JAMA Internal Medicine | Original Investigation

Complication Rates of Central Venous Catheters
A Systematic Review and Meta-Analysis

Bijan Teja, MD; Nicholas A. Bosch, MD, MSc; Calvin Diep, MD; Tiago V. Pereira, PhD; Paolo Mauricio, MD; Michael C. Sklar, MD; Ashwin Sankar, MD, MSc; Harindra C. Wijeysundera, MD, PhD; Refik Saskin, MSc; Allan Walkey, MD; Duminda N. Wijeysundera, MD, PhD; Hannah Wunsch, MD, MSc

IMPORTANCE Central venous catheters (CVCs) are commonly used but are associated with complications. Quantifying complication rates is essential for guiding CVC utilization decisions.

OBJECTIVE To summarize current rates of CVC-associated complications.

DATA SOURCES MEDLINE, Embase, CINAHL, and CENTRAL databases were searched for observational studies and randomized clinical trials published between 2015 to 2023.

STUDY SELECTION This study included English-language observational studies and randomized clinical trials of adult patients that reported complication rates of short-term centrally inserted CVCs and data for 1 or more outcomes of interest. Studies that evaluated long-term intravascular devices, focused on dialysis catheters not typically used for medication administration, or studied catheters placed by radiologists were excluded.

DATA EXTRACTION AND SYNTHESIS Two reviewers independently extracted data and assessed risk of bias. Bayesian random-effects meta-analysis was applied to summarize event rates. Rates of placement complications (events/1000 catheters with 95% credible interval [CrI]) and use complications (events/1000 catheter-days with 95% CrI) were estimated.

MAIN OUTCOMES AND MEASURES Ten prespecified complications associated with CVC placement (placement failure, arterial puncture, arterial cannulation, pneumothorax, bleeding events requiring action, nerve injury, arteriovenous fistula, cardiac tamponade, arrhythmia, and delay of ≥1 hour in vasopressor administration) and 5 prespecified complications associated with CVC use (malfunction, infection, deep vein thrombosis [DVT], thrombophlebitis, and venous stenosis) were assessed. The composite of 4 serious complications (arterial cannulation, pneumothorax, infection, or DVT) after CVC exposure for 3 days was also assessed.

RESULTS Of 11 722 screened studies, 130 were included in the analyses. Seven of 15 prespecified complications were meta-analyzed. Placement failure occurred at 20.4 (95% CrI, 10.9-34.4) events per 1000 catheters placed. Other rates of CVC placement complications (per 1000 catheters) were arterial canulation (2.8; 95% CrI, 0.1-10), arterial puncture (16.2; 95% CrI, 11.5-22), and pneumothorax (4.4; 95% CrI, 2.7-6.5). Rates of CVC use complications (per 1000 catheter-days) were malfunction (5.5; 95% CrI, 0.6-38), infection (4.8; 95% CrI, 3.4-6.6), and DVT (2.7; 95% CrI, 1.0-6.2). It was estimated that 30.2 (95% CrI, 21.8-43.0) in 1000 patients with a CVC for 3 days would develop 1 or more serious complication (arterial cannulation, pneumothorax, infection, or DVT). Use of ultrasonography was associated with lower rates of arterial puncture (risk ratio [RR], 0.20; 95% CrI, 0.09-0.44; 13.5 events vs 68.8 events/1000 catheters) and pneumothorax (RR, 0.25; 95% CrI, 0.08-0.80; 2.4 events vs 9.9 events/1000 catheters).

CONCLUSIONS AND RELEVANCE Approximately 3% of CVC placements were associated with major complications. Use of ultrasonography guidance may reduce specific risks including arterial puncture and pneumothorax.

Invited Commentary
page 482

Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author:
Bijan Teja, MD, St Michael's Hospital, Departments of Anesthesia and Critical Care Medicine, 30 Bond St, Rm 6-504, Donnelly Wing South, Toronto, ON M5B 1W8, Canada (bijan.teja@mail.utoronto.ca).

JAMA Intern Med. 2024;184(5):474-482. doi:10.1001/jamainternmed.2023.8232
Published online March 4, 2024. Corrected on May 20, 2024.

Central venous catheters (CVCs) are widely used to deliver medications, fluids, and parenteral nutrition. Older estimates suggest that 5 million CVCs are inserted in the US annually,[1] and a more recent estimate is that 27 million CVCs are inserted worldwide annually.[2] Despite their frequent use, CVCs are associated with several risks, including immediate insertion-related complications (eg, pneumothorax, arterial cannulation), central catheter-line-associated bloodstream infections (CLABSI), and deep venous thrombosis (DVT).[3]

Recent studies have shown low complication rates from peripheral administration of vasoactive drugs previously thought to require administration via CVC.[4] This has motivated hospitals to create protocols supporting peripheral vasoactive medication administration.[5] Understanding complication rates of different catheter types helps guide development of these policies.

To estimate current rates of complications associated with centrally inserted CVCs and factors influencing complication rates, we conducted a systematic review and meta-analysis of recent studies (2015-2023) examining CVCs in inpatient populations.

Key Points

Question What are the rates of complications from central venous catheter (CVC) use?

Findings This systematic review and meta-analysis of literature from 2015 to 2023 found that rates of complications varied substantially across studies, but on average, the rate of serious complications (arterial cannulation, pneumothorax, infection, or deep vein thrombosis) from a CVC placed for 3 days was estimated to be 30 events per 1000 catheters placed (3%). Use of ultrasonography was associated with lower rates of immediate insertion-related complications.

Meaning This study found that approximately 3% of CVC placements were associated with major complications, with ultrasonography guidance reducing some of the specific risks.

Methods

Search Strategy

This study followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guidelines,[6] and was registered at PROSPERO (CRD42020176851). We searched MEDLINE, Embase, CINAHL, and CENTRAL. We included English-language studies published between July 2015 and September 2023. The search strategy was limited to 2015 to 2023 to ensure that included studies were more representative of current medical practices, including adherence to recent guidelines on CVC placement and use, and increased adoption of ultrasonography guidance (eAppendix 1 in Supplement 1).

Inclusion/Exclusion Criteria

We included observational studies or randomized clinical trials reporting complication rates of short-term centrally inserted CVCs (peripherally inserted central catheters [PICCs] were excluded). Included studies met the following criteria: (1) included data for adult inpatients aged 18 years or older, (2) described centrally inserted CVCs that are typically placed for short-term use, and (3) included data for 1 or more outcomes of interest. We excluded studies that (1) evaluated long-term intravascular devices such as tunneled lines; (2) focused on dialysis catheters not typically used for medication administration; and (3) studied catheters placed by radiologists. We excluded studies in which data for CVCs of interest could not be separated from data on PICCs or dialysis catheters (eTable 1 in Supplement 1).

Study Selection

Pairs of investigators (B.T., C.D., T.V.P., P.M., M.C.S., and/or A.S.) independently screened identified references for inclusion based on title and abstract. Full texts of potentially eligible articles were reviewed by at least 2 of the reviewers. Disagreements were resolved by discussion and, when necessary, consultation with a senior reviewer (H.C.W., D.N.W., or H.W.).

Data Extraction and Risk of Bias

Data were extracted using Covidence[7] by 2 assessors (B.T., C.D., T.V.P., P.M., M.C.S., and/or A.S.). Studies were assessed for quality using an adapted version of the Risk of Bias in Cohort Studies tool[8] (eAppendix 2 in Supplement 1).

Outcomes

We examined complications associated with placement and use of CVCs. We defined CVC-associated complication as any undesirable event not present prior to CVC insertion or any preexisting event that worsened in intensity or frequency following CVC exposure.[9] While this definition did not allow us to differentiate between complications directly related to CVC insertion and those that may have occurred independently of the catheter, the broader definition enabled us to be more comprehensive and accurate in estimating overall risks associated with CVC placement and use.

The 10 prespecified CVC placement complications of interest included placement failure, arterial puncture, arterial cannulation, pneumothorax, bleeding events requiring action, nerve injury, arteriovenous fistula, cardiac tamponade, arrhythmia, and delay in vasopressor administration. The 5 prespecified CVC use complications of interest were malfunctions, CLABSIs, DVTs, thrombophlebitis, and venous stenosis (eTable 2 in Supplement 1).[10] Placement-related complications were modeled as incidence proportions (risks) because they tend to occur immediately after catheter exposure, whereas CVC use complications were modeled as incidence rates because these events are more time-dependent (the risk increases with increasing catheter exposure). We expressed risks as events per 1000 catheters and incidence rates as events per 1000 catheter-days.

Serious complications were defined as those with the potential for grade 3 to 4 morbidity based on National Cancer Institute Common Terminology Criteria for Adverse Events.[11,12] A composite outcome was then developed, including 4 serious complications often considered in clinical decision-making regarding whether to place a CVC: arterial cannula-

tion, pneumothorax, CLABSI, and DVT. Although CVCs are often placed for more than 3 days, we chose a 3-day period to estimate the probability of the composite outcome based on published vasopressor dose trajectories[13] to remain conservative in our estimate.

Statistical Analysis

Continuous variables were described as medians (IQRs). Categorical variables were presented as counts (proportions). We imputed mean follow-up (in catheter-days) using reported summary statistics (eAppendix 3 in Supplement 1).[14]

We used Bayesian random-effects meta-analysis models to pool estimates across studies. We used the binomial likelihood with a logit link to model proportions. For incidence rates, we used the Poisson likelihood with a log link. All models were estimated based on noninformative prior distributions (eAppendix 4 in Supplement 1). We quantified the between-study heterogeneity using 95% predictive intervals.[15]

We fitted Bayesian random-effects meta-regression models to investigate whether moderators (insertion site, ultrasonography use, risk of bias, and study design) were associated with the risk or incidence rate of complications. We prespecified these models for placement failure, arterial puncture, and pneumothorax but did not do so for CLABSI and DVT. We added these nonprespecified analyses based on reviewer recommendations since reducing needle passes with ultrasonography might mitigate the risk of CLABSI and DVT, as suggested by previous studies.[16-18]

We also estimated the probability of patients developing the composite outcome (arterial cannulation, pneumothorax, infection, or DVT) after being exposed to a CVC for 3 days (eAppendix 4 in Supplement 1).

All results were obtained from posterior medians and 2.5th and 97.5th percentiles. We implemented models in OpenBUGS 2.0, and estimates were obtained using Markov chain Monte Carlo simulation via 500 000 iterations (burn-in of 50 000 simulations). Approaches to model diagnostics are described in eAppendix 4 in Supplement 1. We conducted a sensitivity analysis using frequentist random-effects meta-analysis models, specifically mixed-effects logistic and Poisson regression, as these models provide less biased estimates than inverse-variance methods in meta-analyses with few events.[19,20]

Results

Study Characteristics

Our search identified 15 282 records, of which 11 722 were unique peer-reviewed studies. After title/abstract screening and full-text assessment, 130 articles met all eligibility criteria (**Figure 1**). The **Table** shows the study characteristics. Sixty-one (47%) were randomized trials and 50 (38.5%) were prospective cohort studies. The median (IQR) sample size was 160 (91-424) participants. A total of 112 studies (86%) were at low risk of bias (eTable 3 in Supplement 1 and eFigure 1 in Supplement 1). Randomized clinical trials were twice as likely to use ultrasonography guidance: 37 of 61 (61%) randomized clinical trials used ultrasonography guidance in all patients, compared with 23 of 69 observational studies (33%).

Catheter Placement Characteristics

In the 130 included studies, 214 325 central catheters were placed, of which 47 533 were internal jugular (22.2%), 21 540 subclavian (10.1%), and 8201 (3.8%) femoral. Catheters were primarily assessed in participants from intensive care units (ICUs; n = 69 studies; 53.1%) and/or operating rooms (n = 53 studies; 40.8%). The purpose of catheter placement was unspecified in 77 studies (59.2%). Among the 53 studies that reported the purpose, the most common reason was total parenteral nutrition (18 studies), followed by chemotherapy (13 studies), and vasopressors (12 studies) (Table).

Rates of CVC-Associated Complications

Figure 2 summarizes the rates of the 7 CVC-associated complications with sufficient data for meta-analysis. There were insufficient data for meta-analysis for bleeding events requiring action, nerve injury, arteriovenous fistula, cardiac tamponade, arrhythmia, delay of 1 or more hours in vasopressor administration, thrombophlebitis, and venous stenosis.

Placement Failure

In 37 studies on 17 407 catheters, placement failure rates ranged from 0 to 200 per 1000 catheters placed (eFigure 2 in Supplement 1). The pooled rate of catheter placement failure was 20.4 per 1000 catheters placed (95% CrI, 10.9-34.4), with a wide 95% prediction interval (PI) (0.8-326.4 events/1000 catheters), indicating high heterogeneity (Figure 2; and eFigure 2 in Supplement 1).

Arterial Cannulation

In 10 studies on 6489 catheters, the rate of arterial cannulation ranged from 0 to 28 per 1000 catheters placed (eFigure 3 in Supplement 1). The pooled rate of arterial cannulation was 2.8 events per 1000 catheters placed (95% CrI, 0.1-10.0) (Figure 2; and eFigure 3 in Supplement 1). The 95% PI, indicating substantial between-study heterogeneity, spanned from 0.3 to 135.4 events per 1000 catheters placed.

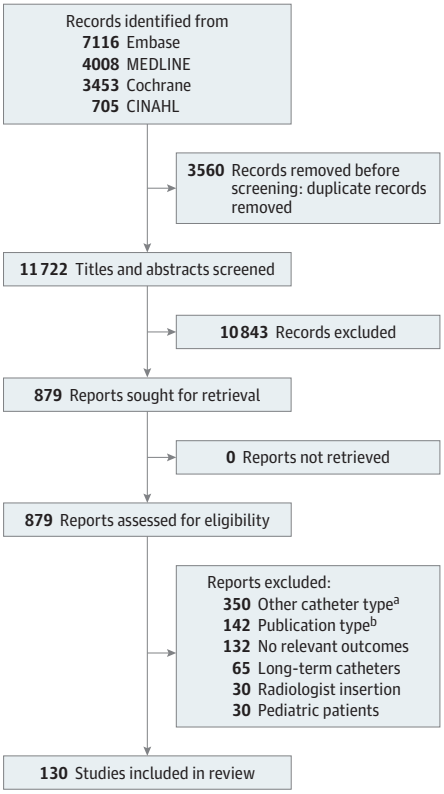
Arterial Puncture

In 67 studies on 22 296 catheters, the rates of arterial puncture ranged from 0 to 144 per 1000 catheters placed (eFigure 4 in Supplement 1). The pooled rate of arterial puncture was 16.2 per 1000 catheters placed (95% CrI, 11.5-22.0) (Figure 2; and eFigure 4 in Supplement 1). The 95% PI, suggesting high between-study heterogeneity, spanned from 1.6 to 139.3 events per 1000 catheters placed.

Pneumothorax

In 65 studies on 32 665 catheters, the rates of pneumothorax ranged from 0 to 100 per 1000 catheters placed (eFigure 5 in Supplement 1). The pooled rate of pneumothorax was 4.4 per 1000 catheters placed (95% CrI, 2.7-6.5). The 95% PI, indicating substantial between-study heterogeneity, ranged from 0.3 to 54.9 events per 1000 catheters placed (Figure 2; and eFigure 5 in Supplement 1).

Figure 1. PRISMA Diagram



[a] Other catheter types such as urinary catheters, peripheral intravenous catheters, midline catheters, peripherally inserted central catheters, and dialysis catheters were excluded from this study.

[b] Other study types such as case reports, case series, study protocols for future research, guidelines, systematic reviews, and surveys were excluded from this study.

Table. Characteristics of the 130 Included Studies

Study characteristic	No. (%)
Setting[a]	
Intensive care unit	69 (53.1)
Ward	18 (13.8)
Emergency department	8 (6.2)
Operating room	53 (40.8)
≥2 categories	25 (19.2)
Other/unclear	11 (8.5)
Catheter placed by[b]	
Attending physician	84 (64.6)
Medical trainees	37 (28.5)
Nurses	3 (2.3)
Other professionals	2 (1.5)
≥2 categories	29 (22.3)
Unclear	36 (27.7)
Purpose[c]	
Vasopressors	12 (9.2)
Total parenteral nutrition	18 (13.8)
Chemotherapy	13 (10)
Other	23 (17.7)
≥2 categories	12 (9.2)
Unclear	77 (59.2)
Study design	
Randomized clinical trial	61 (46.9)
Prospective cohort	50 (38.5)
Retrospective cohort	14 (10.8)
Time series	5 (3.8)
Ultrasonography use	
Yes	60 (46.2)
No	11 (8.5)
Partially[d]	17 (13.1)
Unclear	42 (32.3)
Sample size (No. of participants)	
≤100	38 (29.2)
101-250	39 (30)
251-500	18 (13.8)
501-1000	11 (8.5)
≥1000	14 (10.8)
Unclear	10 (7.7)
Country[e]	
High income	75 (57.7)
Low and middle income	55 (42.3)

[a] The sum of the counts is larger than the number of studies because catheters could be placed in more than 1 location in a given study.

[b] The sum of the counts is larger than the number of studies because catheters could be placed by more than 1 professional category in a given study.

[c] The sum of the counts is larger than the number of studies because a study could have examined catheters for different purposes.

[d] Partial refers to ultrasonography guidance used for some but not all patients.

[e] Based on the classification of countries by the World Bank in 2021.[21]

Catheter Malfunction

In 8 studies examining 23 794.3 catheter-days, catheter malfunction occurred at an incidence rate ranging from 0 to 45.7 per 1000 catheter-days (eFigure 6 in Supplement 1). The pooled incidence rate of catheter malfunction was 5.5 per 1000 catheter-days (95% CrI, 0.6-38.0). The 95% PI indicated extreme heterogeneity across studies (0 to 2054 events per 1000 catheter-days) (Figure 2; and eFigure 6 in Supplement 1).

Central Catheter-Associated Bloodstream Infections

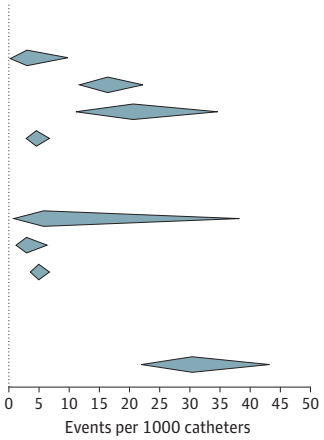
In 48 studies examining 549 246.8 catheter-days, rates of CLABSI ranged from 0 to 23.5 per 1000 catheter-days (eFigure 7 in Supplement 1). The pooled rate of CLABSI was 4.8 per 1000 catheter-days (95% CrI, 3.4-6.6). The 95% PI indicated substantial heterogeneity across studies (0-39.8 events per 1000 catheter-days) (Figure 2; and eFigure 7 in Supplement 1).

Deep Vein Thrombosis

In 14 studies examining 73 895 catheter-days, rates of DVT ranged from 0 to 25.0 per 1000 catheter-days (eFigure 8 in Supplement 1). The pooled incidence rate of DVT was 2.7 per 1000 catheter-days (95% CrI, 1.0-6.2). There was evidence for between-study heterogeneity, with the 95% PI spanning 0.1 to 61.7 events per 1000 catheter-days (Figure 2; and eFigure 8 in Supplement 1).

Figure 2. Summary of Central Venous Catheter-Associated Complications Based on Bayesian Random-Effects Meta-Analysis Models

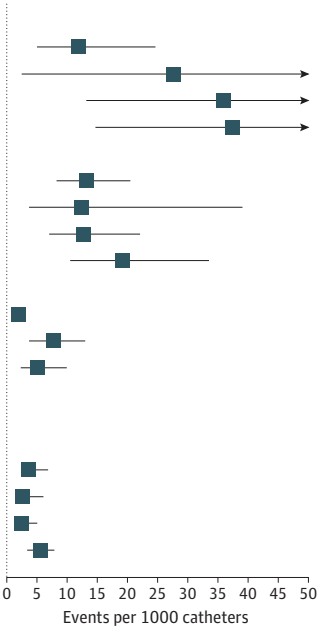
Complication	No. of studies	Events/ catheters	No. of events per 1000 catheters (95% CrI)
Arterial cannulation	10	27/6489	2.8 (0.1-10.0)
Arterial puncture	67	388/22 296	16.2 (11.5-22.0)
Placement failure	37	834/17 407	20.4 (10.9-34.4)
Pneumothorax	65	184/32 665	4.4 (2.7-6.5)
		Events/ catheter-days	Incidence rate per 1000 catheter-days (95% CrI)
Catheter malfunction	8	332/23 794.31	5.5 (0.6-38.0)
Deep vein thrombosis	14	486/73 894.98	2.7 (1.0-6.2)
Infection	48	3427/549 246.8	4.8 (3.4-6.6)
			No. events per 1000 catheters placed for 3 d (95% CrI)
Composite of serious complications	NA	NA	30.2 (21.8-43.0)



95% CrI indicates 95% credible interval; NA, not applicable.

Figure 3. Central Venous Catheter-Associated Complication Rates by Catheter Insertion Site

Catheter type	No. of groups	Events/ catheters	No. of events per 1000 catheters (95% CrI)
Placement failure			
Internal jugular	21	247/8852	11.9 (5.0-24.7)
Femoral	2	58/1200	27.7 (2.5-225.8)
Subclavian	12	401/4253	35.9 (13.2-86.1)
Other	12	128/3102	37.4 (14.7-89.1)
Arterial puncture			
Internal jugular	38	153/10 307	13.3 (8.3-20.5)
Femoral	6	14/1678	12.4 (3.7-39.1)
Subclavian	23	101/5690	12.8 (7.1-22.1)
Other	21	120/4621	19.3 (10.5-33.6)
Pneumothorax			
Internal jugular	31	63/19 312	1.9 (0.9-3.5)
Subclavian	34	80/7111	7.8 (4.3-13.0)
Other	20	41/4883	5.1 (2.3-10.0)
		Events/ catheter-days	Incidence rate per 1000 catheter−days
Infection			
Internal jugular	12	185/50 007.5	3.8 (2.0-6.9)
Femoral	7	58/19 094.46	2.7 (1.1-6.1)
Subclavian	10	57/21 076.05	2.5 (1.2-5.1)
Other	35	3127/459 068.8	5.6 (3.9-7.9)



Placement failure, arterial puncture, pneumothorax, and infection were the only 4 outcomes with sufficient data for comparison across catheter types. The subgroup others encompasses unknown, unclear, or mixed central venous catheter types. For placement failure, the upper bound of the 95% credible interval (CrI) for femoral catheters extends beyond the limits of the graph, and it is not displayed for simplicity. Number of groups refers to the number of patient groups with different insertion sites among studies. For studies that had more than 1 study group (eg, internal jugular vs femoral), each study group was treated separately in the analysis.

Pooled Composite Outcome of Serious Complications

We estimate that 30.2 (95% CrI, 21.8-43.0) of 1000 patients treated with a CVC for 3 days will develop 1 or more serious complications (arterial cannulation, pneumothorax, CLABSI, or DVT).

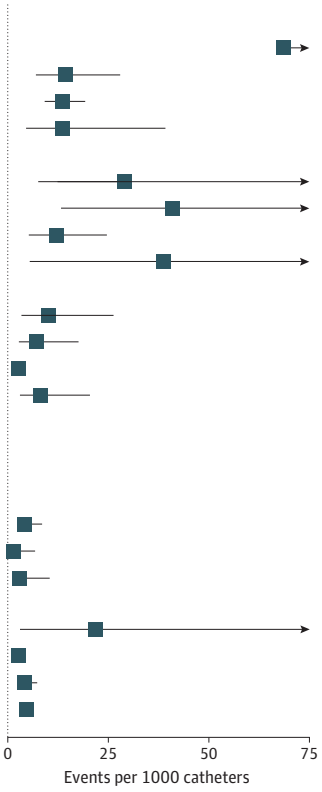
Association of Insertion Site With the Rate of Complications

Figure 3 shows CVC-associated complication rates by catheter insertion site. A total of 124 studies were included in the analysis of complications by insertion site (eFigures 9-12 in Supplement 1 and eTables 4-7 in Supplement 1). All insertion sites were comparable with respect to rates of arterial puncture and placement failure. Insufficient data for arterial cannulation and catheter malfunction precluded model fitting. The subclavian site had a higher risk of pneumothorax than the internal jugular site, with 7.8 events per 1000 events (95% CrI, 4.3-13.0) vs 1.9 events per 1000 catheters (95% CrI, 0.93-3.5), respectively. The corresponding risk ratio (RR) was 4.09 (95% CrI, 1.84-9.48), with 100% posterior probability that the true RR greater than 1 (eFigure 11 in Supplement 1).

Rates of CLABSI were comparable for subclavian and femoral insertions, with rates of 2.5 and 2.7 infections per 1000 catheter days, respectively. Internal jugular insertions were associated with 3.8 infections per 1000 catheter days, but 95% CrIs overlapped across the 3 insertion sites (eFigure 12 in Supplement 1).

Figure 4. Estimates From Meta-Regression Models for the Association of Use of Ultrasonography With the Rate of Complications

Ultrasonography	Studies (events/ catheters)	No. of events per 1000 catheters (95% CrI)
Arterial puncture		
No	8 (94/1267)	68.8 (32.4-137.5)
Partial	11 (75/6789)	14.3 (7.1-27.7)
Yes	46 (199/12 584)	13.5 (9.1-19.2)
Unclear	5 (20/1656)	13.6 (4.4-39.2)
Placement failure		
No	6 (201/2153)	29.0 (7.5-96.3)
Partial	9 (410/4597)	41.0 (13.2-108.3)
Yes	19 (156/9551)	11.9 (5.1-24.6)
Unclear	3 (67/1106)	38.6 (5.3-197.3)
Pneumothorax		
No	9 (31/1581)	9.9 (3.3-26.2)
Partial	9 (33/6193)	6.9 (2.6-17.5)
Yes	40 (81/21 451)	2.4 (1.2-4.3)
Unclear	10 (39/3440)	8.1 (2.9-20.3)
	Studies (events/ catheter-days)	No. of events per 1000 catheter-days (95% CrI)
Deep vein thrombosis		
No		
Partial	3 (21/15 826.49)	3.8 (1.4-8.4)
Yes	12 (410/52 634.44)	1.2 (0.2-6.7)
Unclear	5 (55/5434.052)	2.9 (0.6-10.3)
Infections		
No	1 (122/5427.046)	21.8 (2.9-154.6)
Partial	16 (575/51 501.27)	2.5 (1.2-4.8)
Yes	12 (200/52 989.7)	4.2 (2.3-7.2)
Unclear	35 (2530/43 9328.8)	4.8 (3.3-6.8)



In the context of meta-regression models, each study may contribute 2 distinct estimates, for instance, when 1 group received ultrasound treatment while another group did not. Use of ultrasonography was included as a categorical variable with the following values: 0 for "no," 1 for "partial," 2 for "yes," and 3 for "unclear." 95% CrI indicates 95% credible interval.

Association of Ultrasound Use With the Complication Rates

Ultrasonography-based guidance was associated with lower risk of arterial puncture and pneumothorax compared with partial (used for some but not all patients) or no ultrasonography use (**Figure 4**). Analyses of ultrasonography guidance per insertion site (only internal jugular and subclavian catheters had sufficient data) corroborated the results from the main analysis. Compared with no or partial ultrasonography guidance, use of ultrasonography was associated with lower rates of placement failure, arterial puncture and pneumothorax, irrespective of insertion site (eFigures 13-15 in Supplement 1). However, greater differences were observed in the incidence risk of pneumothorax for internal jugular catheters, with incidence rates of 0.4 events per 1000 catheters under ultrasonography guidance compared with 17.9 events per 1000 catheters without or with partial ultrasonography guidance (RR, 0.02; 95% CrI, 0.001-0.28). The corresponding difference was smaller for subclavian catheters, with rates of 3.2 events per 1000 catheters under ultrasonography guidance vs 12.2 events per 1000 catheters without or with partial ultrasonography guidance (RR, 0.26; 95% CrI, 0.04-1.60) (eFigure 15 in Supplement 1).

Association of Risk of Bias and Study Design With the Rate of Complications

We found no robust association between risk of bias or study design (randomized clinical trials vs observational studies) and the magnitude of complication rates in the included studies (eTables 8-11 in Supplement 1).

Sensitivity Analyses

Estimates derived from frequentist models were comparable to those obtained from Bayesian analyses (eFigures 2-8 in Supplement 1).

Discussion

Main Findings and Potential Implications

In this systematic review, we assessed data from 130 recent studies (2015 to 2023) to determine average rates of complications associated with CVCs, providing comprehensive estimates of potential complications resulting from placement and use of CVCs. The 3 most common complications associated with CVC placement are placement failure (20.4 events/1000 catheters placed), arterial puncture (16.2 events/1000 catheters placed), and pneumothorax (4.4 events/1000 catheters placed). Approximately 30 of 1000 patients with a CVC for 3 days were estimated to have 1 or more of the 4 serious complications: arterial puncture, pneumothorax, infection, or DVT. This rate is relatively high compared with other bedside procedures.[22-24] However, rates were also substantially lower for a number of these complications when ultrasonography guidance was consistently used.

These findings have important implications for informed consent and clinical practice because they highlight the need for widespread use of up-to-date insertion protocols and for clinicians to carefully consider risks and benefits of CVC use, particularly for delivery of medications traditionally thought to require CVC that may be safely administered peripherally with appropriate protocols for a short period of time.[4,5] Studies examining vasopressor dose trajectories and implementation of peripheral vasopressor delivery protocols have shown that approximately 50% of patients requiring vasopressors can avoid need for CVC,[13,25,26] with extravasation of peripheral vasopressors being uncommon, and tissue injury being very rare with monitored peripheral administration.[4,26-29] A recent international survey of ICUs in the US, Australia, the UK, Canada, and Saudi Arabia found that norepinephrine was delivered peripherally in 113 of 132 centers (86%), reducing need for CVCs.[30]

Comparison With Previous Studies

Other reviews have reported complications occurring in 15% to 33% of catheterization attempts.[31,32] The pooled complication rates in the meta-analysis were lower, which may reflect progress in CVC placement and maintenance techniques in our more recent literature search. Historically, central veins were accessed using anatomical landmarks and palpation of anatomic structures, leading to high rates of immediate insertion-related complications, particularly in obese or critically ill patients.[31]

The pooled rates of CLABSI were lowest for subclavian insertions in this study, but 95% CrIs overlapped substantially (eFigure 12 in Supplement 1). A recent review suggested that reduced risk of CLABSI with subclavian insertion may be clearer in the ICU setting but must be balanced against increased risk of immediate insertion-related complications such as pneumothorax.[33] Our findings suggest that the small decrease in CLABSI rates with subclavian insertion may be offset by the increased risk of pneumothorax, which remains relatively high even with use of ultrasonography for subclavian insertion. It is important to note that these results are based on a small number of studies and are associated with considerable uncertainty. Further confirmation is required through more extensive and well-conducted studies.

The 2020 practice guidelines from the American Society of Anesthesiologists recommended that real-time ultrasonography guidance be used for internal jugular vein cannulation and, when feasible, for subclavian and femoral cannulation.[34] Our analyses showed that the rates of arterial puncture and pneumothorax were 5- to 6-fold lower in studies that used ultrasonographic guidance compared with those that did not, similar to prior research.[35]

Limitations

This systematic review has important limitations. First, outcome definitions were not uniform across studies. Although efforts were made to standardize estimates and account for dissimilar follow-up whenever feasible, the wide CrIs and statistical heterogeneity among estimates can be attributed, at least partially, to variation in patient samples, study design, and different definitions of CVC-associated complications. Second, we included many populations in this analysis, such as oncological patients, those in critical care settings, patients undergoing major surgery, and individuals with difficult peripheral venous access. Although these results offer important clinical insights into the overall rates of CVC-associated complications, additional research is required to generate estimates specific to different patient populations. Third, we found that many studies on CVC-associated complications provided suboptimal descriptions of the purpose of catheter use and characteristics of operators inserting catheters. We also could not account for the effect of the experience, type, and skill levels of clinicians in these analyses. Further investigations are required to clarify the association of these factors with CVC-associated complications. Fourth, despite our best efforts including having 2 reviewers screen all titles, abstracts and selected full texts, it is possible that a few articles were missed due to the large number of studies that were screened. Fifth, incomplete adoption of modern infection prevention protocols at some study centers may have increased pooled CLABSI rates. Sixth, if there was correlation between major complications in the composite outcome, this may have led us to overestimate the outcome, whereas our short time period may have led us to underestimate it. Seventh, our choice to use uniform daily risks for CLABSI and DVT in our composite outcome may have oversimplified the risk over time. However, because follow-up time across studies was also variable, our estimate was likely a slight underestimate as well. Eighth, studies using ultrasonography guidance were more likely to be randomized clinical trials than those that did not. Nevertheless, we found no robust differences in complication rates between randomized clinical trials and observational studies, nor between studies with low and high overall bias risk. The potential association between methodological rigor and the magnitude of the CVC complication rates remains uncertain, but merits further investigation. Finally, it is crucial to interpret the results obtained from our metaregression models as suggestive associations, not definitive evidence of causality. Even though the results align with previous evidence indicating that ultrasonography guidance is associated with lower rates of CVC-associated complications,[36] we could not adjust the analyses for patient demographic characteristics, comorbidities, or concurrent treatments due to a lack of individual patient data. Thus, residual confounding may explain the estimates of reduction in complications from ultrasonography use.

Conclusions

In this systematic review of complications following CVC insertion, we found that the rate of major complications was approximately 3%. Ultrasonography use was associated with fewer immediate insertion-related complications. Efforts should be made to limit CVC use when clinically appropriate.

ARTICLE INFORMATION

Accepted for Publication: November 7, 2023.

Published Online: March 4, 2024. doi:10.1001/jamainternmed.2023.8232

Correction: This article was corrected on May 20, 2024, to fix formatting errors in Supplement 1.

Author Affiliations: Interdepartmental Division of Critical Care Medicine, University of Toronto, Toronto, Ontario, Canada (Teja, Sklar); Department of Anesthesiology and Pain Medicine, University of Toronto, Toronto, Ontario, Canada (Teja, Diep, Sklar, Sankar, D. N. Wijeysundera, Wunsch); Department of Anesthesia, St Michael's Hospital, Toronto, Ontario, Canada (Teja, Sklar, Sankar, D. N. Wijeysundera); The Pulmonary Center, Department of Medicine, Boston University Chobanian and Avedisian School of Medicine, Boston, Massachusetts (Bosch, Mauricio); Clinical Trial Unit and Epidemiological Studies Unit, Nuffield Department of Population Health, University of Oxford, Oxford, United Kingdom (Pereira); Department of Emergency Medicine, Boston University Chobanian and Avedisian School of Medicine, Boston, Massachusetts (Mauricio); Division of Cardiology, Schulich Heart Program, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada (H. C. Wijeysundera); ICES Central, University of Toronto, Toronto, Ontario, Canada (Saskin, D. N. Wijeysundera); Division of Health Systems Sciences, University of Massachusetts Medical School, Worcester, Massachusetts (Walkey); Applied Health Research Centre, Li Ka Shing Knowledge Institute, St Michael's Hospital, Toronto, Ontario, Canada (D. N. Wijeysundera); Department of Anesthesiology, Weill Cornell Medicine, New York, New York (Wunsch); Sunnybrook Research Institute, Toronto, Ontario, Canada (Wunsch).

Author Contributions: Dr Teja had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Teja, Bosch, H. Wijeysundera, Saskin, Walkey, D. Wijeysundera, Wunsch.
Acquisition, analysis, or interpretation of data: Teja, Bosch, Diep, Pereira, Mauricio, Sklar, Sankar, Wunsch.
Drafting of the manuscript: Teja, Pereira, Sklar, Sankar.
Critical review of the manuscript for important intellectual content: Bosch, Diep, Pereira, Mauricio, Sklar, Sankar, H. Wijeysundera, Saskin, Walkey, D. Wijeysundera, Wunsch.
Statistical analysis: Teja, Diep, Pereira, Sklar, Sankar.
Obtained funding: Teja.
Administrative, technical, or material support: Diep, Sankar.
Supervision: Bosch, Pereira, H. Wijeysundera, Saskin, Walkey, D. Wijeysundera, Wunsch.

Conflict of Interest Disclosures: Dr Bosch reported funding from Gilead Sciences outside the submitted work. Dr. Pereira received grant support from Johnson & Johnson and Medtronic, which were paid directly to the institution (German Hospital Oswaldo Cruz, Brazil) outside the submitted work, and also disclosed receiving consulting fees from Novartis, Pfizer, and Calecim outside the submitted work. No other disclosures were reported.

Funding/Support: This study was supported by the Acute and Intensive Care Outcomes Research Network (AICORN). Dr Teja was supported by a Foundation Grant from the Department of Critical Care Medicine, Sunnybrook Health Sciences Centre, and three grants from the Canadian Institutes of Health Research (Drug Safety and Effectiveness Cross-Disciplinary Training (DSECT) program; Canada Graduate Scholarships–Masters Award; Frederick Banting and Charles Best Canada Graduate Scholarship Doctoral Award #175965). Dr Teja, Dr Sklar, Dr Sankar, Dr D. Wijeysundera, and Dr Wunsch were supported by Merit Awards from the Department of Anesthesiology and Pain Medicine at the University of Toronto. Dr Diep was supported by an Ontario Graduate Scholarship held at the University of Toronto. Dr D. Wijeysundera was supported by the Endowed Chair in Translational Anesthesiology Research at St Michael's Hospital and the University of Toronto. Dr Wunsch was supported by a Canada Research Chair (tier 2) in Critical Care Organization and Outcomes (CRC-2019-00151).

Role of the Funder/Sponsor: The funding agencies had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Data Sharing Statement: See Supplement 2.

REFERENCES

1. McGee DC, Gould MK. Preventing complications of central venous catheterization. *N Engl J Med*. 2003;348(12):1123-1133. doi:10.1056/NEJMra011883

2. iData Research. Central Venous Catheter Market Size, Share & Trends Analysis, Global, 2020-2026. 2020. Accessed October 26, 2023. https://idataresearch.com/product/vascular-access-devices-market/

3. Timsit JF, Rupp M, Bouza E, et al. A state of the art review on optimal practices to prevent, recognize, and manage complications associated with intravascular devices in the critically ill. *Intensive Care Med*. 2018;44(6):742-759. doi:10.1007/s00134-018-5212-y

4. Tian DH, Smyth C, Keijzers G, et al. Safety of peripheral administration of vasopressor medications: a systematic review. *Emerg Med Australas*. 2020;32(2):220-227. doi:10.1111/1742-6723.13406

5. Munroe E, Claar D, Tamae-Kakazu M, et al. Hospital policies on intravenous vasopressor administration and monitoring: a survey of Michigan hospitals. *Ann Am Thorac Soc*. 2022;19(10):1769-1772. doi:10.1513/AnnalsATS.202203-197RL

6. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Int J Surg*. 2021;88:105906. doi:10.1016/j.ijsu.2021.105906

7. Covidence Systematic Review Tool. Accessed October 28, 2022. covidence.org

8. Risk of Bias in Cohort Studies Tool. Accessed October 28, 2022. Cochrane.org

9. Nilsson ME, Koke SC. Defining treatment-emergent adverse events with the medical dictionary for regulatory activities (MedDRA). *Drug Inf J*. 2001;35(4):1289-1299. doi:10.1177/009286150103500425

10. Practice Guidelines for Central Venous Access. Practice guidelines for central venous access 2020: an updated report by the American Society of Anesthesiologists Task Force on Central Venous Access. *Anesthesiology*. 2020;132(1):8-43. doi:10.1097/ALN.0000000000002864

11. Common Terminology Criteria for Adverse Events. (CTCAE – Version 5.0). Accessed April 5, 2022. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf

12. Parienti JJ, Mongardon N, Mégarbane B, et al; 3SITES Study Group. Intravascular complications of central venous catheterization by insertion site. *N Engl J Med*. 2015;373(13):1220-1229. doi:10.1056/NEJMoa1500964

13. Gandotra S, Wunsch H, Bosch NA, Walkey AJ, Teja B. Reducing central venous catheter use through adoption of guidelines for peripheral catheter-based vasopressor delivery. *Ann Am Thorac Soc*. 2023;20(8):1219-1223. doi:10.1513/AnnalsATS.202212-1060RL

14. Kwon D, Reis IM. Simulation-based estimation of mean and standard deviation for meta-analysis via approximate Bayesian computation (ABC). *BMC Med Res Methodol*. 2015;15:61. doi:10.1186/s12874-015-0055-5

15. IntHout J, Ioannidis JP, Rovers MM, Goeman JJ. Plea for routinely presenting prediction intervals in meta-analysis. *BMJ Open*. 2016;6(7):e010247. doi:10.1136/bmjopen-2015-010247

16. Lamperti M, Bodenham AR, Pittiruti M, et al. International evidence-based recommendations on ultrasound-guided vascular access. *Intensive Care Med*. 2012;38(7):1105-1117. doi:10.1007/s00134-012-2597-x

17. Karakitsos D, Labropoulos N, De Groot E, et al. Real-time ultrasound-guided catheterisation of the internal jugular vein: a prospective comparison with the landmark technique in critical care patients. *Crit Care*. 2006;10(6):R162. doi:10.1186/cc5101

18. Debourdeau P, Kassab Chahmi D, Le Gal G, et al; working group of the SOR. 2008 SOR guidelines for the prevention and treatment of thrombosis associated with central venous catheters in patients with cancer: report from the working group. *Ann Oncol*. 2009;20(9):1459-1471. doi:10.1093/annonc/mdp052

19. Lin L, Chu H. Meta-analysis of proportions using generalized linear mixed models. *Epidemiology*. 2020;31(5):713-717. doi:10.1097/EDE.0000000000001232

20. Spittal MJ, Pirkis J, Gurrin LC. Meta-analysis of incidence rate data in the presence of zero events. *BMC Med Res Methodol*. 2015;15:42. doi:10.1186/s12874-015-0031-0

21. World Bank Data Help Desk. Accessed October 28, 2022. https://datahelpdesk.worldbank.org/

22. Scheer B, Perel A, Pfeiffer UJ. Clinical review: complications and risk factors of peripheral arterial catheters used for haemodynamic monitoring in anaesthesia and intensive care medicine. *Crit Care*. 2002;6(3):199-204. doi:10.1186/cc1489

23. Evans RW. Complications of lumbar puncture. *Neurol Clin*. 1998;16(1):83-105. doi:10.1016/S0733-8619(05)70368-6

24. Cantey EP, Walter JM, Corbridge T, Barsuk JH. Complications of thoracentesis: incidence, risk factors, and strategies for prevention. *Curr Opin Pulm Med*. 2016;22(4):378-385. doi:10.1097/MCP.0000000000000285

25. Yerke JR, Mireles-Cabodevila E, Chen AY, et al. Peripheral administration of norepinephrine: a prospective observational study. *Chest*. 2023; S0012-3692(23)05350-3.

26. Munroe ES, Hyzy RC, Semler MW, et al. Evolving management practices for early sepsis-induced hypoperfusion: a narrative review. *Am J Respir Crit Care Med*. 2023;207(10):1283-1299. doi:10.1164/rccm.202209-1831CI

27. Loubani OM, Green RS. A systematic review of extravasation and local tissue injury from administration of vasopressors through peripheral intravenous catheters and central venous catheters. *J Crit Care*. 2015;30(3):653.e9-653.e17. doi:10.1016/j.jcrc.2015.01.014

28. Owen VS, Rosgen BK, Cherak SJ, et al. Adverse events associated with administration of vasopressor medications through a peripheral intravenous catheter: a systematic review and meta-analysis. *Crit Care*. 2021;25(1):146. doi:10.1186/s13054-021-03553-1

29. Tran QK, Mester G, Bzhilyanskaya V, et al. Complication of vasopressor infusion through peripheral venous catheter: a systematic review and meta-analysis. *Am J Emerg Med*. 2020;38(11): 2434-2443. doi:10.1016/j.ajem.2020.09.047

30. Abu Sardaneh A, Penm J, Oliver M, et al. International pharmacy survey of peripheral vasopressor infusions in critical care (INFUSE). *J Crit Care*. 2023;78:154376. doi:10.1016/j.jcrc.2023.154376

31. Millington SJ, Colvin MO, Shiloh AL, Koenig S, How I. How i do it: ultrasound-guided internal jugular and femoral central venous catheter insertion. *Chest*. 2020;158(6):2425-2430. doi:10.1016/j.chest.2020.06.026

32. Young MPY, Theodore H. Overview of complications of central venous catheters and their prevention in adults. Accessed October 28, 2022. https://www.uptodate.com/contents/central-venous-catheters-overview-of-complications-and-prevention-in-adults

33. O'Grady NP. Prevention of central line-associated bloodstream infections. *N Engl J Med*. 2023;389(12):1121-1131. doi:10.1056/NEJMra2213296

34. Practice Guidelines for Central Venous Access. Practice guidelines for central venous access 2020: an updated report by the American Society of Anesthesiologists Task Force on Central Venous Access. *Anesthesiology*. 2020;132(1):8-43. doi:10.1097/ALN.0000000000002864

35. Millington SJ, Lalu MM, Boivin M, Koenig S. Better with ultrasound: subclavian central venous catheter insertion. *Chest*. 2019;155(5):1041-1048. doi:10.1016/j.chest.2018.12.007

36. Brass P, Hellmich M, Kolodziej L, Schick G, Smith AF. Ultrasound guidance versus anatomical landmarks for internal jugular vein catheterization. *Cochrane Database Syst Rev*. 2015;1(1):CD006962. doi:10.1002/14651858.CD006962.pub2

Invited Commentary

Enhancing Quality and Safety in Critical Care—Challenges and Strategies for Central Venous Catheters

Elie A. Saade, MD, MPH; Francis T. Lytle, MD; Peter J. Pronovost, MD

Central venous catheters (CVCs) are widely used in US critical care settings, providing essential functions such as medication administration, hemodynamic monitoring, and reliable venous access. Despite the benefits of CVCs, complications, particularly infections, have become a major focus of US hospital quality improvement efforts due to federal and state initiatives that emphasize patient safety, transparency, and accountability. The Centers for Medicare & Medicaid Services mandate reporting hospital-acquired infections through the Hospital Inpatient Quality Reporting Program, which significantly affects hospital operations nationwide. The program specifically targets certain hospital-acquired infections, such as central line–associated bloodstream infections (CLABSIs), and can result in financial penalties for hospitals with elevated rates. Additionally, complications that are not solely related to CVC use, such as iatrogenic pneumothorax and deep venous thrombosis, are included in the quality metrics that hospitals must report.[1]

Related article page 474

In their systematic review and meta-analysis in *JAMA Internal Medicine*, Teja et al[2] investigated 15 CVC-related complications. The study found significant rates of placement failure, arterial puncture, pneumothorax, catheter malfunction, infections, and thrombosis. Notably, 3% of patients with a CVC for 3 days experienced serious complications, such as arterial cannulation, pneumothorax, infection, or deep vein thrombosis. A smaller percentage of these complications was tracked by the Hospital Inpatient Quality Reporting Program. The infection rates were similar for subclavian and femoral insertions, with a slightly higher rate observed for internal jugular insertions, although the confidence intervals overlapped, suggesting no significant difference. Arterial puncture and placement failure rates were similar across all CVC insertion sites, and the subclavian site had a significantly higher risk of pneumothorax than the internal jugular site did. The authors underscored the effectiveness of ultrasonography guidance in reducing complications such as arterial puncture, pneumothorax, deep venous thrombosis, and infections.[2]

As new research and changing practices emerge, the traditional reliance on CVCs for various clinical applications is being reevaluated. Studies suggest that peripheral administration of vasopressors for patients with septic or cardiogenic shock, among others, is feasible and safe.[3] International surveys indicate a trend toward peripheral administration of medications such as norepinephrine, which is traditionally administered centrally due to its vesicant nature and risk of extravasation. Advances in parenteral nutrition and chemotherapeutic agent formulations have made peripheral administration more viable, further reducing the need for CVC placement. Recent developments in medical technology have led to minimally invasive and noninvasive hemodynamic monitoring techniques, reflecting a growing focus on patient safety and comfort in critical care settings.[4] However, CVC use remains high, which suggests that additional efforts need to be made to educate and incentivize frontline clinicians to minimize their use; including measures of utilization of CVCs in pay-for-performance programs might be considered for this goal.

The broadened use of point-of-care ultrasonography and other advanced peripheral intravenous access placement techniques has significantly contributed to the reduced need for traditional CVCs in patients with difficult venous access. Despite the technological advancements that enhance the precision and user-friendliness of ultrasonography guidance for