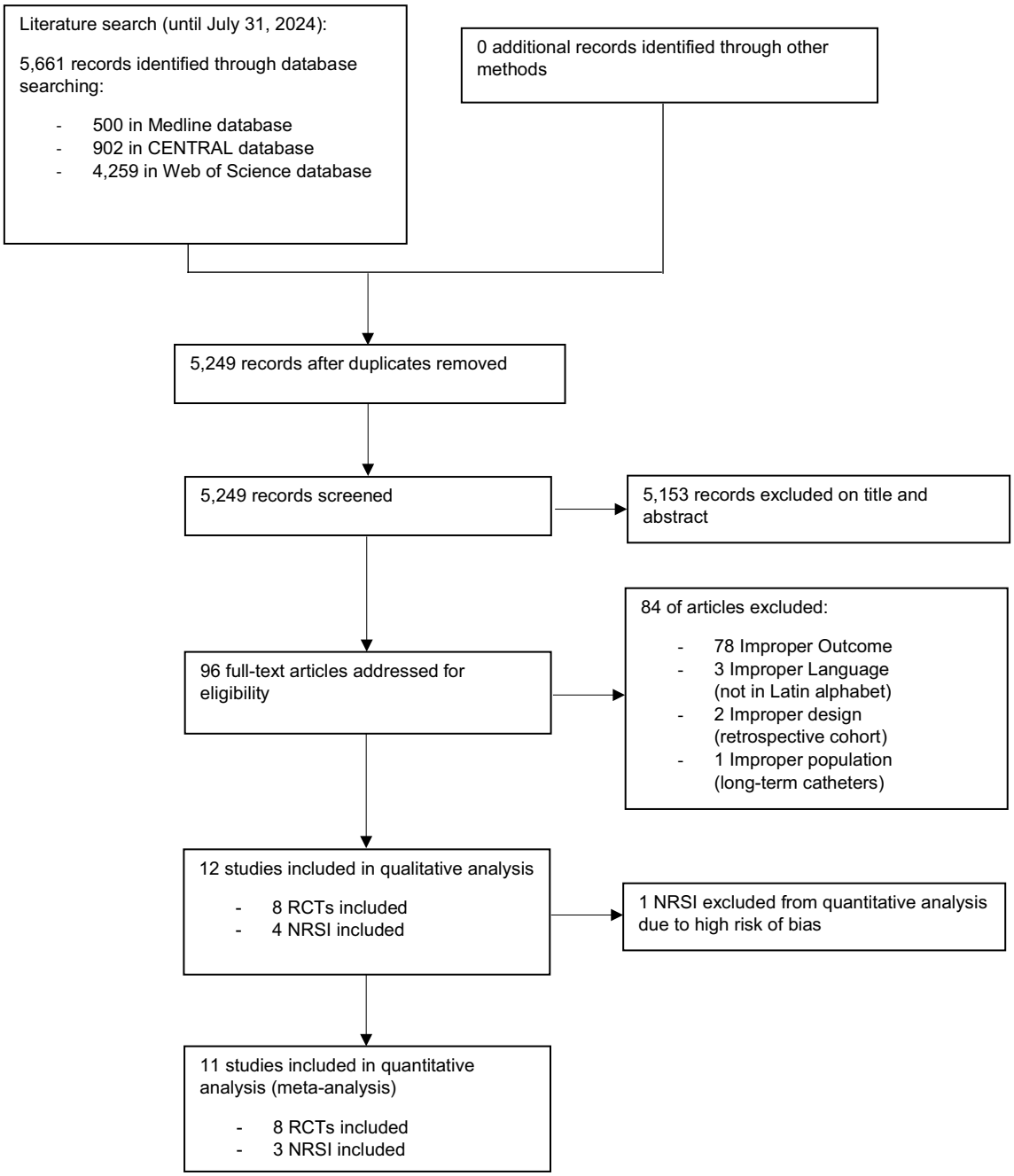

Fig. 1 Flow chart of the study *NRSI* non-randomized studies of intervention, *RCTs* randomized controlled studies

analysis (8 RCTs [14–17, 31–34], and 4 NRSI [35–38]). The Fig. 1 shows the study flow chart.

Studies characteristics (Tables 1, 2, S1, S2)

The twelve included studies [14–17, 31–38] involved 5092 procedures: 2072 (40.7%) US-guided and 3020 (59.3%) AL techniques. Catheter sites were internal jugular vein (n = 4112, 80.8%), subclavian vein (n = 821, 16.1%), and femoral vein (n = 159, 3.1%). Studies were

Table 1 Main characteristics of included study: Randomized controlled trials

Study	Country	Center (s)	Study setting	Number of procedures (n =)	Age (mean ± SD)	Gender = male (n (%))	BMI (kg/m^2) (mean ± SD)	Mechanical ventilation (n(%))	Punctured vessel(s) (n(%))	Puncture side = right (n, %)	Operator (s)	Outcome (s)
Slama [33]	France	1	ICU	79 US = 37 AL = 42	US = 65 ± 17 AL = 66 ± 16	US = 24 (65%) AL = 29 (69%)	NA	US = 14 (37%) AL = 14 (33%)	IJV = 79 (100%)	US = 37 (100%) AL = 42 (100%)	Unknown number, Inexperienced	Undefined infection
Karakitsos [17]	Greece	1	ICU	900 US = 450 AL = 450	US = 58.3 ± 10.3 AL = 59 ± 9.5	US = 252 (56%) AL = 270 (60%)	US = 24.1 ± 5.3 AL = 23.7 ± 5.9	US = 450 (100%) AL = 450 (100%)	IJV = 900 (100%)	US = 228 (50.7%) AL = 232 (51.6%)	56, Experienced	CRBSIs
Shrestha [32]	Nepal	1	ICU	120 US = 60 AL = 60	US = 39 ± 15 AL = 38 ± 15	US = 31 (51.7%) AL = 27 (45%)	NA	US = 26 (43%) AL = 28 (47%)	IJV = 120 (100%)	US = 60 (100%) AL = 60 (100%)	NA	Undefined infection
Airapetian [16]	France	1	ICU	74 US = 36 AL = 38	US = 63 ± 15 AL = 67 ± 16	US: 26 (72.2%) AL: 28 (63.6%)	US: 25 ± 6 AL: 28 ± 6	US = 22 (61%) AL = 29 (76%)	US: IJV = 21 (58%) FV = 15 (42%) AL: IJV = 28 (74%) FV = 10 (26%)	NA	10, Inexperienced	Undefined infection, catheter colonization
Gok [15]	Turkey	1	ICU	194 US = 97 AL = 97	US = 48.9 ± 21.9 AL = 51.8 ± 21.3	US = 47 (48.5%) AL = 45 (46.4%)	US = 27.4 ± 6.2 AL = 26.0 ± 5.1	US = 97 (100%) AL = 97 (100%)	IJV = 194 (100%)	US = 63 (64.9%) AL = 72 (74.2%)	1, Experienced	CRBSIs
Dolu [14]	Turkey	1	Operating room	100 US = 50 AL = 50	US = 53.6 ± 5.8; AL = 53.2 ± 9.10	US = 32 (64%) AL = 33 (66%)	US = 25.7 ± 2.6 AL = 26.6 ± 3.7	NA	IJV = 100 (100%)	US = 20 (40%) AL = 24 (48%)	4, Experienced	Undefined infection
Marín-Rodríguez [31]	Venezuela	1	Emergency Department	276 US = 138 AL = 138	US = 57.8 ± 9.5 AL = 56.2 ± 9.0	US = 77 (55.8%) AL = 83 (60.1%)	US = 25.1 ± 8.4 AL = 25.9 ± 8,5	NA	US: IJV = 52 (37.7%) SV = 86 (62.3%) AL: IJV = 47 (34.1%) SV = 91 (65.9%)	US = 66 (47.8%) AL = 63 (45.7%)	NA	Undefined infection
Ramesh [34]	India	1	Operating Room	90 US = 45 AL = 45	US = 42.6 ± 13.3 AL = 45.1 ± 13.6	US = 19 (42.2%) AL = 25 (55.6%)	US = 23.9 ± 1.2 AL = 23.4 ± 1.7	US = 45 (100%) AL = 45 (100%)	IJV = 90 (100%)	US = 45 (100%) AL = 45 (100%)	Unknown number, Experienced	CRBSIs

AL anatomical landmark, *BMI* body mass index, *CRBSIs* catheter-related bloodstream infections, *FV* femoral vein, *ICU* intensive care unit, *IJV* internal jugular vein, *NA* not available, *SD* standard deviation, *SV* subclavian vein, *US* ultrasound

Table 2 Main characteristics of included study: prospective non-randomized studies of intervention

Study	Country	Center(s)	Study setting	Number of procedures (n =)	Age	Gender = male (n, %)	BMI (kg/m^2)	Mechanical ventilation	Punctured Vessel(s)	Puncture side = right (n, %)	Operator(s) number and experience	Outcome(s)
Hrics [38]	USA	2	Emergency Department	40 US = 32 AL = 8	NA	NA	NA	NA	IJV = 40 (100%)	NA	16, Inexperienced	Undefined infection
Lin [37]	Taiwan	1	Nephrology	190 US = 104 AL = 86	*Mean* ± *SD*: US = 60 ± 16.2 AL = 64.9 ± 14.4	US = 68 (65.4%) AL = 56 (65.1%)	NA	NA	IJV = 190 (100%)	US = 69 (66.3%) AL = 55 (64%)	Unknown number, Inexperienced	Undefined infection
Farré [36]	Spain	1	Operating Room, ICU	546 US = 179 AL = 367	NA	NA	NA	NA	IJV* = 381 (69.8%) SV* = 163 (29.9%) FV* = 2 (0.4%)	NA	NA	CRBSIs
Cartier [35]	Switzerland	1	ICU or ACU	2,483 US = 844 AL = 1639	*Median (IQR)*: US = 65 (51–75) AL = 62 (49–73)	US = 472 (57.1%) AL = 872 (58.7%)	NA	NA	US: IJV = 781 (92.5%) FV = 32 (3.8%) SV = 31 (3.7%) AL: IJV = 1,089 (66.4%) FV = 100 (6.1%) SV = 450 (27.5%)	NA	NA	CLABSIs

ACU acute care unit, *AL* anatomical landmark, *BMI* body mass index, *CLABSIs* central line-associated bloodstream infections, *CLABSIs* central-line associated bloodstream infections, *CRBSIs* catheter-related bloodstream infections, *FV* femoral vein, *ICU* intensive care unit, *IJV* internal jugular vein, *NA* not available, *SD* standard deviation, *SV* subclavian vein, *US* ultrasound

*No distribution details for each arm, but non-statistically significant difference between the 2 groups

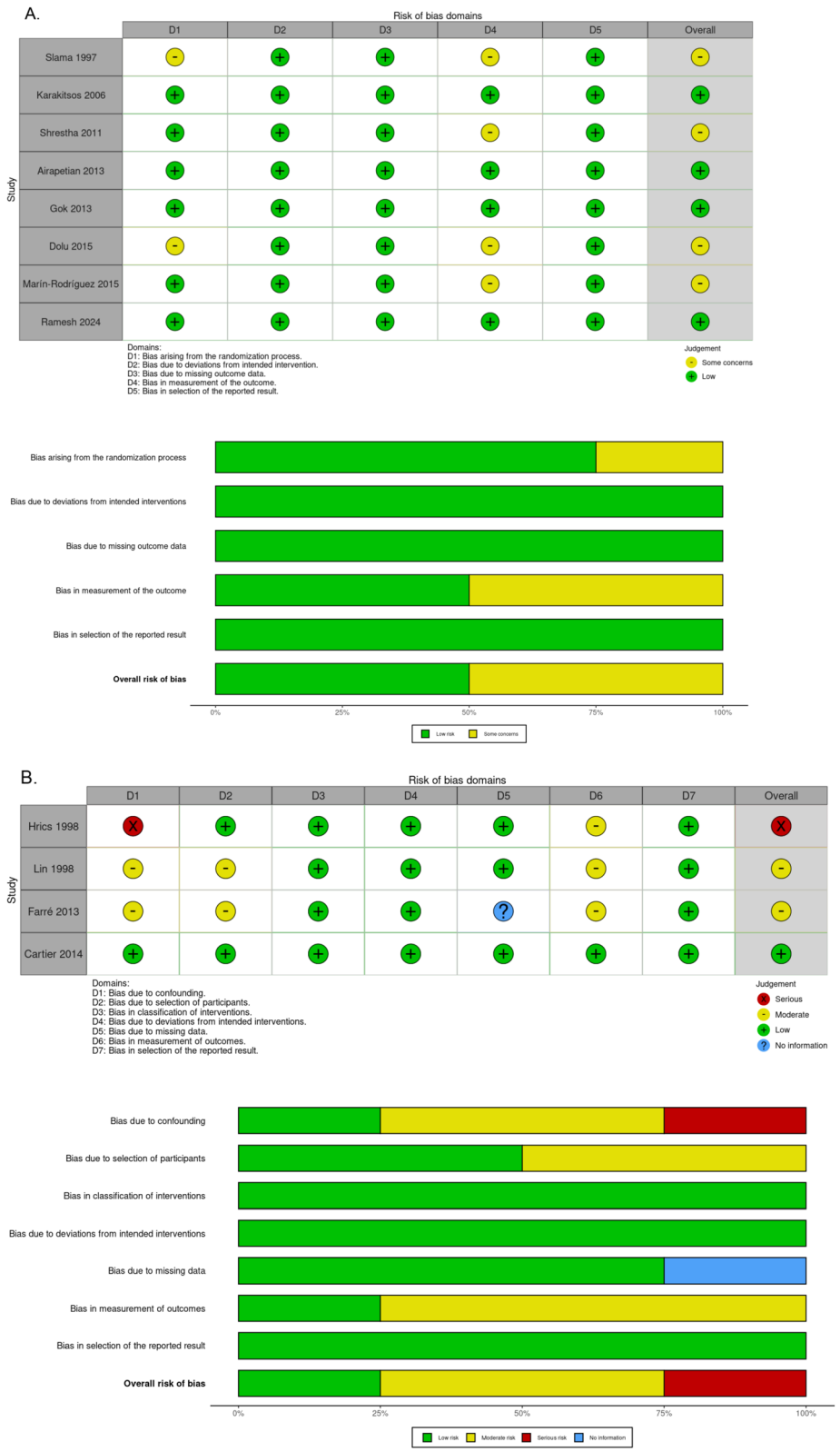

Fig. 2 Assessment of risk of bias. **A** Randomized controlled trials. **B** Non-Randomized Studies of Intervention

undertaken in 10 different countries, in a range of clinical settings (ICU, operating room, emergency department, nephrology, acute care unit), and all except one [38] were single-centered. One RCT [15] and one NRSI [36] reported CRBSIs as the primary outcome. One NRSI reported CLABSI as primary outcome. Microbiological data from two studies [15, 17] are presented in Table S2.

Risk of bias of included studies (Fig. 2)

The eight RCTs [14–17, 31–34] were categorized as low to moderate risk of bias with some deficits in randomization and outcome measurement. One NRSI was excluded from the quantitative analysis due to a serious risk of bias due to confounding [38], whereas the three others [35–37] were categorized as having low to moderate risk of bias. In the absence of funnel plot asymmetry, there is no evidence of publication bias (Figure S1).

Primary outcome: composite outcome of all types of catheter-related infection

The eleven studies [14–17, 31–37] included in the quantitative analysis reported the primary outcome. The

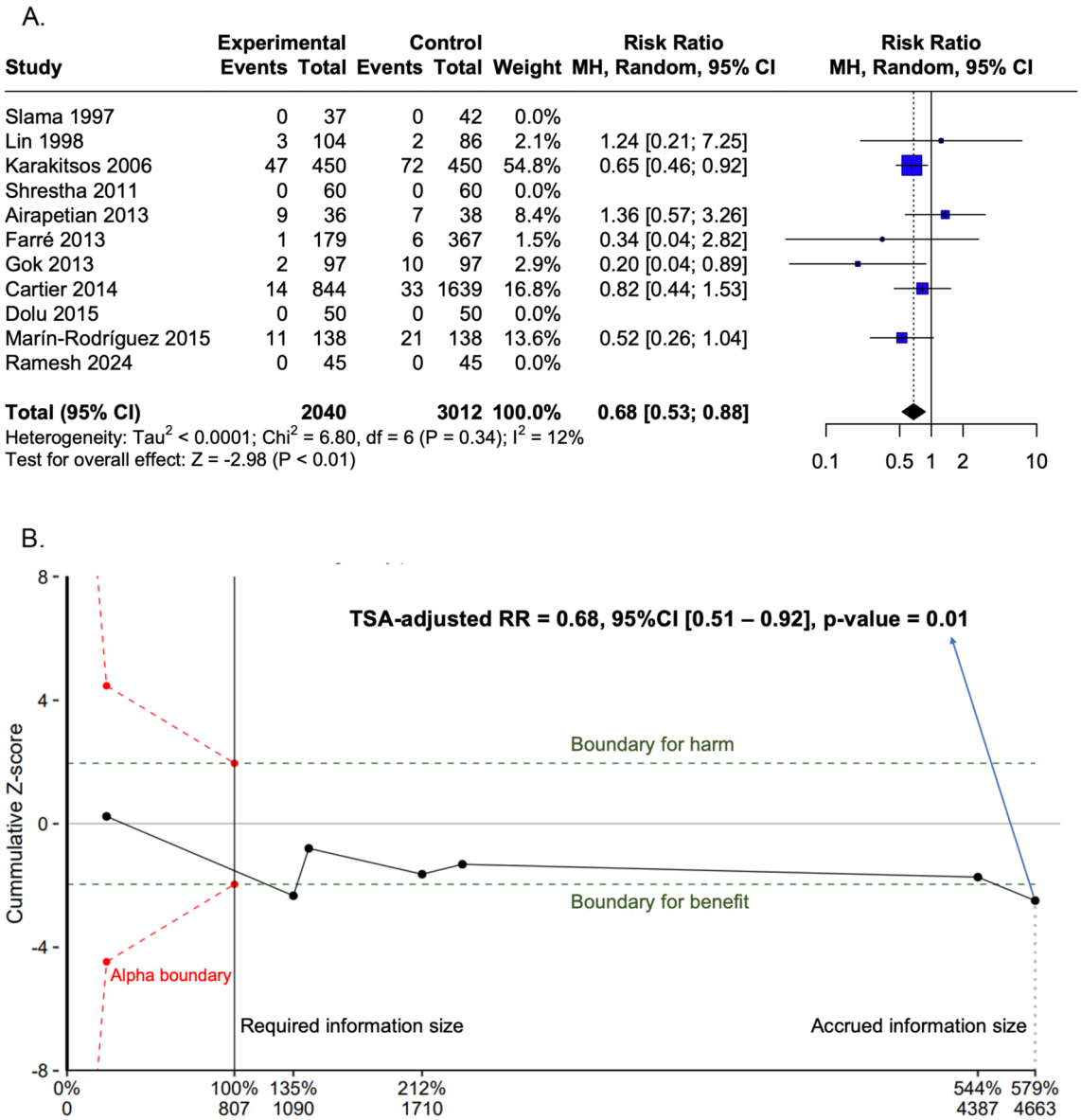

Fig. 3 **A** Forest plot comparing the incidence of central venous catheter infections (composite outcome) between ultrasound-guided versus anatomical landmark technique. **B** Trial Sequential Analysis

pooled RR across all studies was 0.68 (95% CI 0.53–0.88, $p<0.01$), indicating a significant reduction in catheter-related infections with US-guided CVC versus AL technique (Fig. 3A). There was no significant heterogeneity for this outcome (df = 6, $p=0.34$). The corresponding I [2] statistic was 12%.

A cumulative meta-analysis and a meta-regression were performed to assess the effect of time on the primary outcome (Figures S2, S3). No significant difference of risk ratio over time was observed in all types of catheter-related infections ($p=0.76$ in meta-regression).

The forest plot of the leave-one-out sensitivity analysis (Figure S4) did not show any outlier.

TSA showed that the required information size to conclude was of 807 patients, and the accrued information size was of 4663 patients (Fig. 3B). The TSA-adjusted RR was of 0.68 (95% CI 0.51–0.92, $p=0.01$), indicating a significant reduction in catheter-related infections with US-guided CVC versus AL technique.

A preplanned subgroup analysis according to the type of study (RCT or NRSI) was conducted (Table S3). In the RCT subgroup, the pooled RR was 0.65 (95% CI 0.49–0.87, $p<0.01$). In the NRSI subgroup, the pooled RR was 0.81 (95% CI 0.46–1.42, $p=0.45$). There was no significant interaction highlight between these two subgroups ($p=0.50$).

A preplanned subgroup analysis was performed according to operators' experience (Fig. 4, Table S4). In the experienced group, the pooled RR across all studies was 0.60 (95% CI 0.41–0.89, $p=0.01$), indicating a significant reduction in infectious complications with US-guided CVC versus AL technique in this subgroup. In the inexperienced and in the unknown experience subgroups, the pooled RR were not statistically significant (RR = 1.33, 95% CI 0.60–2.97, $p=0.48$, and RR = 0.65, 95% CI 0.41–1.04, $p=0.07$, respectively).

Secondary outcomes

One NRSI [35] reported CLABSI, with no significant difference observed between the US and AL techniques (RR = 0.82; 95% CI 0.44–1.53, $p=0.73$) (Figure S5).

Four studies [15, 17, 34, 36] (3 RCTs, 1 NRSI) reported CRBSI, with a pooled RR of 0.47 (95% CI 0.21–1.05, $p=0.06$), indicating no significant difference in CRBSI risk (Figure S5).

The pooled RR of studies reporting CLABSI and CRBSI was 0.65 (95% CI 0.48–0.87, $p=0.003$), indicating a statistically significant reduction with US-guided CVC when compared to AL technique (Figure S5).

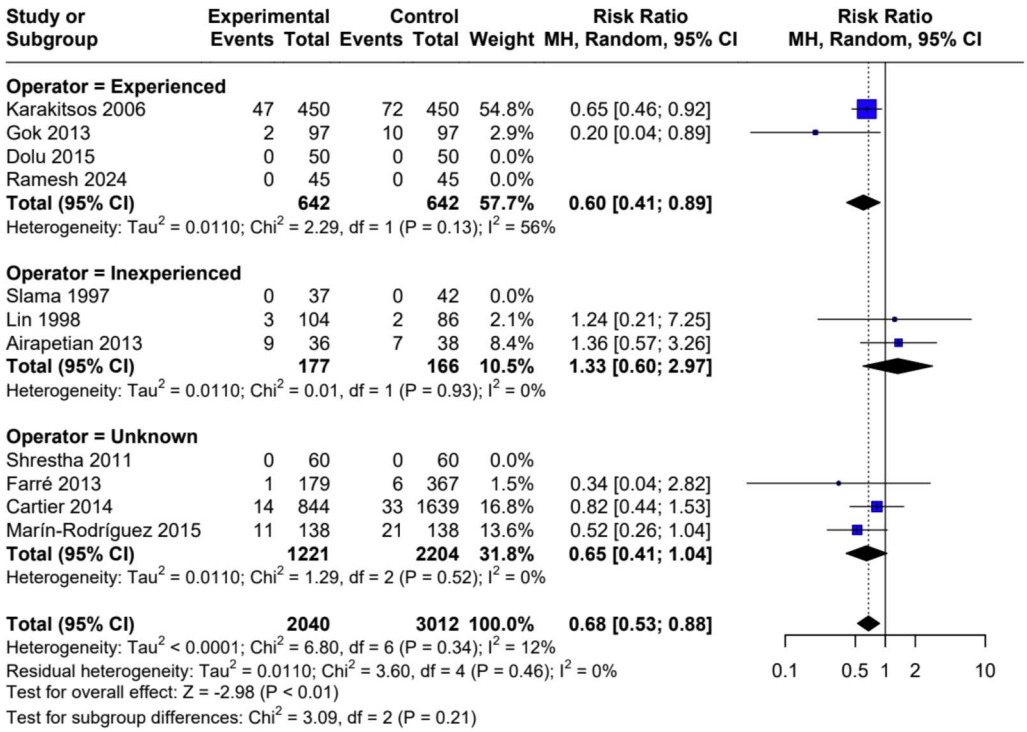

Fig. 4 Forest plot comparing the incidence of central venous catheter infections (composite outcome) between ultrasound-guided versus anatomical landmark technique, according to the operators' experience

One RCT [16] reported catheter colonization, with RR of 1.36 (95% CI 0.57–3.26, $p=0.49$), indicating no significant difference in colonization (Figure S6).

One NRSI [35] reported mortality at day 28, with an RR of 0.69 (95% CI 0.53–0.90, $p=0.0056$), indicating a statistically significant reduction in mortality risk (Figure S7).

Discussion

This systematic review, meta-analysis, trial sequential analysis and meta-regression, which included both RCTs and NRSI, demonstrated that US-guided CVC is associated with a statistically significant reduction of catheter-related infections, compared with the AL puncture technique (RR = 0.68, 95% CI 0.53–0.88). The preplanned subgroup analysis showed that US-guided CVC significantly reduced catheter-related infections when the procedures were performed by experienced operators (RR = 0.60, 95% CI 0.41–0.89), whereas no significant benefit was observed in inexperienced operators. The secondary outcomes further supported our primary findings. While individual analyses of studies measuring CRBSI or CLABSI alone did not reach statistical significance, the pooled analysis of these outcomes (composite secondary outcome) demonstrated a significant reduction of CLABSI or CRBSI with US-guided CVC (RR = 0.65, 95% CI 0.48–0.87). This suggests that US guidance consistently reduces the risk of serious catheter-related infections, although individual studies may be underpowered to detect these differences independently.

All of these findings provide important insights into the ongoing debate surrounding the optimal method of CVC placement [2]. They are consistent with prior studies suggesting that the US guidance minimizes the risk of catheter-related infections, due to fewer skin punctures, fewer risk of hematoma and reduced procedure time, which likely decrease the opportunity for microbial contamination [15, 18]. However, a previous meta-analysis of Takeshita et al. (2022) [13] showed no statistically significant difference in CRBSIs between US-guided and AL puncture in CVC. It should be noted that there were several important differences between their study and the present study. The selection process of the present meta-analysis was much wider, including an additional third database, and not restrict to the English language in the selection of articles, as recommended in PRISMA guidelines [19]. Furthermore, as the number of studies included in their systematic review and meta-analysis was low (four RCTs), we decided to expand the included studies to prospective NRSI. The inclusion of NRSI, following to strict guidelines [39], can provide very valuable information, particularly concerning rare events or adverse effects.

In the present study, the operator experience emerged as a critical factor influencing all types of catheter-related infections, likely due to better infection prevention measures and technique. Given the lack of significance in the primary outcome in the inexperienced operators subgroup, and the lack of interaction between the three subsets (experienced, inexperienced, and unknown), two hypotheses can be formulated. The first one is that there is no difference between the three subgroups, but the unknown and inexperienced groups suffer from a lack of statistical power. The second one is that the statistical difference found in the overall sample is driven by a large effect in the experienced operators, while US-guidance is not influential in the inexperienced operators. This would imply that US guidance may reduce the infectious complications of CVC, in proportion to the operator's level of experience. As well as its role in reducing mechanical complications [40], our study underscores the importance of adequate training and proficiency in US-guided techniques to achieve optimal outcomes [41]. It should also be noted that 2 out of 3 studies conducted in controlled environments, such as operating rooms, reported no catheter-related infections, regardless of the technique used. Thus, the most significant benefits of US-guided CVC insertion might be realized in environments where maintaining strict sterile techniques is challenging.

Our study has several strengths. The present systematic review and meta-analysis has a large sample size, including 5,092 procedures, and the results were deemed robust in TSA, which allowed to reach a high level of certainty. Then, the cumulative meta-analysis (Figure S2) and the meta-regression (Figure S3) led to conclude that there was no dynamic trend of the association result. However, the graphical evolution we have observed, represented by the regression line, suggests that there may be an evolution of the effect in favor of US guidance over time, but not statistically significant with this sample of studies. This hypothesis may be linked to the improvement of CVC practices over the years. The leave-one-out analysis confirmed that absence of outliers among studies included.

Several limitations should be considered when interpreting these results. First, the included studies varied in terms of patient populations, catheter types, insertion sites, and definitions of infectious outcomes, increases the generalizability of our results but may introduce clinical heterogeneity. However, statistical heterogeneity was low ($I^2=12\%$). Most studies lacked some relevant data, such as antibiotic use, catheter dwell time, ICU length of stay, or all-cause mortality. Future studies on catheter-related infections should incorporate these clinically relevant criteria. Second, the risk of bias varied across studies, potentially affecting the overall conclusions.

The inclusion of four NRSI may introduce potential bias, such as selection and confounding bias. This subgroup analysis by study type was preplanned in response to the meta-analysis by Takeshita et al. [13], which included only 4 RCTs, to increase the power and the number of procedures of our study. Even if the NRSI may also lack power to detect an effect, this subgroup analysis also showed that our main result was not strongly influenced by the observational studies and prevented this above-mentioned bias. Moreover, the lack of interaction between the RCTs and NRSIs may be due to insufficient power rather than true equivalence between the two. In addition, many of the included studies were conducted before 2014. Given the significant advancements in US technology and training methods, particularly for novice practitioners, this may have introduced a potential bias, particularly when comparing the differences in outcomes between novice and experienced operators. Third, the secondary outcome of mortality at day 28 was based on a single NRSI [35]. This study was not exempt from bias (in particular, overuse of the femoral site in more severe patients requiring hemodialysis, usually without US guidance), which limits the generalizability of the results. However, demonstrating a benefit on mortality from US guidance seems challenging. This likely explains why few studies have reported this outcome. Fourth, we included catheter colonization in our outcome, although colonization of itself may not be associated with patient symptoms, however our findings were consistent even when the study using this endpoint was removed. Lastly, it should be noted that the cannulation site could be a potential confounder. Indeed, the subclavian site is recommended as first-line choice, to reduce the risk of catheter-related infection, compared with the jugular and femoral sites. The absence of substantial data on US-guided subclavian access represents a gap in the current analysis (821 procedures included, i.e. 16.1%, in 3 studies [31, 35, 36]). However, the preference for the subclavian site is currently being debated since a recent observational study found no excess risk of infection depending on the CVC site [42].

Catheter-related infection prevention [20, 43, 44] and US guidance [2, 7, 45, 46] practices have evolved in recent years, gradually leading to the abandonment of the AL puncture technique, which is encouraged by numerous international guidelines to reduce the incidence of immediate complications (such as pneumothorax or arterial puncture) [1, 6, 8].

US guidance is increasingly accepted as the standard of care for CVC placement. However, although widely recommended, the clinical reality of the systematic use of US guidance for CVC remains problematic. Its utilization is reported in 36–68% of CVC (less than 30% of cases for the subclavian site) [9–11]. Prevention of infections will simply increase overall acceptance in addition to decreasing procedural complications such as bleeding and pneumothorax.

In this context, our study provides an opportunity to counter some of the last remaining arguments in favor of the anatomical landmark technique. Given the overwhelming evidence in favor of US guidance, conducting a new RCT may no longer be justified from an ethical standpoint. Above all, basic infection prevention and control measures must continue to be strictly applied (hand hygiene, skin asepsis, maximal sterile barriers).

Future research should focus on large, multicenter RCTs promoting new workforce training and models, techniques, technologies, or alternative puncture sites to further improve the efficiency, comfort, and safety of CVC [2, 45], whose complications, although rare, can be devastating [47].

Conclusion

In conclusion, this systematic review and meta-analysis provides compelling evidence that US-guided CVC significantly reduces the risk of catheter-related infections compared to the traditional AL technique. This benefit is particularly pronounced in procedures performed by experienced operators, highlighting the importance of training and proficiency in US-guided CVC.

Abbreviations

AL	Anatomical landmark
CI	Confidence interval
CLABSI	Central line-associated bloodstream infection
CRBSI	Catheter-related bloodstream infection
CVC	Central venous catheterization
ICU	Intensive care unit
NRSI	Non-randomized studies of intervention
RCT	Randomized controlled trial
RR	Risk ratio
RRR	Relative risk reduction
TSA	Trial sequential analysis
US	Ultrasound

Supplementary Information

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Additional file 1.

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Author contributions

NB, BO, PFP, OM, CMR, NBu, JYL, LM, and CRo developed the search strategies NB and JYL screened the titles and abstracts of all studies identified by the search and extracted full texts of the included studies. NB and JP designed the data extraction form. NB and JP assessed methodological quality of the studies. JP and BVO carried out the statistical analyses. All authors participated

in the revision of the draft, added valuable comments, read and approved the final manuscript.

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Declarations

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The authors declare no competing interests.

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