Title:
Clinical impact of targeting a narrow vancomycin AUC range of 350–500 mg·h/L without adjustment for MIC in patients with methicillin-resistant Staphylococcus aureus infections

Background:
Vancomycin remains a first-line antibiotic for treating Methicillin-Resistant Staphylococcus aureus (MRSA) infections, with current ASHP guidelines recommending an AUC target of 400–600 mg·h/L. However, emerging data suggest that exposures above 500 mg·h/L may increase nephrotoxicity without added efficacy, and lower AUC values may still be effective. At Middlesex Health, vancomycin regimens are often designed to target a narrower AUC range of 350–500 mg·h/L. This study aims to evaluate whether targeting this range improves global outcomes and reduces toxicity compared to higher AUC exposures in patients treated for culture-confirmed MRSA infections.

Methods:
This is a retrospective cohort study of adult patients who received vancomycin for culture-confirmed MRSA infections at Middlesex Health from June 1, 2023, to June 1, 2025. Patients were stratified into two groups based on predicted steady-state AUCs: 350–500 mg·h/L and >500 mg·h/L. AUCs were retrospectively calculated using population pharmacokinetic modeling since our previous methodology did not require calculation of predicted AUC.
The primary endpoints are the rate of treatment failure– defined as a composite of 30-day mortality, 30-day infection-related readmission, and escalation of antibiotic therapy—and incidence of acute kidney injury (AKI). Secondary outcomes include length of stay, duration of antimicrobial treatment, and the individual components of the treatment failure composite outcome. Categorical outcomes were analyzed using Chi-squared or Fisher's exact test, while continuous data was analyzed using Student's t-test or Mann–Whitney U test as appropriate. This study received approval from the Middlesex Health Institutional Review Board.

Results:
A total of 492 patients were screened, of whom 347 met inclusion criteria. After excluding 187 patients, 160 were included in the final analysis: 48 in the AUC 501–600 group and 112 in the AUC 350–500 (N-AUC) group. Baseline characteristics were generally well balanced between groups. However, the N-AUC group had a higher proportion of persons who inject drugs (8.9% vs 2.1%) and MRSA isolates with a vancomycin MIC of 1 mg/L (48.2% vs 22.9%). The incidence of AKI was significantly lower in the N-AUC group (0.9% vs 12.5%; p = 0.003). The composite treatment failure outcome occurred less frequently in the N-AUC group (15.2% vs 27.1%), although this difference did not reach statistical significance (p = 0.077). Additionally, 90-day all-cause mortality was significantly lower in the N-AUC group (5.4% vs 18.8%; p = 0.015).

Conclusion:
Targeting a narrower vancomycin steady-state AUC of 350–500 mg·h/L in patients with culture-confirmed MRSA infections was associated with significantly lower rates of AKI and all-cause 90-day mortality, along with a numerically lower incidence of treatment failure. These findings support the safety and efficacy of this approach, though prospective studies are needed to confirm these results.