

1 **Clinical significance of methicillin-resistant coagulase-negative**
2 **staphylococci obtained from sterile specimens**

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1 **Abstract**

2 Distinguishing true coagulase-negative staphylococci bacteremia from
3 contamination remains a challenge. We conducted a retrospective analysis of 183
4 patients with methicillin-resistant coagulase-negative staphylococci (MR-CoNS)–
5 positive and methicillin-resistant *Staphylococcus aureus*–positive cultures obtained
6 from sterile sites such as blood, synovial fluid, ascitic fluid, and cerebrospinal fluid. Of
7 the 209 MR-CoNS isolates, 83 (39.7%) were considered infection associated and 126
8 (60.3%) were considered contamination. MR-CoNS isolates cultured from synovial
9 fluid were more likely to be infection associated ($P = 0.009$). The median interval from
10 insertion of a central venous catheter to onset of infection tended to be longer in
11 MR-CoNS infection cases than in methicillin-resistant *S. aureus* infection cases (41
12 days versus 14 days, $P = 0.055$). In conclusion, our results suggest that the proportion of
13 cases of true MR-CoNS infection may be higher than previously reported.

14

15

1 Keywords: Methicillin-resistant coagulase-negative staphylococci, Methicillin-resistant
2 *Staphylococcus aureus*, Contamination, Sterile specimen
3
4 Abbreviations: CoNS, coagulase-negative staphylococci; CRBSI, catheter-related
5 bloodstream infection; MR-CoNS, methicillin-resistant coagulase-negative
6 staphylococci; MRSA, methicillin-resistant *Staphylococcus aureus*.

1 **1. Introduction**

2 Some coagulase-negative staphylococci (CoNS) species are among the main species
3 of the normal resident skin flora (Roth and James, 1988). Therefore, CoNS isolates from
4 clinical specimens are often considered contaminants, especially when the specimens
5 are obtained from sterile sites. However, some reports have indicated the importance of
6 CoNS, which account for more than 30% of blood culture isolates (Gaynes, et al., 1996;
7 Richards, et al., 1999a, 1999b; Wisplinghoff, et al., 2004). Most CoNS infections occur
8 in patients with indwelling medical devices (Otto, 2009). Additionally, the central
9 venous catheterization procedure rate is increasing (Glickman, et al., 2010), suggesting
10 that the number of CoNS infections may also be increasing.

11 It remains difficult and challenging to distinguish true CoNS bacteremia from
12 contamination (Hall and Lyman, 2006). Although several investigators have proposed
13 methods to determine the clinical significance of CoNS isolates from blood cultures,
14 multiple positive blood culture results are not sufficient to determine true bacteremia
15 (Beekmann, et al., 2005; Mirrett, et al., 2001; Seo, et al., 2000; Seybold, et al., 2009).
16 Accordingly, the rate of true CoNS bacteremia has been reported to range from 10% to
17 30% in published reports (Beekmann, et al., 2005; Finkelstein, et al., 2002; Herwaldt, et
18 al., 1996; Mirrett, et al., 2001; Souvenir, et al., 1998; Weinstein, et al., 1997).

1 Many studies of contamination rates only involve blood cultures. Additionally,
2 most of these studies were conducted more than 10 years ago. Therefore, we conducted
3 a retrospective analysis of 183 patients with methicillin-resistant CoNS (MR-CoNS)–
4 positive and methicillin-resistant *Staphylococcus aureus* (MRSA)-positive cultures that
5 were obtained from sterile sites such as synovial fluid, ascitic fluid, and cerebrospinal
6 fluid as well as blood. In this study, we focused on methicillin-resistant isolates, which
7 are important drug-resistant pathogens. MRSA was also included to compare clinical
8 aspects with MR-CoNS.

9

10 **2. Materials and methods**

11

12 *2.1 Study setting*

13 This study was conducted at Toyama University Hospital (Japan), a 612-bed tertiary
14 care and teaching hospital with an annual average of 180,000 patient discharges.

15 Between January 2009 and December 2012, all cultures obtained from sterile sites in
16 adult patients (older than 18 years of age) that yielded MRSA and MR-CoNS were
17 identified through a review of the electronic microbiology records. The sterile sites from
18 which specimens were collected included blood, pleural fluid, ascitic fluid,
19 cerebrospinal fluid, synovial fluid, subcutaneous wounds, and closed abscesses. If more

1 than 3 types of bacteria or fungi were isolated from an ascitic fluid specimen, the result
2 was excluded from the analysis because of the high possibility of contamination with
3 gut flora. Isolate identification and antimicrobial susceptibility testing were assessed by
4 using the MicroScan WalkAway 96 SI (Siemens Healthcare, Erlangen, Germany)
5 according to the manufacturer's instructions. The panels used were MicroScan Dried
6 Pos ID 2 (PID2), MicroScan Dried Gram Pos Combo 6.1J, and MicroScan Dried Gram
7 Pos MIC 6.3J (Siemens Healthcare, Erlangen, Germany).

8

9 *2.2 Definition of infection*

10 Most infections, including bloodstream infections, were defined according to the
11 standard definitions of the US Centers for Disease Control and Prevention (Horan, et al.,
12 2008). Catheter-related bloodstream infection (CRBSI) was diagnosed when the same
13 organism grew from at least one percutaneous blood culture and from a catheter tip
14 culture (Mermel, et al., 2009). Decisions regarding contamination in all specimen types
15 were made after the following factors were considered: the patient's clinical history,
16 physical findings, body temperature at the time of culture, leukocyte count, C-reactive
17 protein level, number of positive blood cultures, culture results of specimens from other
18 sites, imaging results, clinical course, and response to therapy (Weinstein, et al., 1997).

1 Briefly, the absence of specific physical and laboratory findings or an improvement in
2 the response to treatment with ineffective antibiotics such as β -lactams indicated
3 contamination. Episodes that could only be effectively treated with anti-MRSA
4 antibiotics were considered infections. If both MRSA and MR-CoNS were cultured
5 from the same specimen, the specimen was considered MRSA infected but not
6 MR-CoNS infected because MRSA is a more invasive pathogen than MR-CoNS.
7 Culture positive results reported for a given specimen within 1 month were counted as a
8 single episode. The criteria for hospital-acquired infection were as follows: the
9 causative agent was cultured more than 48 h after admission; the patient had a history of
10 hospitalization, surgery, dialysis, or residence in a long-term health care facility within 6
11 months before the culture was obtained; and the patient had an indwelling intravenous
12 line, catheter, or any other percutaneous medical device when the culture was obtained
13 (Huang, et al., 2006).

14

15 *2.3 Data collection*

16 The following data for patients with bloodstream infections (including CRBSIs) were
17 extracted from the clinical records: age; sex; risk factors such as underlying conditions
18 (e.g., diabetes mellitus, neoplasm, and immunosuppressive therapy), the presence of

1 intravascular devices, and previous surgeries; clinical signs; results of laboratory
2 studies; antibiotic therapies; and death within 30 days. The duration of hospital stay,
3 interval from admission to onset, and interval from insertion of a central venous catheter
4 to onset were also examined. For patients transferred from other facilities, the duration
5 of hospital stay included the duration of hospitalization at both institutions.

6

7 *2.4 Statistical analysis*

8 Differences in the group proportions were assessed by using the chi-square or Fisher
9 exact test. Continuous variables were compared by using the Mann-Whitney test.
10 Statistical analyses were performed by using Prism version 5.0 (GraphPad, Inc., San
11 Diego, CA, USA). Differences were considered significant at a *P* value <0.05.

12

13 **3. Results**

14 During the study period, 284 cultures obtained from sterile sites in 183 patients were
15 MRSA or MR-CoNS positive; these yielded 335 microorganisms, including 126 MRSA
16 and 209 MR-CoNS isolates. Ninety-four patients had 106 infection episodes: 58 were
17 MRSA infections and 48 were MR-CoNS infections.

18

1 *3.1 Rate of contamination*

2 Of the 126 MRSA isolates, 115 (91.3%) were considered infection associated and 11
3 (8.7%) were considered contamination. Of the 11 latter isolates, 9 were cultured from
4 blood and 2 were cultured from a closed abscess; the most common reason for
5 considering contamination was that the clinical symptoms and laboratory data improved
6 after treatment with an antimicrobial agent known to be ineffective against MRSA
7 infection, such as a β -lactam. Of the 209 MR-CoNS isolates, 83 (39.7%) were
8 considered infection associated and 126 (60.3%) were considered contamination. The
9 proportions of infection-associated or contaminant isolates for each specimen are shown
10 in Table 1. These proportions remained the same even if the type of specimen was
11 limited to blood (39.6%). If only the initially cultured isolates from the blood of each
12 patient were evaluated, the proportion of infection decreased to 33.3%. MR-CoNS
13 isolates cultured from synovial fluid were significantly more likely to be infection
14 associated than isolates cultured from other specimens (5/83 vs. 0/126, $P = 0.009$).

15 Given the lack of criteria regarding clinical signs or symptoms in the definition of
16 CRBSI, we also confirmed clinical characteristics in patients with CRBSI to avoid
17 overestimating the incidence of infection. Of the 44 CRBSI-associated MR-CoNS
18 isolates in this study, 38 were obtained from patients with fever ($\geq 38^\circ\text{C}$), 4 were

1 obtained from patients with hypotension (<90 mm Hg), and 3 were obtained from
2 patients with neutropenia (<500 cells/ μ L). Some patients had more than one of these 3
3 factors.

4 We also examined the possibility that the study population comprised patients with a
5 potentially higher risk of infection than the general hospital population. Of the 83
6 infection-associated MR-CoNS isolates, only 3 were obtained from patients in the
7 intensive care unit; 77 isolates were from patients in the general ward, and 3 isolates
8 were obtained from patients of the outpatient clinic. None of the study participants were
9 bone marrow transplant recipients. Twelve MR-CoNS isolates were obtained from
10 patients with hematologic malignancies.

11

12 3.2 MR-CoNS species

13 The proportions of each MR-CoNS species obtained from sterile sites are shown in
14 Table 2 and are classified as infection or contamination. *Staphylococcus epidermidis*
15 was the dominant species, responsible for 75.9% of all MR-CoNS infections. Of the 154
16 MR-CoNS blood culture isolates, 101 (65.6%) were of *S. epidermidis*; of these, 45
17 (44.6%) were infection-associated isolates. Among the cases of infection, *S. epidermis*
18 was followed in prevalence by *Staphylococcus hominis* (9.6%), *Staphylococcus capitis*

1 (8.4%), *Staphylococcus warneri* (2.4%), and *Staphylococcus schleiferi* (2.4%). However,
2 among the cases of contamination, *S. epidermidis* accounted for only 60.3% of cases,
3 followed by *S. hominis* (14.0%), *Staphylococcus haemolyticus* (8.1%), *S. capitis* (6.6%),
4 and *Staphylococcus simulans* (5.0%). *S. epidermidis* was more prevalent among the
5 cases of infection ($P = 0.025$); however; *S. haemolyticus* and *S. simulans* were more
6 prevalent among the cases of contamination ($P = 0.007$ and 0.041 , respectively).
7 *Staphylococcus saprophyticus*, which usually causes urinary tract infections, was not
8 detected in this study.

9

10 3.3 Community-acquired or hospital-acquired organisms

11 Of the 335 MRSA- and MR-CoNS–positive cultures, 297 isolates were obtained more
12 than 48 h after admission and 38 were cultured within 48 h of admission; the latter
13 included 12 MRSA isolates (32%) and 26 MR-CoNS isolates (68%). Of the 38 isolates
14 cultured within 48 h, 36 were considered hospital-acquired organisms according to the
15 clinical definition; therefore, 333 isolates were hospital acquired. Only 2 *S. simulans*
16 isolates were considered community-acquired isolates.

17

18 3.4 Difference between MRSA and MR-CoNS infection

1 We next compared the clinical features between the 58 MRSA and 48 MR-CoNS cases
2 of infection. The types of infection are shown in Table 3. The proportion of CRBSIs was
3 higher among MR-CoNS infections than among MRSA infections (62.5% versus 24.1%,
4 $P < 0.001$). In contrast, among bone and joint infections, the proportion of MRSA
5 infections was higher than that of MR-CoNS infections ($P = 0.021$). No single
6 *Staphylococcus* species was isolated among prosthetic joint infections.

7 A comparison between MRSA and MR-CoNS infections with respect to the clinical
8 characteristics of bloodstream infections (including CRBSIs) is summarized in Table 4.
9 The MRSA-infected patients were older than the MR-CoNS–infected patients (68.8
10 years versus 59.7 years, $P = 0.016$). The median interval from insertion of a central
11 venous catheter to the onset of infection tended to be longer in the cases of MR-CoNS
12 infection than in the cases of MRSA infection (41 days versus 14 days, $P = 0.055$). The
13 mortality rate with MRSA infection was 25%, which was higher than that with
14 MR-CoNS infection (2.9%, $P = 0.016$). Vital signs on the day of the positive blood
15 culture were similar. However, leukocyte counts and C-reactive protein levels tended to
16 be higher in the cases of MRSA infection than in the cases of MR-CoNS infection ($P =$
17 0.082 and $P = 0.023$, respectively). Regarding underlying conditions, the rates of use of
18 a central venous catheter exceeded 80% for both infection groups, especially among

1 cases of MR-CoNS infection, for which 33 of 34 episodes involved central venous
2 catheters. The most commonly used initial drugs for the treatment of both MRSA and
3 MR-CoNS infections were vancomycin and teicoplanin. In some cases, removal of a
4 central venous catheter resulted in clinical improvement without antibiotics. In other
5 cases not treated with anti-MRSA drugs, the patients died before the culture results
6 became available.

7

8 **4. Discussion**

9 In this study, we analyzed and compared various aspects of cases involving MRSA
10 and MR-CoNS cultures. Initially, we evaluated each positive culture obtained from
11 sterile sites to distinguish true infection from contamination because some CoNS
12 species are among the main species of normal resident skin flora (Roth and James,
13 1988). In this study, the percentage of MRSA contamination among blood cultures was
14 similar to that in a previous report (6.4%) (Weinstein, et al., 1997).

15 On the other hand, 39.7% of the MR-CoNS–positive cultures were considered true
16 infections, which is a higher proportion than previously reported (5%–30%) (Beekmann,
17 et al., 2005; Finkelstein, et al., 2002; Hall and Lyman, 2006; Herwaldt, et al., 1996;
18 Natoli, et al., 2009; Souvenir, et al., 1998; Weinstein, et al., 1997). There were some
19 differences in the settings of our study and those previously reported. First, various

1 specimen types were included in our study, whereas previously published studies only
2 evaluated blood cultures. Even so, our results limited to blood cultures showed higher
3 infection rates compared with the results of previous studies. Second, the scope of our
4 study was limited to methicillin-resistant species. We chose to study
5 methicillin-resistant isolates only because this would enable precise decisions regarding
6 the presence or absence of a true infection, according to the requirement for anti-MRSA
7 drugs. Third, we adopted a definitive diagnosis of CRBSI that only required the growth
8 of the same organism from at least one percutaneous blood culture and a catheter tip
9 culture. However, we confirmed that most determinations of true infection-associated
10 CRBSI in this study met the requirements defined in previous studies, with regard to,
11 for example, clinical signs. Fourth, multiple samples may have been taken from the
12 same patient over a short interval. However, the proportion of cases of infection among
13 the initially cultured isolates from blood only in each patient remained higher than the
14 proportions reported in previous studies. Fifth, there was no evidence to indicate the
15 possibility that this study population might comprise patients at a potentially higher risk
16 of infection than the general hospital population, such as bone marrow transplant
17 recipients, patients with hematologic malignancies, and patients in intensive care units
18 (Herwaldt, et al., 1996). These results indicated the possibility that the incidence of

1 CoNS infection may have increased in recent years compared with the rate in the 1990s.
2 This is not surprising because patient populations and treatment modes have changed
3 over time and, in particular, the rate of central venous catheterization has increased
4 (Glickman, et al., 2010).

5 One of the objectives of this study was to examine differences in the clinical
6 significance of MR-CoNS infection in blood and other sterile specimens. Most
7 specimens from sterile sites are normally collected via percutaneous puncture, and
8 therefore, microbes from the normal skin flora could likely contaminate those
9 specimens. We therefore expected that the infection-associated rates for each type of
10 specimen would be nearly identical. Indeed, most rates of contamination for other types
11 of specimens were similar to that in blood. However, an MR-CoNS–positive culture
12 from synovial fluid was more likely to be associated with infection. The pretest
13 probability for synovial fluid collection may be higher than that for other sterile
14 specimens (e.g., blood); however, the number of isolates in this study was small, and a
15 larger number of cases would have to be studied to confirm this hypothesis.

16 *S. epidermidis* was the dominant MR-CoNS species in this study and was more likely
17 to be infection associated than contamination, as previously reported (Chu, et al., 2008;
18 Finkelstein, et al., 2002; Herwaldt, et al., 1996; Kloos and Bannerman, 1994).

1 Conversely, *S. haemolyticus* and *S. simulans* were less likely to be infection associated
2 and were always considered contamination in this study. Herwaldt et al. indicated that
3 non-*S. epidermidis* species blood culture isolates were less likely to be infection
4 associated. Another potential concern in this study was the false identification of
5 *Staphylococcus* species. MicroScan WalkAway, which was used for identification, has
6 been reported to have poor reliability for some uncommon CoNS strains (Olendzki, et
7 al., 2014). Unlike other species, the identification of *S. epidermidis*, *S. haemolyticus*,
8 and *S. hominis* was reported to be sufficiently reliable in the same study. The authors
9 also reported that the automated system showed 100% specificity and 90% sensitivity
10 for the detection of oxacillin resistance. Our results indicate the need for careful
11 evaluation, especially for uncommon CoNS strains.

12 In our study, rates of hospital-acquired infection were higher than those in previous
13 studies (Beekmann, et al., 2005; Finkelstein, et al., 2002; Herwaldt, et al., 1996;
14 Weinstein, et al., 1997). The main reason for this difference is that we used the timing
15 criterion of “not only 48 h after admission” as well as other detailed criteria such as a
16 history of hospitalization. Second, we investigated only methicillin-resistant species.
17 Indeed, Cherifi et al. found that *S. epidermidis* CRBSI, which was considered hospital
18 acquired, was significantly resistant to more antibiotics when compared with *S.*

1 *epidermidis* isolates obtained from healthy volunteers (Cherifi, et al., 2013).

2 The clinical features and outcomes differ between *S. aureus* and CoNS infections. *S.*
3 *aureus* is an aggressive pathogen that causes various invasive and fatal infections. In
4 contrast, *S. epidermidis* is usually associated with infections of implanted medical
5 devices such as central venous catheters (Pfaller and Herwaldt, 1988). We confirmed
6 that MR-CoNS caused CRBSI more frequently than MRSA. This finding is compatible
7 with the fact that *S. epidermidis* is responsible for 50% to 70% of catheter-related
8 infections (von Eiff, et al., 2002). Interestingly, the proportion of bone and joint
9 infections was higher among MRSA infections than among MR-CoNS infections. This
10 might have been due to differences in *S. aureus* pathogenicity, including the production
11 of enterotoxins, exotoxins, leukocidins, and leukotoxins that is not observed in *S.*
12 *epidermidis* infection (Gill, et al., 2005).

13 In conclusion, our results suggest that the proportion of true cases of MR-CoNS
14 infection is higher than previously reported. The MR-CoNS contamination rates in
15 blood and other sterile site specimens, excluding synovial fluid, were similar. Because
16 patient populations and treatment modes change over time, we urge the continued
17 monitoring of both *S. aureus* and CoNS infections.

18 **ETHICAL APPROVAL**

1 This study was performed in conformity with the Declaration of Helsinki after approval
2 by the Ethics Committee of University of Toyama. The patients' privacy was fully
3 protected, and personal information was handled such that patients could not be
4 identified.

5

6 **CONFLICT OF INTEREST**

7 Yoshihiro Yamamoto has received lecture fees from Pfizer Inc. Koichi Izumikawa has
8 received honoraria from Pfizer Japan, Inc., Astellas Pharma Inc., and Merck & Co., Inc.

9 No other authors declare any conflicts of interest.

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Table 1. Sterile specimens with isolated methicillin-resistant coagulase-negative staphylococci

Specimens (n)	No. (%) of isolates		<i>P</i> value
	Infection-associated isolates	Contaminants	
Blood (154)	61 (39.6)	93 (60.4)	0.960
Subcutaneous wound (13)	8 (61.5)	5 (38.5)	0.097
Synovial fluid (5)	5 (100.0)	0 (0.0)	0.009
Ascitic fluid (18)	4 (22.2)	14 (77.8)	0.113
Closed abscess (13)	3 (23.1)	10 (76.9)	0.379
Cerebrospinal fluid (4)	2 (50.0)	2 (50.0)	0.650
Pleural fluid (2)	0 (0.0)	2 (100.0)	0.519
All (209)	83 (39.7)	126 (60.3)	

Table 2. Methicillin-resistant coagulase-negative staphylococci isolated from sterile sites^a

Microorganism	No. (%) of isolates per indicated category			<i>P</i> value
	Total (n = 209)	Infection (n = 83)	Contamination (n = 126)	
<i>Staphylococcus epidermidis</i>	139(66.5)	63(75.9)	76(60.3)	0.019
<i>Staphylococcus hominis</i>	25(12.0)	8(9.6)	17(14.0)	0.401
<i>Staphylococcus capitis</i>	15(7.2)	7(8.4)	8(6.6)	0.568
<i>Staphylococcus haemolyticus</i>	10(4.8)	0(0.0)	10(8.1)	0.007
<i>Staphylococcus lugdunensis</i>	6(2.9)	1(1.2)	5(4.1)	0.406
<i>Staphylococcus simulans</i>	6(2.9)	0(0.0)	6(5.0)	0.083
<i>Staphylococcus warneri</i>	4(1.9)	2(2.4)	2(1.7)	0.650
<i>Staphylococcus schleiferi</i>	2(1.0)	2(2.4)	0(0.0)	0.157
<i>Staphylococcus sciuri</i>	1(0.5)	0(0.0)	1(0.8)	1.000
<i>Staphylococcus intermedius</i>	1(0.5)	0(0.0)	1(0.8)	1.000

^aSpecimens were collected from sterile sites, including blood, pleural fluid, ascitic fluid, cerebrospinal fluid, synovial fluid, subcutaneous wounds, and closed abscesses.

Table 3. Comparison of types of infection between MRSA and MR-CoNS infections

Type of infection	No. (%) of episodes per indicated category		
	MRSA (n = 58)	MR-CoNS (n = 48)	P value
Surgical site	16(27.6)	10(20.8)	0.421
Catheter-related bloodstream	14(24.1)	30(62.5)	<0.001
Bloodstream	10(17.2)	4(8.3)	0.177
Bone and joint	9(15.5)	1(2.1)	0.021
Skin and soft tissue	4(6.9)	1(2.1)	0.374
Lower respiratory tract	3(5.2)	0(0.0)	0.250
Gastrointestinal system	1(1.7)	1(2.1)	1.000
Cardiovascular system	1(1.7)	1(2.1)	1.000

MRSA, methicillin-resistant *Staphylococcus aureus*; MR-CoNS, methicillin-resistant coagulase-negative staphylococci.

Table 4. Comparison of clinical characteristics of bloodstream infections^a

Variable	Causative microorganism		P value
	MRSA (n = 24)	MR-CoNS (n = 34)	
Age (years)	68.8 ± 9.5	59.7 ± 15.5	0.016
Male sex	15(62.5)	21(61.8)	0.954
Length of hospital stay (days)	97(20-407)	102(29-525)	0.468
Length from admission to onset (days)	41(0-294)	45(0-437)	0.554
Length from CVC insertion to onset (days)	14(1-537)	41(6-970)	0.055
Duration of antibiotic therapy (days)	15(0-45)	8(0-70)	0.099
Death within 30 days	6(25.0)	1(2.9)	0.016
<u>Vital signs and laboratory data</u>			
Body temperature (°C)	38.6 ± 0.6	38.9 ± 0.8	0.050
Systolic blood pressure (mm Hg)	111.6 ± 19.1	115.7 ± 22.6	0.770
Leukocyte (/μL)	12,033.3 ± 8797.7	7850.6 ± 5290.2	0.082
Hemoglobin (g/dL)	9.2 ± 2.3	9.6 ± 2.2	0.517
Platelet (× 10 ³ /μL)	16.8 ± 12.2	21.4 ± 15.3	0.280
C-reactive protein (mg/dL)	10.2 ± 7.4	6.3 ± 5.8	0.023
Albumin (g/dL)	2.8 ± 0.6	2.8 ± 0.6	0.521
Creatinine (mg/dL)	1.0 ± 0.7	1.0 ± 0.7	0.818
Sodium (mEq/L)	136.0 ± 6.0	136.4 ± 4.8	0.652
<u>Underlying condition</u>			
Recent surgery (previous 30 days)	7(29.2)	9(26.5)	0.820
CVC	20(83.3)	33(97.1)	0.149
Diabetes mellitus	5(20.8)	6(17.6)	1.000
Neoplasm	13(54.2)	19(55.9)	0.897
Immunosuppressive therapy	12(50.0)	11(32.4)	0.176
<u>Initial drug of choice</u>			
Vancomycin	14(58.3)	13(38.2)	
Teicoplanin	5(20.8)	2(5.9)	
Arbekacin	1(4.2)	0(0.0)	

Values are mean ± SD, n (%), and median (minimum to maximum).

^aBloodstream infections in this table include catheter-related bloodstream infection MRSA, methicillin-resistant *Staphylococcus aureus*; MR-CoNS, methicillin-resistant coagulase-negative staphylococci; CVC, central venous catheter; SD, standard deviation.