RESEARCH PAPER

PICC Line Associated Blood Stream Infections: an Analysis of Host and Device Factors

Turki Alkully [a] **Sandra Hensley** [b] **Sadik Khuder** [c] **Naveena Luke** [d] **Mohammed Ruzieh** [e] **and Joan Duggan**[1,f]

Coresponding author(s): [1] joan.duggan@utoledo.edu

[a]Department of Gastroenterology, University of Toledo Medical Center, Toledo, OH 43614, USA,,[b]Division of Infectious Diseases, University of Toledo Medical Center, Toledo OH 43614, USA,,[c]Departments of Medicine and Public Health, University of Toledo Medical Center, Toledo OH 43614, USA,,[d]Department of Physiology and Pharmacology , University of Toledo Medical Center, Toledo OH 43614, USA,,[e]Department of Internal Medicine, University of Toledo Medical Center, Toledo OH 43614, USA,, and [f]Department of Medicine, University of Toledo Medical Center, Toledo OH 43614, USA.

Background: Risk factors for PICC CLABSI (peripherally inserted central venous catheter/ central line associated bloodstream infections) have been evaluated in a limited number of prospective and retrospective studies with conflicting results. Methods: A six year retrospective review of PICC CLABSI within a single institution was performed. PICC CLABSI cases were matched to uninfected controls and host and device data were extracted from comprehensive medical record reviews. A statistical analysis of PICC CLABSI risk factors compared to matched controls was performed. Results: 6756 patients had a PICC line placed during the study period (January 1, 2008 - December 31, 2013). Fifty-six (0.83%) CLABSI were identified and matched to 245 uninfected controls. Factors associated with PICC CLABSI included: sepsis (P<0.0001), history of smoking (P=0.002), hyperlipidemia (P=0.048), duration of PICC (P<0.0001), area of insertion (P=0.019), use of de-clotting agents (P=0.0009), complication after PICC line insertion (P=0.0008), and use of anti-MRSA antibiotics after PICC insertion (P=0.006). In multivariant analysis, there was a significant association between PICC CLABSI and sepsis (OR=4.9, CI 2.2-11.1), history of smoking (OR=2.9, CI 1.3 { 6.2) and gastrostomy (OR=6.5, CI 2.2 { 19.4). Conclusions: Risk factors for PICC CLABSI in an institution with low rates of infection include both host factors (sepsis, smoking, gastrostomy tube) and device factors (area of insertion, complications, use of de-clotting agents, anti-MRSA antibiotics after PICC placement, and PICC duration). Preventative measures targeting modifiable risk factors may decrease rates of PICC CLABSI in the future.

peripherally inserted central venous catheter | blood streem infections

In recent years, peripherally inserted central venous catheters (PICC) have increasingly replaced subclavian or internal jugular central venous catheters (CVC) in both the outpatient and inpatient setting. This significant increase in the use of PICCs can be explained by many factors, including ease of insertion, improved patient comfort, and favorable cost profile (1, 2). PICC are often considered to have a superior safety profile than CVC (3). Some studies have also indicated that PICC have a decreased incidence of central line associated bloodstream infections (CLABSI) when compared with CVC (4-6), but a more recent meta-analysis showed that PICC used in the inpatient setting may have a risk of infection similar to CVC (7).

The risk factors for inpatient CVC and PICC have been evaluated in a number of prospective and retrospective studies (8-10) and multiple strategies to decrease infection rates have been evaluated and successfully implemented. Several studies have examined selected risk factors for CLABSI in PICC (11-13), including patient and device associated risk factors and post-placement line management, with some conflicting results. A deeper understanding of the risk factors for CLABSI in PICC may help in the development of additional appropriate prophylactic strategies to decrease the incidence of infection. Given the increasing number of PICC used in the inpatient and outpatient settings and the devastating consequences of CLASBI, this may result in significant improvements in patient care and safety. In our institution, a dedicated PICC line team used a multi-faceted approach to PICC line insertion and maintenance and achieved one of the lowest rates of CLABSI in the nation sustained for over a 5-year period of time (14). In this current study, a retrospective analysis of PICC-associated bloodstream infections was undertaken using data collected from a six year period of time in an institution which had achieved very low infection rates of CLABSI to evaluate patient and device factors that may be associated with

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inpatient PICC CLABSI in this setting.

Materials and Methods

Study Design and Subjects

The study was approved by the Institutional Review Board at the University of Toledo Medical Center (UTMC) and consisted of a retrospective analysis within the institution of all patients age >18 years who had a PICC line inserted by a dedicated PICC line team using maximal barrier precautions. The study period was between January 1st, 2008 and December 31st, 2013. PICC CLABSI cases were identified using the National Healthcare Safety Network (NHSN) definition for blood stream infections. All PICC CLABSI cases underwent chart review using the NHSN definition. Patients meeting the NHSN CLASBSI definition who had a PICC line inserted outside of UTMC or a PICC CLABSI documented at less than two calendar days from insertion date were excluded from analysis.

Data Collection

PICC CLABSI cases occurring during the study period were obtained from the infection prevention department and also through review of billing codes. Patient information and information regarding the PICC insertion and maintenance were obtained by a comprehensive medical record review and review of billing codes. The International Classification of Diseases - 9th revision (ICD- 9) was used during the period of study. PICC CLABSI cases were matched to uninfected controls with similar age, gender, race and time of admission within a six-month period (January 1 to June 30 and July 1 to December 31).

PICCs insertion and maintenance protocol

All PICC lines were inserted by a dedicated PICC team using portable ultrasonography guidance. Placements were done under maximal sterile barrier precautions, which included sterile gown, sterile gloves, cap and use of a full body drape. Chlorhexidine gluconate 2% was used to sterilize the skin prior to insertion and chlorhexidine gluconate dressings were placed after insertion. The position of the PICC tip was verified by chest radiography prior to usage of the line. The PICC team performed line checks and dressing changes weekly. The PICC line team used the de-clotting agent alteplase in cases of catheter occlusion on an as needed basis as per manufacture instructions.

Definition of variables

The variables collected through chart documentation and billing code review were defined prior to data extraction. Patient demographics of age, race, gender, and time period of insertion (January 1 through June 30 and July 1 through December 31). were collected. Past medical and surgical history, home medications, hospital medications, and the course of the hospitalization including microbiology data were extracted through review of both the electronic medical record and the paper chart as applicable. The duration of the PICC line was calculated in days from insertion until PICC removal or documented CLABSI. Steroid use was defined as any systemic steroid intake within 30 days before or after the PICC placement but not including use of intranasal, inhaled, or topical preparations. Statin and non-steroidal anti-inflammatory drug (NSAID) use was defined as use of any medication in these classes except for topical NSAIDS within 30 days before or after PICC line insertion. Antibiotic therapy was divided into usage of any non-topical antibiotic 30 before or after PICC insertion and was further divided into MRSA coverage if the patients received at least two doses of Vancomycin, Daptomycin, Linezolid, Bactrim or Doxycycline. Active chemotherapy was defined as receipt of oral or intravenous chemotherapy treatment within 30 days before or after PICC line placement. Transfusion of blood products was defined as receipt of any blood products such as packed red blood cells, platelets, or fresh frozen plasma during the hospital observation period.

Statistical Analyses

All data underwent statistical analyses using SPSS 21.0 software. The correlation between PICC CLABSI and risk factors was determined using chi-square test. Multivariate analysis was done using logistic regression. Two tailed P value < 0.05 was considered to be statistically significant.

Results

A total of 6756 patients underwent a PICC line placement during the study period (January 1, 2008 thru December 31, 2013). Fifty-six (0.83%) infected cases were identified and matched to 245 uninfected controls. The final analysis included 301 patients total.

The demographic characteristics, comorbid diseases and medications (statins, NSAIDs, steroids) for both groups are shown in Table 1. There was a significant association between an infected PICC and a diagnosis of sepsis (P<0.0001) hyperlipidemia (P=0.048) or a history of smoking documented on the initial assessment (P=0.002). There was no significant correlation between PICC CLABSI and the use of statins (OR: 0.95, 95% CI [0.52-1.72], P=0.87), NSAIDs (OR: 0.82, 95% CI [0.34-1.97], P=0.67) and/or steroids (OR: 1.01, 95% CI [0.54-1.88], P=0.96) either 30 days before or after insertion (P>0.05).

Device related factors among infected PICC lines and the matched control group are listed in Table 2. There was a correlation between PICC infection and the duration of PICC use (mean: 14 days vs 7 days, P<0.0001). There was significant correlation with PICC line infection and the following use of de-clotting agents (OR:0.22, 95% [CI:0.08-0.57], P=0.0009), complication after PICC line insertion (OR:4.22, 95%CI [1.72-10.34], P=0.0008) and the use of MRSA coverage antibiotics after PICCs insertion but not in the 30 days prior to insertion (OR:2.26, 95%CI [1.24-4.10], P=0.006).

The most common PICC insertion vein was the basilic vein (n=196, 65.11%) and insertion in the median cubital vein was associated with an increased risk of infection (OR:0.32, 95% CI [0.12-0.86], P=0.019). Most of PICC lines were inserted in non-intensive care units including the rehabilitation unit and the general medical/surgical units (n=225, 74.75%). There was no significant correlation between PICC CLABSI and number of lumens in the PICC (P>0.05).

There was a significant association with presence of a gastrostomy tube (OR:0.20, 95%CI [0.09-0.44], P:<0.0001) and mechanical ventilation (OR:1.99,95%CI [1.04-3.80], P=0.03) with PICC CLABSI compared to matched controls (Table 3). There was no correlation between a PICC CLABSI and presence of a Foley catheter or tracheostomy tube, transfusion of blood products after PICC placement or performance of an esophagogastroduodenoscopy (EGD) or colonoscopy during the admission. In the multivariate logistic regression analysis (Table 4), there was a significant association between PICC CLABSI and sepsis (OR:4.92, 95%CI [2.18-11.13], P:<0.0001), history of smoking (OR:2.87, 95%CI [1.33-6.19], P:0.007) and presence of a gastrostomy tube (OR:6.51, 95%CI [2.19-19.39], P>0.0008).

Table 5 demonstrates the microbiological data. The majority of the PICC CLABSI during the study period were caused by coagulase negative staphylococci (n=15, 26.79%), enteric gram negative rods (n= 14, 25.00%), polymicrobic bacterial infections (n= 9, 16.07%), candida species (n=7, 12.50%), or coagulase positive staphylococci (n= 3, 5.36%).

Table 1.Demographics, comorbidities and medications for patients with PICC CLABSI compared to case matched controls.

Characteristic	**PICCs CLABSI n=56**	**Matched Controls n=245**	**P-Value**
Male Gender N,	27(48.21%)	105 (42.86%)	0.46
CHF N,	19(33.93%)	61(24.90%)	0.16
COPD N,)	5 (8.93%)	22 (8.98%)	0.99
DM N,	17(30.36%)	87(35.51%)	0.46
CKD N,	9 (16.07%)	50(20.41%)	0.46
Active Cancer N,)	12(21.43%)	39(15.92%)	0.32
Sepsis N,	26(46.43%)	28 (11.43%)	<0.0001
Hypertension N,	22(39.2%)	110(44.90%)	0.44
Hyperlipidemia N,	18(32.14%)	49(20.00%)	0.048
C. Diff Infection N,	3 (5.36%)	12 (4.90%)	0.88
Acute Pancreatitis N,	5(8.93%)	10(4.08%)	0.13
BMI (kg/m2), Mean $\pm$ SD	28.32 $\pm$ 10.01	30.49 $\pm$ 11.05	0.18
Smoking N,	25(44.64%)	58(24.0%)	0.002
Wound type III or IV, N/	15/35 (42.85%)	47/132 (35.60%)	0.43
Total N (%)			
Statin	22 (39.29%)	99 (40.41%)	0.87
NSAID	7 (12.50%)	36 (14.69%)	0.67
Steroid	18 (32.14%)	78 (31.84%)	0.96

CLABSI= Central line associated blood stream infection, OR= odd ratio, CI: confidence interval, CHF= congestive heart failure COPD= chronic obstructive pulmonary disease, CKD= chronic kidney disease, C.diff infection= Clostridium Difficile infection, BMI= body mass index.

Table 2.Device Factors for Patients with PICC CLABSI compared to Case matched Controls.

Characteristic	PICCs CLABSI n=56	Matched Controls n=245	P-Value
Duration (Days),	Median 14 (7-32.5)	7(4-11)	<0.0001
Unit of Placement			
Non-ICU, N	42 (75.00%)	183 (74.69%)	Ref
MICU/SICU, N (%)	14 (25.00%)	62 (25.51)	0.93
PICCs Insertion Site			
Basilic,N	44(89.80%)	152 (82.61%)	Ref
Cephalic, N	5 (10.20%)	32 (17.39%)	0.22
Median Cubital/Brachial, N	5 (10.20%)	53 (25.85%)	0.019
Indication			
TPN, N	10 (55.56%)	26 (47.27%)	Ref
Antibiotics, N	8 (44.44%)	29 (52.73%)	0.54
Chemotherapy, N	3 (23.08%)	1 (3.70%)	0.055
Use of Declotting Agent			
Yes, N	9 (16.07%)	10 (4.08%)	Ref
No, N	47 (83.93%)	235 (95.42%)	0.0009
Number of Lumens			
Single, N	7 (12.50%)	36 (14.69%)	Ref
Double, N	35 (62.50%)	168 (68.57%)	0.87
Triple, N	14 (25.00%)	39 (15.92%)	0.23
Complication During PICCs Insertion, N	25 (44.64%)	91 (37.14%)	0.29
Complications After PICCs Insertion, N	10 (17.86%)	12 (4.90%)	0.0008
MRSA Coverage Before Placement of PICCs, N	19 (33.93%)	78 (31.97%)	0.77
MRSA Coverage After Placement of PICCs, N	34 (60.71%)	99 (40.57%)	0.006

CLABSI= central line associated blood stream infection, MRSA= Methicillin-resistant Staphylococcus aureus, OR= odd ratio, CI= Confidence interval.

Table 3. Medical Devices and Procedures Comparison of Study Groups.

Characteristic	**PICCs CLABSI n=56**	**Case Control n=245**	OR (95%CI)	**P-Value**
Foley Catheter, N	40 (72.73%)	149 (61.07%)	0.58 (0.30-1.12)	0.10
Gastrostomy, N	15 (26.79%)	17 (6.94%)	0.20 (0.09-0.44)	<0.0001
Tracheostomy, N	1 (1.79%)	11 (4.49%)	0.38 (0.04-3.05)	0.35
EGD, N	3 (5.36%)	7 (2.86%)	1.92 (0.48-7.68)	0.34
Colonoscopy, N	1 (1.79%)	10 (4.08%)	0.42 (0.053-3.40)	0.40
Mechanical Ventilation, N	18 (32.14%)	47 (19.18%)	1.99 (1.04-3.80)	0.03
Blood Product Transfusion,	24 (42.86%)	94 (38.37%)	1.20 (0.66-2.17)	0.53

TPN: total parental nutrition, EGD: Esophagogastroduodenoscopy

Table 4. Multivariate logistic regression an of risk factors associated with PICC CLABSI

Characteristic	**Odds Ratio (95% Confidence Interval) n=56**	**P-Value n=245**
BMI (Kg/M2) 0.98	(0.95-1.02)	0.49
Sepsis	4.92 (2.18-11.13)	<0.0001
Hyperlipidemia	1.98 (0.85-4.63)	0.11
Smoking	2.87 (1.33-6.19)	0.007
Use of Declotting Agent	0.29 (0.08-1.04)	0.059
Antibiotics use Before PICCs Insertion	1.21 (0.79-1.84)	0.36
Antibiotics use After PICCs Insertion	0.83(0.55-1.26)	0.39
TPN	3.88(0.88-17.00)	0.07
Mechanical Ventilation	1.17(0.47-2.93)	0.72
Gastrostomy	6.51(2.19-19.39)	0.0008
Foley catheter	0.98(0.39-2.44)	0.96
Tracheostomy	2.01(0.38-10.52)	0.40

BMI=body mass index; TPN=total parental nutrition.

Table 5. Classes of antimicrobial infections in the PICC CLASBSI cases

Pathogen	PICC CLABSI) n=56
Polymicrobial, N	9 (16.07%)
Candida Species, N	7 (12.50%)
Gram Positive Bacteria	
Coagulase Negative Staphylococcus N	15 (26.79%)
Enterococcus Species, N	5 (8.93%)
MRSA, N	2 (3.57%)
MSSA, N	1 (1.79%)
Gram Negative Bacteria	
Klebsiella Pneumonia, N	7 (25.36%)
Escherichia Coli, N	4 (7.14%)
Serratia, N	3 (5.36%)
Pseudomonas Aeruginosa, N	1 (1.79)
Providencia, N	1 (1.79)
Sphingomonas, N	1 (1.79)

Discussion

CLABSI are potentially catastrophic for patient outcomes and are associated with a significantly increased risk of mortality (15). There have been a number of retrospective and prospective studies that have evaluated risk factors for CLABSI in a variety of settings and with a variety of intravascular devices. Based on the insights generated from these studies, significant strides in the reduction of CLABSI have occurred and successful programs to reduce the rates of CLABSI to near zero have been piloted, primarily in ICU settings (16, 17). In practice, PICC are increasingly being used for longer durations in multiple hospital settings and the rates of CLABSI are often similar to that seen with non-PICC CVC. In this study, a retrospective evaluation for risk factors associated with PICC CLABSI in ICU and non-ICU hospital patients against a background of sustained low rates of CLABSI was undertaken to evaluate potentially novel host and/or device factors in this setting. The 5-year sustained rate of PICC CLABSI was <1% in this study, which is lower than the rate of infection for PICC CLABSI of 1.1% referenced in the prevention guidelines (14, 18).

A number of risk factors identified in this study have also been suggested in previous studies. While use of a declotting agent was identified as a risk factor for infection, this may be a surrogate marker for thrombosis, which has been identified previously as a risk factor for infection in pediatric CLABSI (19, 20). Duration of PICC line placement and complications after insertion, including manipulation of the PICC line have been documented in other studies as risk factors for infection and were demonstrated in this study as well (11). In a previous report of PICC CLABSI in a large tertiary hospital with a higher rate of infection, use of TPN, duration of PICC, mechanical ventilation, and gastrostomy were also reported as risk factors for infection (13). In this study, the number of lumens did not appear to be a risk factor for CLABSI but the majority of lumens in both infected cases and matched controls were, however, single or double lumens with infrequent use of triple lumen catheters (17.6%). In multivariant analysis, there were three risk factors for PICC CLABSI that were significant but were not modifiable { sepsis on admission, presence of a gastrostomy tube, and history of smoking. The presence of significant, non-modifiable risk factors for PICC CLABSI raises the question of whether a target of zero PICC CLABSI is obtainable and sustainable (16).

Nearly one-third of the organisms associated with CLABSI in this study were gram-negative organisms, which is higher than that reported in other reviews of PICC CLABSI (11, 13). In a previous study, gram-negative organisms caused the majority of PICC CLABSI in children with PICU exposure while gram-positive organisms caused the majority of infections in those without PICU exposure (21). Our retrospective study was undertaken in a single institution which had a dedicated PICC team and did not include pediatric patients. CLABSI generally occur from one or more of the following sources { skin, device lumen, bloodstream seeding, and/or rarely the infusate. Skin colonization with secondary catheter colonization and subsequent CLABSI is the most common cause of CVC infections (22, 23) resulting in the high incidence of gram positive skin commensals usually reported in CLABSI studies. In fact, the successful strategies currently in place to reduce CLABSI rely in large part on reduction of skin bacteria at the catheter insertion site. Gastrostomy tubes as a significant risk factor for CLABSI have been previously identified in a pediatric study (24) and may be a marker for severity of illness or poor nutritional status. In the current study, less than half of the PICC CLABSI were caused by gram positive

organisms but interestingly, use of an anti-MRSA antibiotic after, but not before, line placement was associated with an increased risk of infection. Gastrostomy tubes may also represent a route for the transfer of enteric pathogens to the CVC. The route of bacterial transfer is rarely through hematogenous dissemination regardless of the method of placement [25, 26]. A recent study demonstrated, however, that the presence of a gastrostomy tube was associated with an increased risk of axillary colonization with gram negative rods (27). It would be interesting to evaluate the changes in resident axillary skin flora and colonization around the catheter site or other alterations of the microbiome in the presence of gastrostomy tubes especially with respect to the incidence and microbiology of PICC CLABSI.

Previous studies have found an increased incidence of DVT in patients using a PICC line compared to patients using other central venous lines (28-30). Limiting the use of PICC lines in patients predisposed to thrombus formation may be an important consideration. As previously mentioned, PICC used in the inpatient setting have a risk of infection similar to CVC (7, 31). The MPC (Michigan PICC-CLABSI) score currently offers a promising way to determine whether PICC insertion would be the most appropriate method of treatment for certain patient populations as it predicts the risk of PICC-CLABSI development (32).

Conclusion

There were several limitations of this study. This was a review of CLABSI in a single institution with a very limited number of PICC CLABSI observed during the study period. Also, this was a retrospective study and as with all non-prospective studies, not all data points of interest were collected in all patients. This study demonstrated risk factors for PICC CLABSI such as the presence of gastrostomy tubes and history of smoking that may have increased significance as the rates of PICC CLABSI decrease and additional interventions are utilized to achieve the ultimate goal of elimination of morbidity and mortality from central line bloodstream infections.

Conflict of interest

Authors declare no conflict of interest.

Authors' contributions

JD and SH: conceived/designed the review, TA: performed the data collection, TA, MR, SK: performed the data collection reviews and formal analysis, and NL: reviewed and revised the manuscript. All authors wrote the manuscript, read and approved the final document.

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