Early Use of Daptomycin Versus Vancomycin for Methicillin-Resistant *Staphylococcus aureus* Bacteremia With Vancomycin Minimum Inhibitory Concentration >1 mg/L: A Matched Cohort Study

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(See the Editorial Commentary by Weston and Boucher on pages 1570–2.)

**Background.** Recent reports have described decreased effectiveness with vancomycin treatment for methicillin-resistant *Staphylococcus aureus* bacteremia (MRSAB) when the vancomycin minimum inhibitory concentration (MIC) is >1 µg/mL.

**Methods.** This matched, retrospective cohort study compared the clinical effectiveness of daptomycin with that of vancomycin for the treatment of MRSAB with vancomycin MICs >1 µg/mL. The primary outcome was clinical failure, defined as a composite of 30-day mortality or bacteremia persisting for ≥7 days.

**Results.** One hundred seventy patients were matched 1:1 with respect to the antimicrobial administered. In the daptomycin group, all patients received <72 hours of vancomycin (median, 1.7 days [interquartile range, 1.1–2.3 days]) prior to switching to daptomycin. The rate of clinical failure at 30 days was significantly lower in the daptomycin arm compared to the vancomycin arm (20.0% vs 48.2%; *P* < 0.001). Both 30-day mortality and persistent bacteremia were significantly lower in the daptomycin group compared to the vancomycin group (3.5% vs 12.9% [*P* = .047] and 18.8% vs 42.4% [*P* = .001], respectively). Logistic regression confirmed the association between vancomycin treatment and increased risk of clinical failure (adjusted odds ratio, 4.5; 95% confidence interval, 2.1–9.8).

**Conclusions.** This is the first matched study comparing early daptomycin versus vancomycin for the treatment of MRSAB when the vancomycin MIC is >1 µg/mL. Treatment with daptomycin resulted in significantly improved outcomes, including decreased 30-day mortality and persistent bacteremia. These results support the practice of switching early from vancomycin to daptomycin for the treatment of MRSAB when the vancomycin MIC is >1 µg/mL.

**Keywords.** vancomycin; daptomycin; methicillin-resistant *Staphylococcus aureus*; bacteremia.

The increasing prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) has led to widespread, increased use of vancomycin [1]. Subsequently, numerous reports of elevated minimum inhibitory concentrations (MIC) to vancomycin among MRSA isolates have surfaced, concomitant with increased global vancomycin exposure to MRSA [2–4]. Isolates with vancomycin MICs >1 µg/mL have been associated with higher rates of vancomycin treatment failure [4–10].
The question still remains as to whether poorer outcomes when the MIC is >1 µg/mL are due to ineffective treatment or to other microbiological characteristics of the organism. Holmes et al [11] evaluated outcomes of a cohort of patients with *S. aureus* bacteremia and found that vancomycin MIC >1.5 µg/mL was an independent predictor of increased mortality at 30 days even if the isolate was methicillin susceptible. A recent meta-analysis of the literature reported a 2.69-fold (95% confidence interval, 1.21–4.02) increase in treatment failure when the vancomycin MIC is ≥1.5 µg/mL [8]. Current guidelines for MRSA bacteremia (MRSAB) recommend that the decision to switch therapy should not be based solely on MIC; however, alternatives may be considered if the patient’s condition is worsening or the vancomycin MIC is 2 µg/mL and the patient is critically ill [12].

Regardless of the causative factors for poorer outcomes among infections caused by MRSAB with high vancomycin MICs, data to support alternative treatment are of critical importance. The purpose of this study was to compare clinical outcomes associated with vancomycin and daptomycin in the setting of MRSAB when the vancomycin MIC is >1 µg/mL.

**METHODS**

**Study Design and Patient Population**

This was a retrospective, matched cohort study comparing outcomes of patients treated with vancomycin or daptomycin at 4 hospitals within the Detroit Medical Center (Detroit, Michigan) between January 2005 and March 2012. In February 2008, the Detroit Medical Center implemented a treatment guideline in which patients would receive daptomycin for MRSAB if the vancomycin MIC was documented as >1 µg/mL [8]. Current guidelines for MRSA bacteremia (MRSAB) recommend that the decision to switch therapy should not be based solely on MIC; however, alternatives may be considered if the patient’s condition is worsening or the vancomycin MIC is 2 µg/mL and the patient is critically ill [12].

Regardless of the causative factors for poorer outcomes among infections caused by MRSAB with high vancomycin MICs, data to support alternative treatment are of critical importance. The purpose of this study was to compare clinical outcomes associated with vancomycin and daptomycin in the setting of MRSAB when the vancomycin MIC is >1 µg/mL.

All adult patients with susceptible MRSA bloodstream isolates with an initial vancomycin MIC >1 µg/mL who received vancomycin or daptomycin for ≥72 hours were eligible for inclusion. Patients were excluded if the primary source of bacteremia was an intravenous catheter or pneumonia, or if the patient required renal replacement therapy due to acute renal failure or end-stage renal disease. Patients were also excluded if they had received ≥72 hours of alternative MRSA therapy prior to initiation of vancomycin or daptomycin, including patients who were switched from vancomycin to daptomycin.

Data collected from the medical record included demographic information, comorbidities, antimicrobial therapy, and clinical and microbiological laboratory data.

**Matching Criteria**

Patients who received daptomycin were matched in a 1:1 ratio with those who received vancomycin in a blinded fashion. Patients were matched according to age (±5 years), Pitt bacteremia score (<4 or ≥4), and primary source of bacteremia. The Pitt bacteremia score has previously been validated as a scale to help predict mortality in patients with *S. aureus* bacteremia [13]. For the purposes of matching, patients were put into the following categories based on the primary source of bacteremia: endocarditis, bone or joint, complicated skin and soft tissue, or unknown source. The primary source of bacteremia was determined by the treating physician, along with clinical and microbiological data obtained from the medical record.

**Microbiological Data**

Antimicrobial susceptibility was determined by Detroit Medical Center University Laboratories. Susceptibilities to vancomycin and daptomycin were determined via Etest (bioMérieux) from January 2005 and January 2008, and via MicroScan (Siemens) from February 2008 through March 2012.

**Antimicrobial Dosing**

Daptomycin-treated patients received at least 6 mg/kg daily with higher doses based on the discretion of the treating physician. Vancomycin-treated patients received doses targeting serum trough levels between 15 and 20 µg/mL according to hospital protocol. To achieve these targets, vancomycin dosing was based on population pharmacokinetic data and equations [14]. Initial vancomycin serum trough levels were measured prior to the third or fourth dose of vancomycin. Subsequent vancomycin serum trough levels were measured every 4 to 7 days or as clinically indicated. Estimated area under the vancomycin concentration-time curve to MIC (area under the curve [AUC]$_{24}$/MIC) ratios were calculated as previously described [7].

**Definitions**

Duration of bacteremia was calculated as the number of days from the start of MRSA treatment until the day the first negative blood culture was drawn. For patients treated with daptomycin, the initial period of vancomycin treatment prior to daptomycin was included in the duration of bacteremia. For patients receiving empiric MRSA treatment prior to the initial positive blood culture, the duration of bacteremia was calculated from the day the initial positive culture was drawn to the day the first negative culture was drawn. Persistent bacteremia was defined as MRSA bacteremia ≥7 days. Nephrotoxicity was defined as an increase in serum creatinine of either ≥50% or ≥0.5 g/dL (whichever was greater) from baseline on at least 2 consecutive occasions [15]. Creatinine phosphokinase (CPK) levels were documented when available, and increases >5 times the upper limit of normal were considered significant [16].
Outcomes
The primary outcome, clinical failure, was a composite of all-cause mortality within 30 days of the initial positive blood culture or persistent bacteremia. Mortality was verified via public records review using the United States Social Security Death Index.

Secondary clinical outcomes included a survival analysis up to 90 days following the initial positive blood culture, inpatient mortality, hospital readmission within 30 days following discharge, and recurrence of MRSAB within 30 days of discharge or the last day of therapy, whichever occurred first. Secondary microbiological outcomes included duration of bacteremia and the emergence of decreased MRSA susceptibility to vancomycin or daptomycin during inpatient treatment.

Costs of care from the institution’s perspective were compared between the 2 groups, and included the total of all charges accrued during hospitalization, total medication charges, total laboratory charges, and charges for surgical and intensive care services. Data for this analysis were obtained from the Detroit Medical Center Corporate Finance Department.

Statistical Analysis
Using assumptions based on data from our own institution, a power analysis indicated that 44 patients per group were required to detect a 31.5% difference in the proportion of clinical failure between groups with 80% power and a 2-sided 5% level of significance [17]. The $\chi^2$ test and Fisher exact test were used to compare categorical variables, while the Student $t$ test or Mann-Whitney $U$ test was used to compare continuous variables. Independent predictors of clinical failure were determined via backward stepwise logistic regression. The 90-day survival analysis was performed using a Cox proportional hazards model. Variables associated with failure in univariate analysis ($P < .2$) and disparate variables between treatment groups ($P < .2$) were considered for inclusion in both the logistic regression and Cox proportional hazards models. For all analyses, $P$ values <.05 were considered statistically significant. All calculations were performed using PASW, version 20.0 (SPSS).

RESULTS
During the study period, 1863 consecutive cases of MRSAB with a vancomycin MIC $\geq$1 µg/mL were identified and screened for inclusion. A total of 85 daptomycin-treated patients were matched to 85 vancomycin-treated patients. Among the 1652 patients not meeting inclusion criteria, the primary reasons included renal failure, initial vancomycin therapy $\geq$72 hours in the daptomycin group, and cases in which an intravenous catheter was identified as the primary source of bacteremia. Baseline patient characteristics were similar between groups (Table 1). Median Pitt bacteremia score and Charlson comorbidity index did not differ significantly, nor did the proportion of patients requiring admission to the intensive care unit (ICU; Table 1). All patients received surveillance blood cultures during hospitalization. Among patients requiring admission to the ICU, the median ICU length of stay was 7 days (interquartile range [IQR], 2–12 days) in the daptomycin group compared to 5 days (IQR, 2–14 days) in the vancomycin group ($P = .824$). Vancomycin or daptomycin was initiated the day the initial positive blood culture was drawn in 84.1% of cases, and within 2 days for all patients.

The most common primary sources of MRSAB were complicated skin and soft tissue infection, bone or joint infection, and infective endocarditis (Figure 1). Vancomycin susceptibility for the majority of isolates was determined via MicroScan versus Etest (85.3% vs 14.7%). Overall, 160 (94.1%) isolates had vancomycin MICs of 2 µg/mL, while 10 (5.9%) had MICs of 1.5 µg/mL. Seventy-nine (92.9%) patients in the daptomycin group were switched from vancomycin once a vancomycin MIC of $>$1 µg/mL was identified; the remaining 6 patients had MRSA therapy initiated with daptomycin. The median duration of initial vancomycin therapy prior to daptomycin was 1.7 days (IQR, 1.1–2.3 days). In the vancomycin group, the median serum trough concentrations were 17.6 µg/mL (IQR, 14.9–21.2 µg/mL) and the corresponding AUC$_{24}$/MIC was 211.7 (IQR, 155.1–279.9), whereas 10 (12.2%) patients treated with vancomycin had AUC$_{24}$/MIC ratios $>$421 [7]. The median daptomycin daily dose was 8.4 mg/kg (IQR, 6.3–9.9 mg/kg). Concomitant aminoglycoside and rifampin use did not differ significantly between the groups (Table 1). The infectious diseases service was consulted for the majority of cases in each treatment group (Table 1).

Table 2 compares clinical and microbiological outcomes between the daptomycin and vancomycin treatment groups. In the crude analysis, treatment with daptomycin was associated with significantly less clinical failure at 30 days compared to vancomycin (20.0% vs 48.2%; $P < .001$). Both components of clinical failure, mortality at 30 days and persistent bacteremia, were significantly lower in patients receiving daptomycin therapy (Table 2). Among patients who died during admission, 5 of 9 (55.6%) in the vancomycin group remained bacteremic at the time of death compared to 0 of 3 patients in the daptomycin group. These findings were confirmed by multivariate logistic regression analysis, in which vancomycin was associated with a significantly higher risk of clinical failure at 30 days (adjusted odds ratio, 4.5 [95% confidence interval, 2.1–9.8]; Table 3).

The Cox proportional hazards model of survival to 90 days favored treatment with daptomycin (Figure 2). Additionally, patients in the daptomycin treatment group were more likely...
to survive until hospital discharge compared to the vancomycin treatment group (3.5% vs 11.9%; \(P = .047\)). Patients who were switched to daptomycin experienced a shorter duration of bacteremia compared to those treated only with vancomycin (Table 2). However, both duration of therapy and length of stay were similar between the 2 groups (Table 2). Overall charges accrued during hospitalization were similar between the daptomycin and vancomycin treatment groups, with significantly higher medication charges in the daptomycin group (Table 2). Charges related to laboratory (Table 2), intensive care, and surgical services (data not shown) were not significantly different between the 2 groups.

In the daptomycin group, 2 patients (2.6%) experienced elevations in daptomycin MIC to 2 or 4 µg/mL following initiation of daptomycin. In both cases, the vancomycin MIC also increased to 4 µg/mL. Daptomycin monotherapy was continued in one case, while the second patient received gentamicin and rifampin in combination with daptomycin. Both patients survived until discharge with documented clearance of infection, though they did experience persistent bacteremia. There were no cases in which the vancomycin MIC increased without a concomitant increase in daptomycin MIC.

In the vancomycin group, 22 patients (25.9%) experienced nephrotoxicity. Among those with nephrotoxicity, the median vancomycin trough was 18.1 µg/mL (IQR, 16.7–21.1 µg/mL). The median age and primary source of bacteremia was not different between those patients who experienced nephrotoxicity versus those who did not. The proportion of vancomycin-treated patients who experienced nephrotoxicity was higher among those who received concomitant aminoglycoside therapy (50.0% vs 15.9%, \(P = .001\)). One patient in the daptomycin treatment group experienced a significant elevation in

### Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>DAP (n = 85)</th>
<th>VAN (n = 85)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>57 (51–65)</td>
<td>56 (51–64)</td>
<td>.645</td>
</tr>
<tr>
<td>Male</td>
<td>61 (71.8%)</td>
<td>55 (64.7%)</td>
<td>.323</td>
</tr>
<tr>
<td>Pitt bacteremia score</td>
<td>2 (1–3)</td>
<td>2 (1–2)</td>
<td>.362</td>
</tr>
<tr>
<td>ICU admission</td>
<td>27 (31.8%)</td>
<td>27 (31.8%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Hospitalization previous 90 d</td>
<td>34 (40.0%)</td>
<td>44 (51.8%)</td>
<td>.124</td>
</tr>
<tr>
<td>Surgery previous 30 d</td>
<td>14 (16.5%)</td>
<td>18 (21.2%)</td>
<td>.433</td>
</tr>
<tr>
<td>Prosthetic device</td>
<td>25 (29.4%)</td>
<td>18 (21.7%)</td>
<td>.251</td>
</tr>
<tr>
<td>Duration of hospitalization prior to start of antimicrobial treatment, d</td>
<td>1 (0–2)</td>
<td>1 (0–2)</td>
<td>.950</td>
</tr>
<tr>
<td>Charlson comorbidity index</td>
<td>5 (3–7)</td>
<td>4 (3–6)</td>
<td>.306</td>
</tr>
<tr>
<td>Stroke or TIA</td>
<td>7 (8.2%)</td>
<td>11 (12.9%)</td>
<td>.319</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>9 (10.6%)</td>
<td>6 (7.1%)</td>
<td>.417</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>33 (38.8%)</td>
<td>27 (31.8%)</td>
<td>.336</td>
</tr>
<tr>
<td>Active cancer</td>
<td>4 (4.7%)</td>
<td>6 (7.1%)</td>
<td>.746</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>8 (9.4%)</td>
<td>3 (3.5%)</td>
<td>.211</td>
</tr>
<tr>
<td>Pressure ulcer</td>
<td>13 (15.3%)</td>
<td>8 (9.4%)</td>
<td>.244</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>21 (24.7%)</td>
<td>19 (22.4%)</td>
<td>.867</td>
</tr>
<tr>
<td>Creatinine clearance, mL/min</td>
<td>72.6 (51.7–94.8)</td>
<td>79.3 (59.4–102.7)</td>
<td>.182</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>17 (20.0%)</td>
<td>18 (21.2%)</td>
<td>.850</td>
</tr>
<tr>
<td>IVDA</td>
<td>28 (32.9%)</td>
<td>33 (38.8%)</td>
<td>.424</td>
</tr>
<tr>
<td>Antimicrobial use last 90 d</td>
<td>28 (32.9%)</td>
<td>36 (42.4%)</td>
<td>.205</td>
</tr>
<tr>
<td>Vancomycin use last 90 d</td>
<td>17 (20.0%)</td>
<td>24 (28.2%)</td>
<td>.209</td>
</tr>
<tr>
<td>Daptomycin use last 90 d</td>
<td>3 (3.5%)</td>
<td>1 (1.2%)</td>
<td>.621</td>
</tr>
<tr>
<td>MRSA previous year</td>
<td>9 (10.6%)</td>
<td>9 (10.6%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Concomitant MRSA therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aminoglycoside</td>
<td>12 (14.1%)</td>
<td>22 (25.9%)</td>
<td>.055</td>
</tr>
<tr>
<td>Rifampin</td>
<td>14 (16.5%)</td>
<td>18 (21.2%)</td>
<td>.433</td>
</tr>
<tr>
<td>Surgical intervention</td>
<td>39 (45.9%)</td>
<td>35 (41.2%)</td>
<td>.536</td>
</tr>
<tr>
<td>Infectious diseases consultation</td>
<td>85 (100.0%)</td>
<td>81 (95.3%)</td>
<td>.121</td>
</tr>
</tbody>
</table>

Data are presented as No. (%) or median (interquartile range).

Abbreviations: DAP, daptomycin; HIV, human immunodeficiency virus; ICU, intensive care unit; IVDA, intravenous drug abuse; MRSA, methicillin-resistant *Staphylococcus aureus*; MRSAB, methicillin-resistant *Staphylococcus aureus* bacteremia; TIA, transient ischemic attack; VAN, vancomycin.
serum CPK concentration, in which the level increased from 67 units/L to 721 units/L after 17 days of daptomycin 12 mg/kg daily. However, this elevation was not associated with any subjective complaints, including musculoskeletal symptoms. In this patient, discontinuation of daptomycin resulted in a prompt decrease in CPK; vancomycin was administered for the remainder of a 28-day treatment course without further complications. Otherwise, 26 daptomycin-treated patients (30.6%) experienced nonsignificant increases in serum CPK concentrations (median, 92 units/L [IQR, 20–207 units/L]) after a median of 11 days (IQR, 11–17 days) of daptomycin, which did not warrant discontinuation or dose adjustment of daptomycin.

**DISCUSSION**

Recent guidelines recommend that the decision to switch from vancomycin to alternative antimicrobials be guided by individual patient response rather than MIC alone, but data to support such practice are currently lacking. The increased risk of vancomycin failure in this setting is particularly worrisome, considering the paucity of data supporting alternative treatment strategies. This study compares early daptomycin versus dose-adjusted vancomycin the treatment of MRSAB when the vancomycin MIC is >1 μg/mL. Moore et al recently reported that patients with MRSAB exhibiting high vancomycin MICs were more likely to experience a favorable outcome if treated with daptomycin after initial vancomycin failure [18]. In their study, patients were switched to daptomycin after a median of 5 days, and up to 14 days of vancomycin therapy at the discretion of the treating physician. However, switching therapy only after being deemed a failure on vancomycin could potentially favor the daptomycin treatment group. Furthermore, duration of bacteremia was defined from the start of daptomycin in the daptomycin treatment group or from the start of vancomycin in the vancomycin treatment group, a definition that inherently favors daptomycin. In the current report, we defined duration of bacteremia from the start of MRSA therapy (ie, including the initial period of vancomycin therapy in the daptomycin group), which is likely more representative of daptomycin’s treatment effect and more closely reflects current clinical practice. Additionally, we only included patients who were switched early from vancomycin to daptomycin (ie, within 72 hours), thus limiting potential selection biases.

Nearly 50% of vancomycin-treated patients in our cohort met the criteria for clinical failure, which is slightly higher compared with previous reports in the range of 25%–40% [4, 6, 7, 18]. The high proportion of failures noted here could potentially be a reflection of the study design, in which patients were excluded if the primary source of bacteremia was deemed to be an intravenous catheter or other intravenous access device (eg, graft or fistula for hemodialysis). Patients with deep-seated infections, which comprised a majority of...
infections in this study, are more likely to experience a prolonged duration of bacteremia, which in turn has been associated with poor clinical outcomes including mortality [10, 19]. Indeed, the finding of intravenous drug use as an independent predictor of clinical failure may be reflective of this point; endocarditis was identified as the primary source of bacteremia in a significantly higher proportion of patients with a history of intravenous drug use compared to those without (36.1% vs 16.5%, respectively; \( P = .004 \)). Consultation to an infectious diseases physician is thought to improve patient outcomes in the setting of \( S. \) aureus bacteremia [20, 21]. The infectious diseases service was consulted in 97.6% of cases in the current study, although none of the 4 patients without an infectious diseases consultation experienced clinical failure.

Resistance to daptomycin has been reported to emerge during treatment, and may represent one drawback compared to vancomycin. Three patients experienced elevations in daptomycin MICs up to 4 \( \mu g/mL \) during therapy in the current cohort, which is similar to that reported previously [22]. Of note, all 3 patients survived until hospital discharge, though did experience persistent bacteremia, perhaps reflecting the impact of elevated daptomycin MIC on antistaphylococcal activity.

![Figure 2. Cox proportional hazards model of survival to 90 days.](https://academic.oup.com/cid/article-abstract/56/11/1562/303519/early-daptomycin-for-mrsa-bacteremia)
Several factors may have led to the significantly improved outcomes among patients treated with daptomycin compared to vancomycin. Experience with vancomycin over time has demonstrated that trough levels between 15 and 20 µg/mL are needed to effectively treat complicated MRSA when the vancomycin MIC is ≤1 µg/mL. If the vancomycin MIC is >1 µg/mL, patients are not likely to safely tolerate vancomycin doses that would be required to achieve the AUC24/MIC target (>421) that has been shown to optimize activity against MRSA [7, 26]. The high rate of clinical failure in the current study despite median serum vancomycin trough levels ≥15 µg/mL is potentially a reflection of the inability to reach the AUC24/MIC target when the vancomycin MIC exceeds 1 µg/mL. If the vancomycin MIC is >1 µg/mL, patients are not likely to safely tolerate vancomycin doses that would be required to achieve the AUC24/MIC target (>421) that has been shown to optimize activity against MRSA [7, 26]. The high rate of clinical failure in the current study despite median serum vancomycin trough levels ≥15 µg/mL is potentially a reflection of the inability to reach the AUC24/MIC target when the vancomycin MIC exceeds 1 µg/mL. If the vancomycin MIC is >1 µg/mL, patients are not likely to safely tolerate vancomycin doses that would be required to achieve the AUC24/MIC target (>421) that has been shown to optimize activity against MRSA [7, 26]. The high rate of clinical failure in the current study despite median serum vancomycin trough levels ≥15 µg/mL is potentially a reflection of the inability to reach the AUC24/MIC target when the vancomycin MIC exceeds 1 µg/mL. If the vancomycin MIC is >1 µg/mL, patients are not likely to safely tolerate vancomycin doses that would be required to achieve the AUC24/MIC target (>421) that has been shown to optimize activity against MRSA [7, 26].

In fact, 65.7% of vancomycin-treated patients failed to attain concentrations >15 µg/mL. Daptomycin’s rapid bactericidal and concentration-dependent activity may have contributed to the more favorable outcomes observed in this study [23]. Of note, the doses administered in this cohort were on average higher on a mg/kg basis compared with those used in initial clinical trials evaluating daptomycin 6 mg/kg daily [22]. Given that daptomycin’s bactericidal activity is dependent upon the AUC24/MIC ratio and peak concentration to MIC ratio, the use of higher doses could have positively impacted patient outcomes [23]. Daptomycin dosing regimens greater than the FDA-approved dose of 6 mg/kg daily have been associated with safe and potentially more favorable outcomes in previous observational studies of patients with bacteremia [18, 24, 25].

A comparison between vancomycin- and daptomycin-treated patients demonstrated that total charges accrued during hospitalization were similar, although charges related to medications were greater in the daptomycin group. But because the high variability in total hospital charges, as reflected by the range of charges (Table 2), this study may not have been adequately powered to detect a difference in overall cost of care. The data suggest that the majority of costs incurred during the treatment of MRSA bacteremia may not be due to drug therapy, but rather to length of stay.

The present study was retrospective and examined patients from one regional medical center, thus limiting external validity to an extent. Although all patients were followed up to assess mortality within 90 days, readmissions to outside institutions during the follow-up period could have been missed. A multicenter, prospective study involving patients from various regions both nationally and internationally may be able to better characterize the potential benefit of switching therapy from vancomycin to daptomycin once the vancomycin MIC is known to be >1 µg/mL. Although patients receiving ≥72 hours of vancomycin prior to switching to daptomycin were excluded, initial vancomycin exposure may have influenced the outcome of patients treated with daptomycin. The potential for selection bias was minimized in this study as patients with high vancomycin MICs were recommended to switch to daptomycin according to hospital guidelines. The potential that confounding variables impacted clinical failure was minimized by matching based on site of infection, age, and severity of illness. Furthermore, analysis of clinical failure using multivariate logistic regression confirmed that vancomycin treatment was an independent predictor of clinical failure. The majority of isolates were tested via the MicroScan automated susceptibility testing system, while a small proportion was determined via Etest. The use of 2 different susceptibility testing methodologies may have the potential to confound our results; however, a subgroup analysis of cases with MIC determined via MicroScan (n = 145) revealed outcomes similar to the entire population; clinical failure in the subgroup analysis occurred in 25.3% of patients in the daptomycin group compared to 41.9% in the vancomycin group (P = .034).

In conclusion, early use of daptomycin was associated with significantly less clinical failure compared to vancomycin in the setting of MRSA with high vancomycin MICs (ie, >1 µg/mL). Both 30-day mortality and persistent bacteremia were significantly decreased in the daptomycin treatment group. For the treatment of bacteremia caused by deep-seated MRSA infections with high vancomycin MICs, early daptomycin may offer improved clinical outcomes compared to dose-optimized vancomycin.

Note

Potential conflicts of interest. M. J. R. has consulted for Cubist, Astellas, Forest, and Cepheid; has received research grants from Cubist, Cerexa, Clinical Therapeutics, Forest, the National Institutes of Health, and the Michigan Department of Community Health; and has served on the speaker’s bureaus of Cubist, Forest, Novartis, Rib-X, and Theravance. K. S. K. has received research grants from Cubist, Pfizer, and Forest; has served as a consultant to Cubist, Pfizer, and Forest, and has served on speaker’s bureaus for Cubist, Pfizer, and Forest. R. K. has served on the speaker’s bureau for Cubist and Forest Pharmaceuticals, and is on the board of Optimer. S. L. D. has consulted for Forest and has received grants from Cerexa. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

3. Hawser SP, Bouchillon SK, Hoban DJ, Dowzicky M, Babinchak T. Rising incidence of Staphylococcus aureus with reduced susceptibility MICs recommended to switch to daptomycin according to hospital guidelines. The potential that confounding variables impacted clinical failure was minimized by matching based on site of infection, age, and severity of illness. Furthermore, analysis of clinical failure using multivariate logistic regression confirmed that vancomycin treatment was an independent predictor of clinical failure. The majority of isolates were tested via the MicroScan automated susceptibility testing system, while a small proportion was determined via Etest. The use of 2 different susceptibility testing methodologies may have the potential to confound our results; however, a subgroup analysis of cases with MIC determined via MicroScan (n = 145) revealed outcomes similar to the entire population; clinical failure in the subgroup analysis occurred in 25.3% of patients in the daptomycin group compared to 41.9% in the vancomycin group (P = .034).

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