

The Effect of Infectious Diseases Consultation on Mortality in Hospitalized Patients With Methicillin-Resistant *Staphylococcus aureus*, *Candida*, and *Pseudomonas* Bloodstream Infections

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We evaluated the association between infectious disease consultation and bloodstream infection outcomes, including methicillin-resistant *Staphylococcus aureus*, *Candida*, and *Pseudomonas*. No infectious diseases consultation was associated with over 4-fold increased hazard of death at 3 months and 6-fold increased hazard of death in hospital.

Keywords. bacteremia; bloodstreams infections; infectious diseases consultation.

Bloodstream infections result in high morbidity and mortality [1]. Multiple studies have demonstrated that infectious diseases (ID) consultation is associated with improved outcomes, especially in *Staphylococcus aureus* bacteremia and candidemia [2]. Infectious diseases consultation is not mandatory at our facility. The purpose of our study was to investigate the impact of ID consultation on mortality of hospitalized patients with 3 common bloodstream infections: methicillin-resistant *S aureus* (MRSA), *Candida*, and *Pseudomonas*.

METHODS

We performed a retrospective cohort study of bloodstream infections at the University of Minnesota Medical Center, an 874-bed, academic, tertiary referral center. Through our hospital's infection control database, we reviewed all blood cultures positive for MRSA, *Candida*, and *Pseudomonas* between January 1, 2016 and December 31, 2018. We included adults (≥ 18 years)

and reviewed electronic medical records for demographic information, comorbidities, Charlson comorbidity index, treatment information, and vital status 3 months after index positive blood culture draw. We recorded whether an ID consultation note was present in the electronic medical record, time to appropriate antibiotics, and whether the hospitalization included an intensive care unit (ICU) stay. Appropriate antibiotics was defined as receipt of an antistaphylococcal, antifungal, or antipseudomonal antimicrobial during hospitalization. The primary outcome was 3-month mortality. Institutional review board approval was obtained through the University of Minnesota.

Categorical variables were compared using the χ^2 test, and continuous variables were compared using the Student *t* test. Hazard ratios and 95% confidence intervals (CIs) were estimated using multivariable Cox proportional hazards regression models adjusted for risk factors for mortality. Those who died on the day of index positive blood culture were removed from analyses. Statistical significance was defined as $P < .05$. We used IBM SPSS Statistics, version 24 (IBM Corp., Armonk, NY) for analyses.

RESULTS

In total, we identified 229 bloodstream infections between 2016 and 2018; 99 with MRSA, 69 with *Candida*, and 61 with *Pseudomonas*. Overall, 181 (79%) of bloodstream infections had an ID consultation, and 48 did not. The groups were comparable with regard to demographics and comorbidities (Supplemental Table 1). Three-month mortality was 36% for all bloodstream infections combined. In multivariate analysis, patients without ID consultation had 4.5 increased hazard of death at 3 months (95% CI, 2.7–7.3; $P < .0001$) compared with those who received ID consultation, controlling for age, sex, ICU stay, solid organ transplant, and Charlson comorbidity index (Figure 1). Removing those who died 1 day after blood culture draw, the hazard of death was 3.4 times without ID consultation (95% CI, 1.9–5.9; $P < .0001$), compared with with ID consultation controlling for age, sex, ICU stay, solid organ transplant, and Charlson comorbidity index. Furthermore, removing those who died within 2 days of blood culture draw, there was a 2.9 increased hazard of death without ID consultation (95% CI, 1.6–5.3; $P = .0001$). Those without ID consultation had a 5.9 increased hazard of death in hospital compared with those who received an ID consultation (95% CI, 3.2–11.0, $P < .0001$).

Patients who received ID consultation were 9 times more likely to receive appropriate antibiotics or antifungals (95% CI, 1.7–53.3; $P = .011$), 6 times more likely to have central lines removed (95% CI, 1.7–20.9; $P = .008$), and 4 times

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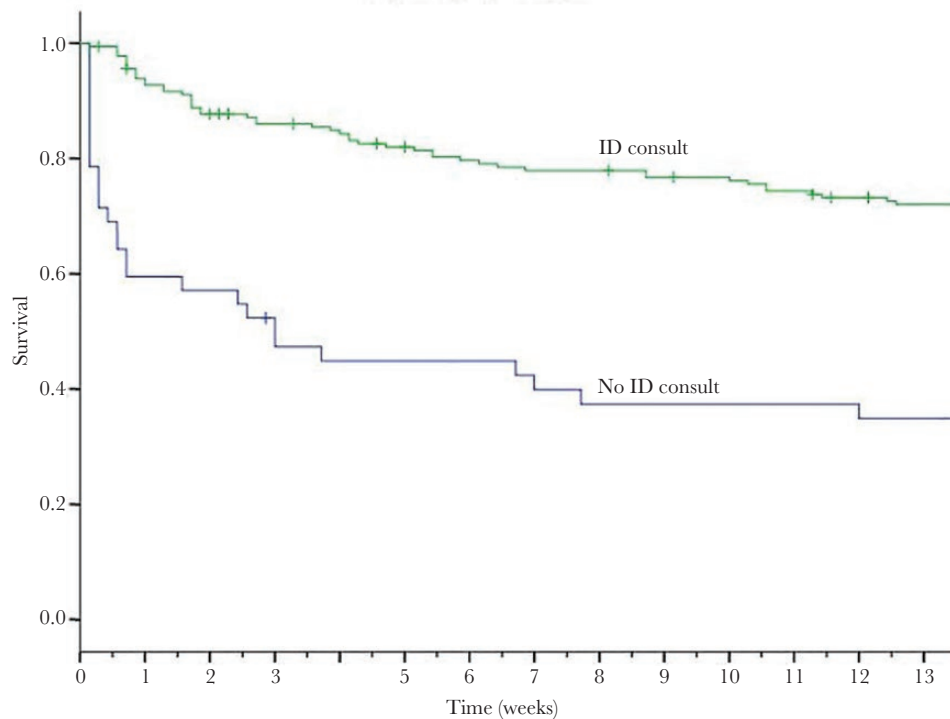


Figure 1. Overall 3-month survival in those with bloodstream infections with and without an infectious diseases (ID) consultation (73% vs 36% survival; log rank; $P < .0001$).

more likely to have echocardiography (transthoracic or transesophageal) performed to evaluate for endocarditis (95% CI, 1.6–11.8; $P = .008$).

Methicillin-Resistant *Staphylococcus aureus* Bacteremia

Of those 99 cases of MRSA bacteremia, 3-month mortality was 28%. All 99 cases were placed on antistaphylococcal antibiotics within 1 day of blood culture draw. Mortality with ID consultation was 22% (19 of 87), but mortality without ID consultation was 67% (9 of 12) ($P = .0001$). The median time to death in those without an ID consultation was 2 days (interquartile range [IQR], 1–5), whereas with an ID consultation was 27 days (IQR, 10–61). Median time to ID consultation was 2 days (IQR, 1–2). Controlling for age, sex, ICU stay, solid organ transplant, and Charlson comorbidity index, persons without ID consultation had 11.1 increased hazard of death (95% CI, 3.7–33.3; $P < .0001$), compared with persons with an ID consultation, and 6.7 increased hazard of death in hospital (95% CI, 2.1–21.6, $P = .001$) without ID consultation compared with persons with ID consultation. Infectious diseases consultation was associated with obtaining a transesophageal echocardiogram ($P = .039$), and early ID consultation (within 72 hours of blood culture draw) was associated with central line removal ($P = .018$).

Candidemia

There were 68 cases of candidemia: 38% ($n = 26$) were *Candida albicans*; 34% ($n = 23$) were *Candida glabrata*; and 15% ($n = 10$)

were *Candida parapsilosis* and 10 other species of *Candida*. Overall 3-month mortality for patients with candidemia was 35%. Without ID consultation, 63% (5 of 8) died, compared with 32% (19 of 60) who died with ID consultation ($P = .120$). Median time to ID consultation was 2 days (IQR, 0–3). Adjusting for age, sex, ICU stay, and Charlson comorbidity index, no ID consultation was associated with 3.8 increased hazard of death (95% CI, 1.2–11.4; $P = .020$) and 5.9 increased hazard of death before hospital discharge (95% CI, 1.6–21.2; $P = .007$). Median time to death in patients with an ID consultation was 18 days (IQR, 5–39), whereas for patients without ID consultation median time to death was 4 days (IQR, 1–11). Early ID consultation (within 72 hours of blood culture draw) was associated with central line removal ($P = .050$). Infectious diseases consultation was associated with obtaining echocardiography within 2 weeks of candidemia ($P = .005$) and obtaining ophthalmology evaluation—although this was not statistically significant (70% vs 38%, $P = .109$).

Pseudomonas Bacteremia

In the subgroup with *Pseudomonas* bacteremia, significantly more people without ID consultation had malignancy compared with those who received ID consultation (33% [8 of 24] vs 12% [4 of 34], $P = .054$). Of the 58 persons with *Pseudomonas* bacteremia, mortality was 45% at 3 months. Mortality at 3 months was 63% (15 of 24) without an ID consultation and 32% (11 of 34) with an ID consultation ($P = .033$). Median time to ID consultation was 2.5 days (IQR, 1–4). Median time to death was

5 days (IQR, 1–21) without ID consultation and 36 days (IQR, 9–41) with an ID consultation. After controlling for age, sex, ICU stay, solid organ transplant, and Charlson comorbidity index, no ID consultation was associated with 3.2 times increased hazard of death (95% CI, 1.4–7.3; $P = .005$) at 3 months and 5.3 times increased hazard of death in hospital (95% CI, 1.5–18.8; $P = .010$), compared with persons with ID consultation.

DISCUSSION

Our study determined that 3-month, all-cause mortality of 3 common bloodstream infections at our institution is 36%. The adjusted hazard ratio for 3-month mortality of patients who did not receive an ID consultation is 4.5 times higher than patients who received ID consultation. In-hospital mortality is also 6 times higher without ID consultation. In addition to mortality benefit, ID consultation is associated with a significantly higher rate of appropriate antimicrobial therapy, central line removal, and echocardiography to evaluate for endocarditis. From the perspective of hospital administrators, if hospitalized patients with bloodstream infections are more likely to receive appropriate treatment with ID consultation, then automatic ID consultation should be considered to improve patient outcomes.

For *S aureus* bacteremia, retrospective studies have consistently demonstrated the association between ID consultation and improved hospital outcomes [3]. The benefit of ID consultation in our study is not from appropriate antibiotics but from timely central line removal and pursuit of echocardiography to determine duration of therapy.

For candidemia, a recent, large, retrospective cohort study of 1691 candidemia cases (the largest to date) demonstrated a 19% survival benefit at 90 days with ID consultation [4]. Our study corroborates this finding: the absence of ID consultation was associated with a 3.8 increased hazard of death and 5.9 increased hazard of in-hospital death.

Pseudomonas bacteremia has an overall poor prognosis with a 30-day mortality rate ranging from 25% to 39% [5]. Previous studies failed to demonstrate the benefit of ID consult in multidrug-resistant *Pseudomonas* infection [6]. Our study demonstrated that *Pseudomonas* bacteremia had the highest 3-month mortality at 45% and the lowest proportion of ID consultations among the 3 subgroups in our hospital. Mortality of patients without ID consultation was 63% at 3 months.

The major limitation of this study is its retrospective nature, which could result in immeasurable confounding or bias.

For example, patients without ID consultation may be more likely to have serious comorbidities. In particular, those with *Pseudomonas* bacteremia without ID consultation were more likely to have a malignancy, resulting in variations in goals of care, which could potentially affect overall mortality regardless of ID consult. The patient population is too small for propensity score matching between 2 groups; however, we attempted to adjust for such confounding by controlling for age, ICU stay, solid organ transplant, and Charlson comorbidity index, and we removed those who died on the same day of blood culture draw, to reduce this bias.

CONCLUSIONS

Our study demonstrates that ID consultation is associated with significantly lower 3-month mortality and lower inpatient mortality in persons with bloodstream infections. The benefit of ID consultation was found for MRSA, candidemia, and extended to *Pseudomonas* bacteremia. Mandatory ID consultation may have the potential to improve patient survival; prospective evaluation of such an intervention is warranted.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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