American Journal of Infection Control 43 (2015) 38-43

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major article

Health care–associated methicillin-resistant *Staphylococcus aureus* infections increases the risk of postdischarge mortality

Richard E. Nelson PhD [a,b,*], Vanessa W. Stevens PhD [a,c], Makoto Jones MD [a,b], Matthew H. Samore MD [a,b], Michael A. Rubin MD, PhD [a,b]

[a] *IDEAS Center, Veterans Affairs Salt Lake City Health System, Salt Lake City, UT*
[b] *Department of Internal Medicine, University of Utah School of Medicine, Salt Lake City, UT*
[c] *Department of Pharmacotherapy, Pharmacotherapy Outcomes Research Center, University of Utah College of Pharmacy, Salt Lake City, UT*

Key Words:
Methicillin-resistant *Staphylococcus aureus*
Health care–associated infection
Mortality
Veterans affairs

Background: Although many studies have estimated the impact of health care–associated methicillin-resistant *Staphylococcus aureus* (MRSA) infections on mortality during initial hospitalization, little is known about the long-term risk of death in these patients. The purpose of this study was to quantify the effect of MRSA health care–acquired infections (HAIs) on mortality after hospital discharge.

Methods: Our study cohort consisted of patients with inpatient admission within the U.S. Department of Veterans Affairs system between October 1, 2007, and September 30, 2010. Of these patients, we identified those with a positive MRSA culture from electronic microbiology reports. We constructed multivariable Cox proportional hazards regressions to assess the impact of a positive culture on postdischarge mortality in the 365 days following discharge using both the full cohort and a propensity score–matched subsample.

Results: In our analysis cohort of 369,743 inpatients, positive MRSA cultures were recorded in 3,599 (1.0%) patients. We found that positive cultures resulted in an increased risk of postdischarge mortality both in the full cohort (hazard ratio = 1.42, $P < .001$) and in the subset of propensity score–matched patients (hazard ratio = 1.37, $P < .0001$).

Conclusion: We found that MRSA HAIs significantly elevate the long-term risk of mortality. These results underscore the importance of infection prevention efforts in the hospital.

Staphylococcus aureus is a gram-positive organism that causes a wide range of clinically significant infections and is carried in the nares of up to 40% of healthy individuals.[1-3] Methicillin-resistant *S aureus* (MRSA) was first described in the early 1960s, just 2 years after the first anti-staphylococcal penicillin, methicillin, was introduced into clinical practice.[4] Since then, estimates of the proportion of *S aureus* isolates that are methicillin-resistant range from 43%-64%.[5-7] Despite observed decreases in incidence since 2005,[8] infections caused by MRSA remain a significant contributor to morbidity, mortality, and health care utilization in the United States.[9]

The impact of an MRSA health care–acquired infection (HAI) on the risk of in-hospital mortality is well known. Serious MRSA bloodstream infections have been associated with mortality rates of 20%-40% in both intensive care unit (ICU) and non-ICU settings.[10-12] Among patients with ventilator-associated pneumonia, those with MRSA infections have a 20% absolute higher risk (59.4% vs 40%, $P = .02$) of mortality than patients with methicillin-sensitive *S aureus* (MSSA) infections.[13] Similarly, patients with MRSA surgical site infections have been shown to be at an increased risk of dying within 90 days when compared with patients with MSSA infections.[14]

Although a number of studies have examined the impact of MRSA infection on mortality outcomes in the short run, either compared with no infection or MSSA infection, there is

* Address correspondence to Richard E. Nelson, PhD, George E. Whalen Department of Veterans Affairs Medical Center, 500 Foothill Dr, GRECC-182, Salt Lake City, UT 84148.
E-mail address: richard.nelson@utah.edu (R.E. Nelson).

Disclaimer: The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the United States government.

Funding/support: The research reported here was supported by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, and Health Services Research and Development Service (CDA 11-210), with Dr. Nelson as the principal investigator.

Conflicts of interest: None to report.

0196-6553/$00.00 - Published by Elsevier Inc. on behalf of the Association for Professionals in Infection Control and Epidemiology, Inc.
http://dx.doi.org/10.1016/j.ajic.2014.09.014

relatively little information about long-term postdischarge mortality following a hospital-acquired MRSA infection. Three previous studies have examined long-term mortality in MRSA patients,[15-17] but 2 of these studies only compared MRSA infections with patients with MRSA colonization,[15,17] 1 only evaluated the impact of MRSA colonization on mortality,[16] and all 3 studies were single-center evaluations. The objective of this study was to shed light on the long-term impacts of MRSA HAIs by evaluating the impact of these infections on the risk of mortality during the 1-year period following hospital discharge and to evaluate variability in estimates across facilities in a large multicenter setting.

METHODS

Study design and population

We conducted a retrospective cohort study of patients hospitalized at 1 of 123 Department of Veteran Affairs (VA) acute care facilities during the period from October 1, 2007-September 30, 2010. The VA health care system is the largest integrated health care system in the United States, providing care for >8.7 million veterans each year.[18] Patients may have been hospitalized more than once during the study period. For the purposes of this analysis, the first hospitalization during the study period was chosen. Patients were excluded from the study cohort if they were hospitalized for ≤2 days, had a positive MRSA culture on admission, died prior to discharge, or if they had <365 days of preadmission observation time in the VA health care system. Approval for this study was obtained from the University of Utah Institutional Review Board and the Salt Lake City VA's Office of Research & Development.

MRSA definition

Beginning on October 1, 2007, the VA implemented the National MRSA Prevention Initiative with a goal to reduce transmission of MRSA in hospitals.[19] To achieve this goal, all patients were tested on admission to a VA hospital, when being transferred between hospital wards, and on discharge. Results of the surveillance cultures are entered into the VA electronic medical record. We used a previously developed Natural Language Processing algorithm[20] to retrieve information on microorganisms and antibiotic susceptibilities from the unstructured data in the infection control reports.

The primary independent variable in this study was a positive MRSA culture during hospitalization. In accordance with surveillance definitions from the Centers for Disease Control and Prevention's National Healthcare Safety Network, we defined health care–acquired MRSA as identification of MRSA from a clinical culture >48 hours after admission and 48 hours following discharge.[21] Although some of these positive cultures were in fact infections, a great many of them were likely noninfection-related MRSA colonizations. We applied a recently published algorithm that uses electronic data in the VA to classify positive MRSA cultures as HAIs if they were from a sterile site or if the patient had a pharmacy record for MRSA-active antimicrobials at any point during the 5 days before or 5 days after the positive MRSA culture.[22] Positive cultures not classified as infections using this algorithm were considered colonizations.

Outcome assessment

Patients were followed after hospital discharge (index date) until death or until 365 days postdischarge, at which point patients were censored if they had not died. Death was defined as death from any cause during the study period and was obtained from the VA Corporate Data Warehouse, the national repository for electronic data from several administrative and clinical data sources.[23]

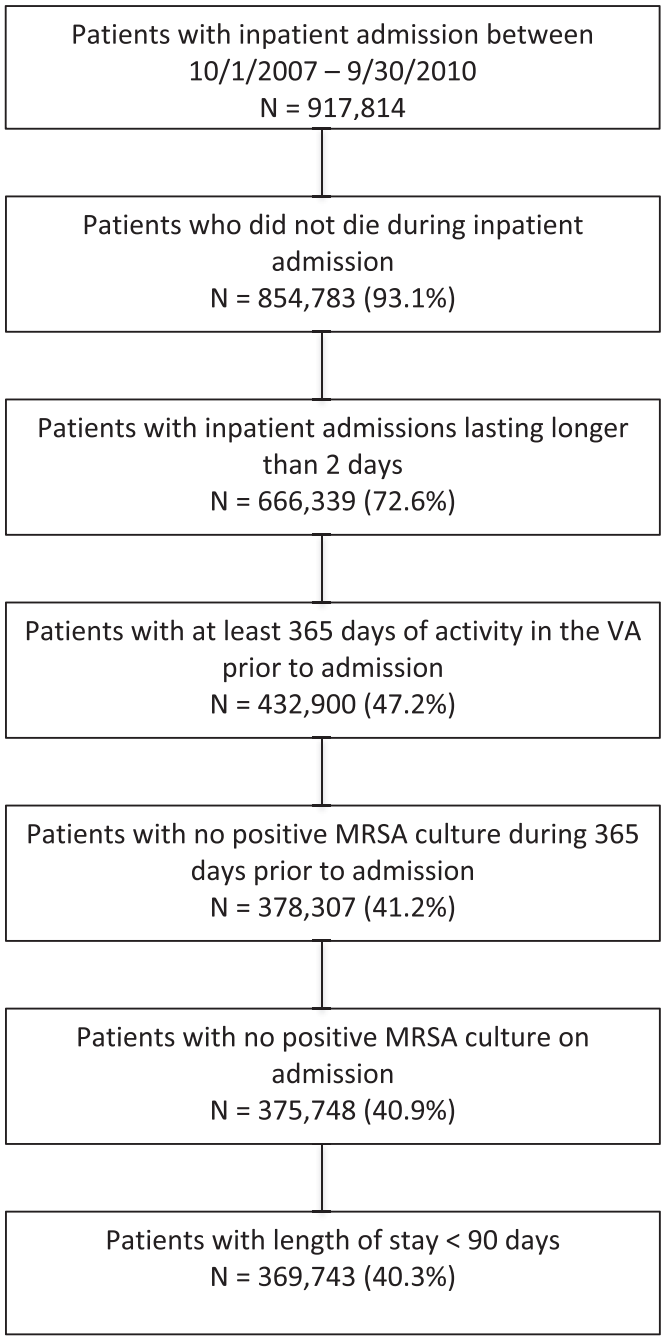

Fig 1. Patient attrition summary. *VA*, veterans affairs.

Propensity score matching

Propensity score matching was undertaken using the psmatch2 command in Stata (StataCorp, version 12, College Station, TX) to improve baseline comparability of MRSA and non-MRSA patient groups. Multivariable logistic regression was used to model the probability of developing a positive MRSA culture as a function of baseline characteristics, which were identified in the 365 days prior to the index date to avoid the possibility of including intermediary variables in the causal pathway. Variables were candidates for inclusion in the model if they were considered to be confounders in