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Comparing complication rates of midline catheter vs. Peripherally inserted central catheter (PICC). A systematic review and meta-analysis

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Background: Peripherally inserted central catheters (PICC) and midlines are commonly used devices for reliable vascular access. Infection and thrombosis are the main adverse effects of these catheters. We aimed to evaluate the relative risk of complications from midlines and PICC.

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Methods: We conducted a systematic review and meta-analysis of randomized controlled trials (RCT) and observational. The primary outcomes were catheter-related bloodstream infection (CRBSI) and thrombosis. Secondary outcomes evaluated included mortality, failure to complete therapy, catheter occlusion, phlebitis, and catheter fracture. The certainty of evidence was assessed using the GRADE approach.

Results: Of 8,368 citations identified, 20 studies met eligibility criteria, including one RCT and nineteen observational studies. Midline use was associated with fewer patients with CRBSI compared to PICC (OR: 0.24; 95% CI: 0.15 to 0.38). This association was not observed when we evaluated risk per catheter. No significant association was found between catheters when evaluating risk of localized thrombosis and pulmonary embolism. A subgroup analysis based on location of thrombosis showed higher rates of superficial venous thrombosis in patients using midline (OR: 2.30; 95% CI: 1.48 to 3.57). We did not identify any significant difference between midline and PICC for the secondary outcomes.

Conclusion: Our findings suggest that patients who use midline might experience fewer CRBSI than those who use PICC However, the use of midline catheter was associated with greater risk of superficial vein thrombosis. These findings can help guide future cost-benefit analyses and direct comparative RCTs to further characterize efficacy and risks of PICC versus midline catheters.

Keywords: Midline, PICC, infection, thrombosis, catheter

INTRODUCTION

Peripherally inserted central catheters (PICCs) have become ubiquitous in the care for hospitalized patients. These lines are associated with low insertion risk, low rates of complications, and allow for durable outpatient intravenous (IV) access, thereby facilitating timely dismissal of patients requiring prolonged IV infusions and frequent blood draws.[1] A systematic review by Chopra and colleagues in 2013 demonstrated a lower risk of Central Line Associated Bloodstream Infection (CLABSI) with PICC lines, when compared to central venous catheters (CVC).[2] The convenience of these devices, however, have led to misuse and overuse, including the utilization of PICC lines in patients with reliable peripheral access and no need for centrally administered medications. The increasing use of PICCs have made the drawbacks of these devices obvious; the long-term lines are associated with thrombotic events, risk of luminal occlusion, and pose risk of infection similar to other CVC.[2-4]

The midline catheter has emerged as an alternative to PICC lines. It is a shorter catheter inserted into the arm, like a PICC, but terminating at the basilic or axillary vein rather than in the central venous circulation. These devices provide the benefit of durable access, but with shorter length and lower surface area reducing the theoretical risk of thrombosis and contamination, as well as

possibly lower rates of infection.[5] Midline catheters have a shorter indwell time (up to 4 weeks) compared to PICC (weeks to months), but are considerably more durable than peripheral IV. They represent an attractive option for short-to-medium term venous access in the inpatient and outpatient setting and are the preferred line for this indication by The Michigan Appropriateness Guide for Intravenous Catheters (MAGIC).[6, 7]

As midline catheters are not considered CVC, their infection rates are not routinely reported as part of the CLABSI metrics.[8] Increased use of midline catheters should lead to a reduction in reported CLABSIs, but it is less clear whether this is attributable to a true decrease in the risk of infection versus under-reporting of metrics. The increasing use of midline catheters makes it important to critically assess complications of these devices and ensure that these apparent improvements are not artifacts of definitions.[7, 9-11]

Despite the emerging data regarding the efficacy of these devices, there is limited evidence comparing device outcomes and risks, specifically the risk of catheter-related bloodstream infection (CRBSI) and thrombosis. For this reason, we conducted a systematic review to evaluate the relative risk of complications from midline catheters and PICC.

METHODS

This review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statements. The study protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO ID: 42018088270).

Literature search

We searched Embase, Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE, Cochrane Central Registrar of Controlled Trials, Ovid Cochrane Database of Systematic Reviews, and Scopus from inception to June 24, 2022. The literature search strategy was developed by an experienced medical librarian with input from the senior researchers. Search strategy in detail is available in Table 1 in the supplement.

Study selection

Eligible studies 1) were randomized controlled trials (RCT) and comparative observational studies; 2) included adult patients (≥ 18 years old) requiring venous access using PICC or midline catheters for >24 hours; and 3) were published in English. We excluded studies with more than 50% of patients on chemotherapy, total parenteral nutrition, or dialysis on any group (PICC or midline). Other comparators such as port devices, implanted devices, tunnel catheters, dialysis catheters, short term CVC, femoral catheters, internal jugular catheters, Hickman catheters, and palindrome catheters were not considered for outcome analysis.

Titles and abstracts of all citations were screened in pairs. Studies included by either reviewer were retrieved for full-text screening. Independent reviewers, working in overlapping duplicates, screened the full-text version of eligible studies. In this phase, any disagreements between the reviewers were harmonized by a third senior investigator. These activities were conducted using the online software DistillerSR (Evidence Partners, Ottawa, Canada).

Data extraction and quality assessment

A standardized data extraction form was developed to extract relevant study characteristics and outcome data. Reviewers worked independently to extract study data. We assessed the risk of bias of the included RCT using the Cochrane Collaboration's Risk of Bias 2 tool which evaluates the randomization process, deviations from the intended interventions, missing outcome data, measurement of the outcome, and selection of the reported results. [12] For observational studies, we adopted selected items from the Newcastle-Ottawa Scale assessing selection, comparability, outcome.[13]

The certainty of evidence was graded using the GRADE approach, categorized as "high", "moderate", "low", and "very low". RCTs without important limitations provide high quality evidence and observational studies without special strengths or important limitations provide low quality evidence. Factors that downrate the quality of evidence are risk of bias, inconsistency, indirectness, imprecision, and publication bias. The process of rating followed the GRADE handbook [14] and the evidence profile table was generated using the software GRADEpro GDT.[15]

The two primary outcomes were CLABSI (in the case of PICCs) or CRBSI (in the case of midlines) and thrombosis. We also evaluated mortality, failure to complete therapy, catheter occlusion, phlebitis, and catheter fracture. Outcomes were reported and analyzed per patient or per catheter in the individual studies because they are considered different unit of analysis (i.e. one patient could have more than one catheter in a study time). The reported definitions of the primary outcomes were provided by each individual study (Table 2 in the supplement). The authors judged whether a given set of studies could be pooled in the outcome analysis based on these definitions.

Data synthesis and analysis

All statistical analyses were based on the "intention-to-treat" (ITT) principle for RCTs, and for observational studies the number of patients that received the intervention at the beginning of the study. For this study, the ITT principle considered all randomized participants. We calculated odds ratio (OR) for binary outcomes. Meta-analyses were conducted using the random effects model. We evaluated statistical heterogeneity between studies using the I^2 estimate, where values closer to 100% represent considerable statistical heterogeneity.[16] Additionally, we conducted subgroup analyses based on thrombosis localization: deep venous thrombosis (DVT) or superficial venous thrombosis (SVT). A two-sided p-value of <0.05 was deemed statistically

significant. We estimated the optimal information size (OIS) of the main outcomes using 0.05 for type 1 error (α). We repeated the analysis using fixed values for type 2 error (β) of 80%, 85% and 90%. The control event rates were calculated and the minimally important clinical differences were set at 0.5%, 1%, and 1.5%.

Analysis was performed using OpenMeta analysis software and R (4.2.0)

RESULTS

The literature search identified 8,368 records. 7,947 studies were excluded in the title or abstract screening level and 421 were eligible for full text, of which 20 were selected for inclusion to the analysis. The flow diagram of the systematic literature review is illustrated in Figure 1.

Study characteristics

We included one RCT[7] and nineteen observational studies.[9-11, 17-32] published between 1997-2022. Twelve studies were conducted in the USA, one in the USA and Canada, two in United Kingdom, two in Australia, two in Italy, and one in Korea. Thirteen studies were conducted in an inpatient setting, six in an outpatient setting, and one in a palliative care unit. Additional information and characteristics of each study are presented in Table 1. Risk of bias assessment is presented in Tables 3 and 4 in the supplement. GRADE evidence profile is depicted in Table 5 in the supplement.

Primary outcomes: CLABSI/CRBSI and thrombosis

Sixteen studies reported the number of patients with CLABSI and/or the number of catheters with an associated bloodstream infection. Overall, midline use was associated with fewer patients with CRBSI compared to PICC (OR: 0.24; 95% CI: 0.15 to 0.38, I^2: 0.00%; 9 studies; 12,478 patients; very low certainty), the results of the meta-analyses are summarized in Figure 2. We estimated that we would need a sample of 926 (with 80% power and α 0.05) to detect a plausible difference in treatment effect for midline compared to PICC on catheter-related bloodstream infections, corresponding to a relative risk reduction of 1.5% (Table 6 in the supplement). No association was observed when we evaluated risk of bloodstream infection per catheter (OR: 0.70; 95% CI: 0.39 to 1.27, I^2: 81.99%; 9 studies; 49,426 catheters; very low certainty).

Thrombosis was reported as either localized thrombosis (SVT, DVT, any other thrombosis) or pulmonary embolism. No association was noted when we evaluated localized thrombosis per catheters (OR: 1.05; 95% CI: 0.69 to 1.57, I^2: 74.02%; 6 studies; 48,177 catheters; very low certainty) and per patients (OR: 1.31; 95% CI: 0.74 to 2.30, I^2: 60.24%; 9 studies; 14,555 patients; very low certainty). Inconsistency in the results and heterogeneity in the reporting of the outcome was noted. Our estimated showed that we would need a sample of 28,321 (with 80%

power and α 0.05) to detect a relative risk reduction of 0.5% for midline compared to PICC on localized thrombosis (Table 6 in the supplement). A subgroup analysis based on type of localized thrombosis revealed higher rates of SVT in patients using midline (OR: 2.30; 95% CI: 1.48 to 3.57, I^2: 0.00%; very low certainty), but no significant difference was observed in rates of DVT (OR: 0.99; 95% CI: 0.70 to 1.41, I^2: 55%; very low certainty). Figure 3 presents the results of the subgroup analysis.

We did not observe any correlation between catheter type and risk of pulmonary embolism (OR: 0.87; 95% CI: 0.53 to 31.44, I^2: 0.00%; 2 studies that included 13,440 patients; very low certainty; and OR: 0.80; 95% CI: 0.37 to 1.72, I^2: 0.00%; 2 studies that included 12,464 catheters; very low certainty).

Secondary outcomes

Mortality was reported in one study, which did not observe any difference in this outcome between catheter type (OR: 1.90; 95% CI: 0.82 to 4.41; 406 patients; very low certainty).

The use of PICC was associated with more patients failing to complete therapy compared to midline (OR: 1.92; 95% CI: 1.01 to 3.66; I^2=32.08%; 6 studies, 13,653 patients; very low certainty). No difference was observed between catheter type and failure to complete therapy when analyzed by catheters (OR: 2.08; 95% CI: 0.53 to 8.15; I^2=69.27%; 3 studies, 31,071 catheters; very low certainty).

No difference was observed between catheter type and catheter occlusion when evaluated per patient (OR: 0.46; 95% CI: 0.18 to 1.18; I^2=34.06%; 5 studies, 11,515 patients; very low certainty) or per catheter (OR: 2.28; 95% CI: 0.19 to 27.58; I^2=98.08%; 4 studies, 43,220 catheters; very low certainty).

Rates of phlebitis were similar among patients who used midline versus PICC catheters (OR: 0.91; 95% CI: 0.39 to 2.15; I^2=0%; 5 studies, 659 patients; very low certainty), as well as when evaluated per catheter (OR: 1.74; 95% CI: 0.41 to 7.36; 1 study, 406 catheters; very low certainty).

Lastly, we did not note any differences between midline and PICC with respect to proportion of patients with a fractured catheter (OR: 0.84; 95% CI: 0.08 to 9.36; 1 study, 328 patients; very low certainty) or with the proportion of fractured catheters (OR: 1.11; 95% CI: 0.88 to 1.40; 1 study, 30,987 catheters; very low certainty).

DISCUSSION

1. Summary of findings

This meta-analysis identified 20 studies that compared primary outcomes including risk of CRBSI and thrombosis between midline catheters and PICC. Our findings suggest lower rates of bloodstream infection in patients who used midline in comparison to PICC. However, the use of midline catheter was associated with greater risk of SVT, albeit similar rates of overall localized thrombosis (SVT and DVT) and pulmonary embolism. PICC was associated with more patients failing to complete therapy. We did not find any significant difference between midline and PICC for the secondary outcomes assessed including mortality, phlebitis, and rates of fractured catheter.

2. Implications to clinical practice

CRBSI and catheter-related thrombosis are the main adverse events associated with vascular catheters and have been widely investigated.[33] Catheter related infection is a serious and frequent complication that varies according to the device used.[34] The risk can be influenced by setting, experience of proceduralist, frequency of catheter access and care, duration of placement, and patient specific characteristics. A prior meta-analysis has demonstrated the risk of CRBSI for several catheter types at 0.1% for peripheral, 0.4% for midline, 2.4% for PICC, 4.4% for CVC.[1] Historically, PICC has been associated with reduced risk of CLABSI relative to CVC.[2]

Interestingly, midline catheters may have an even lower infection rate compared to PICC.[1] Our study suggested that rates of CRBSI per patient were lower with midline catheters when compared to PICC. This association was not present when the outcome was analyzed per catheter. It is important to note that CLABSI rates being higher in PICC is largely being driven by one cohort (Swaminathan et al 2022).[32]A prior meta-analysis by Lu and colleagues found no difference in rates of CRBSI between PICC and midline (RR: 0.77; 95% CI: 0.50 to 1.17).[5]

Catheter-related venous thrombosis is a second significant complication of catheter insertion. This outcome can be categorized into minor complications like superficial thrombophlebitis and major complications such as DVT and PE. PICC has been associated with an increased risk of thrombosis in several studies. A prior meta-analysis by Chopra and colleagues comparing PICC vs. other CVC, reported an increased risk of PICC-associated deep vein thrombosis (OR: 2.55; 95% CI 1.54 to 4.23).[35] The difference in risk of thrombosis between midline and PICC is not clear. Our study demonstrated lower rates of SVT with PICC, when compared to midline. However, we did not identify any significant difference in rates of DVT or PE between catheter types. This is consistent with a prior cohort study comparing midline vs. PICC, which did not find a significant difference in the risk of DVT or PE (OR: 0.93; 95% CI: 0.63 to 1.37; and OR: 1.29; 95% CI: 0.46 to 3.61, for DVT and PE, respectively).[32] In contrast, a prior small, prospective trial by Lescinskas et al (n=113) found that 14.5% of patients with PICC developed

DVT compared to no patients in the midline group.[20] Part of the difference observed in rates of DVT and PE between our meta-analysis and prior prospective trials may be secondary to significant heterogeneity and imprecision of outcomes as noted.

The number of patients included in the analysis is only the 51% of the 28,321 we calculated was required, which is the number of patients needed to reliably reject a difference in effect of midline and PICC on localized thrombosis based on a relative risk reduction of 0.5% and a control event rate of about 2.7%. Our analysis showed that the current evidence for a clinically relevant difference of midline and PICC for localized thrombosis is still inconclusive. Although more head-to-head data is needed to compare risk of thrombosis between midline and PICC, the overall risk of serious thrombotic events including PE appears to be low with both vascular catheters.

3. Strengths and limitations

This study included a comprehensive search strategy of relevant medical databases such as OVID, MEDLINE, and Scopus, with systematic screening to facilitate identification, assessment, and synthesis of the body of current evidence relevant to the study question. The majority of the included studies had a prospective, longitudinal design, which facilitated correlation of sequence of events, starting from catheter insertion to observation of outcomes of interest. The primary and secondary outcomes were analyzed by rate of events per patients or per catheters according to reporting within the original study. This strategy allowed us to be inclusive of all studies that reported the outcomes of interest.

This study has several limitations. First, most of the data came from observational studies and only one small RCT (n=54) at high risk of bias, which ultimately accounted for overall very low certainty in the evidence. While observational studies have proven useful when assessing risk factors, RCTs are better accepted as an optimal design to compare the efficacy and effectiveness of medical interventions, offering less heterogeneity between studies and lower risk of bias due to confounding and overestimation of treatment effects. Second, inclusion of head-to-head prospective studies were rare. These types of trials are critical in evaluating direct comparison of outcomes and providing insight into shared decision-making among all the available options. Third, we did not exclude any records by publication year, thus including some studies from ≥20 years ago (1997-2002). This may falsely skew towards worse outcomes as newer catheters, medical equipment, and procedural techniques likely offer better safety profiles. Fourth, many included studies were at high risk of bias. The most frequent source of bias was the comparability between interventions due to lack of matching, which introduced risk of critical confounders such as catheter usage time. Finally, imprecision was a concern for certain important primary outcomes including rates of pulmonary embolism, likely driven by low event rates.

4. Future research

Further head-to-head RCTs in patients who are candidates to receive either PICC or midline are needed. Clinically important outcomes including infection and thrombosis (both local and systemic) should be considered by trialists. Furthermore, relative contribution of SVT and DVT to overall risk of thrombosis needs to be further delineated, as our data supports that the higher rates of thrombosis with midline may largely be SVT.

These RCTs should ideally consider evaluating treatment-subgroups by setting (inpatient vs outpatient), site of insertion of midline (i.e. basilic vs. brachial vs. cephalic), expertise of the proceduralist, duration of placement, we well as patient, device, or healthcare-related characteristics. Furthermore, cost-benefit analyses are needed to further guide decision making for clinicians and patients when deciding on the type of catheter that best fit the patients' needs.

5. Conclusions

Bloodstream infections and thrombosis are important healthcare consequences of vascular catheters. This meta-analysis compared the rates of these primary outcomes between PICC and midline. Our findings suggest that patients who use midline might experience fewer CRBSI than those who use PICC. However, the use of midline catheter was associated greater risk of thrombosis with more patients having SVT. The relative risk of DVT and PE remains unknown. These findings warrant future cost-benefit analyses and direct comparative RCTs to further characterize efficacy and risks of PICC versus midline catheters.

NOTES

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Table 1. Study characteristics

Author, Year	Study design, Country	Setting	Intervention	Population Characteristics	Device Characteristic
Bahl, 2019[9]	Retrospective cohort, USA	Inpatient (non-critical)	Midline	1,094 patients aged 63.70±17.80 years; 65.50% female	Place of insertion: 59.80% basilic, 32.60% brachial, 6.50% cephalic, 1.10% other; 36.20% antibiotic therapy; 52.30% poor vascular access; 0% TPN; 11.50% other
			PICC	1,483 patients aged 63.70±16.90 years; 47.50% female	Place of insertion: 69.80% basilic, 26.60% brachial, 2.60% cephalic, 1% other; 62.40% antibiotic therapy; 6.50% poor vascular access; 12.80% TPN; 18.20% other
Barr, 2012[17]	Retrospective cohort, United Kingdom	Outpatient	Midline	648 catheters	100% antibiotic therapy
			PICC	43 catheters	100% antibiotic therapy
Bing, 2022[29]	Retrospective cohort, USA	Inpatient and ICU	Midline	1,772 patients (2049 catheters) aged 57±17.7 years; 54% female; race: Hispanic 2%, non-Hispanic 98%	NA
			PICC	1,636 patients (2502 catheters) aged 57±16.29 years; 51% female; Hispanic 2%, non-Hispanic 98%.	NA

Author, Year	Study design, Country	Setting	Intervention	Population Characteristics	Device Characteristic
Caparas, 2014[7]	RCT, USA	Inpatient (non-critical)	Midline	29 patients (30 catheters) aged 72 years; 69% female	100% basilic, brachial and cephalic; catheter dwell-time 5.80±2.75 days, 100% antibiotic therapy
			PICC	25 patients (28 catheters) aged 69 years; 48% female	100% basilic, brachial and cephalic; catheter dwell-time 6.30±6 days, 100% antibiotic therapy
Caserta, 2022[30]	Retrospective cohort, Italy	ICU	Midline	42 patients (42 catheters) [Midline]	34% antibiotic therapy; 66% poor vascular access; 0% TPN
			PICC	61 patients (61 catheters) [PICC]. Total population: Aged 74±10 years; 53% female	58.50% antibiotic therapy; 54.70% poor vascular access; 26.80% TPN
Dickson, 2019[18]	Retrospective cohort, Australia	Outpatient	Midline	38 patients; 31.60% female	Catheter dwell-time 25.20±17.90 days, 100% antibiotic therapy
			PICC	33 patients; 45.50% female	Catheter dwell-time 35.40±28.01 days, 100% antibiotic therapy
Khalidi, 2009[19]	Prospective cohort, USA	Inpatient (non-critical)	Midline	44 patients (Midline) 116 patients (PICC). Total population 43.10% female; race: 75.60% White, 13.10% African American, 11.30% other	Place of insertion: 54.40% basilic, 24.40% cephalic, 20.60% other; 82% antibiotic therapy, 18% other
			PICC		
Kim, 2022[31]	Retrospective cohort, Korea	Inpatient (non-critical)	Midline	20 patients (20 catheters) aged	Catheter dwell-time 15.10±18.75 days, 65%

Author, Year	Study design, Country	Setting	Intervention	Population Characteristics	Device Characteristic
				57±18.40 years; 40% female	poor vascular access; 10% TPN; 25% other
			PICC	10 patients (10 catheters) aged 67.7±20.70 years; 70% female	Catheter dwell-time 28.70±38.50 days, 70% poor vascular access; 20% TPN; 10% other
Lescinskas, 2020[20]	Prospective cohort, USA	Inpatient (non-critical)	Midline	58 patients aged 49.10±12.90 years; 62% female; race: 48% White, 46% African American, 40% Asian, American Indian, Hispanic and other	12% antibiotic therapy; 52% poor vascular access; 28% other
			PICC	63 patients aged 45.50±13.90 years; 27% female; race: 68.30% White, 28.60% African American, 58.70% Asian, American Indian, Hispanic and other	11.10% antibiotic therapy; 11.10% poor vascular access; 12.70% other
Magnani, 2019[21]	Prospective cohort, Italy	Palliative care unit	Midline[a]	8 patients (Midline) 24 patients (PICC). Total population aged 73±13 years; 47.80% female	Place of insertion: 87.50% basilic, 12.50% brachial, 0% cephalic
			PICC[a]		Place of insertion: 75% basilic, 25% brachial, 0% cephalic
Moureau, 2002[22]	Retrospective cohort, USA	Outpatient	Midline	5,397 patients (5,423 catheters); 48% female	NA
			PICC	25,590 patients (25,707 catheters); 45% female	
Mushtaq,	Retrospective	Inpatient and ICU	Midline	411 patients aged	19.40% antibiotic

Author, Year	Study design, Country	Setting	Intervention	Population Characteristics	Device Characteristic
2018[23]	cohort, USA			58.79±17.72 years; 55.20% female	therapy; 76.60% poor vascular access; 0% TPN; 2.90% others.
			PICC[b]	282 patients aged 56.62±17.76; 45.70% female	23.70% antibiotic therapy; 48.90% poor vascular access; 1.70% TPN; 25.10% others.
Sargent, 1997[24]	Retrospective cohort, United Kingdom	Inpatient (non-critical)	Midline	12 catheters	Catheter dwell-time 7 days
			PICC	18 catheters	Catheter dwell-time 21 days
Seo, 2019[31]	Retrospective cohort, USA	Outpatient	Midline	82 patients aged 66.39± 21.23 years; 43.90% female	Place of insertion: 29.30% basilic, 22% brachial, 24.40% cephalic; catheter dwell-time 10.65±7.43 days
			PICC	50 patients aged 61±20 years; 60% female	Place of insertion: 66% basilic, 30% brachial, 4% cephalic; catheter dwell-time 29±15.50 days
Sharp, 2014[11]	Retrospective cohort, Australia	Outpatient	Midline	231 patients; 44% female	NA
			PICC	97 patients; 39% female	
Swaminathan, 2022[32]	Retrospective cohort, USA	Inpatient and ICU	Midline	5,105 patients aged 64.80±16.81 years; 58.20% female; race: 56.40% White, 39.20% African American, 0.60% Asian	Place of insertion: 48.70% basilic, 37.10% brachial, 14.20% other; catheter dwell-time 6±6.66 days; 40.10% antibiotic therapy; 72.40% poor vascular

Author, Year	Study design, Country	Setting	Intervention	Population Characteristics	Device Characteristic
					access; 0.10% TPN; 1.30% others.
			PICC	5,758 patients aged 64.90±16 years; 48.10% female; race: 75.90% White, 18.50% African American, 0.50% Asian	Place of insertion: 60.60% basilic, 32.50% brachial, 6.80% other; catheter dwell-time 14±14.81 days; 71.20% antibiotic therapy; 40.10% poor vascular access; 3.80% TPN; 5.50% others.
Tokars, 1999[26]	Prospective cohort, USA and Canada	Outpatient	Midline[c]	155 catheters (Midline) 324 catheters (PICC). Total population aged 52 years; 41.50% female	Total population: 67.50% antibiotic therapy; 10.20% TPN; 4.20% chemotherapy
			PICC[c]		
Tso, 2017[27]	Retrospective cohort, USA	Inpatient (non-critical)	Midline	100 catheters (Midline) 205 catheters (PICC). Total population aged 38±12.16 years; 74% female	NA
			PICC		
Vanek, 1997[28]	Case series, USA	Inpatient (non-critical)	Midline	2,169 catheters	NA
			PICC	61 catheters	
Xu, 2016[10]	Retrospective cohort, USA	Inpatient and ICU	Midline	172 patients (200 catheters) aged 62.50±13.16 years; 54.70% female	0% antibiotic therapy; 97% poor vascular access
			PICC	185 patients (206 catheters) aged 60±11.33 years; 38.40% female	63.60% antibiotic therapy; 35.40% poor vascular access

ICU = intensive care unit; NA = not available; PICC = peripherally inserted central catheter; RCT = randomized controlled trial; TPN = total parenteral nutrition

[a] Total population includes patients with midline, PICC and "short" midline insertion

[b] Included patients with CVC lines (peripherally inserted central catheter, internal jugular, subclavian, or femoral)

[c] These numbers belong to the total population (n= 827), not only PICC and midline patients.

FIGURES

Figure 1: Selection of trials for inclusion in the review and meta-analysis

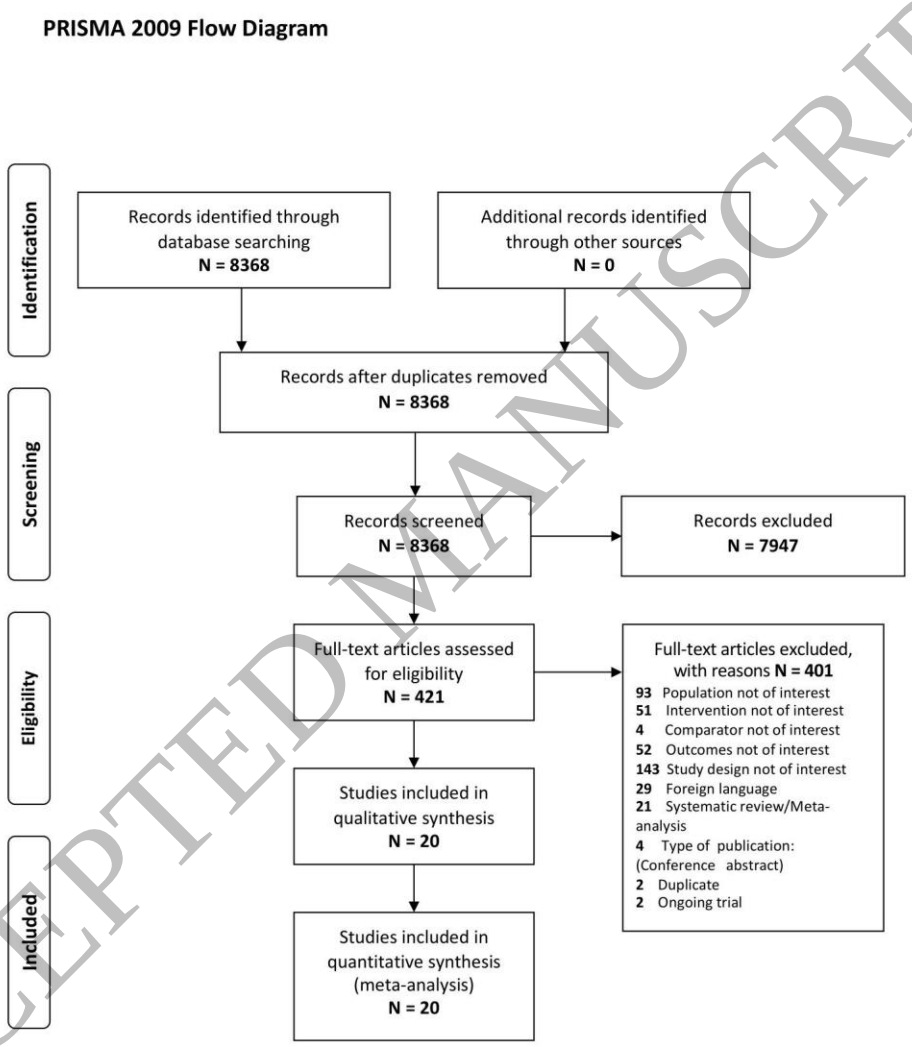

Figure 2: Forest plot comparing rates of CRBSI in patients with midlines vs PICC

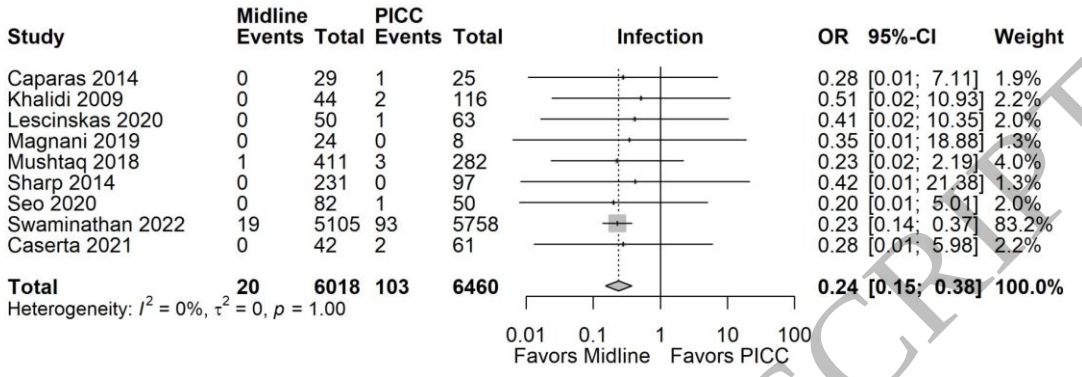

Figure 3: Subgroup analysis based on thrombosis localization