


# Risk factors associated with increased incidences of catheter-related bloodstream infection

Kiyoshi Moriyama, MD\* , Tadao Ando, MD, Mariko Kotani, MD, Joho Tokumine, MD, PhD, Harumasa Nakazawa, MD, Akira Motoyasu, MD, Tomoko Yorozu, MD, PhD

## Abstract

We have implemented several preventive measures to reduce central line-associated bloodstream infection (CLABSI) in the general intensive care unit (ICU) of a university hospital in Japan. Here, we analyzed the factors associated with CLABSI in patients with central venous catheter (CVC) insertions and evaluated the effects of our implemented preventive measures. From July 2013 to June 2018, data was collected from the medical records of 1472 patients with 1635 CVC insertions, including age, sex, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, duration of ICU stay, duration of catheter insertion, insertion site, and mechanical ventilation status. During weekly conferences, a surveillance team comprising intensive care and infection control doctors and nurses determined the patients' CLABSI status. The analyzed factors were compared between CLABSI and central line patients without bloodstream infection. Multivariate analysis revealed three factors associated with CLABSI. Adjusted odds ratios with 95% confidence intervals were as follows: duration of ICU stay, 1.032 (1.019–1.044); duration of catheter insertion, 1.041 (1.015–1.066); and APACHE II score, 1.051 (1.000–1.105). The prominent risk factors were associated with the severity of the initial condition and exacerbation of the clinical condition of the patients during their stays in the ICU. Further strategies to reduce CLABSI must be developed.

**Abbreviations:** APACHE II = Acute Physiology and Chronic Health Evaluation II, CI = confidence interval, CLABSI = central line-associated bloodstream infections, CVC = central venous catheter, ICU = intensive care unit, NHSN = National Healthcare Safety Network, OR = odds ratio.

**Keywords:** catheter-related bloodstream infection, central venous catheters, intensive care unit

## 1. Introduction

The Centers for Disease Control and Prevention claim that although central line-associated bloodstream infections (CLABSI) are preventable, they are responsible for thousands of deaths each year, and billions of dollars in added costs to the U.S. healthcare system.<sup>[1]</sup> In 2008, the Japanese Healthcare Associated Infection Surveillance system began nationwide device-related infection surveillance according to the National Healthcare Safety Network (NHSN) guidelines in Japan.<sup>[2]</sup> Krein et al<sup>[3]</sup> reported that nearly all hospitals in Thailand and the United States monitor CLABSI, ventilator-associated pneumonia, and catheter-associated urinary tract infection rates. However, only CLABSI rates were monitored by the majority of hospitals in Japan between 2012 and 2014. In addition, the authors reported that the use of generally established recommendations, regardless of the type of infection, seemed to be lower among hospitals in Japan.

To reduce CLABSI, it is important to measure the effects of preventive efforts using data derived from evidence-based

surveillance.<sup>[4]</sup> Sakamoto et al<sup>[5]</sup> reported that in Japan, the use of chlorhexidine gluconate for insertion site antiseptics, antimicrobial dressings with chlorhexidine, and central line insertion bundles for CLABSI have increased from 2012 to 2017. In addition, Greene et al<sup>[6]</sup> reported that although several recommended practices for ventilator-associated pneumonia, CLABSI, and catheter-associated urinary tract infection were implemented, established surveillance systems were lacking in Dutch, Swiss, and Japanese hospitals.

Our institution has implemented several CLABSI preventive measures since July 2013, when we began CLABSI monitoring with the Japanese Healthcare-Associated Infection Surveillance. Here, we analyzed the factors associated with CLABSI in patients with central venous catheter (CVC) insertions in a single-center general intensive care unit (ICU) in Japan and evaluated the effects of our implemented preventive measures. Because there are few detailed reports on CLABSI in Japan, we compiled our accumulated data over five years to elucidate the risk factors of CLABSI.

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The requirement for obtaining informed consent was waived because of the study's retrospective nature.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

This observational study was approved by the Kyorin University Ethical Committee (approval no. 382–01). The requirement for obtaining informed consent was waived because of the study's retrospective nature.

Department of Anesthesiology, Kyorin University School of Medicine, Tokyo, Japan.

\* Correspondence: Kiyoshi Moriyama, Department of Anesthesiology, Kyorin University School of Medicine, 6-20-2 Shinkawa, Mitaka, Tokyo 181-8611, Japan (e-mail: mokiyokeio@gmail.com).

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## 2. Materials and Methods

### 2.1. Study design and data collection

This observational study was approved by the Kyorin University Ethical Committee (approval no. 382-01). Obtaining informed consent was waived because of the study's retrospective nature and the study complied with the ethical standards of the Declaration of Helsinki. The observation period was from July 2013 to June 2018. All patients with CVC insertions were enrolled for surveillance in an 18-bed general ICU of the 1058-bed Kyorin University Hospital in Japan. Peripherally inserted central catheters and cases with unknown insertion sites were excluded from the analysis. The initial CLABSI preventive bundles and other preventive measures we have implemented are summarized in Table 1. At weekly conferences, a surveillance team, including intensivists, infection control doctors, and infection control nurses, determined the patients' CLABSI status.

### 2.2. Definition of CLABSI

Our surveillance team used the criteria of the Patient Safety Component Manual of the NHSN. Briefly, laboratory-confirmed bloodstream infection must meet one of the following criteria when an organism(s) identified in the blood is not related to an infection at another site; patient of any age has a recognized bacterial or fungal pathogen, not included on the NHSN common commensal list, identified from one or more blood specimens obtained by a culture or identified to the genus or species level by non-culture based microbiologic testing methods. Patient of any age has at least one of the following signs or symptoms: fever ( $>38.0$  °C), chills, or hypotension and the same NHSN common commensal is identified by culture from two or more blood specimens collected on separate occasions. Patient  $\leq 1$  year of age has at least one of the following signs or symptoms: fever ( $>38.0$  °C), hypothermia ( $<36.0$  °C), apnea, or bradycardia and the same NHSN common commensal is identified by culture from two or more blood specimens collected on separate occasions.

### 2.3. Statistical analyses

To statistically determine factors associated with CLABSI, data were collected from patient medical records, including: age, sex, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, duration of ICU stay, duration of catheter insertion, insertion site, and mechanical ventilation status.

**Table 1**

#### Interventions to prevent CLABSI.

Initial CLABSI preventive bundles

- Hand hygiene with rubbing alcohol for sterilization
- Maximal barrier precautions
- 1% chlorhexidine alcohol skin antisepsis
- Femoral insertion or not (checked by nurses)

The preventive measures added to our protocol

- 1) The skin cover sheets are changed to gauze if an impermeable sheet is soaked with sweat (from November 2014).
- 2) The side tubes of three-way stopcocks in the central venous infusion tubes are wiped twice with alcohol before and after an injection (from April 2015).
- 3) Infection control nurses carry out regular inspections of the condition of the cover sheet fixations and change dressings at regular intervals, and use protective gloves when changing the infusion tubes (from September 2015).
- 4) Drug preparation area is fixed to a clean bench (from July 2017).
- 5) Skin cover sheets must be soaked in chlorhexidine (from Jan 2018).

CLABSI = central line-associated bloodstream infections.

Data are presented as means  $\pm$  standard deviations and medians  $\pm$  interquartile ranges for normally and non-normally distributed continuous variables, respectively. Unpaired *t*-tests and Wilcoxon rank-sum tests were used for normally and non-normally distributed continuous variables, respectively.

Mann–Whitney *U* and chi-square tests were used to analyze the differences between CLABSI and non-CLABSI cases, where appropriate. For the multivariate analysis of factors associated with CLABSI, logistic regression analysis with a backward-stepwise procedure was used. Covariates were selected based on clinical knowledge and previous studies and were used in the multivariate analysis if  $P < .1$  was observed in the univariate analysis. During multivariate analysis, covariates were retained if they were found to change the model significantly ( $P < .05$ ). The statistical output is reported as an odds ratio (OR) and a 95% confidence interval (CI). All statistical analyses were done with IBM SPSS Statistics version 24 (IBM statistics, IBM Corporation, Chicago, IL). Significance was set at  $P < .05$ .

## 3. Results

A total of 1472 patients with 1635 CVCs were analyzed. Figure 1 shows the rate of CLABSI assessed once every 3 months from July 2013 to June 2016 and once every 6 months from July 2016 to June 2018 in accordance with the preventive measures added to our protocol. Although we gradually added preventive measures, the rate of CLABSI fluctuated, and no added preventive measures seemed to decrease the rate of CLABSI.

All patients with CVCs were enrolled for surveillance. The rates of CLABSI were assessed once every 3 months from July 2013 to June 2016, and once every 6 months from July 2016 to June 2018. The initial CLABSI preventive bundles and other preventive measures we have implemented are summarized in Table 1.

Baseline characteristics of the CLABSI (+/–) patients are summarized in Table 2, in accordance with the results of the univariate analysis. Patients with CLABSI had higher APACHE II scores, longer ICU stays, and longer durations of catheter insertion than those without CLABSI. The rates of mechanical ventilation were greater in CLABSI cases.

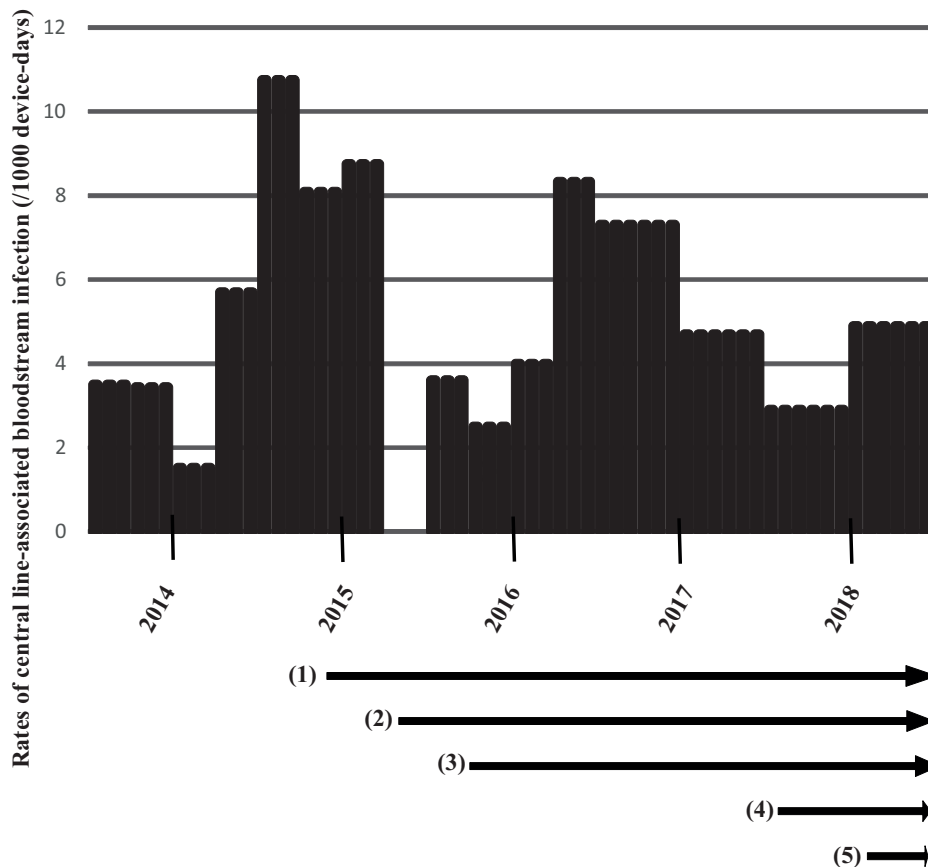
Table 3 shows the results of the multivariate analysis of factors associated with CLABSI. Adjusted ORs with 95% CIs were as follows: duration of ICU stay, 1.032 (1.019–1.044); duration of catheter insertion, 1.041 (1.015–1.066); and APACHE II score, 1.051 (1.000–1.105). Multivariate analysis showed that severely ill patients with longer stays in the ICU and longer durations of CVC insertion tended to have CLABSI at higher rates.

Table 4 shows the causative bacterial agents of CLABSI at our institution. Most of the causative bacterial agents were not skin-indigenous microorganisms but bacteria of the *Enterobacteriaceae* family.

## 4. Discussion

### 4.1. Key findings

In this observational study, we evaluated the effects of our additional preventive measures in reducing the rates of CLABSI in our general ICU and analyzed the factors associated with CLABSI over 5-years. We found that the rate of CLABSI fluctuated every 3 months, and therefore did not reduce as we expected with our CVC bundles and additional preventative measures. Statistical analysis showed that the severity of illness in patients seemed to have affected the CLABSI rate, as logistic regression analysis revealed that the factors associated with CLABSI were higher APACHE II scores, longer stays in the ICU, and longer duration of catheter insertion. These results suggest that CLABSI is highly associated with a patient's severity of illness.



**Figure 1.** The rates of CLABSI assessed weekly and summarized every 3-6 months, in accordance with the preventive measures added. A surveillance team comprising intensivists, infection control doctors, and infection control nurses determined the patients' CLABSI status at weekly conferences. CLABSI = central line-associated bloodstream infections.

**Table 2**  
**Baseline characteristics of 1472 patients, and results of univariate analysis of factors associated with CLABSI.**

		CLABSI (+)	CLABSI (-)	P value
Number of catheters		63	1479	
Age (years)	Mean (SD)	70.9 ± 13.0	67.8 ± 15.8	n/a
Male/female sex		40/23	929/535	n/a
Height	Mean (SD)	159.6 ± 14.9	159.8 ± 13.3	n/a
Weight	Mean (SD)	58.0 ± 13.8	56.3 ± 26.3	n/a
Apache II score	Mean (SD)	22.1 ± 8.1	16.5 ± 7.4	P < .01
Duration of hospital stay (days)	Mean (SD)	112.3 ± 72.0	63.9 ± 79.9	P < .01
Duration of ICU stay (days)	Mean (SD)	62.4 ± 58.0	13.0 ± 21.2	P < .01
Duration of catheter insertion (days)	Mean (SD)	29.9 ± 45.6	7.8 ± 8.0	P < .01
Mechanical ventilation	no. (%)	57/63 (90.5%)	832/1409 (59.0%)	P < .01
Insertion site	no. (%)			n/a
IJV		46 (74.2%)	1205 (83.1%)	
Subclavian		2 (3.2%)	28 (1.9%)	
Femoral		14 (22.6%)	217 (15.0%)	

The student's *t*-test, Mann-Whitney *U* test, and Chi-square test were used to analyze the differences between patients with and without CLABSI. Peripherally inserted central catheters and cases with unknown insertion sites were excluded from the analysis. A *P* value of <.05 was considered statistically significant.

Apache II = Acute Physiology and Chronic Health Evaluation II, CLABSI = central line-associated blood stream infection, ICU = intensive care unit, IJV = internal jugular vein, SD = standard deviation.

**4.2. Relationship to previous studies**

The risk of CLABSI in ICU patients is high,<sup>[7]</sup> because of the frequent insertion of multiple or specific types of catheters (e.g., pulmonary artery catheters) and because catheters are frequently placed in emergency circumstances, repeatedly accessed each day, and often needed for extended periods. We

showed that risk factors of CLABSI were higher APACHE II scores, longer ICU stays, and longer duration of catheter insertion. We interpreted that these factors were associated with the severity of the patient's illness, which is consistent with previous findings.<sup>[8]</sup> Meyer et al<sup>[9]</sup> found that males and advanced acute myeloid leukaemia were the risk factors for bloodstream infections in neutropenic patients who have undergone

**Table 3****Multivariate analysis of four factors associated with catheter-related blood stream infection.**

	Adjusted OR (95% CI)	P value
Duration of ICU stay (days)	1.032 (1.019–1.044)	<.001
Duration of catheter insertion (days)	1.041 (1.015–1.066)	.001
Apache II score	1.051 (1.000–1.105)	.048

Apache II = Acute Physiology and Chronic Health Evaluation II, CI = confidence interval, ICU = intensive care unit, OR = odds ratio.

**Table 4****Remarkable causative bacterial agents of CLABSI.**

<i>Pseudomonas aeruginosa</i>	11%	<i>Klebsiella pneumoniae</i>	10%
<i>Escherichia coli</i>	8%	<i>Enterobacter cloacae</i>	7%
<i>Serratia marcescens</i>	7%	<i>Staphylococcus aureus</i> (MRS)	6%
<i>Staphylococcus epidermidis</i>	6%	<i>Klebsiella oxytoca</i>	5%
<i>Candida albicans</i>	4%	coagulase (-) <i>Staphylococcus</i>	4%
<i>Enterobacter aerogenes</i>	4%	<i>Enterococcus faecalis</i>	4%

CLABSI = central line-associated blood stream infection.

peripheral blood stem cell transplantation. Lipitz-Snyderman et al<sup>[10]</sup> found that long-term CVC use increases the likelihood of bloodstream infections in older adults with cancer. These results suggest that prominent risk factors were associated with the severity of the initial condition and exacerbation of the patient's clinical condition during their ICU stay.

#### 4.3. Significance and implications

In our study, we found that the insertion site did not increase the incidence of CLABSI, and infectious disease-causing bacteria were not skin-indigenous microorganisms, but bacteria of the *Enterobacteriaceae* family. In accordance with the fact that the mean duration of catheter insertion was 29.9 days, we speculate that the initial preventive bundles did play a minor role in reducing the incidence of CLABSI in its early stages, because our initial bundles included preventive measures at insertion. In addition, the fact that insertion sites were not related to the infection rates might be due to our thorough care for femoral insertion sites. However, although we implemented several preventive measures for CLABSI, the rates remained unchanged.

#### 4.4. Strengths and limitations

Several limitations should be mentioned. First, although we monitored CLABSI, we did not monitor catheter-related bloodstream infections, as we do not routinely monitor bloodstream infections related to peripherally insert central catheters or peripheral intravenous catheters. However, there are certain risks of bloodstream infection for any intravascular device,<sup>[11]</sup> and the risks of catheter-related infection of arterial catheters may be similar to the short-term risks of CVCs.<sup>[12]</sup> Because we monitored only CLABSI, catheter-related infection of arterial or venous catheters could have increased the incidence of CLABSI when a patient has a CVC and an arterial and venous catheter. Although point incidence rates of bloodstream infections with arterial catheters seem to be lower than infection with CVCs, infection from these devices might have increased the rates of catheter-related bloodstream infections in our study. Unlike CVCs, routine replacement of peripheral intravenous catheters decreased catheter-related bloodstream infections.<sup>[13]</sup> As Mermel suggests,<sup>[14]</sup> we may need to include not only CVCs but also arterial catheters and

peripheral venous catheters as concurrent catheters in future surveillance.

Second, the mean duration of catheter insertion of 29.9 days in patients with CLABSI was relatively long, and this result may suggest that we had unnecessary catheter use. Because routine replacement of CVC is not recommended,<sup>[8]</sup> we do not routinely replace CVCs. Routine changing of catheters can decrease the number of infections per catheter but does not modify the number of infections per day of catheter insertion,<sup>[15]</sup> and may even increase the risk of mechanical complications. In addition, temporary vascular catheters were frequently inserted in CLABSI (+) patients. Syed-Ahmed et al<sup>[16]</sup> suggested that chronic kidney disease is associated with a proinflammatory milieu and immune dysfunction encompassing all aspects of innate and acquired immunity. A stronger effort is needed to avoid unnecessary catheterization and to encourage prompt removal of CVCs that are no longer required, particularly for longer-dwelling catheters.<sup>[8]</sup>

## 5. Conclusion

We found that the factors associated with CLABSI were higher APACHE II scores, longer ICU stays, and longer durations of catheter insertion. The results of our study suggest the need to avoid unnecessary catheterization and encourage timely removal.

## Author contributions

**Conceptualization:** Tomoko Yorozu.

**Data curation:** Kiyoshi Moriyama, Mariko Kotani, Tadao Ando.

**Formal analysis:** Tomoko Yorozu.

**Funding acquisition:** Tomoko Yorozu.

**Supervision:** Tomoko Yorozu.

**Writing – original draft:** Kiyoshi Moriyama.

**Writing – review & editing:** Akira Motoyasu, Joho Tokumine, Harumasa Nakazawa, Mariko Kotani, Tomoko Yorozu.

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