The Local Hospital Milieu and Healthcare-Associated VRE Acquisition

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Background

- Vancomycin-resistant *Enterococcus* (VRE) causes 4% of all healthcare-associated infections (HAIs) in the United States.[1]
- Rates of gastrointestinal VRE colonization on admission to intensive care units (ICUs) range from 4% to 30%.[2]
- In the ICU, VRE-colonized patients have longer ICU stays, increased hospital costs, and increased mortality compared to non-colonized patients.[3]
- The relationship between the local hospital environment and VRE acquisition is not fully understood, and the relative effectiveness of standard infection control approaches in controlling VRE acquisition in reducing transmission is unclear.

Objectives

To determine the importance of specific factors within the local hospital environment in healthcare-associated VRE acquisition.

Study Methods

Study Design and Subjects

- Retrospective cohort study including adults ≥18 years old admitted to any of 6 ICUs affiliated with a large academic medical center from January 1, 2012 to December 31, 2016.
- Inclusion criteria: having a negative VRE surveillance rectal swab within 24 hours of ICU admission.

Variables

- Factors related to the local presence of VRE immediately preceding and during each patient's hospitalization and factors related to the local use of vancomycin, as well as co-variables such as laboratory values and treatment received.
- VRE colonization pressure was defined to encapsulate the circulating VRE burden during the at-risk patient's ICU stay:

$$\sum \frac{Daily\ Exposure\ to\ VRE - positive\ patients\ (sum\ VRE\ pressure)}{Length\ of\ time\ at\ risk}$$

- VRE importation pressure was defined to encapsulate the VRE burden at the time of ICU admission:

$$\sum \frac{Number\ of\ patient - days\ of\ VRE - positivity\ in\ prior\ 30\ days}{\sum Number\ of\ all\ patient - days}$$

Endpoints and Statistics

- Primary outcome: healthcare-associated VRE acquisition (positive subsequent VRE surveillance swab performed at any time after the initial negative surveillance swab during the same hospitalization).
- Multivariable analysis was constructed using a Cox proportional hazards model with patients followed from the time of ICU admission until death, VRE acquisition, or for a maximum of 30 days.

Table 1: Clinical characteristics

Characteristics	VRE acquisition (n = 161)	No VRE acquisition (n = 8,324)	Total (n = 8,485)	p-value
Baseline demographics and comorbidities				
Male sex	91 (57%)	4,384 (53%)	4,475 (53%)	0.33
Age				
18 – 49 years	63 (39%)	2,766 (33%)	2,829 (33%)	0.06
50 – 70 years	58 (36%)	2,770 (33%)	2,828 (33%)	
>70 years	40 (25%)	2,788 (33%)	2,828 (33%)	
Race				
Black	16 (10%)	848 (10%)	864 (10%)	0.93
Hispanic	41 (25%)	2,293 (28%)	2,334 (28%)	
White	51 (32%)	2,601 (31%)	2,652 (31%)	
Other/unknown	53 (33%)	2,582 (31%)	2,635 (31%)	
Season of admission*				
Winter	44 (27%)	2,148 (26%)	2,192 (26%)	0.78
Spring	40 (25%)	1,978 (24%)	2,018 (24%)	
Summer	41 (25%)	2,035 (24%)	2,076 (24%)	
Fall	36 (22%)	2,163 (26%)	2,199 (26%)	
ICU location				
1	11 (7%)	1,989 (24%)	2,000 (24%)	<0.01
2	2 (1%)	84 (1%)	86 (1%)	
3	42 (26%)	3,020 (36%)	3,062 (36%)	
4	1 (0.6%)	31 (0.4%)	32 (0.4%)	
5	50 (31%)	1,704 (20%)	1,754 (21%)	
6	55 (34%)	1,496 (18%)	1,551 (18%)	
Charlson comorbidity index				
0-1	43 (27%)	2,840 (34%)	2,883 (34%)	0.06
1-2	49 (30%)	2,597 (31%)	2,646 (31%)	
≥3	69 (43%)	2,887 (35%)	2,956 (35%)	
Laboratory values at ICU admission				
Sodium <135 or >145 mEq/L	46 (29%)	2,210 (27%)	2,256 (27%)	0.57
Creatinine >2 mg/dL	54 (34%)	1,555 (19%)	1,609 (19%)	<0.01
Albumin <2.5 g/dL	54 (34%)	1,736 (21%)	1,790 (21%)	<0.01
Hematocrit <35%	23 (14%)	991 (12%)	1,014 (12%)	0.36
White blood cells <4 or >12 x 10^9/L	77 (48%)	3,373 (41%)	3,450 (41%)	0.06
Sodium <135 or >145 mEq/L	46 (29%)	2,210 (27%)	2,256 (27%)	0.57
Treatment received in ICU				
Antibiotics	126 (78%)	5,964 (72%)	6,090 (72%)	0.07
Immunosuppressants	102 (63%)	3,356 (40%)	3,458 (41%)	<0.01
Proton pump inhibitors	90 (56%)	4,071 (49%)	4,161 (49%)	0.08
Recent surgery	26 (16%)	2,063 (25%)	2,089 (25%)	0.01
Mechanical ventilation	112 (70%)	4,264 (51%)	4,376 (52%)	<0.01
Dialysis	30 (19%)	591 (7%)	621 (7%)	<0.01

Results

Patient Characteristics

- Among 8,485 patients included in the study, 161 patients (2%) acquired VRE.
- Patients with VRE acquisition were more likely to be admitted to the tertiary care medical ICUs, have had recent surgery, required dialysis, required mechanical ventilation, received immunosuppressants, had elevated creatinine, or had hypoalbuminemia.

Factors Associated with VRE Acquisition

- On univariate analysis, patients with VRE acquisition were more likely to have received vancomycin, have had a neighboring patient who received vancomycin, have high VRE importation pressure, or have high VRE colonization pressure.
- High VRE colonization pressure was the most important covariate, with a VRE acquisition rate of 42% for those with high VRE colonization pressure versus 21% for those with low VRE colonization pressure (log-rank p <.01).
- On multivariable analysis, only high VRE colonization pressure was an independent predictor of VRE acquisition (aHR 1.79, 95% CI 1.19 - 2.70).
- Similar results were obtained in the sensitivity analyses, specifically when the analysis was restricted to 1,131 patients who were rechecked for VRE during the index hospitalization (aHR 1.86, 95% CI 1.03 - 3.36), or when the analysis was restricted to 3,305 patients admitted to the tertiary referral medical ICUs (aHR 1.90, 95% CI 1.12 - 3.23).

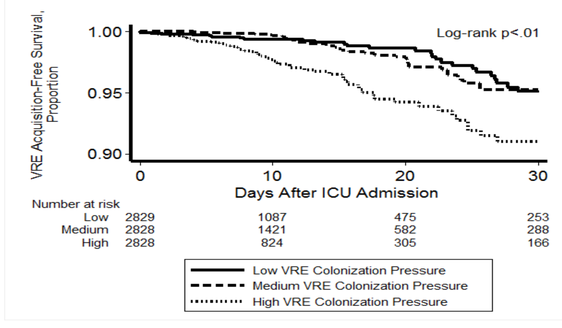
Table 2. Local hospital milieu factors, stratified by VRE acquisition

Characteristics	VRE acquisition (n = 161)	No VRE acquisition (n = 8,324)	Total (n = 8,485)	p-value
At-risk patient				
Vancomycin use	132 (82%)	4,721 (57%)	4,853 (57%)	<0.01
Prior bed occupant				
VRE colonization	69 (43%)	3,487 (42%)	3,556 (42%)	0.81
Vancomycin use	75 (47%)	3,331 (40%)	3,406 (40%)	0.09
Neighboring patient(s)				
VRE colonization	35 (22%)	1,497 (18%)	1,532 (18%)	0.22
Vancomycin use	64 (40%)	2,677 (32%)	2,741 (32%)	0.04
Unit-level				
VRE colonization pressure				
Low	33 (21%)	2,836 (34%)	2,869 (34%)	<0.01
Medium	61 (38%)	2,806 (34%)	2,867 (34%)	
High	67 (42%)	2,682 (32%)	2,749 (32%)	
VRE importation pressure				
Low	42 (26%)	2,787 (34%)	2,829 (33%)	0.01
Medium	48 (30%)	2,780 (33%)	2,828 (33%)	
High	71 (44%)	2,757 (33%)	2,828 (33%)	
Vancomycin use				
Low	59 (37%)	2,781 (33%)	2,840 (33%)	0.55
Medium	48 (30%)	2,799 (34%)	2,847 (34%)	
High	54 (33%)	2,744 (33%)	2,798 (33%)	

Table 3. Multivariable model of risk factors for VRE acquisition

Risk factor	VRE acquisition Adjusted hazard ratio (95% CI)
VRE colonization pressure	
Low	Reference
Medium	0.82 (0.54 – 1.26)
High	1.79 (1.19 – 2.70)
ICU location	
1	0.40 (0.21 – 0.79)
2	0.62 (0.15 – 2.60)
3	0.71 (0.47 – 1.09)
4	0.94 (0.13 – 7.00)
5	Reference
6	1.18 (0.80 – 1.73)
Charlson comorbidity index	
0-1	Reference
1-2	1.12 (0.74 – 1.69)
≥3	1.27 (0.86 – 1.88)
Creatinine >2 mg/dL	1.52 (1.09 – 2.13)

Figure 1. VRE acquisition-free survival, stratified by VRE colonization pressure



Conclusions

- VRE colonization pressure was the most important risk factor for healthcare-associated VRE acquisition in the ICU, regardless of VRE importation pressure or local use of vancomycin.
- The increased rates of VRE acquisition among patients who faced high VRE colonization pressure, regardless of importation pressure, may suggest that an important mechanism of VRE transmission is from known VRE-positive patients via healthcare workers or shared fomites as opposed to VRE transmitted from shared surfaces from prior patients.
- Interventions seeking to reduce healthcare-associated VRE acquisition may wish to focus on ways to minimize transmission of VRE between patients with known VRE and the local hospital environment.

References:

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3. Jung E, et al. Vancomycin-resistant Enterococcus colonization in the intensive care unit: clinical outcomes and attributable costs of hospitalization. *American journal of infection control*. 2014;42:1062-6.

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