IDWeek #276

Molecular Epidemiology of MRSA and VRE Co-colonization among Hospitalized Adults in Detroit

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ABSTRACT (Updated)

Background: Co-colonization with methicillin-resistant *S. aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE) is a key factor in the emergence of vancomycin-resistant *S. aureus*. Our objective is to describe the molecular epidemiology of MRSA co-colonization through comparison of MRSA *spa*types between co-colonized cases and matched controls.
Methods: We conducted a prospective study among adult inpatients in six hospitals in and around Detroit, Michigan. Cases were defined as individuals with positive cultures for MRSA and VRE within 7 days of one another. Controls with a positive culture for MRSA and not VRE were matched to cases by hospital, infection type, healthcare associated infection, and requirement for intensive care unit (ICU) care. Patient demographics and clinical data were collected by medical record review. *spa* typing was conducted by sequencing of the staphylococcal protein a (spa) gene, and sequences were analyzed using DNAGear. Molecular characteristics were compared between matched study groups using generalized estimating equations.
Results: 163 MRSA isolates were analyzed from 80 MRSA and VRE co-colonized case patients and 72 MRSA-only control patients. Isolates were most frequently identified from acute bacterial skin and skin structure infections (46%) and bloodstream infections (19%). Thirty-one percent of clinical cultures were collected within 72 hours of admission. The most common *spa* types were t002 (n=51; 31%), t008 (n=41; 25%), t1094 (n=15; 9%), or t688 (n=11; 7%). The t002 type was significantly more common among co-colonized cases (n=42; 47%) than among MRSA-only controls (n=9; 12%) (p<0.001). Conversely, the t008 type was significantly more common among controls (n=26; 36%) than among cases (n=15; 17%) (p=0.006).
Conclusion: Patients with MRSA and VRE co-colonization were more likely to be infected with USA100-associated type t002. In contrast, patients with MRSA-only were more likely to be infected with USA300-associated type t008. This difference in molecular epidemiology may represent underlying differences in the medical history of patients at risk for co-colonization.

INTRODUCTION

- The majority of VRSA identifications in the United States have occurred in patients treated in Southeastern Michigan.[1]
- VRSA isolates typically belong to *S. aureus* clonal complex 5, which is comprised of USA100-associated MRSA strain types.[1]
- The emergence of VRSA requires co-colonization with MRSA and VRE, in addition to other elements, for the transfer of the *vanA* gene to *S. aureus*.[2]
- Our objective was to describe the molecular epidemiology of MRSA among patients with MRSA and VRE co-colonization in Detroit, Michigan and the surrounding areas.

METHODS

- We conducted a prospective study of adult inpatients admitted to 6 Detroit Medical Center hospitals in and around Detroit, Michigan from 2012 through 2014.
- Patients with MRSA & VRE Co-colonization (defined as positive clinical cultures occurring within 7 days of each other) were identified through automatic surveillance (Theradoc).
- Comparison patients with MRSA and *no* VRE detection were matched based on intensive care unit admission, healthcare-associated infection and infection site.
- *spa* type was determined based on Sanger sequencing of the *Staphylococcal* protein A gene and sequence type determination was performed using DNAGear.[3]
- Type distribution was compared between patients with co-colonization and matched comparison patients using multivariate generalized estimating equations with clusters identified by matched pairs.

RESULTS

Figure 1. Ascertainment of Study Patients

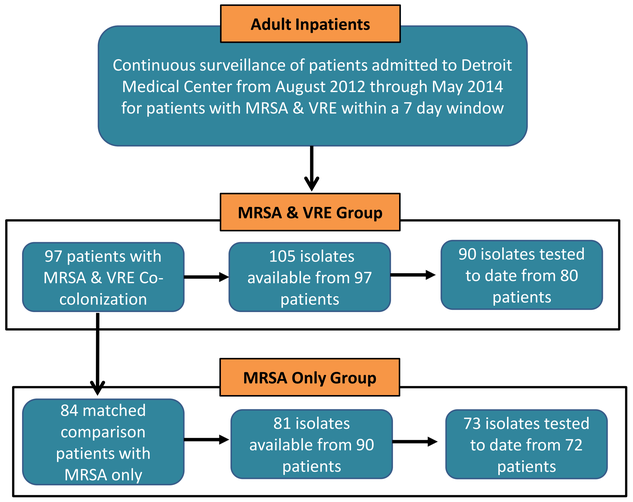

Table 1. Patient Characteristics by Study Group, n(%)
Study characteristics were relatively similar between co-colonization and single infection groups

	MRSA & VRE Group (N=80)	MRSA Only Group (N=72)
Male	53 (67)	36 (55)
Race		
White	14 (18)	6 (9)
Black	63 (81)	54 (84)
Other	1 (1)	0 (0)
Unknown	0 (0)	4 (6)
Admitted to Intensive Care Unit*	26 (33)	16 (24)
>72 hours Stay Prior to 1st Culture*	23 (29)	21 (32)
MRSA Infection Site*		
ABSSSI	36 (46)	30 (45)
Blood	14 (18)	13 (20)
Urinary Tract	7 (9)	5 (8)

Valid percent is presented.
*These characteristics were matched between study groups

References: (1)Limbago et al. J Clin Microbiol. 2014, 52(3):998. (2) Zhu et al. Antimicrob Agents Chemother. 2013 Jan; 57(1):212-9. (3) AL-Tam et al. BMC Res Notes. 2012 Nov 19;5:642.

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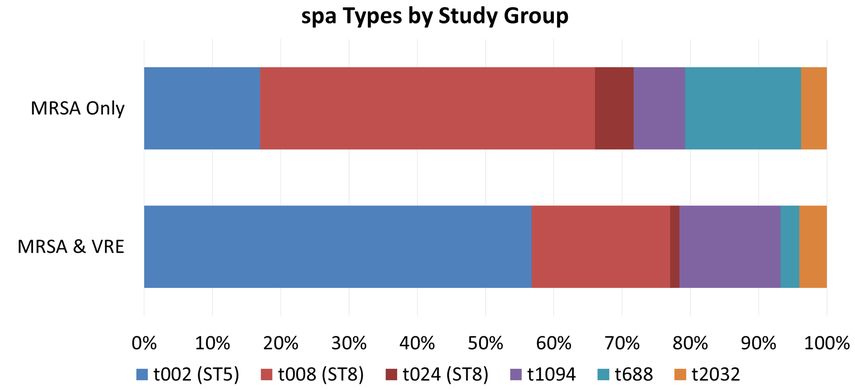

Figure 2. Distribution of *spa* types. Percent in study group with each *spa* type detected. Sequence type (ST) numbers are estimated based on commonly associated types (Ridom *spa* server). *t002*, an ST5-associated type, was predominantly found in patients with MRSA & VRE co-colonization. Conversely, ST8-associated types, including *t008* and *t024* were predominantly found in patients with MRSA but no VRE co-colonization.

Table 2. Multivariate Models for Association Between Study Group and *MRSA spa* Type
Study group was associated with *t002* type (for co-colonized group) and *t008* type (for MRSA only group) even after controlling for intensive care using admission and healthcare associated infection.

	Model 1: MRSA spa t002 OR (95% C.I.); p (N=154)	Model 2: MRSA spa t008 OR (95% C.I.); p (N=154)
MRSA & VRE Co-Colonization	6.2 (2.5, 15.5); <0.001	0.4 (0.2, 0.8); 0.01
Admitted to Intensive Care Unit	2.6 (1.2, 5.8); 0.02	0.7 (0.3, 1.8); 0.48
>72 hours Stay Prior to 1st Culture	0.6 (0.3, 1.4); 0.29	0.9 (0.4, 2.1); 0.81

CONCLUSION

- Patients with MRSA and VRE co-colonization were more likely to be infected with USA100-associated *spa* type *t002.*
- Conversely, patients with MRSA infection without VRE co-colonization had a higher prevalence of USA300-associated *spa* type *t008*.
- VRSA isolates identified in the United States typically belong to *t002*-related clonal complexes (CC-5). Our finding of increased VRE-detection among patients with MRSA *t002* corresponds with the molecular epidemiology of VRSA.
- Lower prevalence of VRE co-colonization with MRSA *t008* may mediate a lower risk of VRSA emergence among more virulent community-associated MRSA clonal complexes.