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BRIEF REPORT

Peripheral Intravenous Catheter Placement Is an Underrecognized Source of *Staphylococcus aureus* Bloodstream Infection

Eloise D. Austin,[1] Sean B. Sullivan,[1] Susan Whittier,[2] Franklin D. Lowy,[1,2] and Anne-Catrin Uhlemann[1]

[1]Department of Medicine, Division of Infectious Diseases, and [2]Department of Pathology and Cell Biology, Clinical Microbiology Laboratory, Columbia University Medical Center, New York

Few studies have focused on the risks of peripheral intravenous catheters (PIVs) as sources for *Staphylococcus aureus* bacteremia (SAB), a life-threatening complication. We identified 34 PIV-related infections (7.6%) in a cohort of 445 patients with SAB. Peripheral intravenous catheter-related SAB was associated with significantly longer bacteremia duration and thrombophlebitis at old PIV sites rather than current PIVs.

Keywords. bacteremia; MRSA; peripheral IV; *Staphylococcus aureus*.

Peripheral intravenous catheter (PIV) insertion is a common procedure among hospitalized patients, but few studies have focused on the risks associated with PIV infections [1, 2]. Bacteremia as a complication of PIV placement is considered rare and estimated to occur in 0.1% patients with PIV infections [3]. However, the large number of PIVs that are placed annually mean that the public health burden associated with this low-frequency event can be substantial [4]. Furthermore, most PIV-related bacteremias are due to *Staphylococcus aureus* and are associated with the most severe complications, with a mortality rate that can approach 20%–30% [5].

The true burden of *S. aureus* disease due to PIVs is unknown. Phlebitis is a finding often missed on exam, and for this reason PIV-related infections likely contribute significantly to the number of bloodstream infections where the initial focus of infection is never identified. Although national rates of central line-associated bloodstream infections continue to decrease, particularly for *S. aureus* infections [6], little data exist on infections due to peripheral catheters. In this study, we examined the frequency and characteristics of PIV catheter-related *S. aureus* bacteremia (SAB) cases at our center over a 2-year period.

METHODS

We retrospectively reviewed all *S. aureus* bloodstream infections in adult patients that occurred between January 1, 2010 and December 31, 2011 at our tertiary care medical center, which includes a 745-bed academic and 300-bed community hospital. For patients with multiple episodes of bacteremia, we reviewed the initial episode. We extracted information from the medical charts on basic demographics, comorbidities, and outcomes, including 30-day and 90-day mortality. We calculated the duration of bacteremia as the number of days with positive blood cultures and categorized these as >1 day and >3 days. Patients with a single positive blood culture and either no follow-up negative culture or death within 1 day of developing bacteremia were excluded from duration analyses. Peripheral intravenous catheter-related bacteremia was defined when visible infection (thrombophlebitis) at a PIV site was documented in daily progress notes within 10 days before and after the start of bacteremia and no alternative source was identified. These criteria were independently reviewed by two Infectious Diseases (ID) specialists. Antibiotic susceptibility testing (Microscan) and staphylococcal protein A (*spa*) typing were performed on all isolates as described [7]. To compare differences in outcomes between PIV and non-PIV-related SAB, we performed χ^2 test to analyze categorical variables, and when appropriate we used the Fisher's exact test. For continuous variables, we used Student's *t* test and Wilcoxon rank–sum test for variables with nonparametric distribution. To compare the time to blood culture clearance, we used Kaplan–Meier estimates, censoring patients at time of death, and analyzed these using the Wilcoxon and log-rank tests. Data were analyzed using SAS 9.4 (SAS Institute Inc., NC). Our research protocol was reviewed and approved by the Columbia University Institutional Review Board.

RESULTS

During the 2-year study period, we observed 445 cases of SAB (258 methicillin-sensitive *S. aureus* [MSSA] and 187 methicillin-resistant *S. aureus* [MRSA]), 34 (7.6%) of which were due to thrombophlebitis at a PIV site (Table 1). Of the 34 PIV cases, 21 were caused by MSSA and 13 by MRSA. Sources of SAB were never identified in 17% (n = 32) of the MRSA and 21% (n = 55) of MSSA infections. The PIV and non-PIV groups did not differ significantly in comorbidities, Charlson Comorbidity Index scores, complications, or the frequency of ID consultations (Table 1).

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Correspondence: A-C. Uhlemann, Department of Medicine, Columbia University Medical Center, New York, NY 10032 (au2110@cumc.columbia.edu).

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Table 1. Characteristics of PIV-Associated *Staphylococcus aureus* Bloodstream Infections

Characteristics of PIV-Related SA Bloodstream Infection (BSI) Cases				
Variables	All BSI N = 445, N (%)	PIV BSI N = 34, N (%)	Non-PIV BSI N = 411, N (%)	*P* Value
MSSA	258 (58)	21 (62)	237 (58)	.64
MRSA	187 (42)	13 (38)	174 (42)	
Average age (range)	61 (18–101)	63 (28–96)	61 (18–101)	.44
Age >65	172 (39)	14 (41)	158 (38)	
ID consult	262 (59)	20 (59)	242 (59)	.99
Comorbidities				
Coronary artery disease	94 (21)	5 (15)	89 (22)	.34
Diabetes	157 (35)	11 (32)	146 (36)	.71
Renal disease	140 (31)	7 (21)	133 (32)	.16
Malignancy	89 (20)	10 (29)	79 (19)	.13
Average Charlson Score	5.6 ± 3.0 (6)	5.5 ± 3.2 (6)	5.6 ± 3.0 (6)	.83[a]
Complications				
Endocarditis	80 (18)	4 (12)	76 (18)	.33
Metastatic Spread to other sites	92 (21)	5 (15)	87 (21)	.19
Overall				
30-Day Mortality	91 (20)	4 (12)	90 (22)	.16
90-Day Mortality	137 (31)	9 (26)	128 (31)	.57
Death while Bacteremic	46 (10)	1 (2.9)	45 (11)	.24[b]
Average Duration	2.7 ± 3.2	3.6 ± 2.7	2.7 ± 3.3	.002[c]
Duration >1 d[d]	183/395[d] (46)	25 (74)	158/361[d] (44)	.0009
Duration >3 d[d]	99/395[d] (25)	15 (44)	84/361[d] (23)	.007[b]
MSSA Only	All (N = 258)	MSSA PIV (N = 21)	MSSA Non-PIV (N = 237)	
30-Day mortality	46 (18)	2 (10)	44 (19)	.39
90-Day mortality	69 (27)	5 (24)	64 (27)	.75
Death while bacteremic	20 (7.8)	0	20 (8.4)	.39[b]
Average duration	2.4 ± 2.1	2.8 ± 1.9	2.4 ± 2.1	.12[c]
Duration >1 d[d]	101/223[d] (45)	13 (62)	88/202[d] (44)	.11
Duration >3 d[d]	52/223[d](23)	8 (38)	44/202[d] (22)	.11
MRSA Only	All (N = 187)	MRSA PIV (N = 13)	MRSA Non-PIV (N = 174)	
30-Day mortality	48 (26)	2 (15)	46 (26)	.52
90-Day mortality	68 (36)	4 (31)	64 (37)	.77
Death while bacteremic	26 (14)	1 (7.7)	25 (14)	1[b]
Average duration	3.4 ± 4.3	4.8 ± 3.5	3.2 ± 4.3	.002[c]
Duration >1 d[d]	82/172[d] (48)	12 (92)	70/159[d] (44)	.0008
Duration >3 d[d]	47/172[d] (27)	7 (54)	40/159[d] (25)	.046[b]

Abbreviations: BSI, bloodstream infections; ID, infectious diseases; IV, intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; PIV,peripheral IV catheter.

[a] Student's *t* test.

[b] Fisher's exact test.

[c] Wilcoxon rank-sum test.

[d] Duration data missing for 50 patients (35 patients from MSSA group and 15 patients from MRSA group, with all missing data from non-PIV patients) because either clearance of bloodstream infection was never confirmed by negative culture, death occurred after single initial culture obtained, or if initial cultures were collected at outside facility and exact culture dates could not be obtained.

The 30-day (12% vs 22%) and 90-day (26% vs 31%) mortality was lower for the PIV compared with the non-PIV group, although these differences were not statistically significant, including when patients with an unknown primary source were excluded. The average duration of bacteremia was significantly longer in the PIV group (3.6 ± 2.7 vs 2.7 ± 3.3 days, $P = .002$), and a higher proportion of patients was still bacteremic at >1 and >3 days (Table 1). This difference was driven by the MRSA-infected PIV group (4.8 ± 3.5 vs 3.2 ± 4.3 days, $P = .002$; Table 1) and was not due to delays in initiation of effective antibiotic therapy (average number of days from initial culture to effective antibiotics, 0.85 ± 0.93 days). To further exclude that death biased these results, we applied Kaplan–Meier estimates of time to blood culture clearance. The differences in duration remained significant for the Wilcoxon test ($P = .007$), which weighs earlier observations more heavily, but not the log-rank test ($P = .26$).

Infectious Diseases consults were called in 56% (n = 19) of the PIV SAB cases and in 59% of the non-PIV cases. In 29% (n = 10) of these, ID consultants identified IV-related thrombophlebitis that had not previously been recognized by the

primary team. In the majority of cases (n = 27, 79%), the thrombophlebitis was observed at an old site where the PIV had already been removed. Approximately one quarter of these (24%, n = 8) involved phlebitis at IV sites from a separate, prior admission or outpatient visit, with an average of 4.9 days between discharge and positive culture. Most infections occurred at proximal upper extremity IV sites (59% proximal forearm, n = 8; antecubital fossa, n = 8) and less frequently at the hand (n = 5, 19%) or the wrist (n = 6, 22%).

There were no significant differences in the antibiotic susceptibility profiles between the PIV and non-PIV SAB groups (Table 1). *S. aureus* clonal types causing PIV-associated bacteremia, as ascertained by *spa* typing, were reflective of *spa* patterns for the overall bacteremia group. In the MRSA PIV group, t002 (31%, n = 4) and t008 (31%, n = 4) predominated, whereas t002 (19%, n = 4) was most frequently represented among MSSA infections. This group was otherwise heterogeneous in genetic background with more than 15 *spa* types.

DISCUSSION

Few studies in the recent past have evaluated PIV-related *S. aureus* bloodstream infections and their complications. In this study, we identified that, despite validated prevention guidelines, PIVs continue to represent a significant source of SAB associated with longer duration in MRSA PIV-related bacteremia. This included the frequency of bacteremia lasting >3 days, a predictor of major complications (mortality, recurrence of infection, and metastatic foci) [8]. Although patients with PIV-related SAB had a trend to fewer early complications, their 90-day mortality rates were comparable. Our observation of longer bacteremia in PIV-related infections suggests the need for consideration of a PIV source in patients with continued positive *S. aureus* cultures. More importantly, the majority of these infections were related to old IV sites, highlighting the critical need for thorough skin care and surveillance after PIV removal.

These infections occurred despite hospital-wide PIV infection prevention guidelines based on current Centers for Disease Control and Prevention recommendations [9], which include the frequent assessment of catheter sites and removal of catheters either every 72 hours or when signs of phlebitis appear [10–12]. These guidelines do not address the care of old PIV sites where a residual burden of microorganisms or subclinical phlebitis might lead to a delayed infection days after catheter removal. Our study also suggests that the proximal upper extremity catheter sites are more frequent sites of phlebitis leading to SAB. This could reflect more frequent use of such sites, the difficulty of maintaining sterility of proximal sites, or different burdens of *S. aureus* skin colonization across these areas.

The pattern of antibiotic resistance and clonal types mirrored that of the overall SAB population and did not suggest clonal outbreaks or in-hospital transmission events. These findings also highlight the important contribution of nonmultidrug-resistant organisms such as MSSA as a cause of hospital-associated infections.

Several limitations to our study need to be considered. This study represents the experience of a single tertiary care hospital. Although we included approximately 450 cases, the study was not powered to detect differences of mortality given the cumulative incidence of PIV cases, which would have required a sample size approximately 3-fold higher. More importantly, due to the retrospective nature of this study and our use of strict criteria for PIV-related infection, these numbers likely underestimate the true burden of PIV-related bacteremia. Up to 20% of bloodstream infections were due to an unknown primary site, which may have included additional PIV-related infections that were missed, not documented, or where the PIV itself served as a nidus for biofilm formation and portal of entry into the bloodstream. Likewise, patients with documented thrombophlebitis might have had alternative sources of infection. Our ability to accurately estimate bacteremia duration was dependent on the frequency of collecting blood cultures. In cases in which culture collection was prematurely stopped, or in the event of death, duration may have been underestimated. We excluded single positive cultures lacking follow-up negative culture, which occurred only in the non-PIV group. Therefore, these exclusions may have led to a bias toward the null hypothesis, making differences in bacteremia duration less pronounced.

CONCLUSIONS

Our findings suggest that PIV infections as a preventable source of *S. aureus* bloodstream infection remain a major concern. This phenomenon might be partly attributed to a delay in diagnosing and controlling the underlying source, which was almost always infection at an old IV site and not one currently used and monitored. Our data suggest that site monitoring after removal of PIVs should be a priority in preventive efforts. More prospective studies are needed, both to assess the true incidence and burden of PIV-related SAB and to evaluate effective novel prevention strategies, such as checklists for PIV insertion, monitoring of old PIV sites, or use of antimicrobial-coated peripheral catheters.

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