Predictors of Clinical Success Among a National Veterans Affairs Cohort With Methicillin-Resistant *Staphylococcus aureus* Pneumonia

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ABSTRACT

Background: The treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia is exceedingly complicated, which is concerning because of the high mortality rate associated with the infection. Identification of independent predictors of clinical success can optimize patient care by assisting clinicians in treatment decisions.

Objectives: Our goal was to identify independent predictors of clinical success in a national Veterans Affairs (VA) cohort of patients with MRSA pneumonia.

Methods: A nested case-control study was conducted among a cohort of VA patients with MRSA pneumonia receiving linezolid or vancomycin between January 2002 and September 2010. Cases included those demonstrating clinical success, defined as discharge from the hospital or intensive care unit by day 14 after treatment initiation, in the absence of death, therapy change, or intubation by day 14. Control subjects represented nonsuccess, defined as therapy change, intubation, intensive care unit admission, readmission, or death between treatment initiation and day 14. The potential predictors assessed included treatment, patient demographic and admission characteristics, previous health care and medication exposures, comorbidities, and medical history. Odds ratios (ORs) and 95% CIs were calculated from logistic regression.

Results: Our study included 2442 cases of clinical success and 1290 control subjects. Demographic characteristics varied between the clinical success and nonsuccess groups, including age, race, and region of facility. A current diagnosis of chronic respiratory disease (46% vs 42%) and diagnosis of pneumonia in the year before the MRSA pneumonia admission (37% vs 32%) were both more common in the clinical success group. Despite these significant differences, only 2 predictors of clinical success were identified in our study: previous complication of an implant or graft, including mechanical complications and infections, in the year before the MRSA pneumonia admission (adjusted OR, 1.55 [95% CI, 1.17–2.06]) and treatment with linezolid (adjusted OR, 1.53 [95% CI, 1.12–2.10]). Predictors of nonsuccess (adjusted OR [95% CI) included diagnosis of concomitant urinary tract infection (0.82 [0.70–0.96]), intravenous line (0.76 [0.66–0.89]), previous coagulopathy (0.74 [0.56–0.96]), previous amputation procedure (0.72 [0.53–0.98]), current coagulopathy diagnosis (0.71 [0.53–0.96]), dialysis (0.54 [0.38–0.76]), multiple inpatient procedures (0.53 [0.45–0.62]), inpatient surgery (0.48 [0.41–0.57]), and previous endocarditis (0.24 [0.07–0.81]).

Conclusions: MRSA pneumonia tends to affect patients with complex care, and identification of the predictors of clinical success is useful when considering different therapeutic approaches. In this national cohort of VA patients with MRSA pneumonia, treatment was the only modifiable variable predicting clinical success. (*Clin Ther*. 2014;36:552–559) Published by Elsevier HS Journals, Inc.

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INTRODUCTION

Pneumonia is the leading cause of infectious disease–related deaths in the United States.[1] A prominent pathogen causing pneumonia in both health care and community settings is methicillin-resistant *Staphylococcus aureus* (MRSA).[2] In recent years, rates of community-associated MRSA pneumonia have been steadily increasing, while MRSA was also becoming a leading cause of health care–associated pneumonia, including ventilator-associated pneumonia.[3,4]

Limited options exist for the treatment of MRSA pneumonia. Vancomycin has been the mainstay of treatment for MRSA infections for years; however, rates of treatment failure for pneumonia as high as 40% have been reported.[5] Linezolid is a well-studied alternative to vancomycin that has been available for >10 years. Several studies have demonstrated clinical equivalence between the 2 drugs,[6–9] but some data suggest a significant benefit for linezolid compared with vancomycin for the treatment of pneumonia.[10–12] Currently, both drugs are recommended as first-line options for the treatment of MRSA pneumonia.[2]

In addition to treatment-related factors, host and pathogen characteristics can affect clinical outcomes for patients with MRSA pneumonia. For example, age, underlying comorbidities, severity of illness, multiple lobe involvement, and need for intensive care unit (ICU) admission have been associated with poor clinical outcomes.[9–11,13,14] There are multiple differences among MRSA strains on a molecular level, including staphylococcal cassette chromosome *mec* type, presence of the toxin Panton-Valentine leukocidin, and MIC, which can also affect clinical outcomes.[14–16]

MRSA pneumonia is a complex disease associated with significant morbidity and mortality. Despite the large public health impact of MRSA pneumonia, there are limited published data examining clinical predictors of success or failure. Identification of independent predictors of clinical success could optimize patient care by assisting clinicians in treatment decisions. It was therefore the aim of the present study to identify independent predictors of clinical success among a national Veterans Affairs (VA) cohort of patients with MRSA pneumonia.

PATIENTS AND METHODS

The study design and methods were defined a priori in the study protocol, which was reviewed and approved by the institutional review board and research and development committee of the Providence Veterans Affairs Medical Center.

Data Sources

The Veterans Health Administration has used an electronic medical record system since 1999. Our study included national standardized databases capturing patient care variables: *International Classification of Diseases, Ninth Revision* (ICD-9) diagnostic and procedure codes, pharmacy records for prescriptions, laboratory tests, select laboratory test results, mortality, and patient vital signs.[17,18]

Patient Population and Study Design

Our nested case-control study was conducted among an original cohort of patients admitted to VA hospitals between January 1, 2002, and September 30, 2010, with an ICD-9 code for MRSA (038.12, 041.12, 482.42, or V09.0) and pneumonia (482.40–482.42, 482.49, 482.89, 482.9, 484.8, 485–486, 510.0, 510.9, or 513.0–513.1).[19] Patients aged ≥18 years were selected for inclusion if they were initiated on linezolid or vancomycin treatment during the admission, in the absence of linezolid or vancomycin therapy in the 7 days before the hospitalization, with at least 3 days of therapy dosed per hospital protocol. Patients were excluded if they died or were discharged within 3 days of treatment initiation, were initiated on vancomycin or linezolid therapy in the nursing home before their hospital admission, or were exposed to >2 consecutive days of anti-MRSA antibiotics in the 3 days before treatment initiation or during treatment with linezolid or vancomycin. Only the first admission within the study period meeting all inclusion and exclusion criteria was included.

To identify independent predictors of clinical success among our MRSA pneumonia cohort, we identified cases of clinical success and a nonsuccess control group. Clinical success was defined as discharge from the hospital and/or from the ICU by day 14 after treatment initiation, in the absence of therapy change, intubation, admission to the ICU, re-admission, and/or death by day 14.[19] Nonsuccess was defined as therapy change, intubation, ICU admission, discharge and readmission, or death between treatment initiation