POSTER # 293

Healthcare-associated methicillin-resistant *Staphylococcus aureus* infections increase the risk of post-discharge mortality

Richard E. Nelson PhD, Vanessa W. Stevens PhD, Makoto Jones MD, Matthew H. Samore MD, Michael A. Rubin MD PhD

VA Salt Lake City Health Care System

University of Utah

Background

- *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].
- Despite observed decreases in incidence since 2005, [2] infections due to methicillin-resistant *Staphylococcus aureus* (MRSA) remain a significant contributor to morbidity, mortality, and healthcare utilization in the United States [3].
- The impact of an MRSA healthcare-acquired infection (HAI) on the risk of in-hospital mortality is well known [4,5].
- However, there is relatively little information about long-term post-discharge mortality following a hospital-acquired MRSA infection.

Objective

- Examine the impact of MRSA HAIs on the risk of mortality during the one-year period following hospital discharge.

Methods

Data

- Beginning on October 1, 2007, the VA implemented a nationwide MRSA Prevention Initiative with a goal of reducing MRSA HAIs [6].
- Our team developed a natural language processing system to extract microorganisms mentioned in these reports as well as antibiotic susceptibilities [7].
- Data on mortality and patient characteristics were drawn from the VA Corporate Data Warehouse.

Outcome assessment

- Patients were followed after hospital discharge (index date) until death or until 365 days post-discharge, at which point, patients were censored if they had not died.
- Death was defined as death from any cause during the study period.

Independent variables

- The key independent variable in our models was an indicator for a positive MRSA culture.
- 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 five days before or five days after the positive MRSA culture [8].
- Positive cultures not classified as infections using this algorithm were considered colonizations.
- We also controlled for potential confounders, including
  - (1) demographic characteristics,
  - (2) VA healthcare costs in the 365 days prior to admission,
  - (3) length of stay at risk for MRSA infection during index hospitalization,
  - (4) admitting diagnosis for index hospitalization,
  - (5) indicator for surgery within first 48 hours of index hospitalization, and
  - (6) comorbidities, as measured using a risk score that combines the Charlson and Elixhauser measures [9].

Regression model

- We used a Cox proportional hazard model to estimate the attributable post-discharge mortality for MRSA HAI.

For more information contact:

Richard E. Nelson, Ph.D.
Phone: (801) 582-1565 x4049
E-mail: Richard.Nelson@utah.edu

UNIVERSITY OF UTAH SCHOOL OF MEDICINE

Methods

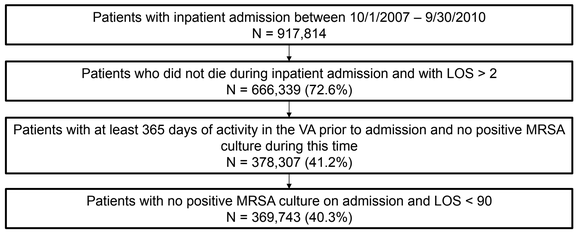
Propensity score matching

- We ran our analyses on a subgroup of propensity score-matched patients in order to balance observable characteristics between patients with and without a positive MRSA culture.

Study design and population

- We employed a historical cohort study design and used data from the VA healthcare system from October 1, 2007 and September 30, 2010.
- Patients were excluded from the cohort if they (1) died during this index hospitalization, (2) had a length of stay that exceeded 90 days, (3) were discharged from the hospital in 2 days or less, (4) had a prior positive clinical culture for MRSA or (5) did not have at least 365 days of observation in the VA prior to their index hospitalization.
- Our final sample consisted of 369,743 patients (**Figure 1**).

Figure 1: Patient attrition summary



Results

Patient characteristics

- Characteristics of our patient cohort are shown in **Table 1**.

Table 1: Patient characteristics

	Full cohort		Propensity score-matched cohort	
	No MRSA	MRSA	No MRSA	MRSA
Total (n)	366,144	3,599	3,592	3,592
Age (mean)	64.3	65.9	66.0	65.9
Male (%)	94.9	96.0	96.0	96.0
Race (%)				
White	69.2	67.6	67.6	67.6
Black	19.4	21.1	20.2	21.1
Other	6.7	6.9	7.7	6.8
Unknown	4.6	4.5	4.5	4.5
CCI/Elixhauser (mean)	1.3	1.4	1.9	1.8
Outpt cost prior yr (mean)	$9,703	$10,711	$16,783	$13,483
LOS (mean)	9.3	22.4	23.2	20.1

Kaplan-Meier curves

- **Figure 2a** and **Figure 2b** show that post-discharge mortality was more common in patients when compared with those without positive MRSA cultures and that patients with MRSA HAIs had the highest mortality rate.

Results

Figure 2a: K-M curve – positive MRSA culture, no positive MRSA culture

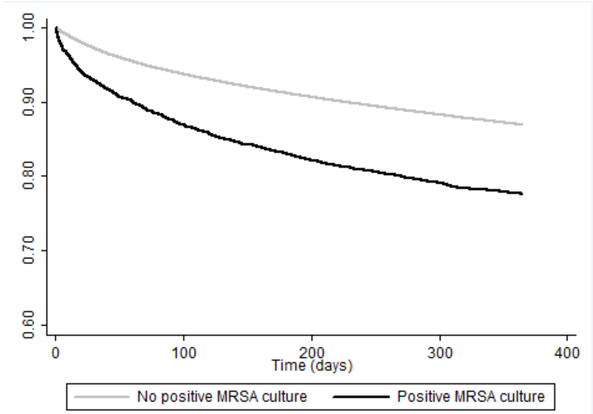
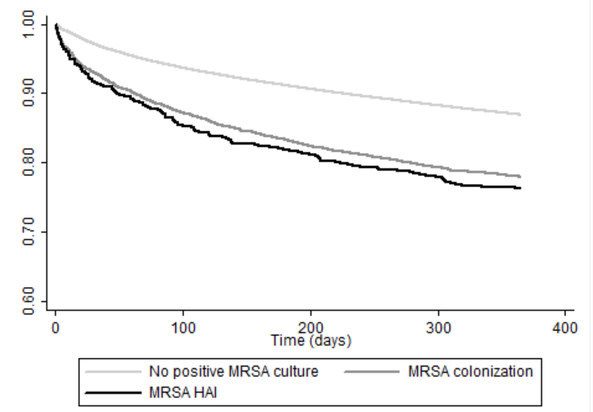


Figure 2b: K-M curve – MRSA HAI, MRSA colonization, no MRSA culture



Results

Multivariable regressions

- The results of the multivariable Cox Proportional Hazards regression models are shown in **Table 3**.
- In the full cohort, MRSA patients were significantly more likely to die than non-MRSA patients, after accounting for the effects of covariates.
- This was true both for MRSA colonizations and HAIs.
- Estimates were similar in the propensity score-matched sample.

Table 4: Results. MRSA HAI vs. MRSA colonization vs. no positive MRSA culture

Independent variables	Estimate	95% CI	
		Lower	Upper
Positive MRSA culture vs. no positive MRSA culture			
Full cohort (N = 369,743)			
No positive MRSA culture (ref)	-	-	-
Positive MRSA culture	1.420	1.322	1.525
Propensity score matched (N = 7,184)			
No positive MRSA culture (ref)	-	-	-
Positive MRSA culture	1.370	1.231	1.524
MRSA HAI vs. MRSA colonization vs. no positive MRSA culture			
Full cohort (N = 369,743)			
No MRSA (ref)	-	-	-
MRSA colonization	1.406	1.301	1.520
MRSA HAI	1.489	1.261	1.758
Propensity score matched (N = 7,184)			
No MRSA (ref)	-	-	-
MRSA colonization	1.351	1.209	1.510
MRSA HAI	1.464	1.212	1.769

Summary & Conclusions

- Using electronic data from 123 VA hospitals in the US, we find that patients with positive MRSA cultures are at greater risk for mortality in the 1-year post-discharge period than those without positive MRSA cultures.
- Whether those positive cultures were due to colonization or to HAI, the impact on mortality was similar.
- This was the first large, multi-center study to evaluate the impact of MRSA infection on the long-term risk of mortality when compared to patients without MRSA infection.
- There are several possible explanations for these long-term mortality effects.
- First, the increased risk of death may be due to recurrent infections, which are common in patients with MRSA infection [10].
- Second, recent evidence suggests that *Staphylococcus aureus* HAIs can lead to long-term disabilities such as chronic ventilator dependence and dialysis-dependent end-stage renal disease, which may also increase the risk of death [11].

References

1. Choi CS, Yin CS, Bakar AA, et al. **J Microbiol Immunol Infect**. 2006;39(6):458-464.\
2. Dantes R, Mu Y, Belflower R, et al. **JAMA Intern Med.** 2013;173(21):1970-1978.
3. Zimlichman E, Henderson D, Tamir O, et al. **JAMA Intern Med.** 2013;31(3)2953-301.
4. Cosgrove SE, Qi Y, Kaye KS, Harbarth S, Karchmer AW, Carmeli Y. **ICHE** 2005;26(2):166-174.
5. Stevens V, Lodise TP, Tsuji B, et al. **ICHE** 2012;33(6):558-564.
6. Jain R, Kralovic SM, Evans ME, et al. **NEJM** 2011;364(15):1419-1430.
7. Jones M, DuVall SL, Spuhl J, Samore MH, Nielson C, Rubin M. **BMC Med Inform Decis Mak** 2012;12:34.
8. Branch-Elliman W, Strymish J, Gupta K. **ICHE** 2014;35(6):692-698.
9. Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. **J Clin Epidemiol** 2011;64(7):749-759.
10. Huang SS, Hinrichsen VL, Datta R, et al. **PLoS One** 2011;6(9):e24340.
11. Su CH, Chang SC, Yan JJ, Tseng SH, Chien LJ, Fang CT. **PLoS One** 2013;8(8):e71055.