American Journal of Infection Control 47 (2019) 208–210

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Brief Report

# Comparison of the epidemiology and microbiology of peripheral line– and central line–associated bloodstream infections

Motoyuki Tsuboi MD [a], Kayoko Hayakawa MD, PhD [a,*], Kazuhisa Mezaki MT [b], Yuichi Katanami MD [a], Kei Yamamoto MD [a], Satoshi Kutsuna MD, PhD [a], Nozomi Takeshita MD, PhD [a], Norio Ohmagari MD, MSc, PhD [a]

[a] Disease Control and Prevention Center, National Center for Global Health and Medicine, Tokyo, Japan
[b] Microbiology Laboratory, National Center for Global Health and Medicine, Tokyo, Japan

*Key Words:*
Peripheral venous catheter
Central venous catheter
Bacteremia
Causative organism
Enterobacteriaceae

A B S T R A C T

We retrospectively studied the epidemiology and microbiology of peripheral line–associated bloodstream infection (PLABSI) in comparison with central line–associated bloodstream infection (CLABSI). Among 2,208 bacteremia episodes, 106 (4.8%) PLABSI and 229 (10.4%) CLABSI were identified. In PLABSI, gram-negative rods, especially Enterobacteriaceae, were more frequently identified than in CLABSI, and infectious disease consultation was more frequently involved. The 7-day mortality rate was similar between the 2 groups, suggesting similar adverse effects of PLABSI and CLABSI on patient outcomes.


## BACKGROUND

Short-term peripheral venous catheters (PVCs) are 1 of the most frequently used medical devices. Approximately 20%-30% of inpatients are hospitalized with PVCs, and PVCs account for 80%-95% of all types of intravascular catheters.[1]

The incidence of peripheral line–associated bloodstream infection (PLABSI) was shown to be 0.18% among 85,063 PVCs; PVCs accounted for a mean of 6.3% and 23% of nosocomial bloodstream infections (BSIs) and nosocomial catheter-related BSIs, respectively.[1] BSI is a major cause of morbidity and death in hospitalized patients,[2] and attention should be focused on both PLABSI and central line–associated bloodstream infection (CLABSI). However, many reports of PLABSI have been limited to those caused by *Staphylococcus aureus*.[3-5] The aim of this study was to elucidate the epidemiology and microbiology of PLABSI as compared with CLABSI.

## METHODS

We conducted a retrospective cohort study at the National Center for Global Health and Medicine in Tokyo, Japan, between April 2012 and March 2015. This study was approved by the Human Research Ethics Committee (NCGM-G-001131-02).

All positive blood culture results were reviewed by infectious disease (ID) specialists, and microbiologic tests were conducted as per Clinical and Laboratory Standards Institute (CLSI) criteria (M100-S22).

PLABSI was defined as bacteremia with at least 1 of the following conditions: (1) the presence of phlebitis or (2) resolution of clinical symptoms after PVC withdrawal with the careful exclusion of another focus of bacteremia.[6] CLABSI was defined according to the guideline.[7] The clinical significances of pathogens known as contaminants (eg, coagulase-negative staphylococci [CoNS], *Corynebacterium* species, and *Bacillus* species) were decided on the basis of previous reports[8] and decisions by ID specialists. Peripheral catheters (Surflo; Terumo, Tokyo, Japan) were mostly placed on forearms and rarely on upper arms or lower extremities. The site of insertion of each case was not available for review in this study. Transparent dressings were used for nurses to observe the insertion sites on a daily basis.

*Address correspondence to Kayoko Hayakawa, MD, PhD, Disease Control and Prevention Center, National Center for Global Health and Medicine, 1-21-1, Toyama, Shinjuku, Tokyo 162-8655, Japan.

Funding/support: This work was supported by Grants for International Health Research from the Ministry of Health, Labour, and Welfare of Japan (28S1106).

The need for informed consent was waived by the Human Research Ethics Committee of NCGM because of the retrospective nature of the analysis, which used anonymized information contained in medical charts and records.

Author contributions: M.T. and K.H. designed the study and analyzed the data. M.T. and K.H. wrote the first draft of the manuscript. K.M., K.Y., Y.K., S.K., and N.T. contributed to data collection. All authors contributed to interpretation of data and revision of the manuscript and approved the final version of the manuscript before submission.

Conflicts of interest: None to report.

https://doi.org/10.1016/j.ajic.2018.08.016
0196-6553/

**Table 1**
Baseline characteristics of the study patients

| | PLABSI (n = 106) No. (%) | CLABSI (n = 229) No. (%) | *P* value |
|---|---|---|---|
| Age (IQR), y | 76 (61-83) | 68 (56-79) | .006 |
| Male sex | 57 (53.8) | 147 (64.2) | .069 |
| Hospital onset* | 100 (94.3) | 203 (88.6) | .099 |
| Consultation with ID specialists | 69 (65.1) | 115 (50.2) | .011 |
| Comorbidities | | | |
| DM | 12 (11.3) | 33 (14.4) | .441 |
| CKD | 5 (4.7) | 47 (20.5) | <.001 |
| CHF | 10 (9.4) | 23 (10.0) | .862 |
| COPD | 3 (2.8) | 11 (4.8) | .401 |
| Hematologic malignancy | 5 (7.0) | 33 (14.4) | .009 |
| Solid tumor | 24 (22.6) | 65 (28.4) | .268 |
| Corticosteroid | 12 (11.3) | 23 (10.0) | .722 |
| Biologic agent use | 1 (0.9) | 1 (0.4) | .576 |
| HIV | 2 (1.9) | 6 (2.6) | .683 |

*CHF*, congestive heart failure; *CKD*, chronic kidney disease; *CLABSI*, central line–associated bloodstream infection; *COPD*, chronic obstructive pulmonary disease; *DM*, diabetes mellitus; *ID*, infectious disease; *IQR*, interquartile range; *PLABSI*, peripheral line–associated bloodstream infection.
*Hospital onset was defined as a positive blood culture obtained from patients who had been hospitalized ≥48 hours.

Bivariate analyses were performed using the Fisher exact test or the $\chi^2$ test for categorical variables and the Mann-Whitney U test for continuous variables. Statistical significance was defined as 2-sided $P < .05$. All statistical analyses were performed using Statistical Package for the Social Sciences software version 23.0 (IBM, Chicago, IL).

## RESULTS

Among all-cause–positive blood culture episodes (n = 2,208), 335 (15.2%) were considered to be catheter-related BSIs: 106 (4.8%) were PLABSI and 229 (10.4%) were CLABSI. The baseline characteristics of study patients are summarized in Table 1. The median age was 71 years (interquartile range, 58.3-80.3 years), and 204 (60.9%) patients were men. Most episodes of both PLABSI and CLABSI occurred in hospital settings (94.3% and 88.6%, respectively). ID consultations were more frequently observed in PLABSI (PLABSI vs CLABSI: 65.1% vs 50.2%, *P* = .011). Compared with PLABSI, CLABSIs were more frequently detected in patients of younger age, those with chronic kidney diseases, and those with hematologic malignancy (*P* = .006, *P* < .001, and *P* = .009, respectively).

With regard to their microbiology (Table 2), gram-positive cocci were the main cause of both PLABSI and CLABSI (47.2% and 58.1%, respectively). Gram-negative rods (GNRs) were more frequently identified in PLABSI (n = 35 [33%]) than in CLABSI (n = 43 [18.8%]) (*P* = .004). Enterobacteriaceae (eg, *Enterobacter cloacae* [n = 8], *Klebsiella pneumoniae* [n = 5], and *Serratia marcescens* [n = 4]) accounted for most PLABSI-causing GNRs and were more frequently isolated from PLABSI (n = 27 [25.5%]) than from CLABSI (n = 28 [12.2%]) (*P* = .002). The prevalence of nonfermenting GNRs did not differ between PLABSI and CLABSI. CLABSI was significantly associated with CoNS (PLABSI vs CLABSI: 19.8% vs 31.9%, *P* = .022), enterococci (PLABSI vs CLABSI: 2.8% vs 8.7%, *P* = .047), and *Candida* species (PLABSI vs CLABSI: 11.3% vs 20.5%, *P* = .040).

The 7-day mortality rate was similar between PLABSI and CLABSI (4.7% vs 6.1%, *P* = .601), whereas CLABSI tended to have higher 30-day mortality rates (PLABSI vs CLABSI: 12.6% vs 21.9%, *P* = .053).

## DISCUSSION

We found significant epidemiologic and microbiologic differences between PLABSI and CLABSI. Our finding that Enterobacteriaceae are the most frequently identified organism in PLABSI is different from that of previous reports,[6,9] in which *S aureus* was identified as the most frequent cause of PLABSI. There are a few possible explanations for this discrepancy. First, the prevention methods for PLABSI differ; in this study, peripheral catheters were regularly replaced at least once every 96 hours to reduce risk of infection, whereas catheters

**Table 2**
Comparison of causative organisms between PLABSI and CLABSI

| | PLABSI (n = 106) No. (%) | CLABSI (n = 229) No. (%) | OR (95% CI) | *P* value |
|---|---|---|---|---|
| Gram-positive cocci | 50 (47.2) | 133 (58.1) | 0.64 (0.41-1.02) | .062 |
| Coagulase-negative staphylococci | 21 (19.8) | 73 (31.9) | 0.53 (0.30-0.92) | .022 |
| *Staphylococcus aureus* | 26 (24.5) | 39 (17.0) | 1.58 (0.90-2.77) | .107 |
| MRSA | 13 (12.3) | 19 (8.3) | 1.55 (0.73-3.26) | .317 |
| *Enterococcus* species | 3 (2.8)* | 20 (8.7)† | 0.30 (0.09-1.05) | .047 |
| Gram-positive rods | 10 (9.4)‡ | 12 (5.2)§ | 1.88 (0.79-4.51) | .150 |
| GNRs | 35 (33.0) | 43 (18.8) | 2.13 (1.26-3.60) | .004 |
| Enterobacteriaceae | 27 (25.5)‖ | 28 (12.2)¶ | 2.45 (1.36-4.42) | .002 |
| Nonfermenting GNR | 8 (7.5)** | 16 (7.0)†† | 1.09 (0.45-2.63) | .853 |
| ESBLE | 1 (0.9) | 1 (0.4) | 2.17 (0.13-35.05) | .585 |
| CRE | 1 (0.9) | 0 | NA | NA |
| Polymicrobial | 6 (5.7) | 23 (10.0) | 0.54 (0.21-1.36) | .185 |
| *Candida* species | 12 (11.3) | 47 (20.5) | 0.49 (0.25-0.98) | .040 |

*CI*, confidence interval; *CLABSI*, central line–associated bloodstream infection; *CRE*, carbapenem-resistant Enterobacteriaceae; *ESBLE*, extended-spectrum β-lactamase–producing Enterobacteriaceae; *GNRs*, gram-negative rods; *MRSA*, methicillin-resistant *Staphylococcus aureus*; *NA*, not applicable; *OR*, odds ratio; *PLABSI*, peripheral line–associated bloodstream infection.
*Including *Enterococcus faecalis* (n = 3).
†Including *E faecalis* (n = 10), *Enterococcus faecium* (n = 7), *Enterococcus avium* (n = 1), *Enterococcus gallinarum* (n = 1), *Enterococcus raffinosus* (n = 1).
‡Including *Bacillus cereus* (n = 7), *Corynebacterium* species (n = 2), *Bacillus subtilis* (n = 1).
§Including *Corynebacterium* species (n = 10), *B cereus* (n = 2).
‖Including *Enterobacter cloacae* (n = 8), *Klebsiella pneumoniae* (n = 5), *Serratia marcescens* (n = 4), *Citrobacter freundii* (n = 3), *Escherichia coli* (n = 3), *Enterobacter aerogenes* (n = 2), *Klebsiella oxytoca* (n = 2), *Cedecea* species (n = 1), *Enterobacter agglomerans* (n = 1) (2 bacteria were isolated from the same episode).
¶Including *E cloacae* (n = 8), *E coli* (n = 6), *K pneumoniae* (n = 6), *S marcescens* (n = 4), *C freundii* (n = 1), *E aerogenes* (n = 1), *K oxytoca* (n = 1), *Proteus vulgaris* (n = 1), *Pantoea* species (n = 1) (1 bacteria were isolated from the same episode).
**Including *Pseudomonas aeruginosa* (n = 3), *Acinetobacter lwoffii* (n = 2), *Acinetobacter baumannii* (n = 1), *Pseudomonas fluorescens* (n = 1), and *Stenotrophomonas maltophilia* (n = 1).
††Including *P aeruginosa* (n = 10), *S maltophilia* (n = 3), *A baumannii* (n = 2), and *Chryseobacterium* species (n = 1).

were left in place until the occurrence of complications in the previous study.[6,9] Second, different practices in the use of PVCs and central venous catheters among studies might have influenced the results. For example, it is common practice in Japan to complete relatively long courses of intravenous treatment (eg, infective endocarditis) by PVCs rather than central venous catheters. In this study, it is unlikely that other frequent causes of bacteremia caused by GNRs (eg, urinary tract infections) were misclassified as PLABSI, because ID specialists reviewed medical charts and diagnosed PLABSI, and ID consultants were frequently involved (>65%) in its management.

Gram-positive cocci and *Candida* species were more frequently isolated from patients with CLABSI in this study. This result was consistent with previous reports that identified CoNS as the most common organism among CLABSI cases.[6,9]

This study demonstrated 2 other important findings. First, PLABSI and CLABSI should receive greater focus as targets for infection control, given the similar 7-day mortality rates between both BSIs and the observation that PLABSI accounted for 4.8% of all-cause positive blood culture episodes. Although the 30-day mortality rate tended to be higher in CLABSI than in PLABSI, this is probably because of a higher rate of comorbidities in patients with CLABSI. Second, ID consultations were more frequently observed in episodes of PLABSI. This might be owing to the difficulty of diagnosing PLABSI and a lack of awareness of PLABSI as a cause of bacteremia among physicians.

As limitations, in addition to the retrospective nature of this study, our finding on the relation of ID consultations and PLABSI might not be generalizable to other health care systems.

In conclusion, PLABSI has similar adverse effects on patient outcomes as CLABSI. Appropriate prevention and treatment measures are just as necessary for PLABSI as for CLABSI, which might have been underestimated previously.

## Acknowledgments

The authors thank the clinical staff of the Disease Control and Prevention Center and the clinical laboratory for their help in completing this study.

## References

1. Mermel LA. Short-term peripheral venous catheter-related bloodstream infections: a systematic review. Clin Infect Dis 2017;65:1757-62.
2. Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB. Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. Clin Infect Dis 2004;39:309-17.
3. Trinh TT, Chan PA, Edwards O, Hollenbeck B, Huang B, Burdick N, et al. Peripheral venous catheter-related *Staphylococcus aureus* bacteremia. Infect Control Hosp Epidemiol 2011;32:579-83.
4. Rhodes D, Cheng AC, McLellan S, Guerra P, Karanfilovska D, Aitchison S, et al. Reducing *Staphylococcus aureus* bloodstream infections associated with peripheral intravenous cannulae: successful implementation of a care bundle at a large Australian health service. J Hosp Infect 2016;94:86-91.
5. Austin ED, Sullivan SB, Whittier S, Lowy FD, Uhlemann AC. Peripheral intravenous catheter placement is an underrecognized source of *Staphylococcus aureus* bloodstream infection. Open Forum Infect Dis 2016;3, ofw072.
6. Pujol M, Hornero A, Saballs M, Argerich MJ, Verdaguer R, Cisnal M, et al. Clinical epidemiology and outcomes of peripheral venous catheter-related bloodstream infections at a university-affiliated hospital. J Hosp Infect 2007;67:22-9.
7. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009;49:1-45.
8. Hall KK, Lyman JA. Updated review of blood culture contamination. Clin Microbiol Rev 2006;19:788-802.
9. Coello R, Charlett A, Ward V, Wilson J, Pearson A, Sedgwick J, et al. Device-related sources of bacteraemia in English hospitals—opportunities for the prevention of hospital-acquired bacteraemia. J Hosp Infect 2003;53:46-57.