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Prolonged Colonization with the Methicillin-Resistant *Staphylococcus aureus* Strain USA300 among Residents of Extended Care Facilities

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Abstract

We performed a retrospective cohort study ($n = 129$) to assess whether residents of extended care facilities who were initially colonized or infected with the methicillin-resistant *Staphylococcus aureus* (MRSA) strain USA300 were less likely to have prolonged colonization than were residents colonized or infected with other MRSA strains. We found no difference in prolonged colonization (adjusted odds ratio, 1.1 [95% confidence interval, 0.5–2.4]).

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People can be colonized with methicillin-resistant *Staphylococcus aureus* (MRSA) for years. Molecular typing of *S. aureus* isolates has shown that patients with prolonged colonization frequently carry the same genotype over time. The USA300 MRSA strain has emerged as a major cause of community-acquired skin and soft tissue infections¹ and is now spreading in healthcare facilities.^{2,3} Recent reports from long-term care facilities have identified 8%–40% of residents colonized with the USA300 MRSA strain.^{3,4} Data from studies on USA300 MRSA infections in outbreak and nonoutbreak settings report a lower rate of nasal colonization than would be expected, compared with other strains of *S. aureus*, including MRSA strains other than USA300.^{5,6} Because of this, researchers have hypothesized that prolonged colonization with USA300 MRSA is less frequent than prolonged colonization with other *S. aureus* strains.⁷ The purpose of our study was to assess whether residents of extended care facilities who were initially colonized or infected with USA300 MRSA are less likely to have prolonged colonization, compared with residents who were initially colonized or infected with other MRSA strains.

Methods

The Veterans Affairs (VA) Maryland Health Care System has 270 beds in 5 extended care units at 2 centers. Surveillance for MRSA colonization (by use of culture) is performed at admission and every 3 months for infection control purposes. The University of Maryland Baltimore institutional review board and the VA Maryland Health Care System's Research and Development Committee approved the study protocol.

This was a retrospective cohort study of residents of extended care facilities of the VA Maryland Health Care System during the period from 2004 through 2007. Our study population was defined at the time of enrollment and included residents who had (1) their first MRSA isolate recovered from either surveillance or clinical culture within 1 year after study enrollment, (2) a length of stay at the time of study enrollment of greater than 3 weeks, and (3) their first MRSA isolate available for molecular testing. At the time of study enrollment, all eligible residents had samples cultured prospectively for 3 weeks to assess for prolonged colonization (Figure 1). Eligible residents had swab samples obtained from the anterior nares, perineum, axilla, and the largest area of skin breakdown, if present.

The primary study variable was whether a resident's first MRSA isolate was USA300 or non-USA300 MRSA. First MRSA isolates were retrieved retrospectively from the VA Maryland Health Care System's clinical microbiology laboratory, which routinely saves the first MRSA isolate of each patient. All samples were tested for MRSA by use of standard microbiological procedures. MRSA isolates were characterized by use of the polymerase chain reaction assay to amplify Pantone-Valentine leukocidin (PVL) and arginine catabolic mobile element (ACME) genes.⁸ Each MRSA isolate was characterized by use of DNA amplification and DNA sequencing of the protein A (*spa*) gene hypervariable region.⁹ A resident's MRSA isolates, recovered from the first culture and from the 3 weekly MRSA screening cultures, were categorized as USA300 or non-USA300 by use of an established genetic algorithm of having the *spa* type motif MBQBLO and the presence of PVL and ACME genes as a marker of USA300 MRSA.³

The outcome variable was prolonged MRSA colonization. A resident was identified as having prolonged colonization with MRSA if he or she had an MRSA isolate recovered from at least 1 anatomic site within the 3-week evaluation period that had the same genotype as his or her first recovered MRSA isolate. We also determined whether a resident's first MRSA isolate represented either colonization or infection.¹⁰ Data on all the other variables were collected by reviewing the resident's electronic medical record. We used logistic regression to assess the relationship between the primary study variable and the outcome

variable while adjusting for other covariables. In the final model, we included variables that were statistically significantly associated with the outcome variable; a *P* value of less than .2 was considered to be statistically significant. All statistical analyses were 2-sided and were performed by use of SAS statistical software, version 9.1 (SAS Institute).

Results

Of the 355 residents with a history MRSA colonization or infection, 129 (36%) met our eligibility criteria and participated in our study. Of the 226 residents who were not included, 119 had their first MRSA isolate recovered more than 1 year before the start of our study, 28 residents had a length of stay at an extended care facility of less than 3 weeks, 22 residents had a first MRSA isolate that was not available for molecular testing, and 57 residents declined to participate. The study population was predominantly male: 126 (98%) of 129 residents were men, and the mean age was 74 years. Most participants were in residential care (92 residents [71%]). On the basis of molecular typing of the first MRSA isolates recovered, it was determined that 53 residents (41%) carried USA300 MRSA and 76 residents (59%) carried non-USA300 MRSA. Compared with the residents with non-USA300 MRSA, the residents with USA300 MRSA were younger (mean age [$\pm$ standard deviation], 77 ± 10 years vs 71 ± 13 years; $P < .01$) and were 4 times as likely to be in short-term rehabilitation or post-acute care (5 [7%] of 76 residents vs 15 [28%] of 53 residents; $P < .01$). Compared with residents with non-USA300 MRSA, residents with USA300 MRSA were more likely to have their first culture represent an infection (11 [14%] of 76 residents vs 17 [32%] of 53 residents; $P = .02$).

Of the 129 residents, 62 (48%) remained colonized with the same MRSA genotype as their first MRSA isolate, which was determined by *spa* typing. Table 1 compares the demographic and clinical characteristics of residents with prolonged colonization with the same genotype ($n = 62$) with the demographic and clinical characteristics of residents without prolonged colonization with the same genotype ($n = 67$). There was no difference in prolonged colonization between residents with USA300 and residents with non-USA300 (odds ratio [OR], 0.9 [95% confidence interval {CI}, 0.5–1.9]; $P = .87$). Two factors were statistically significantly associated with prolonged colonization: (1) the number of positive culture results prior to enrollment and (2) whether the first MRSA isolate represented colonization or infection. Residents who had only 1 MRSA-positive culture result were less likely to have prolonged colonization, compared with residents who had more than 1 MRSA-positive culture result (OR, 0.4 [95% CI, 0.2–0.9]; $P = .02$). Residents whose first culture result represented an infection were less likely than other residents to have prolonged colonization (OR, 0.5 [95% CI, 0.2–1.05]; $P = .06$). In the logistic regression analysis, we found little change in the association between USA300 MRSA and prolonged colonization (adjusted OR, 1.1 [95% CI, 0.5–2.4]), even when adjusted for whether the first MRSA isolate represented an infection (adjusted OR, 0.4 [95% CI, 0.2–0.9]) and for whether the resident had only 1 MRSA-positive culture result (adjusted OR, 0.4 [95% CI, 0.2–0.8]).

Discussion

Researchers have suggested that nasal colonization plays a less prominent role in USA300 MRSA infection pathogenesis, compared with non-USA300 MRSA infection, because of the observed low frequency of nasal colonization.⁷ We found no difference in prolonged colonization between residents colonized or infected with USA300 MRSA and residents colonized or infected with non-USA300 MRSA, even after adjusting for other factors associated with prolonged colonization. Our findings, however, are not generalizable to community-dwelling persons who had MRSA detected from a clinical culture representing

an infection. The epidemiology of USA300 MRSA colonization in the community is likely to differ from that in the healthcare setting.

Our results also demonstrate that the risk of prolonged MRSA colonization is lower for patients whose first isolate represents an infection as opposed to colonization. The low colonization rates for patients who had MRSA infection could be the result of their prescribed antibiotic therapy, which could have reduced the likelihood of MRSA colonization while treating the MRSA infection. Patients who had only 1 MRSA-positive culture result may have been transiently colonized.

Our results are limited by the relatively small sample size. In addition, we determined whether MRSA isolates were USA300 MRSA by the presence of specific genes and a specific *spa* type. Although this is an indirect method, it has been validated in our study population and by others.^{3,11} Our study also has a number of strengths. We cultured samples obtained from multiple body sites on a weekly basis for 3 weeks to obtain an accurate measurement of prolonged colonization. In addition, we determined the genotype of our isolates in order to determine whether the same MRSA genotype was responsible for prolonged colonization, thus allowing us to make specific conclusions about prolonged colonization with USA300 MRSA.

In conclusion, the emergence of USA300 MRSA in healthcare facilities, including extended care facilities, is a concern from an infection control perspective.^{2,3} We found no difference in the risk of prolonged colonization in extended care facilities between residents colonized or infected with USA300 MRSA and residents colonized or infected with non-USA300 MRSA. Because colonized patients serve as a source of transmission to others, this finding helps explain how USA300 MRSA is spreading in the healthcare setting.

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Figure 1.

Schematic representation of our retrospective cohort study of residents of extended care facilities of the Veterans Affairs Maryland Health Care System during the period from 2004 through 2007. MRSA, methicillin-resistant *Staphylococcus aureus*.

Table 1
Comparison of Demographic and Clinical Characteristics of Residents of Extended Care Facilities in the Veterans Affairs Maryland Health Care System Who Were Colonized with Methicillin-Resistant *Staphylococcus aureus* (MRSA), 2004–2007

Characteristic	Residents with prolonged colonization with the same genotype (<i>n</i> = 62)	Residents no longer colonized with same genotype (<i>n</i> = 67)	<i>P</i>
First MRSA isolate recovered was USA300	25 (40)	28 (42)	.87
No. of days since first MRSA-positive culture result	111 ± 97	125 ± 85	.39
Time of first MRSA-positive culture result			.22
<3 months before enrollment	35 (56)	29 (43)	
3 to <6 months before enrollment	1 (2)	5 (7)	
6 to <9 months before enrollment	21 (34)	29 (43)	
9–12 months	5 (8)	4 (6)	
Age, years	76 ± 12	73 ± 12	.14
Race			.58
White	39 (63)	39 (58)	
African American	23 (37)	28 (42)	
Level of care			.09
Residential care, hospice, or respite	49 (79)	42 (63)	
Long-term rehabilitation	5 (8)	13 (19)	
Short-term rehabilitation or post-acute care	8 (13)	12 (18)	
Level of dependency			.19
Minimal assistance	20 (32)	20 (30)	
Moderate assistance	24 (39)	18 (27)	
Requires assistance with most activities of daily living	18 (29)	29 (43)	
History of diabetes	27 (44)	27 (40)	.71
Presence of skin breakdown ^a	28 (45)	38 (57)	.19
First MRSA isolate represents			.005
Infection	7 (11)	21 (31)	
Colonization	55 (89)	46 (69)	
No. of MRSA-positive culture results before enrollment			.02
1 positive culture result	25 (40)	41 (61)	
>1 positive culture result	37 (60)	26 (39)	

Note. Categorical data are no. (%) of residents, and continuous data are mean values (± standard deviation).

^a Defined as the presence of a percutaneous device or a pressure ulcer, or receipt of surgery.