

infection including epidural abscess development, septic arthritis, and musculoskeletal abscesses. This case highlights the wide range of infectious possibilities associated with severe GBS infection.

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**261. A Single-Center Case Series of Methicillin-Resistant *S. aureus* Bacteremia with Elevated Minimal Inhibitory Concentrations to Vancomycin**

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**Session:** P-9. Bacteremia

**Background:** Methicillin-resistant *Staphylococcus aureus* (MRSA) is a serious nosocomial pathogen, and is listed as a “High Priority Pathogen” by the WHO due to concerns of antimicrobial resistance and lack of novel therapeutics. Even in vancomycin-susceptible MRSA, increased rates of treatment failure occur in the setting of an increased minimum inhibitory concentration (MIC) to vancomycin, which is considered the gold-standard of therapy. We performed a case series of 25 patients infected with MRSA with an elevated MIC to vancomycin. Additionally, we describe the use of combination therapy with beta-lactams for the management of these highly complex cases.

**Methods:** We conducted a retrospective case series of 25 patients hospitalized at MSH between 8/2014–5/2019 who were treated for MRSA bacteremia where the isolate had an MIC ≥ 2. Data was centralized into the REDCap program. Clonal typing of bacteria and analysis of clinical features were performed in SAS and R.

**Results:** In total, 25 patients developed MRSA bacteremia with a vancomycin MIC ≥ 2. The majority of cases involved infection from vascular access, arteriovenous fistula/graft, and septic joint/osteomyelitis. All 25 patients were initially treated with vancomycin, with modification of therapy varying widely depending on clinician. The most common vancomycin-alternative was daptomycin (14/25 patients, alone and in combination). Combination therapy with vancomycin or daptomycin and a beta-lactam was used in 9 cases (36% of cases). Average number of days to clearance was 18.3 (range 1–69 days). Univariate and multivariate analyses revealed significant correlation MRSA bacteremia with vancomycin MIC ≥ 2 and admission from a nursing home or skilled nursing facility (p=0.02), history of MRSA colonization (p=0.006), and persistent bacteremia (bacteremia >7 days) (p<.0001).

**Conclusion:** With few novel therapeutics under development, management of MRSA bacteremia with a rising MIC to vancomycin is a clinical challenge for practitioners. In our case series we found that treatment is largely patient and practitioner-dependent, and far from standardized. Further definition of the clinical risk factors for development and novel therapeutic strategies will enable understanding of how to best manage these challenging infections.

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**262. A Systematic Review and Meta-Analysis of the Impact of Delayed Appropriate Antibiotic Therapy on Mortality in Patients with Gram-Positive Bacteremia**

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**Session:** P-9. Bacteremia

**Background:** Antibiotic resistance is common and frequently leads to unintentional delays in appropriate antibiotic therapy. The detrimental impact of delayed therapy is well-accepted, but the majority of evidence focuses on gram-negative infections. A review and synthesis of the evidence evaluating the impact of delayed appropriate antibiotic therapy in serious gram-positive infections does not exist. Such data would define the scope of the problem in this important patient population where antibiotic resistance is common. The objective of this systematic review and meta-analysis was to assess the impact of delayed appropriate antibiotic therapy on mortality in patients with gram-positive bacteremia.

**Methods:** Pubmed and Embase were searched from inception to March 30, 2020 to identify clinical studies of patients with bacteremia due to staphylococci, enterococci, or streptococci that reported the association between delayed appropriate antibiotic therapy and mortality. Three independent reviewers screened search results. Study quality was assessed via Newcastle-Ottawa Assessment Scale. Meta-analyses evaluating association between delayed therapy and mortality were conducted via random effects models in Review Manager 5.3. The primary analysis included unadjusted effect estimates from studies reporting unadjusted data. Secondary analysis included adjusted effect estimates from studies adjusting for confounding.

**Results:** Of 3684 search results, 16 cohort studies encompassing 4173 bacteremias were included. Ten studies involved *S. aureus*, 5 enterococci, and 2 *S. pneumoniae*. One-third (33.7%) of the 3659 patients in the primary analysis received delayed appropriate antibiotic therapy. The primary meta-analysis of 15 studies reporting unadjusted data showed a statistically significant association between delayed therapy and mortality (figure 1). Results from secondary analysis using adjusted point estimates from 9 studies were similar (figure 2).

Figure 1. Forrest plot of meta-analysis of unadjusted association between delayed therapy and mortality

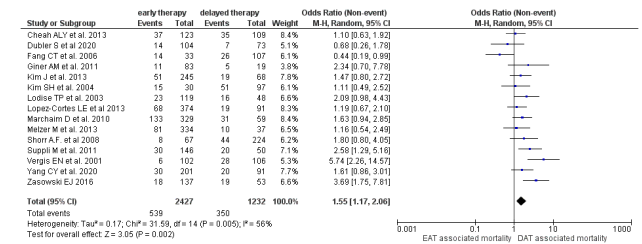
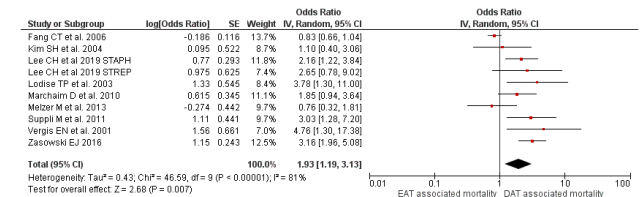


Figure 2. Forrest plot of meta-analysis of covariate adjusted association between delayed therapy and mortality



**Conclusion:** Delayed appropriate therapy was common and associated with increased mortality in patients with gram-positive bacteremia. These findings underscore the need for continued antimicrobial stewardship efforts to ensure expeditious appropriate antibiotic therapy for patients with gram-positive bacteremia.

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**263. An Evaluation of Quality Indicators for the Management of *Staphylococcus aureus* Bacteremia: A Nested Case-Control Study**

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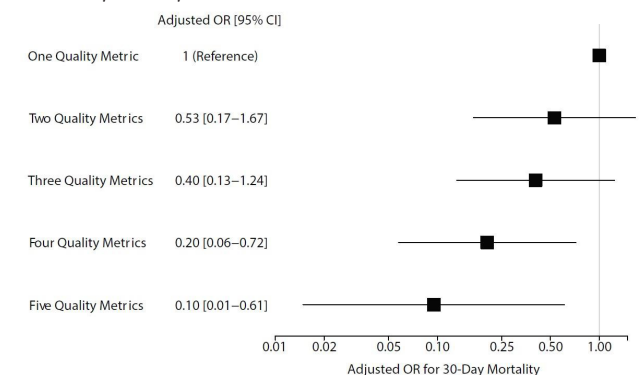
**Session:** P-9. Bacteremia

**Background:** Community-acquired *Staphylococcus aureus* bacteremia (CA SAB) is a common infection with high mortality. Ten Oever *et al.* recently used expert consensus methods to develop a set of 25 quality indicators for SAB care in five domains (i.e., follow up blood cultures, echocardiography, non-antibiotic interventions including source control, antibiotic treatment, and other management aspects). Associations between these quality indicators and patient outcomes have not been evaluated. We assessed associations between proposed quality indicators and all-cause 30-day mortality among patients with CA SAB.

**Methods:** We conducted a nested case-control study within a described national multicenter cohort of patients with SAB in the Veterans Health Administration (VHA). The cohort included 2,093 patients who were: 1) admitted to acute care hospitals between 1/2012 and 12/2014 for CA SAB (the first positive blood culture before or within 48 hours of admission with no recent healthcare exposure); 2) survived at least 96 hours after the SAB onset. We identified paired cases (who died within 30 days) and controls (who survived an equal time), matched 1:1 for age (+/- 5 years), gender, admission year and month, and methicillin susceptibility of isolates. We reviewed charts to extract information for quality indicators. We estimated associations between quality indicators and mortality using logistic regression, adjusting for patient demographics and comorbidity.

**Results:** 164 patients (82 cases and 82 controls) were included. The median patient age was 68.5 (IQR: 62–80) years, and 74 (45.1%) had methicillin-resistant isolates. All patients received at least one domain of quality indicator (median: 3 [IQR: 2–4]). When analyzed individually, only two domains (follow-up blood cultures: OR 0.27 [95% CI: 0.11–0.68]; source control: OR: 0.13 [0.05–0.31]) were associated with mortality. There was a dose-response relationship in which more domains received was associated with decreased mortality (Figure).

Association Between the Number of Satisfied Quality Indicator Domains and All-Cause 30-day Mortality



**Conclusion:** Among patients with CA-SAB, the number of satisfied quality indicator domains was associated with 30-day mortality with a dose-response relationship. This finding supports the relevance of these quality indicators for SAB management.

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**264. Anti-platelet Therapy Significantly Reduces Inpatient Mortality in Patients with *Staphylococcus aureus* Bacteremia**

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**Session:** P-9. Bacteremia

**Background:** There is a growing body of evidence which suggests that P2Y12 inhibitors may have antibacterial properties in vivo. To our knowledge, this has not been previously examined using real world clinical data from patients with specific infections.

**Methods:** Our retrospective cohort study included patients admitted to Veterans Affairs hospitals between 2010–2018 with blood cultures positive for *S. aureus* and treated with appropriate antibiotics within 48 hours of culture collection. We included patients treated with P2Y12 inhibitors for at least the 30 days prior to admission and continued use for at least 5 days after admission. Non-users included patients without P2Y12 inhibitor use in the year prior to admission through discharge. We compared clinical outcomes during the *S. aureus* bacteremia admission among P2Y12 users and non-users using propensity score matched Cox proportional hazards regression models.

**Results:** We identified 371 P2Y12 inhibitor users (clopidogrel, prasugrel, ticagrelor, cangrelor) and 13,298 non-users. Mean age was 70 years and 69 years, respectively. Over 98% were male in both the groups, and the overall inpatient mortality rate was 8.7%. We were able to match 199 users and non-users, which were well matched in terms of baseline covariates. Inpatient mortality was significantly lower among P2Y12 inhibitor users (hazard ratio [HR] 0.08, 95% confidence interval [CI] 0.01–0.64), and 30-day mortality was non-significantly lower (HR 0.57, 95% CI 0.31–1.03). There was no difference between the groups in readmission or re-infection within 30 days of discharge.

**Conclusion:** Among patients with *S. aureus* bacteremia, those treated with P2Y12 inhibitors in the days leading up to admission and continuing through the initial period of antibiotic treatment, had a 92% lower risk of inpatient mortality. Identifying adjunctive therapies which improve clinical outcomes among patients with *S. aureus* bacteremia is highly important in order to improve patient outcomes and to increase the understanding of the pathophysiology of the disease. Prospective clinical studies are needed to further define the potential benefits of P2Y12 inhibitors in *S. aureus* bacteremia and possibly other infection types.

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**265. Blood culture results pre- and post- antimicrobial administration in the Medicine Intensive Care Unit: a retrospective study in South Bronx**

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**Session:** P-9. Bacteremia

**Background:** It is intuitive that obtaining blood cultures prior to administering antibiotics can increase the likelihood of a positive blood culture result. Surviving Sepsis Campaign Hour-1 bundle stipulates that obtaining a blood culture and administering antibiotics within 1 hour is a critical determinant of survival. However, the

diagnostic sensitivity shortly after antibiotic administration remains unknown. In clinical practice, some health care providers delay antibiotic administration in order to first obtain a blood culture.

**Methods:** Adult patients (> 18 years of age) admitted to the Medicine Intensive Care Unit in Lincoln Medical Center, located in South Bronx, New York City, from 09/2019 to 12/2019. Patients needed to have at least one blood culture obtained within 12 hours of admission and have received intravenous antibiotics during the admission to the Medicine Intensive Care Unit.

**Results:** Of 327 patients screened, 196 met enrolment criteria and 253 sets of blood cultures underwent analysis. Blood cultures grew bacteria in 21.8% of pre-antimicrobial group whereas 26.9% in post-antimicrobial group (p=0.37). 25.9% of patients received antibiotics within 1 hour before blood culture sampling, while 34.0% of patients received antibiotics >1 hour prior to obtaining blood culture. Blood culture results positive for coagulase-negative staphylococci were more prevalent in the pre-antimicrobial group.

Table 1. Patient Characteristics

|   | Blood culture before antibiotic (N = 118) | Blood culture after antibiotic (N = 78) | p value  |
|---|---|---|----------|
| Age (mean +/- SD)                         | 54.7 +/- 17.3                             | 59.2 +/- 15.3                           | p= 0.09  |
| Male, n (%)                               | 64 (54.2%)                                | 43 (55.1%)                              | p= 1.00  |
| <b>Comorbidities, n (%)</b>               |   |   |          |
| Hypertension                              | 69 (58.4%)                                | 45 (57.7%)                              | p= 1.00  |
| Diabetes mellitus                         | 45 (38.1%)                                | 28 (35.9%)                              | p= 0.77  |
| Chronic lung disease (asthma, COPD, ILD)  | 38 (32.2%)                                | 31 (39.7%)                              | p= 0.29  |
| End stage renal disease                   | 11 (9.3%)                                 | 4 (5.1%)                                | p = 0.41 |
| Stroke / TIA                              | 15 (12.7%)                                | 3 (3.8%)                                | p = 0.05 |
| Coronary artery disease                   | 22 (18.6%)                                | 8 (10.3%)                               | p = 0.16 |
| Heart failure                             | 20 (16.9%)                                | 17 (21.7%)                              | p = 0.46 |
| Intravenous drug user                     | 30 (25.4%)                                | 19 (24.4%)                              | p = 1.00 |
| HIV                                       | 11 (9.3%)                                 | 11 (14.1%)                              | p = 0.36 |
| Malignancy                                | 11 (9.3%)                                 | 13 (16.7%)                              | p = 0.18 |
| <b>Severity of disease, n(%)</b>          |   |   |          |
| qSOFA >= 2                                | 54 (45.8%)                                | 46 (59.0%)                              | p = 0.08 |
| T >38°C or <36°C                          | 38 (32.2%)                                | 29 (37.2%)                              | p = 0.54 |
| HR >90                                    | 66 (55.9%)                                | 50 (64.1%)                              | p = 0.30 |
| RR >20                                    | 64 (54.2%)                                | 47 (60.3%)                              | p = 0.46 |
| WBC >12000 or <4000                       | 69 (58.5%)                                | 50 (64.1%)                              | p = 0.46 |
| <b>Presume source of infection, n (%)</b> |   |   |          |
| Central nerve system                      | 2 (1.7%)                                  | 3 (3.8%)                                | p = 0.39 |
| Respiratory tract system                  | 56 (47.5%)                                | 33 (42.3%)                              | p = 0.56 |
| Endocarditis                              | 1 (0.8%)                                  | 1 (1.3%)                                | p = 1.00 |
| Gastrointestinal system                   | 7 (0.6%)                                  | 9 (11.5%)                               | p = 0.19 |
| Hepatobiliary system                      | 2 (1.7%)                                  | 2 (2.6%)                                | p = 0.65 |
| Urogenital system                         | 9 (7.6%)                                  | 7 (9.0%)                                | p = 0.79 |
| Skin and soft tissue                      | 3 (2.5%)                                  | 2 (2.6%)                                | p = 1.00 |
| Unknown                                   | 38 (32.2%)                                | 21 (26.9%)                              | p = 0.52 |

Table 2. Number of blood cultures obtained and blood culture result

|   | Blood culture before antibiotic | Blood culture after antibiotic | p value  |
|---|---------------------------------|--------------------------------|----------|
| <b>Total number of blood culture obtained</b>       | 149                             | 104                            |          |
| Positive blood culture result                       | 32 (32/149, 21.8%)              | 28 (28/104, 26.9%)             | p = 0.37 |
| <b>Number of blood culture obtained per patient</b> |                                 |                                |          |
| <b>1 set</b>  | 89 patients                     | 53 patients                    |          |
| Positive culture                                    | 17 (17/89, 19.1%)               | 10 (10/53, 18.9%)              | p = 1.00 |
| <b>2 sets</b>                                       | 27 patients                     | 24 patients                    |          |
| Positive within 1 set                               | 3 (3/27, 11.1%)                 | 2 (2/24, 8.3%)                 | p = 1.00 |
| Positive within 2 set                               | 6 (6/27, 22.2%)                 | 8 (8/24, 33.3%)                | p = 0.53 |
| <b>3 sets</b>                                       | 2 patients                      | 1 patient                      |          |
| 3 sets negative                                     | 2                               | 1                              |          |