Original Article

Extravasation, thrombosis, and infection with vasopressor infusion through peripheral intravenous catheters: a systematic review and meta-analysis

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Background: The safety of administering vasopressors through peripheral venous catheters (PVCs) remains controversial, primarily due to concerns regarding extravasation, thrombosis, and catheter-related infections. This study aimed to systematically summarize the prevalence of these complications through a meta-analysis.

Methods: The PubMed, Excerpta Medical Database (Embase), Cochrane Library, Web of Science (WOS), China National Knowledge Infrastructure (CNKI), Wanfang (WF), Chinese Science and Technology Journal Database (VIP), and China Biology Medicine disc (CBMdisc) databases were systematically searched (from database establishment 16 August 2025) to retrieve pertinent articles, and study quality was rated via the Joanna Briggs Institute (JBI) scale and Newcastle-Ottawa Scale (NOS). The data analysis was conducted using the meta package in R, and random/fixed-effects models were applied to combine the complication rates based on heterogeneity. Sensitivity and subgroup analyses were also carried out.

Results: A total of 19 studies comprising 6,852 patients across 10 counties, including Sweden, the USA, and China, were encompassed in the meta-analysis, with the majority being intensive care unit (ICU) patients. The overall rates of extravasation, thrombosis, and infection were 1.43% [95% confidence interval (CI): 0.72–2.32%; I^2=71%], 1.47% (95% CI: 0.32–3.18%; I^2=86%), and 0.72% (95% CI: 0.14–1.60%; I^2=63%), respectively. The subgroup analysis peripherally inserted central catheters (PICCs) carried a higher risk of thrombosis, while midline catheters (MCs) had the lowest risk of extravasation. In relation to the catheter-related infection risks, PVCs showed the lowest incidence, whereas PICCs had the highest. Limited direct comparative evidence indicated no statistically significant differences between PVCs and central venous catheters (CVCs).

Conclusions: Under standardized procedures, PVCs may be a viable option for vasopressor infusion, particularly MCs, which showed the lowest risk of extravasation. Caution is warranted with PICCs due to the potential risk of thrombosis, while traditional PVCs should be limited to short-term or emergency use. Future well-designed studies with standardized definitions are needed to strengthen the reliability and clinical applicability of the evidence.

Keywords: Vasopressors; peripheral venous catheters (PVCs); adverse event (AE); systematic review; meta-analysis

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Introduction

As indispensable tools in clinical practice, peripheral venous catheters (PVCs) are broadly applied in surgical procedures, intensive care, and chronic disease management, providing convenient venous access for drug infusion (1,2). Recent advances in medical technology have led to the increased use and broader clinical application of novel PVCs, such as peripherally inserted central catheters (PICCs) and midline catheters (MCs) (3). These catheters not only reduce patient discomfort and the risk of infection linked to repeated punctures but also provide reliable options for long-term or specialized drug infusions. However, despite significant technical advances in PVCs, safety concerns, particularly those regarding the potential risks linked to the infusion of specific drugs, still require thorough investigation (4-6).

Vasopressors are critical medications in treating hypotensive states like shock or sepsis, and function by inducing potent vasoconstriction to rapidly elevate blood pressure and improve tissue perfusion (7,8). However, the hyperosmolarity and vascular irritancy of drugs (such as norepinephrine, dopamine, and epinephrine) may lead to severe complications, including local vascular injury, thrombosis, and even tissue necrosis. Conventionally, vasopressors are administered via central venous catheters (CVCs) because their larger diameter and faster blood flow effectively dilute the drug, reducing vascular wall irritation (9). However, in emergencies or when central venous access cannot be promptly established, clinicians may be compelled to use PVCs as an alternative (10,11). Although this approach may provide a temporary solution for drug infusion, evidence supporting its long-term safety and efficacy is insufficient (12,13).

Currently, research on the use of PVCs for the infusion of vasopressors is limited, and conflicting conclusions have been reached (10,14,15). There is a study showing that the risk of phlebitis and vasopressor extravasation was similar between the PVC and CVC groups (16). However, other studies indicate that the use of PVCs may increase the risks of extravasation, thrombosis, and infection (17,18). More importantly, the reported prevalence and incidence of these complications vary widely across studies. For example, the incidence of PICC-related thrombosis has been reported to range from less than 1% to over 30%, depending on patient populations, diagnostic methods, and prophylactic strategies (19). Likewise, catheter-related bloodstream infection rates are substantially lower in outpatients compared with inpatients (20), and rates of extravasation during vasopressor infusion also differ considerably among studies, reflecting variations in catheter type, insertion technique, and monitoring protocols. In oncology populations, PICCs have consistently shown a higher risk of thrombosis than totally implantable venous access ports (21). Furthermore, recent multicenter surveillance has indicated a rising proportion of PICC-related bloodstream infections as their clinical use increases (22). These wide variations underscore that the true risks of extravasation, thrombosis, and infection among patients with PVCs remain uncertain. It should be noted that, according to the Infusion Therapy Standards of Practice (23), PICCs are categorized as central venous access devices rather than peripheral catheters. Nevertheless, in real-world practice, PICCs are frequently utilized as alternatives to peripheral routes for vasopressor infusion when central venous catheterization is not feasible. Therefore, in this study, PICCs were included for analysis but evaluated independently from traditional PVCs and MCs in subgroup comparisons to avoid misclassification. Currently, there is a lack of unified clinical guidelines on whether to use CVCs or PVCs for the infusion of vasopressors. Therefore, a systematic review and meta-analysis are necessitated to synthesize existing evidence and lay a solid scientific foundation for clinical practice.

Highlight box

Key findings

- The risks of complications vary depending on the type of catheter used for peripheral vasopressor administration: midline catheters (MCs) have the lowest extravasation risk (0.68%), traditional peripheral venous catheters (PVCs) show a higher extravasation risk (1.69%), and peripherally inserted central catheters (PICCs) carry the highest risk of thrombosis (4.41%).

What is known and what is new?

- Due to safety concerns with peripheral routes, central venous catheters (CVCs) serve as the standard route for vasopressor administration.
- This meta-analysis provides updated pooled prevalence estimates of adverse events related to peripheral vasopressor infusion. MCs appear to lower the risk of extravasation, while PICCs are associated with increased thrombosis risk. Importantly, limited direct comparisons revealed no statistically significant differences in safety between PVCs and CVCs.

What is the implication, and what should change now?

- MCs may be preferred when aiming to minimize the risk of extravasation, PVCs demonstrated the lowest infection rate, and careful monitoring is required for PICC-associated thrombosis. Future well-designed multi-center randomized controlled trials with standardized outcome definitions are needed to validate these findings and guide clinical practice.

Further, with the introduction of novel catheter technologies, a deeper comparison of the performance of different types of PVCs in vasopressor infusion is warranted.

This study sought to comprehensively evaluate the safety and efficacy of PVCs (including PICCs, MCs, and traditional PVCs) in the infusion of vasopressors via a systematic review and meta-analysis. Specifically, this study endeavored to: (I) quantify the incidences of extravasation, thrombosis, and infection during the PVC infusion of vasopressors; (II) compare the complication risks between different types of PVCs; and (III) where possible, compare the safety differences between PVCs and CVCs. By integrating high-quality research data, our study makes evidence-based recommendations for clinical practice that should assist healthcare providers in selecting the optimal administration route based on risk-benefit analysis and ultimately enhance patient safety and treatment outcomes. We present this article in accordance with the PRISMA reporting checklist (24) (available at https://cdt.amegroups.com/article/view/10.21037/cdt-2025-290/rc).

Methods

The study protocol was prospectively registered on PROSPERO (https://www.crd.york.ac.uk/PROSPERO/) (registration No. CRD420251022812).

Search strategy

The PubMed, Excerpta Medical Database (Embase), Cochrane Library, Web of Science (WOS), China National Knowledge Infrastructure (CNKI), Wanfang (WF), Chinese Science and Technology Journal Database (VIP), and China Biology Medicine disc (CBMdisc) databases were searched to retrieve relevant articles published from database establishment to August 16, 2025. A search strategy combining medical subject headings (MeSH) and free-text terms with Boolean logic constructs was employed. The key search terms included vasopressors, norepinephrine, dopamine, epinephrine, and other drug-related terminology, as well as terms related to administration routes such as PVC, peripheral veins, and MC. The search process had no restrictions regarding countries or languages. The complete search strategy is detailed in Appendix 1.

Literature selection and eligibility criteria

The literature selection was independently performed by two researchers. First, duplicate articles were excluded using EndNote 21 (Clarivate Analytics). Second, the titles and abstracts of the articles were reviewed. Third, the full texts of potentially eligible studies were reviewed. Any disagreements between the two researchers were resolved by discussion or by consulting a third researcher.

Studies were included in the meta-analysis if they met the following inclusion criteria: (I) included patients who required vasopressor therapy due to shock or major surgery; (II) utilized catheters inserted via peripheral venous access (including traditional PVCs, MCs, and PICCs), regardless of whether the catheter tip terminated in a peripheral or central vein; (III) reported at least one outcome measure, such as extravasation, thrombosis, or catheter-related infection; and (IV) a adopted either randomized controlled trial (RCT) or non-randomized study designs.

Articles were excluded from the meta-analysis if they met any of the following exclusion criteria: (I) was non-original research (e.g., reviews, commentaries, or editorials); (II) comprised case reports or case series; (III) contained incomplete data from conference abstracts; (IV) reported on animal studies or studies involving children; and/or (V) included unpublished or non-peer-reviewed literature.

Data extraction

The following data were independently extracted by two researchers using Excel for data extraction and organization: basic study information (authors, year, country, and sample size), baseline characteristics of patients (e.g., age, sex, and disease type), and the incidence of adverse events (AEs) (i.e., extravasation, thrombosis, and infection). All the extracted data were cross-checked, and any issues were resolved via discussion with a third researcher. Missing data were supplemented by contacting the original authors or marked as "not reported".

In this study, extravasation was defined as the unintended leakage of intravenously infused fluids, drugs, or other substances from the vessel into the surrounding tissues, with the main clinical manifestations including local erythema, swelling, and bleeding (25). Thrombosis referred to the formation of blood clots within blood vessels; if the article reported thrombotic phlebitis, it was also categorized under thrombosis (26). Catheter-related infection was defined as an infection associated with the use of a peripheral catheter, which could occur at the insertion site, within the catheter, or along the catheter pathway (27). Other types of infections were not considered within the scope of this study. In subsequent analyses, subgroup analyses were conducted according to different peripheral catheter-based administration methods, specifically including PVCs, MCs, and PICCs.

Quality assessment

Quality assessment was independently performed by two researchers. In case of any discrepancies in the evaluation results, a third party assisted in the discussion to make the final decision on the article's quality.

The Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Prevalence Studies was used to assess the quality of the single-arm studies. This tool comprises nine items, including items related to sample representativeness, data collection methods, outcome measurement standardization, and statistical analysis. A score ≥7 indicates high quality, 4–6 moderate quality, and ≤3 low quality (28).

The Newcastle-Ottawa Scale (NOS) was used to assess the quality of the cohort studies. The NOS comprises eight items, including those related to the representativeness of the exposed cohort, the comparability between groups, and outcome assessment. A maximum of 2 points can be awarded for comparability, resulting in a total possible score of 9. A score ≥7 indicates high quality, 5–6 moderate quality, and ≤4 low quality (29).

Statistical analysis

Data analysis was conducted using the meta package in R software (version 4.4.1, R Foundation for Statistical Computing). For binary outcomes, incidence rates with corresponding 95% confidence intervals (CIs) were calculated from the number of events and total sample size. We utilized the meta package in R version 4.4.1, applying the function metaprop with sm = "PFT", which uses the Freeman-Tukey double arcsine transformation. This approach stabilizes the variance and enables the inclusion of studies with zero events in the pooled estimates, thereby reducing computational bias. Consequently, since some studies reported zero events, we employed both the PFT and inverse variance methods for analysis. This approach stabilizes the variance and enables the inclusion of studies with zero events in the pooled estimates, thereby reducing computational bias. Sensitivity analyses were performed using the "leave-one-out" method. Subgroup analyses were conducted based on peripheral catheter-based administration methods and vasoactive drugs to identify potential sources of heterogeneity. Publication bias tests with funnel plots and Egger's test were conducted when 6 or more studies were included in the pooling process of an outcome. If asymmetry was observed or Egger's P<0.05, publication bias was considered significant, and the "trim and fill" method was used to assess its influence on the stability of results and to further explore its source.

Results

Literature retrieval

In total, 3,244 relevant articles were retrieved through systematic searching. After removing duplicate articles, 1,030 articles remained. Following the title and abstract review, 2,214 articles were further excluded. Ultimately, 50 articles were retained for the full-text evaluation. During the full-text screening process, 21 studies were excluded because the research outcomes did not meet the criteria, three studies used inappropriate catheter types, 3 studies had uncleared or overlapping catheter types, two studies had an inappropriate study population, and two studies were excluded due to very poor quality (Table S1).

After rigorous screening, 19 studies (14-16,30-45) were eligible for the meta-analysis. The screening process is detailed in the PRISMA flowchart (*Figure 1*).

Basic characteristics

In total, the 19 studies included in this meta-analysis collectively reported data from 6,852 patients across 10 countries, including Sweden, the USA, and China. The study populations primarily comprised intensive care unit (ICU) patients, including septic shock patients, neurological ICU patients, and other critically ill patients. The types of used catheters included PVCs, MCs, PICCs, and CVCs (the type was only used for the inter-group comparisons). The reported incidence rates ranged from 0% to 5.2% for extravasation, 0% to 7.3% for thrombosis, and 0% to 2.8% for infection (these are data from the PVC group. The infection rate in the CVC group reached as high as 6.5%). The reporting methods regarding catheter insertion site, specific types of vasoactive drugs, and infusion duration varied across studies, and these details have been summarized in the baseline information table (*Table 1*).

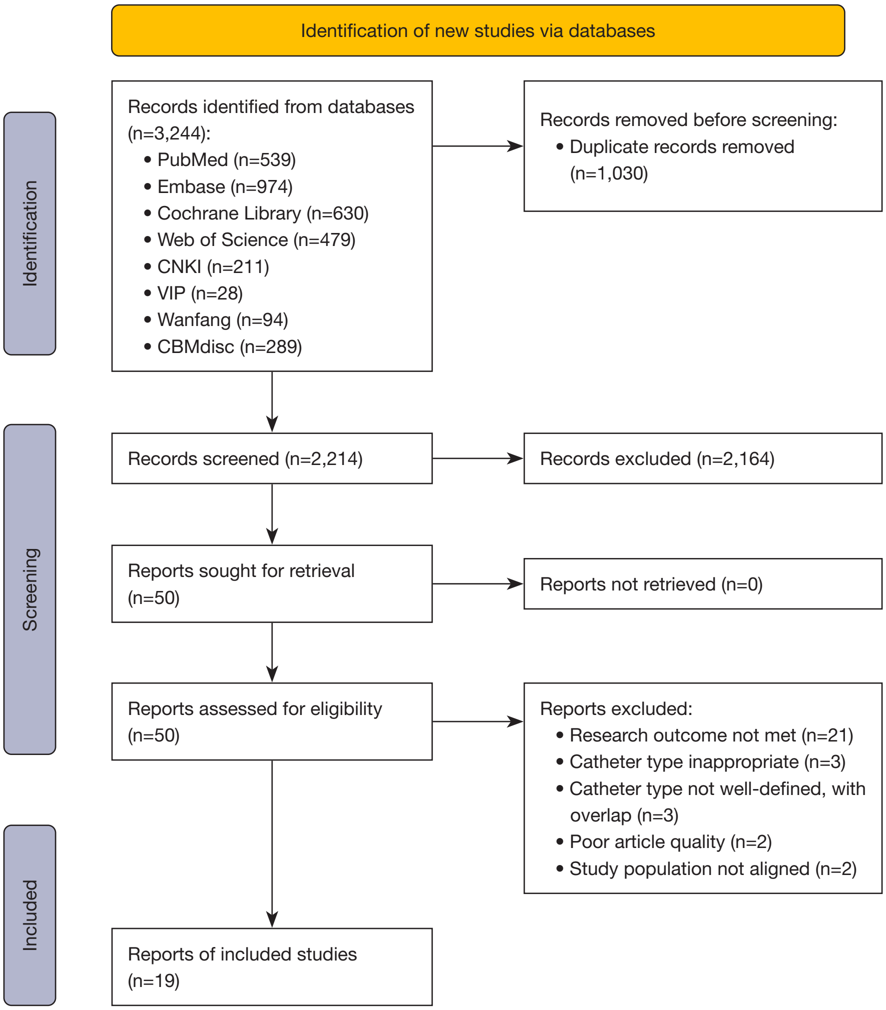

Figure 1 PRISMA literature screening flow chart. CBMdisc, China Biology Medicine disc; CNKI, China National Knowledge Infrastructure; VIP, Chinese Science and Technology Journal Database; WOS, Web of Science.

Quality evaluation

All included cross-sectional and cohort studies were assessed using the JBI critical appraisal tool (*Table 2*) (15,30,32-39,42,43,45). The results indicated that most studies (15,30,32-34,36,38,39,42,43) performed well in terms of participant selection, description of study setting and subjects, condition identification, standardized measurement, and statistical analysis. Most studies received a "Yes" rating on all nine items, suggesting overall high methodological quality. A few studies (35,37,45) showed limitations regarding sample size adequacy and response rate reporting, which may have affected external validity and the stability of results. Overall, the JBI appraisal suggested a low risk of bias across included studies with generally reliable quality.

For cohort studies, NOS was applied (*Table 3*) (14,16,31,40,41,44). The results showed that all studies achieved high scores across selection of cases, the selection of controls, the assessment of exposure, and the handling of non-response rate, with overall ratings ranging from 7 to 8 stars. This indicates that the included case-control studies demonstrated strong methodological reliability with a low risk of bias. In summary, the overall quality of the included studies was satisfactory, with a generally low risk of bias, providing a solid evidence base for the conclusions of this systematic review.

Table 1 Basic information

First author [year]	Country	Population	Route	Sample size	Age (years), mean ± SD or median [IQR]	Gender (M/F)	Extravasation, n/N (%)	Thrombosis, n/N (%)	Infection, n/N (%)	Puncture site	Drug category	Infusion duration (h), mean ± SD or median [IQR]
Karlsson [2024] (32)	Sweden	Septic shock	MC	472	73.5 [65–80]	281/191	1/472 (0.2)	10/472 (2.1)	7/472 (1.5)	Basilic vein, brachial vein, cephalic vein	Norepinephrine	21 [9–38]
Gershengorn [2023] (31)	USA	Mixed patients who received vasopressors	MC	287	68.7 [58.6–75.7]	142/145	6/287 (2.1)	21/287 (7.3)	2/287 (0.7)	Basilic vein, brachial vein, etc.	Norepinephrine, dopamine, epinephrine, vasopressin, etc.	NA
			PICC	1,660	66.6 [57.1–75.0]	875/785	NA	82/1,660 (4.9)	46/1,660 (2.8)			NA
Prasanna [2021] (33)	USA	ICU (septic/distributive shock most common)	MC	248	66 [57–76]	117/131	1/248 (0.4)	1/248 (0.4)	6/248 (2.4)	Basilic vein, brachial vein, cephalic vein	Norepinephrine, epinephrine, vasopressin, etc.	7.8±9.3 (days)
Lewis [2019] (34)	USA	ICU	PVC	202	75 [64–83]	107/95	8/202 (4.0)	NA	NA	Forearm, antecubital fossa, hand, etc.	Norepinephrine, epinephrine, vasopressin, etc.	11.5 (median)
Medlej [2018] (35)	Lebanon	Circulatory shock	PVC	55	70 (mean)	34/21	2/55 (3.6)	1/55 (1.8)	0/55 (0.0)	Antecubital fossa, dorsum of the hand, upper arm, etc.	Norepinephrine, dopamine	Norepinephrine: 13 [6.5–31.5]; dopamine: 53 [15.5–113]
Datar [2018] (36)	USA	Neurological ICU	PVC	277	65±15	129/148	9/277 (3.2)	NA	NA	Proximal upper extremity, hand, etc.	Phenylephrine	19±18
Delgado [2016] (37)	USA	Neurologic ICU	PVC	20	62 (14–90)†	11/9	0/20 (0.0)	0/20 (0.0)	0/20 (0.0)	Upper extremity, proximal to the wrist	Phenylephrine	14.29 (1–54.3)†
Han [2024)] (38)	China	Neurologic ICU	PVC	273	64 [55–71]	188/85	1/273 (0.4)	NA	NA	Bilateral external jugular veins	Metaraminol	88.4 [54.5–131.6]
Guo [2024] (30)	China	Respiratory ICU	PICC	44	72.64±2.30	22/22	1/44 (2.3)	1/44 (2.3)	0/44 (0.0)	Middle 1/3 area between the antecubital fossa and the axilla	Norepinephrine, dopamine, epinephrine	Norepinephrine: 62.00 [37.00–92.00], dopamine: 47.50 [29.75–75.00], epinephrine: 0.18 [0.12–0.32]
		Respiratory ICU	MC	44	69.45±2.31	30/14	1/44 (2.3)	0/44 (0.0)	0/44 (0.0)			
Christensen [2024] (39)	Sweden	Perioperative	PVC	1,004	71±12	556/448	23/1,004 (2.3)	NA	NA	Hand, forearm, etc.	Norepinephrine	175.5 [105–276] mins
Asher [2023] (16)	Israel	Cardiogenic shock (ICCU)	PVC	108	72±12.3	70/38	1/108 (0.9)	NA	1/108 (0.9)	Above the wrist	Norepinephrine, dopamine, etc.	NA
			CVC	31	64±19.6	21/10	1/31 (3.2)	NA	2/31 (6.5)	Jugular vein in nearly half, femoral vein, subclavian vein		
Marques [2022] (40)	Rwanda	ICU	PVC	64	49 [33–65]	29/35	2/64 (3.1)	NA	NA	Antecubital fossa, upper arm, etc.	Adrenaline, norepinephrine, etc.	19 [8.5–37]
Groetzinger [2022] (41)	USA	ICU	PVC	87	65 [56–74]	42/45	1/87 (1.1)	NA	NA	Forearm, upper extremity, etc.	Norepinephrine	1–68†
He [2022] (42)	China	Septic shock	PVC	640	54.35±6.73	380/260	27/640 (4.2)	NA	NA	Forearm, arm, etc.	Norepinephrine	NA
Feng [2021] (43)	China	Septic shock	PVC	116	52.91±18.69	39/77	6/116 (5.2)	NA	NA	Forearm, arm, etc.	Norepinephrine	NA
Padmanaban [2020] (15)	India	ICU	PVC	122	55±4	66/56	1/122 (0.8)	NA	NA	Forearm, hand, etc.	Norepinephrine, vasopressin, etc.	Norepinephrine: 9 [6–14], vasopressin: 4 [2.7–9], epinephrine: 6 [4–10], dopamine: 7.5
Delaney [2020] (14)	Australia	Early septic shock	CVC	548	65.7 [53.6–76.0]	330/218	3/548 (0.5)	1/548 (0.2)	1/548 (0.2)	Internal jugular vein, subclavian vein, etc.	Norepinephrine, epinephrine, etc.	4.9 [3.5–6.6]
			PVC	389	65.4 [52.4–75.3]	233/156	0/389 (0.0)	0/389 (0.0)	0/389 (0.0)	Above the wrist		2.4 [1.3–4.1]
Powell [2023] (44)	USA	Shock	PVC	36‡	69.5 [57.0–78.0]	63/35	0/36 (0.0)	0/36 (0)	0/36 (0.0)	Upper forearm (basilic or cephalic vein), upper arm (basilic or cephalic vein), antecubital fossa	Norepinephrine	6 [3.3–11.3]
Ballieu [2021] (45)	USA	ICU	PVC	125	59.3 (mean)	52/73	2/125 (1.6)	1/125 (0.8)	NA	Above the wrist	Phenylephrine	NA

†, reported as a range instead of IQR; ‡, there were originally 98 cases, among which 62 were subsequently converted to CVC, therefore, only 36 patients received vasopressor infusion via PICC catheters from start to finish. CVC, central venous catheter; ICU, intensive care unit; ICCU, intensive coronary care unit; IQR, interquartile range; MC, midline catheter; NA, data not available; PICC, peripherally inserted central catheter; PVC, peripheral venous catheter; SD, standard deviation.

Table 2 Joanna Briggs Institute scale risk of bias score

First author [year]	Q1: Appropriate sample frame?	Q2: Appropriate sampling?	Q3: Adequate sample size?	Q4: Detailed setting & subjects?	Q5: Sufficient data coverage?	Q6: Valid condition identification?	Q7: Standardized measurement?	Q8: Appropriate statistical analysis?	Q9: Adequate response rate?
Karlsson [2024] (32)	Y	Y	Y	Y	Y	Y	Y	Y	Y
Prasanna [2021] (33)	Y	Y	Y	Y	Y	Y	Y	Y	Y
Lewis [2019] (34)	Y	Y	Y	Y	Y	Y	Y	Y	Y
Medlej [2018] (35)	Y	Y	N	Y	Y	Y	Y	Y	Y
Datar [2018] (36)	Y	Y	Y	Y	Y	Y	Y	Y	Y
Delgado [2016] (37)	Y	Y	N	Y	Y	Y	Y	Y	Y
Han [2024] (38)	Y	Y	Y	Y	Y	Y	Y	Y	Y
Guo [2024] (30)	Y	Y	Y	Y	Y	Y	Y	Y	Y
Christensen [2024] (39)	Y	Y	Y	Y	Y	Y	Y	Y	Y
Ballieu [2021] (45)	Y	Y	N	Y	Y	Y	Y	Y	N
He [2022] (42)	Y	Y	Y	Y	Y	Y	Y	Y	Y
Feng [2021] (43)	Y	Y	Y	Y	Y	Y	Y	Y	Y
Padmanaban [2020] (15)	Y	Y	Y	Y	Y	Y	Y	Y	Y

N, no/unclear; Y, yes.

Table 3 Newcastle-Ottawa Scale risk of bias score

First author [year]	Q1: Is the case definition adequate?	Q2: Is the selection of cases representative?	Q3: Are controls selected appropriately?	Q4: Is the definition of controls adequate?	Q5: Are cases and controls comparable on the basis of the design or analysis?	Q6: Is the exposure of interest assessed reliably?	Q7: Is the method of exposure assessment similar for cases and controls?	Q8: Is the non-response rate addressed?
Gershengorn [2023] (31)	★	★	★	★	★★	★	★	★
Asher [2023] (16)	★	★	★	★	★	★	★	★
Delaney [2020] (14)	★	★	★	★	★	★	★	★
Powell [2023] (44)	★	★	★	★	★	★	★	★
Groetzinger [2022] (41)	★	★	★	★	★	★	★	★
Marques [2022] (40)	★	★	★	★	★	★	★	★

★, the criterion is adequately met (for Q5, it indicates partial satisfaction); ★★, full satisfaction of the criterion (applicable only to Q5).

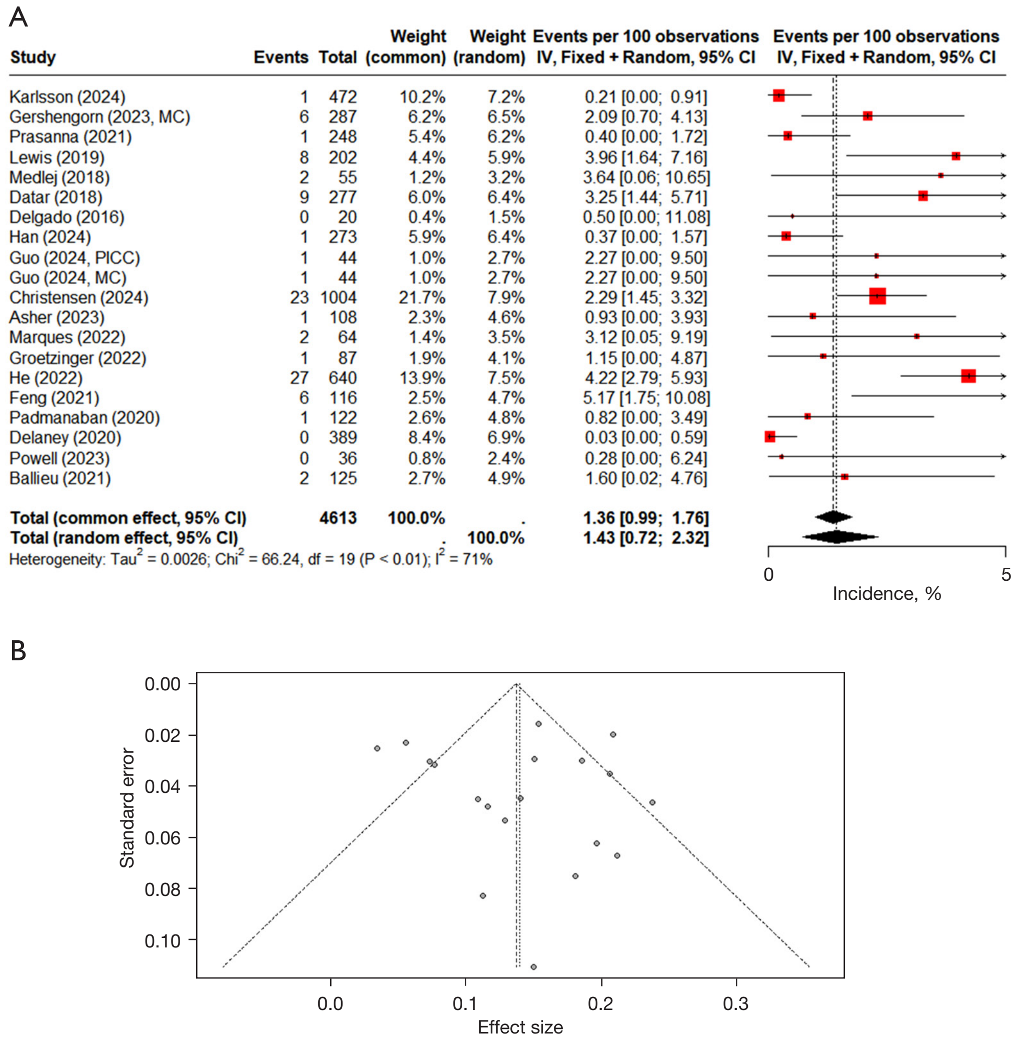

Figure 2 Result of extravasation. (A) Forest plot. (B) Funnel plot. CI, confidence interval; MC, midline catheter; PICC, peripherally inserted central catheter.

Extravasation

In total, 19 studies, comprising 4,613 patients, reported on extravasation. Notably, Guo *et al.* in 2024 included patients from the same hospital but across different admission periods, which could be regarded as two approximately independent cohorts (30). As the meta-analysis revealed significant heterogeneity (I^2=71.0%, P<0.001), a random-effects model was used, yielding an extravasation rate of 1.43% (95% CI: 0.72–2.32%) (*Figure 2A*). The sensitivity analysis showed the robustness of the results (Figure S1), while the funnel plot (*Figure 2B*) and Egger's test (P=0.76) revealed no evidence of publication bias.

A subgroup analysis was conducted according to infusion method (traditional PVC, MC, and PICC). The analysis revealed marked heterogeneity across different catheter types. The risk of extravasation in the PICC subgroup reached 2.27% (95% CI: 0.00–10.06%), which may be higher than that in the PVC subgroup [1.69% (95% CI: 0.81–2.80%)] and the MC subgroup [0.68% (95% CI: 0.00–2.05%)] (Figure S2). However, as only one study was included in the PICC subgroup, we performed a sensitivity analysis using the remaining studies. The overall extravasation rate was 1.42% (95% CI: 0.70–2.23%), with a minimal change of 0.02%, which can be considered negligible. Therefore, we conclude that the single PICC

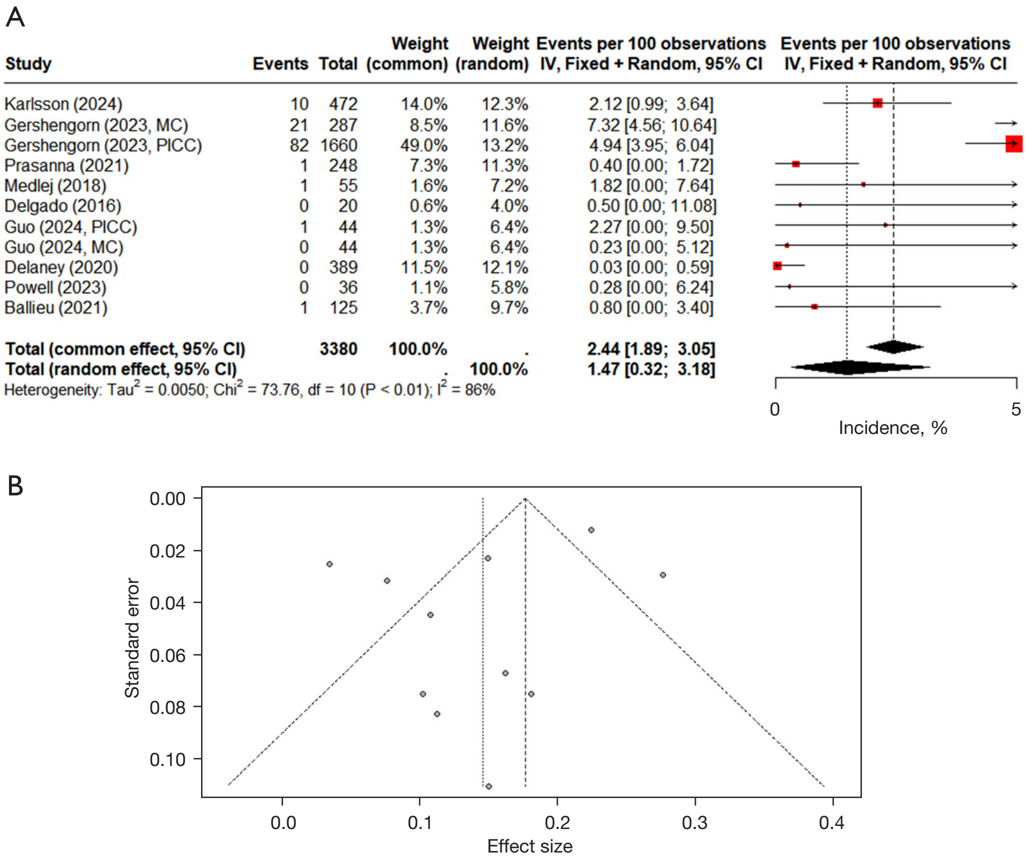

Figure 3 Result of thrombosis. (A) Forest plot. (B) Funnel plot. CI, confidence interval; MC, midline catheter; PICC, peripherally inserted central catheter.

subgroup does not significantly affect the overall results of the study (Figure S3).

Subgroup analyses were further conducted according to the type of vasoactive agent administered. The incidence of thrombosis in the norepinephrine subgroup was 0.28% (95% CI: 0.49–3.92%), in the phenylephrine subgroup was 2.01% (95% CI: 0.68–3.81%), and in the mixed-drug subgroup was 1.29% (95% CI: 0.37–2.61%) (Figure S4).

Thrombosis

Nine studies, comprising 3,380 patients, reported on the occurrence of thrombosis. As the meta-analysis revealed significant heterogeneity (I^2=86%; P<0.001), a random-effects model was used, yielding a thrombosis rate of 1.47% (95% CI: 0.32–3.18%) (*Figure 3A*). The sensitivity analysis showed the robustness of the results (Figure S5), while the funnel plot (*Figure 3B*) and Egger's test (P=0.24) revealed no evidence of publication bias.

Subgroup analysis showed that the risk of thrombosis in the PICC subgroup reached 4.41% (95% CI: 3.43–5.49%), which may be higher than that in the PVC subgroup [0.09% (95% CI: 0.00–1.31%)] and the MC subgroup [2.06% (95% CI: 0.11–5.70%)] (Figure S6). Beyond catheter type, subgroup analyses were also performed according to the vasoactive agents administered, in order to explore whether different drugs contributed to the risk profile. In norepinephrine subgroup reached 1.49% (95% CI: 0.46–2.92%), phenylephrine subgroup reached 0.27% (95% CI: 0.00–2.54%), and the mixed subgroup reached 1.83% (95% CI: 0.22–4.53%) (Figure S7).

Catheter-related infections

Nine studies (including 11 groups), comprising 3,363 patients, reported the incidence of catheter-related infections. Among these, Guo *et al.* in 2024 and Gershengorn *et al.* in 2023 included both the PICC and MC

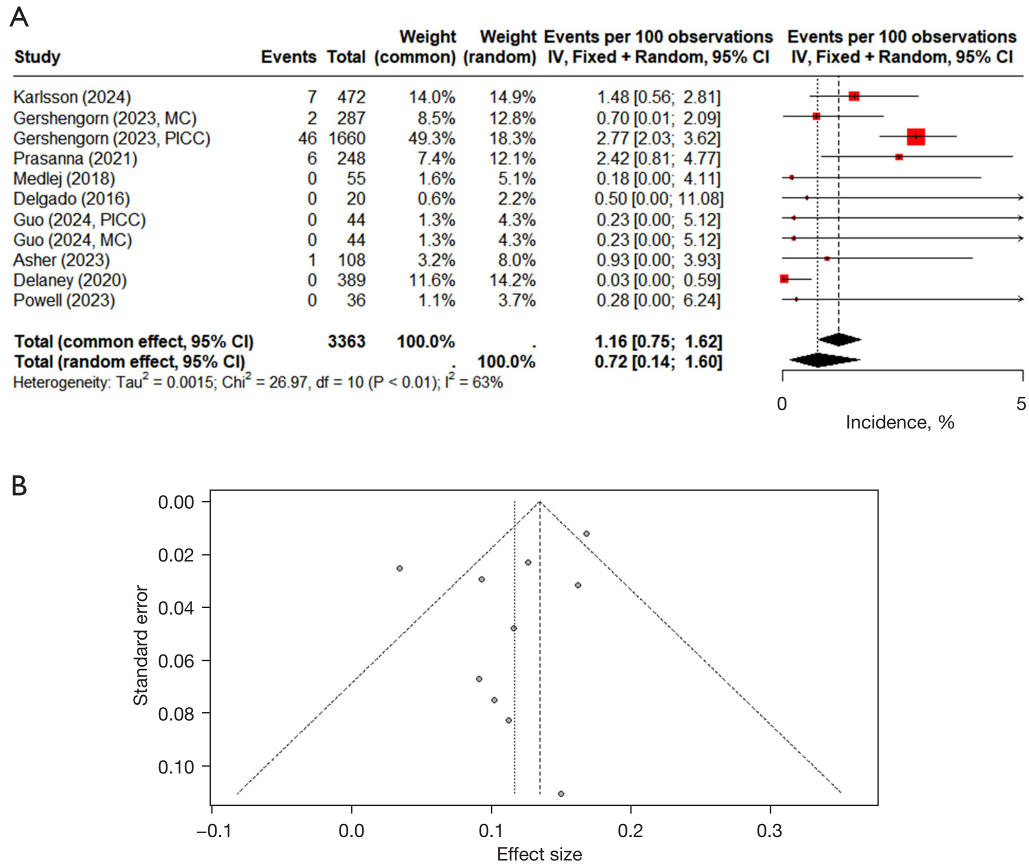

Figure 4 Result of infection. (A) Forest plot. (B) Funnel plot. CI, confidence interval; MC, midline catheter; PICC, peripherally inserted central catheter.

methods for the peripheral administration of vasopressors (30,31). As the meta-analysis displayed low heterogeneity (I^2=63%; P=0.003), a random-effects model was used. The pooled results indicated a catheter-related infection rate of 0.72% (95% CI: 0.14–1.60%) (*Figure 4A*). The sensitivity analysis showed the robustness of the results (Figure S8). The funnel plot (*Figure 4B*) and Egger's test (P=0.21) suggested no evidence of publication bias. Subgroup analysis further indicated that the PICC group had the highest infection risk [2.22% (95% CI: 1.50–3.05%)], followed by the MC group [1.18% (95% CI: 0.54–2.01%)] and the PVC group [0.00% (95% CI: 0.00–0.77%)] (Figure S9). Subgroup analyses were further conducted according to the type of vasoactive agent administered. The incidence of thrombosis in the norepinephrine subgroup was 0.92% (95% CI: 0.14–2.16%), in the phenylephrine subgroup was 0.50% (95% CI: 0.00–11.84%), and in the mixed-drug subgroup was 0.81% (95% CI: 0.12–1.91%) (Figure S10).

Inter-group comparison

Two studies [Asher *et al.* in 2023 (16) and Delaney *et al.* in 2020 (14)] reported the AE rates following the use of PVCs and CVCs; however, no significant difference in the occurrence of infection-related AEs [relative risk (RR) =0.14; 95% CI: 0.01–1.45] and extravasation-related AEs (RR =0.14; 95% CI: 0.01–2.10) was found (Figures S11,S12). Two studies [Guo *et al.* in 2024 (30) and Gershengorn *et al.* in 2023 (31)] reported AE rates following the use of PICCs and MCs; however, no statistical difference between the two methods was found in terms of infection (RR =3.89; 95% CI: 0.97–15.63) and thrombosis (RR =0.70; 95% CI: 0.44–1.11) (Figures S13,S14).

Discussion

The primary aim of this study was to summarize the prevalence of AEs (extravasation, thrombosis, and catheter-related infections) associated with the administration of vasopressors through PVCs, rather than to compare the superiority of different catheter types. This study systematically assesses the risk of complications linked to the infusion of vasopressor drugs through PVCs (including traditional PVCs, MCs, and PICCs) via a meta-analysis. The results revealed that the overall incidence rates of extravasation, thrombosis, and catheter-related infections were 1.44%, 0.34%, and 0.39%, respectively, which were lower than the previously reported complication rates for the infusion of conventional drugs through peripheral veins (46). This discrepancy may arise from the implementation of more stringent catheter management strategies during vasopressor infusion, including strategies related to predefined vasopressor targets, limited infusion times, and intensive monitoring in ICU (47,48). However, the single-group rate analysis does not account for confounding effects from underlying patient conditions (e.g., sepsis-related endothelial damage), which could influence the interpretation of risk attribution.

The subgroup analysis suggested differences in risks among various catheter types: the PICC subgroup showed potentially higher risks of extravasation (2.27%), thrombosis (4.41%), and infection (2.22%) compared with PVCs and MCs. The higher incidence of thrombosis is possibly related to the anatomical positioning of PICCs. However, it is important to note that the single-group rate data only reflect actual in-group occurrences. Therefore, causality cannot be established. For example, the higher thrombosis rate in the PICC group may be a result of clinical selection bias (i.e., PICC was more likely to be selected for sicker patients with coagulopathy rather than the catheter itself directly causing thrombosis) (49,50). Therefore, these results should be interpreted as a risk description of specific clinical scenarios rather than as an evaluation of the superiority of catheter types.

Subgroup analyses according to the type of vasoactive agent administered did not reveal substantial heterogeneity, and the incidence of AEs remained relatively low across all drug categories. Specifically, norepinephrine—the most commonly used vasopressor—showed relatively lower rates of thrombosis and extravasation, whereas phenylephrine and mixed-drug regimens demonstrated numerically higher but overlapping risks. These findings suggest that the pharmacologic agent itself may not be the major determinant of catheter-related complications. Instead, the concentration of the infused solution and infusion practices are likely more critical, as highly concentrated vasopressors can cause endothelial irritation, venous spasm, and tissue injury regardless of the drug used (10). Previous studies have also indicated that more diluted norepinephrine infusions are associated with a lower risk of local complications when administered peripherally (51). Therefore, future investigations should aim to incorporate standardized reporting of drug concentration and infusion practices to better elucidate the determinants of vasopressor-related AEs.

Among the limited direct comparison evidence (see *Inter-group comparison* section), no statistically significant difference in complication risks was found between PVCs and CVCs in infection- or extravasation-related risks; similarly, PICCs and MCs showed no significant differences in infection or thrombosis risks. There could be two reasons for these results. First, under standardized procedures, the complication risks of PVCs (particularly MCs) are comparable to those of CVCs (20,52). Second, the limited samples of the existing studies (which only included two head-to-head trials) resulted in insufficient power to detect clinically meaningful differences. For instance, the CI for the infection risk comparison between PVCs and CVCs (0.01–1.45) suggests that the results could range from a "99% reduction in infection risk" with PVCs to a "45% increase in risk", underscoring the uncertainty and fragility of the comparative evidence.

Based on both the single-group rate and comparative data, the following stratified decision-making framework was proposed: MCs (extravasation rate: 0.68%, thrombosis rate: 2.06%, infection rate: 1.18%) can be considered a safer option when minimizing the risk of extravasation; PVCs (extravasation rate: 1.69%, thrombosis rate: 0.09%, infection rate nearly 0) demonstrated the lowest infection and thrombosis risks but a higher extravasation rate than MCs, suggesting that their use should be accompanied by careful monitoring; PICCs (thrombosis rate: 4.41%) require individualized risk-benefit analysis given their higher thrombosis risk. The current evidence is insufficient to overturn the status of CVCs as the gold standard for hyperosmolar or long-term infusions, but it provides a risk baseline for transition options in critically ill patients in whom a central line cannot be established.

This study had limitations. First, the vasopressor drugs, concentrations, and dwell times in the original studies were not standardized, and consistent grouping criteria were unavailable, which prevented the control of confounders.

Therefore, differences in risks across the catheter groups are possibly influenced by nursing standards, infusion practices drug formulations, and other variables. Second, the scarcity and heterogeneity of the comparative studies (e.g., inconsistent infection definitions) limit the external validity of the results. Third, given the limitations of the original studies, adjustments for the modifiable factors such as catheter dwell time, drug osmolarity, and infusion concentration could not be performed, making it difficult to elucidate the mechanisms underlying the risks. Future research should include multi-center RCTs employing standardized definitions for complications [e.g., Infusion Nurses Society (INS) extravasation grading and Centers for Disease Control and Prevention (CDC) infection criteria]. Finally, local variations in catheter care protocols and nursing standards were not accounted for, which may substantially influence complication rates. The lack of detailed or standardized reporting of these factors in the included studies made it impossible to quantify or adjust for their effects. Therefore, clinicians should interpret our findings in the context of the specific care protocols and standards implemented in their own institutions.

Conclusions

Our meta-analysis indicates that the overall complication risk linked to vasopressor infusion via PVCs is relatively low. Specifically, the incidence rates of extravasation, thrombosis, and catheter-related infections were 1.43%, 1.47%, and 0.72%, respectively. Although direct comparative evidence between PVCs and CVCs was limited, no statistically significant differences in complication risks were observed. However, due to limitations in sample size and heterogeneity, these conclusions should be interpreted with caution. Future multi-center RCTs are necessitated to standardize complication definitions, control for confounders, and further validate the long-term safety and applicable patient populations for different catheter types. It should be emphasized again that the central value of this study lies in summarizing the prevalence of AEs (extravasation, thrombosis, and catheter-related infections) associated with the administration of vasopressors through PVCs. Further high-quality and detailed data are still needed to validate and expand upon our findings.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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