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# Characterization of Recurrent Methicillin-resistant *Staphylococcus aureus* Blood Infections

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## Abstract

**Introduction**
Little is known about clinical characteristics of patients (pts) with methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infection (BSI) that are associated with recurrent BSI (RBSI).

**Methods**
A retrospective chart review study was done in an integrated 4 hospital health system in Michigan. 1173 consecutive individual pts with MRSA BSI were evaluated from 2005 to 2014. RBSI was defined as a positive blood culture ≥30 days after completing treatment (tx) for the initial BSI (IBSI). Pts were compared to ones without RBSI. Deceased pts and pts with RBSI < 30 days from end of tx were excluded. Vancomycin (VAN) and daptomycin (DAP) susceptibility was determined using Etest. Isolates were typed using pulsed field gel electrophoresis (PFGE). Comparisons were done using chi-square and t-test in SAS 9.4.

**Results**
Out of 1173 pts with MRSA BSI, 896 met criteria. 71 (7.9%) experienced RBSI in a median of 258.5 days (range 31-2288). The average age in RBSI was 52.2 vs 59.1 years in the control group p <0.001. Table 1 shows characteristics of the pts. The average duration of IBSI in pts with RBSI was 4.3 (± 3.8) days; 15.5% cases had a duration ≥ 7 days. The source of RBSI was the same as in IBSI in 43 cases (61%): line in 39.5% and endocarditis in 32.6% of cases. Among MRSA isolates, the mean VAN MIC in IBSI was 1.6 (± 0.2) µg/ml vs 1.56 (± 0.39) µg/ml for RBSI. 84.5% had same or decreased VAN MIC in RBSI. For DAP, mean MIC was 0.52 (±0.17) µg/ml in IBSI and 0.66 µg/ml (± 0.44) for RBSI, with increase in DAP MIC in 45.7%. In IBSI, USA 300 (46.5%) and USA 100 (40.8%) were the most common strains. Of the RBSI, 76% had same CDC group as in IBSI.

**Conclusion**
MRSA RBSI, though uncommon, is generally of the same source and with isolates of the same CDC group. VAN is the most commonly used tx, with 84.5% of isolates showing no increase in VAN MIC of RBSI. Source, epidemiological acquisition and comorbidities are risk factors associated with RBSI.

## Background

- *Staphylococcus aureus* is a major cause of bloodstream infection (BSI) around the world. Mortality remains high, up to 30%.
- Recurrence of infection is an important complication of MRSA BSI, playing a role in the morbidity, mortality, hospital readmissions and cost. Estimated rate of recurrence of *S. aureus* bacteremia varies between 5%-12%.
- Recurrence of *S. aureus* may be due to relapse (the emergence of the original infecting organism) or reinfection (infection with a different strain), being more frequent the first one 80-90% of recurrence.
- Little is known about clinical characteristics and molecular epidemiology of recurrence after a first episode of MRSA BSI.

## Objectives

This study aims:

- to describe the characteristics of recurrent MRSA bacteremia infections;
- to evaluate the strains of MRSA isolates causing the recurrent bacteremia using pulsed-field gel electrophoresis.

## Methods

**Study design**

This was a retrospective study, performed in an integrated 4 hospital health system in southeast Michigan. Consecutive individual patients with MRSA BSI were evaluated over a 9-year period, from July 2005 to June 2014. Deceased patients and patients with RBSI < 30 days from end of treatment were excluded. Demographic, clinical and microbiology data was obtained via review of electronic medical records.

## Methods

**Definition of variables**

Recurrent bloodstream infection (RBSI) was defined as the first positive blood culture ≥30 days after completing treatment for the first MRSA BSI.

*Duration of bacteremia* was defined as the number of days between the first positive culture and the first clear blood culture.

Epidemiological acquisition: *community-acquired* and *hospital-acquired* infections were defined as a positive blood culture collected less than 48 hours and more than 48 hours after hospital admission respectively; *healthcare-associated* infection was defined as a positive blood culture collected less than 48 hours in a patient with invasive device on admission, history of MRSA infection or colonization, history of surgery, hospitalization, dialysis, nursing home residence within previous year.

**Laboratory methods**

Initial identification and in vitro susceptibility testing was done in all MRSA isolates by the clinical microbiology lab. MICs to vancomycin (VAN) and daptomycin (DAP) were determined by Etest. Pulsed-field gel electrophoresis (PFGE) patterns were compared and isolates were considered to be in the same PFGE group if they had ≥80% similarity using the Dice coefficient.

**Statistical analysis** were done using chi-square and t-test analysis in SAS 9.4.

Characteristics comparisons were done in the following groups

1. Initial BSI vs Recurrent BSI, in pts with recurrence
2. Pts with RBSI vs pts without RBSI
3. Pts with Relapse (same CDC group) vs Reinfection (different CDC group)

## Results

Out of 1173 patients with MRSA BSI, 896 met inclusion criteria. 71 (7.9%) experienced RBSI in a median of 258.5 days (range 31-2288) and 825 did not. The average age in RBSI was 52.2 (± 14.2) vs 59.1 (± 17.2) years in the control group (p <0.001). Table 1 shows characteristic of the initial BSI and recurrent BSI in pts with recurrence. Table 2 shows characteristics of pts with RBSI vs those that did not. No significant difference was found in characteristics between relapse vs reinfection.

**Table 1 : Characteristics of the Initial BSI vs the Recurrent BSI**

| Variable | Initial BSI N=71 | Recurrent BSI N=71 |
|---|---|---|
| **Source** - 58% had the same source as the first BSI | | |
| Line | 43.6% | 34% |
| Endocarditis | 18.3% | 27% |
| Wound/skin | 15.5% | 20% |
| Other | 24 % | 20% |
| **CDC group -** 76% had the same CDC group as the first BSI | | |
| CDC 100 | 38% | 41% |
| CDC 300 | 49.3% | 47% |
| Other | 12.7% | 12% |
| **Vancomycin MIC** | 1.60 (± 0.2) µg/ml | 1.56 (± 0.39) µg/ml |
| 84.5% had the same or decreased MIC in 2nd BSI | | |
| **Daptomycin MIC** | 0.52 (±0.17) µg/ml | 0.66 µg/ml (± 0.44) |
| 45.7% had an increase in MIC in 2nd BSI | | |

**Table 2 : Characteristics of pts with RBSI vs pts without RBSI**

| Variable | Pts with RBSI N = 71 | Pts without RBSI N = 825 | p value |
|---|---|---|---|
| **Race %** | | | |
| Caucasian | 19 | 35 | 0.012 |
| African-American | 78 | 60 | |
| Other | 3 | 4 | |
| **Source %** | | | |
| Graft infection | 6 | 2 | <0.001 |
| Line | 41 | 20 | |
| Intraabdominal | 0 | 1 | |
| None | 11 | 19 | |
| Respiratory | 1 | 8 | |
| Skin/wound | 17 | 36 | |
| GU tract | 1 | 6 | |
| Osteomyelitis | 1 | 1 | |
| Endocarditis | 21 | 9 | |
| **Epidemiological acquisition %** | | | |
| Community-acquired | 17 | 33 | 0.016 |
| Healthcare-associated | 65 | 52 | |
| Hospital-acquired | 18 | 15 | |
| **Duration of antibiotics (days)** | 34.7 ± 20.8 | 29.3 ± 21.7 | 0.043 |
| **Comorbidities %** | | | |
| Acute renal failure | 3 | 16 | 0.003 |
| Chronic renal failure | 44 | 32 | 0.042 |
| Dialysis | 41 | 20 | <0.001 |
| Hepatitis | 28 | 15 | 0.041 |
| **VAN MIC (mean)** | 1.6 ± 0.2 | 1.6 ± 0.3 | 0.580 |

## Conclusion

- Our data shows MRSA RBSI is uncommon, however when it does occur, it is generally of the same source and with isolates of the same CDC group.
- VAN is the most commonly used antimicrobial, with 84.5% of isolates showing no increase in VAN MIC of the RBSI.
- Characteristics of source, acquisition and comorbidities should be considered when evaluating possible risk factors associated with RBSI.

## References

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