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# Risk Factors for 30-Day Mortality in Patients with Methicillin-Resistant Staphylococcus aureus Bloodstream Infections

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SUMMARY

*Objectives:* Methicillin-resistant *Staphylococcus aureus* (MRSA) blood stream infections (BSI) are a major health care problem accounting for a large percentage of nosocomial infections. The aim of this study was to identify risk factors associated with 30-day mortality in patients with MRSA BSI.
*Methods:* This was a retrospective study performed in Southeast Michigan. Over a 9- year period, a total of 1,168 patients were identified with MRSA BSI. Patient demographics and clinical data were retrieved and evaluated using electronic medical health records.
*Results:* 30-day mortality during the 9-year study period was 16%. Significant risk factors for 30-day mortality were age, cancer, heart disease, neurologic disease, nursing home residence and Charlson score >3 with Odds Ratio (OR) of 1.03 (CI 1.02–1.04), 2.29 (CI 1.40–3.75), 1.78 (CI 1.20–2.63), 1.65 (CI 1.08–2.25), 1.66 (CI 1.02 – 2.70) and 1.86 (CI 1.18 – 2.95) correspondingly. Diabetes mellitus, peripheral vascular disease (PVD), and readmission were protective factors for 30-day mortality with OR of 0.53 (CI 0.36–0.78), 0.46 (CI 0.26–0.84) and 0.13 (CI0.05 – 0.32) respectively.
*Conclusions:* Our study identified significant risk factors for 30-day mortality in patients with MRSA BSI. Interestingly, diabetes mellitus, PVD and readmission were protective effects on 30-day mortality. There was no statistically significant variability in 30-day mortality over the 9-year study period.


## Introduction

MRSA infection was first described in 1961 and continues to be a major public health concern, accounting for significant nosocomial and increasing community-acquired infections (Barber, 1961; Pastagia et al., 2012). From 1993 to 2009, septicemia related hospitalizations increased to 153 percent, adding to healthcare cost, up to 15.4 billion dollars (Elixhauser et al., 2011). Recent data show that the incidence is still increasing (Elixhauser et al., 2011). In the 2013 National Center for Health Statistics Report showed an overall decrease in mortality but an increase in bloodstream related deaths by 17% (Hall et al., 2013). In the 2010 National Healthcare Safety Network (NHSN) report on antimicrobial-resistant pathogens associated with healthcare infections, *S. aureus* was the most common pathogen reported, of which 54.6% were methicillin-resistant (Sievert et al., 2013). MRSA BSI can cause devastating complications with mortality reported up to 39% (Pastagia et al., 2012; Keynan and Rubinstein, 2013; Mansur et al., 2012; Wi et al., 2012; Lee et al., 2013; Gasch et al., 2013a). Identifying risk factors associated with mortality is essential to improving patient outcomes. Studies have shown that the most important factors determining patient outcomes in MRSA BSI are age, presence of comorbidities, and appropriate initial antibiotic treatment (Pastagia et al., 2012; Keynan and Rubinstein, 2013; Ok et al., 2013). This study aims to identify possible predictors of 30-day mortality in MRSA BSI patients and to evaluate changes in mortality rate over a 9 year period.

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## Methods

### Study Design and Patient Identification

This was a retrospective study performed at an integrated 4-hospital health system in southeast Michigan. The primary outcome of this study was 30-day all-cause mortality in patients with MRSA BSI. All patients ≥ 18 years of age with confirmed MRSA BSI were identified over a 9-year period, from July 2005 to June 2014, via review of microbiology laboratory records. Electronic medical health records were utilized to obtain clinical information, patient demographics and 30-day mortality. Thirty-day all cause mortality was defined as death within 30 days of index blood culture. Patient demographics and comorbidities included: age, gender, presence of immunosuppressive disease, cancer, heart disease, gastrointestinal (GI) disease, neurological disease, renal disease, diabetes mellitus, human immunodeficiency virus (HIV), neutropenia, solid organ transplant recipient, intravenous drug use (IVDA), peripheral vascular disease (PVD) and connective tissue disease. The following healthcare exposures were analyzed: prior hospitalization including admission to intensive care unit (ICU), recent surgery within the past 1 year, nursing home residence (NHR), and presence of indwelling central venous catheter (CVC). Source of acquisition was categorized as follows: CVC related, osteomyelitis, endocarditis, graft infection, skin or wound infections, intra-abdominal (IA), respiratory, urinary tract (UTI) or undetermined source. Duration of bacteremia and recurrence were evaluated. Recurrence was defined as positive blood culture within 30 days of completing treatment; duration of bacteremia was divided in 3 groups: ≤3 days, 4–6 days and ≥ 7 days. Patients with recurring positive blood cultures during one admission were included once. Readmission was defined as any infection-related readmissions within 30 days of completing therapy. The Charlson Comorbidity Index was calculated to compare patients' comorbidities and 30-day mortality (Charlson et al., 1987).

### Statistical Analysis

Continuous data were described using means and standard deviations, while all categorical data were presented as counts and percentages. Five patients were excluded from the analysis because of incomplete data. Univariate two-group tests were performed to compare clinical and demographic data between patients who expired within 30 days from index blood culture with alive patients. All predictors of mortality with univariate P-value <0.2 were included in a multivariable logistic regression model. A final model was produced using manual backwards selection, meaning non-significant predictors were removed one by one in descending P-value order and the model re-run each time until each predictor remaining was significant. Variability in 30-day all-cause mortality over the 9-year study period was determined using

**Table 1**
Univariate and Multivariate Logistic Regressionn Analysis.

| Predictor | Demographics and Clinical Characteristics | Univariate Logistic Regression | | | Multivariate Logistic Regression | | |
|---|---|---|---|---|---|---|---|
| | | Unadjusted OR | 95% CI | P-Value | Adjusted OR | 95% CI | P-Value |
| Age, years, mean(SD) | 60.3 (17.6) | 1.04 | 1.03-1.05 | <**0.001** | 1.03 | 1.02-1.04 | <**0.001** |
| Gender, male | 689 (59%) | 1.13 | 0.83-1.55 | 0.4417 | | | |
| Race | | | | | | | |
| African American | 694 (60%) | | | | | | |
| Caucasian | 407 (35%) | | | | | | |
| Other | 56 (5%) | | | | | | |
| Cancer | 140 (12%) | 2.73 | 1.84-4.07 | <**0.0001** | 2.29 | 1.40-3.75 | **0.001** |
| Connective tissue | 23 (2%) | 1.12 | 0.38-3.36 | 0.8341 | | | |
| CVC | 127 (11%) | 0.61 | 0.34-1.08 | 0.0913 | | | |
| Diabetes | 467 (40%) | 0.75 | 0.54-1.04 | 0.0800 | 0.53 | 0.36-0.78 | **0.0015** |
| Duration of bacteremia, days (SD) | 3.9 | 1.32 | 0.78-2.23 | 0.3099 | | | |
| GI disease | 238 (20%) | 1.06 | 0.73-1.55 | 0.7486 | | | |
| Heart disease | 329 (28%) | 2.25 | 1.64-3.10 | **0.0001** | 1.78 | 1.20-2.63 | **0.0039** |
| HIV | 35 (3%) | 0.30 | 0.07-1.26 | 0.1009 | | | |
| Immunosuppressive disease | 75 (6%) | 1.83 | 1.06-3.15 | **0.0306** | | | |
| IV drug use | 206 (18%) | 0.40 | 0.24-0.68 | **0.0006** | | | |
| Neurologic disease | 236 (20%) | 2.44 | 1.73-3.43 | **0.0001** | 1.65 | 1.08-2.52 | **0.02** |
| Neutropenia | 13 (1%) | 3.20 | 1.04-9.89 | **0.0432** | | | |
| Nursing home resident | 129 (11%) | 2.67 | 1.77-4.02 | <**0.0001** | 1.66 | 1.02-2.70 | 0.0421 |
| Prior hospitalization | 597 (51%) | 1.25 | 0.92-1.70 | 0.1599 | | | |
| Prior ICU stay | 183 (16%) | 1.31 | 0.88-1.96 | 0.1876 | | | |
| Prior surgery | 102 (9%) | 1.10 | 0.65-1.89 | 0.7165 | | | |
| PVD | 149 (13%) | 0.66 | 0.39-1.11 | 0.1191 | 0.46 | 0.26-0.84 | **0.0106** |
| Readmit infection | 169 (14%) | 0.13 | 0.05-0.33 | <**0.0001** | 0.13 | 0.05-0.32 | <**0.001** |
| Recurrence 30d | 84 (7%) | 0.24 | 0.09-0.65 | **0.0055** | | | |
| Renal disease | 550 (47%) | 1.29 | 0.95-1.76 | 0.1077 | | | |
| Respiratory disease | 208 (18%) | 2.10 | 1.47-3.01 | <**0.0001** | | | |
| Solid organ transplant | 31 (3%) | 1.79 | 0.79-4.05 | 0.1655 | | | |
| Source: Graft | 31 (3%) | 1.22 | 0.49-3.01 | 0.6675 | | | |
| Source: CVC | 244 (21%) | 0.63 | 0.41-0.96 | **0.0316** | 0.39 | 0.24-0.63 | 0.0001 |
| Source: IE | 0 | N/A | | N/A | | | |
| Source: IA | 10 (1%) | 2.18 | 0.56-8.52 | 0.2609 | | | |
| Source: None | 247 (21%) | 1.91 | 1.36-2.70 | **0.0002** | | | |
| Source: Respiratory | 97 (8%) | 2.26 | 1.41-3.62 | **0.0007** | | | |
| Source: Skin/Wound | 370 (32%) | 0.51 | 0.35-0.75 | **0.0005** | 0.48 | 0.31-0.71 | 0.001 |
| Source: GU | 61 (5%) | 1.14 | 0.58-2.24 | 0.6986 | 0.40 | 0.18-0.88 | 0.022 |
| Source: Osteomyelitis | 7 (1%) | 0.00 | 0.001->999 | 0.9838 | | | |
| Source: Endocarditis | 106 (9%) | 0.89 | 0.51-1.55 | 0.6779 | | | |
| Charlson Score, N, mean (SD) | 1154, 3.2 (2.4) | 1.77 | 1.11-1.25 | <**0.001** | | | |
| Charlson Score Category (>=3 vs <3) | | 2.40 | 1.69-3.40 | <**0.001** | 1.86 | 1.18-2.95 | **0.0079** |