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Predicting high vancomycin minimum inhibitory concentration isolate infection among patients with community-onset methicillin-resistant *Staphylococcus aureus* bacteraemia

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Summary *Objectives:* Methicillin-resistant *Staphylococcus aureus* (MRSA) isolates with an elevated vancomycin MIC ≥2 mg/L have been increasingly identified in many countries. We aimed to develop a clinical score to predict vancomycin MIC ≥2 mg/L in patients with community-onset MRSA bacteraemia.
Methods: This retrospective cohort study enrolled 394 patients with MRSA bacteraemia. Vancomycin MICs of all MRSA isolates were determined by agar dilution method. Clinical

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characteristics between patients with high (≥2 mg/L) and low (≤1 mg/L) vancomycin MIC MRSA bacteraemia were compared. Independent predictors of high vancomycin MIC isolate infection were identified and used to create a score-based predictive model.
Results: Among the 394 study patients, 56 (14.2%) had MRSA isolates with a vancomycin MIC ≥2 mg/L. The final regression model included 6 independent predictors: chronic liver disease (adjusted odds ratio [aOR], 2.99; 95% confidence interval [CI], 1.39—6.42), prior recovery of MRSA from respiratory tract specimen (aOR, 2.54; 95% CI, 1.15—5.61), end-stage renal disease (aOR, 2.53; 95% CI, 1.33—4.78), severe sepsis or septic shock on presentation (aOR, 2.39; 95% CI, 1.28—4.44), prior vancomycin exposure (aOR, 2.21; 95% CI, 1.13—4.30), and recent hospitalization within 3 months (aOR, 2.11; 95% CI; 1.01—4.40). All independent predictors had a value of one point. Youden's index statistics indicated a score of ≥3 as best cutoff value that had a sensitivity of 69.6% and specificity of 78.4%.
Conclusions: Simple decision rule helps clinicians stratify the risk of high vancomycin MIC MRSA infection when deciding empirical therapy for patients with community-onset infections.

Introduction

Patients with methicillin-resistant *Staphylococcus aureus* (MRSA) infection have significant morbidity and mortality.[1—3] Although various antimicrobial agents are available for the treatment of MRSA infection, vancomycin remains the most commonly used anti-MRSA agent in many countries because of its predictable pharmacological activity against MRSA.[4] The successful treatment of MRSA infection with vancomycin, however, is threatened by increasing evidence showing higher mortality or risk of treatment failure among patients with bacteraemia infected with an MRSA isolate with a vancomycin minimum inhibitory concentration (MIC) at the higher end of the susceptible range.[5,6] The situation is further complicated by increasing reports of vancomycin MIC creep in MRSA isolates in the susceptibility window in many institutions.[7—9]

Theoretically, patients in the community are less expected to be infected with high vancomycin MIC MRSA than hospitalized patients because of lower use of antibiotics and colonization pressure in non-hospital environments. However, the spread of an infection with nosocomial high vancomycin MIC MRSA isolates among patients in the community introduces a significant risk of treatment failure even though vancomycin has been frequently included in empirical antibiotic regimens in patients at risk for MRSA infection.[10—14] Though the impact from delay treatment of MRSA infection remains inconclusive,[15,16] earlier identification of patients in the community at risk for high vancomycin MIC MRSA infection and subsequent vancomycin treatment failure is important to augment plausible benefit from timely appropriate antimicrobial therapy.[17,18] This information could be helpful for first-line clinicians to consider alternative therapy for patients with suspected or confirmed MRSA infection,[19] but this is difficult in practice because microbiology and antimicrobial susceptibility results are not available when deciding on empirical antibiotic therapy. Therefore, a prediction rule that helps clinicians with early recognition and timely treatment of patients with high vancomycin MIC MRSA infection becomes crucial to improve clinical outcomes. However, there are no studies that specifically focus on the development of a clinical prediction rule for high vancomycin MIC MRSA infection among patients with community-onset infection.

The objective of the current study was to determine the independent predictors of high vancomycin MIC isolate infection among patients with community-onset MRSA bacteraemia and to develop a score-based prediction rule to help clinicians with clinical decision making on patient management.

Patients and methods

Study design, setting, and participant selection

This emergency department (ED)-based retrospective cohort study was conducted at National Taiwan University Hospital, a 2500-bed university-affiliated teaching hospital providing both primary and tertiary care in northern Taiwan. This hospital discharges an average of 67,000 patients each year and has an average of 100,000 ED visits annually. All ED patients aged 15 years or older diagnosed with MRSA bacteraemia from January 1, 2001, to December 31, 2011, were initially recruited. Patients referred from other hospitals who had been hospitalized for 48 h or longer or patients who had been discharged from any hospital less than 48 h earlier were considered as hospital-acquired bacteraemia. They were excluded in this study because our primary interest was to develop a high vancomycin MIC MRSA prediction score among patients with community-onset infection. For patients with repeated episodes of MRSA bacteraemia during the study period, only the first episode was included. Patients with MRSA bacteraemia were also excluded if the bloodstream isolate was not available for antimicrobial susceptibility testing or if the clinical data were missing or incomplete. Therefore, only non-duplicate adult patients with community-onset MRSA bacteraemia with available clinical data and a bloodstream isolate entered the final analysis. This study was approved by the institutional review board of the hospital, and the requirement for informed consent from each patient was waived.

Data collection and information on variables

Demographic data, pre-hospital living arrangement, prior health care-associated exposure history within the past