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Prevalence, persistence, and microbiology of *Staphylococcus aureus* nasal carriage among hemodialysis outpatients at a major New York Hospital^{★,★}

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Abstract

The study aimed to determine the natural history of *Staphylococcus aureus* nasal colonization in hemodialysis outpatients. Surveillance cultures were taken from patients presenting for hemodialysis or routine care to identify *S. aureus* nasal carriers. A prospective cohort study was performed to identify risks for persistent colonization. Detailed microbiologic and molecular studies of colonizing isolates were performed. Only 23/145 (15.9%) dialysis patients were persistently colonized, and only HIV-positive status was associated with persistence ($P=0.05$). Prior hospitalization was the only risk factor for methicillin-resistant *S. aureus* carriage (OR 2.5, $P=0.03$). In isolates from patients with ≥ 42 days of vancomycin exposure, vancomycin minimum bactericidal concentrations (MBCs) increased with duration of exposure. Among dialysis patients, *S. aureus* colonization was limited and transient; only HIV status was associated with persistence. Nevertheless, duration of vancomycin exposure was associated with increasing vancomycin MBCs. Vancomycin exposure in *S. aureus* carriers may be involved in increasing resistance.

Keywords

Staphylococcus aureus; Hemodialysis; Colonization; Vancomycin

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1. Introduction

Staphylococcus aureus is a leading cause of infection-related morbidity and mortality in the United States (Kleves et al., 2007). Among hemodialysis patients, *S. aureus* is the cause of 70–90% of vascular access infections and related bacteremias that are frequently complicated by endocarditis, metastatic infection, or sepsis, with mortality rates of 20–40% (del Rio et al., 2009; Gould, 2007). Previous studies have established nasal colonization with *S. aureus* as a key risk factor in the epidemiology of these infections (Elie-Turenne et al., 2010; von Eiff et al., 2001). Nasal colonization provides a natural reservoir that facilitates maintenance and propagation of *S. aureus* in human populations. Nasal colonization with *S. aureus* has thus been associated with an increased risk of invasive *S. aureus* infection. (von Eiff et al., 2001) Patients on chronic hemodialysis have been reported to have over twice the rate of *S. aureus* nasal colonization as healthy controls. (Mermel et al., 2010) In cohort studies of dialysis patients, decolonization of *S. aureus* has conversely been shown to decrease *S. aureus* infections (Doebbeling et al., 1994; Kluytmans et al., 1996), albeit transiently due to frequent recolonization. (Bommer et al., 1995) Surprisingly, no prior study has prospectively examined either the natural history of nasal colonization in dialysis patients or the relationship between cumulative antibiotic use and the microbiology of colonizing isolates. We conducted a 2-center, cross-sectional analysis to define risk factors for *S. aureus* nasal colonization in patients receiving chronic hemodialysis and those receiving routine medical care at a major New York City hospital. We then followed the dialysis cohort over a 1-year period to determine the rate of persistent colonization, the incidence of new colonization, and the association between various patient characteristics (including duration of vancomycin exposure) and the microbiology/antimicrobial susceptibility of colonizing isolates.

2. Methods

2.1. Patient population

Chronic hemodialysis patients were recruited from the Rogosin Institute's dialysis centers in Queens and Manhattan, NY. Internal medicine controls were recruited as a convenience sample of patients presenting to the Cornell Internal Medicine Associates clinic in Manhattan, NY. Consenting patients were enrolled from December 28, 2006, to February 9, 2007. At enrollment, all patients completed a basic health questionnaire and underwent nasal cultures for *S. aureus*. In addition to completing the questionnaire, medical records of dialysis patients from the preceding year were reviewed for information on receipt of antibiotics, presence of indwelling catheters/fistulas, and medical history. The dialysis cohort was then followed for a 1-year period, concluding on February 2, 2008. During this period, patients were reevaluated every 4 months by questionnaire and nasal swab for *S. aureus*. Patients who transferred care to another dialysis center, began home or peritoneal dialysis, underwent transplant, died, or refused participation were audited. Institutional review board approval from the Weill Cornell Medical College/New York-Presbyterian Hospital was obtained.

2.2. Data collection

The initial enrollment questionnaire consisted of questions on demographics, history of incarceration or participation in the military, prior Contact Precautions, comorbidities (including HIV, prior intravenous drug use, diabetes, hypertension, liver disease, peripheral vascular disease, chronic obstructive pulmonary disease, cancer, and transplantation), hospitalization in the past year, hospitalization in the past 3 months, use of antibiotics in the past year, and use of antibiotics in the past 3 months. The questionnaire for dialysis patients

also included questions on the reason for hemodialysis, length of time on dialysis, and method of dialysis (catheter, fistula, graft).

2.3. Microbiologic studies

Nasal colonization was defined as any nasal culture positive for *S. aureus*. Persistent colonization was ascertained by repeated nasal swabs in the hemodialysis cohort. Persistent colonization was defined as the presence of 2 or more *S. aureus* isolates of the same clonal complex over at least 2 periods during the study duration. Transient colonization was defined as isolates not associated with persistent colonization. Nasal swabs were obtained by Aimes culturettes using 5 rotations per nares. Swabs were plated within 6 h of collection onto mannitol-salt plates and incubated overnight at 37 °C. Isolates positive for growth on mannitol-salt were plated on tryptic soy + 5% sheep's blood agar plates and incubated overnight at 37 °C. Growth of *S. aureus* on blood agar plates was confirmed by 2 independent methodologies: Staphyloslide reagent (BD, Franklin Lakes, NJ) and VITEK (bioMérieux, Durham, NC) analysis. Resistance to β -lactam agents was determined by ability to grow on Mueller–Hinton (MH) agar with 4% sodium chloride and 6 μ g/mL oxacillin. Minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) testing was determined for each isolate in duplicate. Where results of duplicate testing did not agree, testing was performed a third time, and the mode of 3 tests was taken as the final result. MICs to vancomycin, daptomycin, oxacillin, and linezolid were determined by broth microdilution on Sensititer GPN4F MIC plates using an inoculum of 10^5 CFU/mL in sterile cation-adjusted MH broth (Trek Diagnostics, Cleveland, OH), per Clinical and Laboratory Standards Institute guidelines. Of note, daptomycin wells within Sensititer plates contain calcium, such that the calcium concentration after addition of MH broth is 50 μ g/mL. (Clinical and Laboratory Standards Institute, 2009; Koeth and Thorne, 2010) Aliquots from clear wells were plated onto tryptic soy + 5% sheep's blood agar plates for determination of MBCs to daptomycin, vancomycin, and linezolid. All samples were incubated at 35 °C for 24 h. (Rybak et al., 2008) Vancomycin heteroresistance was determined for each isolate by the Macro Etest-GRD strip, as previously described. (Rybak et al., 2008; Yusof et al., 2008) Isolates that tested positive for vancomycin hetero-resistance were confirmed by repeat Etest-GRD strip analysis. Again, where results of repeat testing did not agree, a third test was performed and the mode of all 3 tests was used as the final result. Molecular analyses included *spa* typing, *SCCmec* typing, and targeted PCR for the Pantón–Valentine leukocidin (PVL) gene and the arginine-catabolic mobile element (ACME), as described in detail elsewhere. (Diep et al., 2008; Mathema et al., 2008; Sinsimer et al., 2005) Multilocus sequence typing (MLST) clonal complexes (CCs) were inferred from *spa* repeat patterns, as described previously (Strommenger et al., 2006).

2.4. Statistical analyses

2.4.1. Patient-level analysis—Logistic regression models were used to determine significant predictors of *S. aureus* (both methicillin-resistant *S. aureus* [MRSA] and methicillin-susceptible *S. aureus* [MSSA]) nasal carriage during the cross-sectional study component as well as predictors of persistent nasal *S. aureus* carriage among the dialysis patient cohort. Variables that were found to be significant predictors of nasal carriage on univariate analysis were included in a multivariate logistic regression model. Fisher exact 2-tailed test was then used to determine the association of HIV status (as a dichotomous variable) with frequency of persistent versus transient *S. aureus* nasal carriage in colonized patients.

2.4.2. Isolate-level analysis—Shapiro–Wilk tests were used to test for normality of vancomycin and daptomycin MBC distributions. As these data were not normally distributed, Spearman rank correlation coefficient was used to determine the strength of

association between these 2 variables. A Jonckheere–Terpstra test for ordered alternatives was used to compare the mean vancomycin and daptomycin MBCs among patients with 0, 1–7, 8–21, 21–42, and greater than 42 days of vancomycin exposure. For all tests and models, statistical significance was set at $\alpha = 0.05$ and 95% CIs. All graphs and calculations were performed using the STATA-11 software (StataCorp LP, College Station, TX).

3. Results

3.1. Risk factors for nasal colonization with *S. aureus*

A total of 320 patients (160 hemodialysis and 160 controls) were recruited, of which 316 (157 hemodialysis and 159 controls) completed enrollment. Characteristics of enrolled patients and the number of patients who completed each follow-up period are shown in Table 1. During period 1, nasal carriage of *S. aureus* was found in 60 patients (19.0%), of which 26 were chronic dialysis patients (43.3%) and 34 were controls (56.7%) (see Table 2). Although the point prevalence of nasal *S. aureus* carriage was numerically higher in the control group than the dialysis group, this difference was not statistically significant. Patients who were colonized with *S. aureus* during period 1 were compared to patients who were not colonized to determine possible risk factors for nasal colonization (see Table 2). This analysis identified no significant risk factors for *S. aureus* nasal carriage when both methicillin-susceptible and -resistant strains were included. A subgroup analysis of MRSA-colonized patients was then performed to determine risk factors specifically associated with MRSA colonization. Although receipt of hemodialysis was associated with an increased risk of MRSA colonization on univariate logistic regression (OR 5.3, $P = 0.03$), this association was not significant on multivariate regression (OR 4.1, $P = 0.08$). On univariate regression, the number of hospitalizations within the prior 3 months (OR 3.2, $P = 0.005$) and in the prior year (OR 1.6, $P = 0.004$) also emerged as risk factors for colonization with MRSA. Because these factors were colinear and hospitalization in the past 3 months was stronger predictor of MRSA colonization, we used this variable for multivariate analysis where it remained significant (OR 2.5, $P = 0.03$), after adjusting for receipt of hemodialysis (see Table 3).

3.2. Patient-specific risk factors for persistent colonization

Among the 157 chronic hemodialysis patients who completed enrollment, factors associated with any and persistent colonization were examined. Sixty-five percent (60/93) of patients who completed follow-up in all 4 study periods were never colonized. In patients who completed at least 2 nasal samplings (not necessarily contiguous), 15.2% (22/145) were transiently colonized and 15.9% (23/145) were persistently colonized (with the same clonal complex strain). Of those patients who were transiently colonized, 2.0% (3/145) had 2 or more positive nasal samplings, but with isolates from a different clonal complex. We identified no significant differences in age, gender, or number of hospitalizations between persistently colonized and non-persistently colonized patients. Among all patients with *S. aureus* colonization, however, HIV-positive status was significantly associated with persistent colonization (4/4 or 100% of HIV-positive patients versus 19/43 or 44.1% of HIV-negative patients were persistently colonized, $P = 0.05$) on analysis by Fisher exact test.

3.3. Microbiology of colonizing isolates and effects of cumulative vancomycin exposure

To examine the relationship between patient characteristics and the microbiology of colonizing isolates, we first compared the antimicrobial susceptibility patterns of colonizing isolates in hemodialysis and control patients. We next examined the association between cumulative vancomycin exposure and the microbiology of colonizing isolates from our hemodialysis cohort to determine if selective antibiotic pressure exerted a change in the antimicrobial resistance pattern of these isolates. Finally, we examined the relationship

between bacterial *spa* type and likelihood of persistent colonization in our hemodialysis cohort to determine if certain bacterial lineages were associated with an increased likelihood of persistent colonization, as previously reported (Hu et al., 1995; Van Belkum et al., 1997).

3.4. Isolates from chronic dialysis patients

Eighty-six *S. aureus* isolates were collected from the 45 dialysis patients with at least one positive culture. Of these, 26 (30.2%) were methicillin resistant. MICs to vancomycin and daptomycin were all within the susceptible range, although one MSSA isolate from the dialysis cohort had a daptomycin MIC of 2 µg/mL—the upper limit of susceptible. MICs to linezolid were within the susceptible range for 59/60 (98.3%) MSSA isolates and 25/26 (96%) MRSA isolates. The remaining 2 isolates had linezolid MICs of 8 µg/mL (Table 4). Screening for vancomycin heteroresistance by Macro Etest-GRD strip testing identified 4/85 (4.8%) MSSA isolates with an MIC 12 to teicoplanin alone or 8 to vancomycin and teicoplanin. No MRSA isolates were identified as vancomycin heteroresistant. Minimum bactericidal testing (MBC) of *S. aureus* isolates against vancomycin and daptomycin revealed a majority of both MSSA and MRSA isolates (78% and 73%, respectively) with vancomycin MBCs of 2 µg/mL or less. The remaining isolates had vancomycin MBCs ranging from 4 to over 16 µg/mL. Similarly, the majority of both MSSA and MRSA isolates had daptomycin MBCs of 0.5 µg/mL or less. Within the remaining MSSA isolates, 3 (5%) had daptomycin MBCs of 1, 4 (6%) had daptomycin MBCs of 2, and 1 (2%) had a daptomycin MBC of 4. There was a slight upward shift in the daptomycin MBCs of the remaining MRSA isolates compared to the MSSA isolates: 5 isolates (19%) had MBCs of 1, and 2 isolates (8%) had MBCs of 2. The distribution of vancomycin and daptomycin MBCs by methicillin susceptibility within each patient cohort is shown in Table 5.

3.5. Isolates from control patients

Of 35 *S. aureus* isolates obtained from control subjects, only 2 (5.7%) were methicillin resistant. All isolates had vancomycin MICs of 0.5 µg/mL, daptomycin MICs of 0.25 µg/mL, and linezolid MICs of 4 µg/mL (see Table 4). In addition, a majority (70% (23/33), $n = 23$) of MSSA isolates from this cohort had MBCs of 2.0 µg/mL or less to vancomycin and MBCs of 0.5 µg/mL or less to daptomycin (51.5%, $n = 17$). Among the remaining MSSA isolates, vancomycin MBCs ranged from 4 to 16 µg/mL and daptomycin MBCs ranged 1–2 µg/mL. One isolate was confirmed as vancomycin heteroresistant by Etest-GRD strip. The remaining MRSA isolates had MBCs of 8 and 16 µg/mL (see Table 5). Neither were vancomycin heteroresistant by Etest GRD strip.

Analyzing all isolates from both dialysis patients and controls, we identified a significant positive association between vancomycin MBC and daptomycin MBC by Spearman rank correlation coefficient ($\rho = 0.52$, $P < 0.0001$).

3.6. Effects of cumulative vancomycin exposure

Analyzing isolates from patients with 42 days of vancomycin exposure, we observed a stepwise increase in vancomycin MBC that paralleled the duration of cumulative vancomycin exposure. In patients with 0 and 1–7 days of cumulative vancomycin exposure, the mean vancomycin MBC was 1.9 (SD 1.1) and 2 (SD 2.2), respectively. Among patients with 8–21 days, 21–42 days, and over 42 days of exposure, mean vancomycin MBCs increased to 3.6 (SD 5.3), 4.1 (SD 6), and 2.3 (SD 2.5), respectively. By contrast, we observed no relationship between cumulative vancomycin exposure and daptomycin MBCs (see Fig. 1). Of note, the overall prevalence of prior vancomycin exposure was high in our dialysis cohort, with 65 patients (41%) having received vancomycin in the prior year and 27 patients (17%) having received vancomycin in the prior 3 months.

3.7. Genotyping of colonizing isolates

No particular *spa* type was associated with an increased risk of persistent colonization. Within the control group, all MRSA isolates belonged to eGenomics *spa* type 2 (Ridom t002), corresponding to MLST CC5. Among the hemodialysis group, 11 MRSA isolates belonged to CC5 (10 *spa* type 2/t002; 1 *spa* type 14/t214); 8 belonged to CC8 (5 *spa* type 1/t008, 2 *spa* type 930/unknown Ridom type, and 1 *spa* type 7/t064); 1 belonged to CC1 (*spa* type 131/t128); and 1 belonged to CC30 (*spa* 16/t018). Of note, all 11 colonizing isolates in the 4 HIV-positive patients belonged to *spa* type 7/t064 (CC8), associated with USA500. Of these, 10 were MSSA, and only 1 was MRSA. By contrast, only 2 *spa* type 1/t008 isolates were consistent with USA300, as determined by targeted PCR for PVL, ACME, and *SCCmec* subtype IVa (see Supplemental Table 1).

4. Discussion

S. aureus is an important cause of infectious-disease morbidity and mortality, largely due to increasing antibiotic resistance among strains (DeLeo and Chambers, 2009). Nasal colonization plays a significant role in both the pathogenesis of staphylococcal infections and the spread of resistance among *S. aureus* strains.(Elie-Turenne et al., 2010; Wagenvoort et al., 2005) Further understanding of the prevalence, natural history, and microbiology of colonizing *S. aureus* strains is therefore key to guiding efforts aimed at reducing the spread of antibiotic-resistant strains. As such, our study aims were to (1) determine the patient risk factors for *S. aureus* nasal carriage and (2) define the natural history, microbiology, and molecular epidemiology of colonizing *S. aureus* strains among chronic dialysis patients.

In the cross-sectional component of our study, we observed a point prevalence of 19% for *S. aureus* nasal carriage among all patients, with a MRSA-specific point prevalence of 4%, similar to prior studies that found an overall prevalence of 16–24% and a MRSA-specific prevalence of 3–7%.(Hidron et al., 2005; Jernigan et al., 2003; Lu et al., 2005) There were no patient-specific risk factors associated with *S. aureus* nasal carriage overall, and only prior hospitalization was found to be a significant risk factor for MRSA-specific nasal carriage (Table 3). Within the hemodialysis cohort, only 31% of patients were positive for *S. aureus* nasal colonization at any time, and only 16% were persistently colonized, consistent with prior studies of *S. aureus* nasal carriage in hemodialysis patients (Table 1). (Johnson et al., 2009; Kluytmans et al., 1996) HIV-positive status was the only risk factor associated with persistent colonization on univariate analysis. Nasal carriage in HIV-infected patients was exclusively due to *spa* type 7/t064 (CC8), an observation that has been reported by others (Cespedes et al., 2005; Roberts et al., 1998; Shet et al., 2009), although the association of *spa* type 7/t064 with persistence has not been reported. In contrast to other studies, we found a very small percentage ($n = 2$, 1.6%) of MRSA strains consistent with USA300 CA-MRSA (Klevens et al., 2007). This likely reflects local epidemiology in the distribution of these strains (as has been detailed in prior studies) (Bhattacharya et al., 2007).

We observed a high degree of vancomycin susceptibility among colonizing isolates in both patient groups, despite considerable prior vancomycin exposure in the hemodialysis cohort. Indeed, only a small number of isolates exhibited MICs at the upper limit of susceptible (2.0 µg/mL), which has been associated with poor treatment responses to vancomycin.(Sakoulas et al., 2004) Notwithstanding, we did note an apparent dose-dependent relationship between cumulative vancomycin exposure and vancomycin MBCs. While this association was lost after 42 days of cumulative exposure, it is interesting to note that 42 days is beyond the duration of most continuous antibiotic courses. As such, this loss of effect at over 42 days may be explained by increasing drug-free intervals in these patients. In contrast, there was no effect of cumulative vancomycin exposure on daptomycin MBCs, suggesting that while heavy vancomycin utilization may slowly erode the susceptibility of *S. aureus* to

vancomycin, it may have a decreased or delayed effect on daptomycin susceptibility. While our analysis did not control for potential confounders, such as duration of hospitalization, the association between prior vancomycin use and vancomycin bactericidal activity has been reported in a previous study by Moise et al. (2008). Interestingly, this study also failed to find a relationship between antecedent vancomycin exposure and daptomycin bactericidal activity. (Moise et al., 2008) The association between cumulative vancomycin exposure and decreased vancomycin susceptibility among colonizing isolates is particularly concerning in light of the high degree of vancomycin exposure in our dialysis cohort (17% exposed within the prior 3 months). As vancomycin bactericidal activity has been shown to predict treatment responses to vancomycin, such changes in bactericidal activity could be an early indicator of decreasing vancomycin efficacy. (Moise et al., 2007; Sakoulas et al., 2004) Future microbiological studies of *S. aureus* colonization may thus wish to include MBC testing given recent concerns for increasing vancomycin resistance in *S. aureus* strains.

Limitations of this study include a relatively small size and significant loss to follow-up within the hemodialysis cohort. Additionally, the point prevalence (in period 1) of *S. aureus* nasal carriage among hemodialysis patients was lower in our study (17%) than in prior studies, (Chow and Yu, 1989; Kluytmans et al., 1996; Mermel et al., 2010) which may have further limited the power of our study to detect patient-specific risk factors associated with persistent colonization. Finally, our limited study size prevented us from analyzing the relationship between HIV status and persistent versus transient colonization by multivariate logistical regression, as there were no transiently colonized HIV-positive patients. As such, our finding that HIV status was associated with an increased likelihood of persistent colonization must be interpreted with some caution, though it has been reported elsewhere. (Miller et al., 2007) Our finding that only prior hospitalization was an independent risk factor for MRSA colonization also echoes results of prior studies (Hidron et al., 2005; Jernigan et al., 2003; Lu et al., 2005) and is important in targeting patient groups for MRSA surveillance, particularly in clinical microbiology laboratories with restricted resources (Harris et al., 2010).

Advantages of this study include its unique cross-sectional/cohort design and prospective surveillance for *S. aureus* carriage. Moreover, it is (to our knowledge) the only study to investigate the relationship between duration of antibiotic exposure and the antimicrobial susceptibility of colonizing isolates.

In conclusion, we report that *S. aureus* nasal carriage among chronic hemodialysis patients is both limited and transient, with only HIV-positive status acting as a significant risk factor for persistent colonization. While most isolates were both methicillin- and vancomycin-susceptible, we found a subtle but potentially significant population-level effect of cumulative vancomycin exposure on vancomycin MBCs. This would suggest that chronic vancomycin exposure in colonized hemodialysis patients may play a role in the emergence of vancomycin resistance among *S. aureus* strains. Additional studies are needed to determine the extent to which vancomycin exposure in colonized patients promotes increasing resistance.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1.

Relationship of cumulative vancomycin exposure group to mean vancomycin minimum bactericidal concentrations (MBCs) (black bars) and mean daptomycin MBCs (gray bars). Mean MBC (in $\mu\text{g/mL}$) is shown above each bar. Group number is displayed on the x -axis. Group 0 = no vancomycin exposure ($n = 31$), group 1 = 1–7 days ($n = 13$), group 2 = 8–21 days ($n = 21$), group 3 = 21–42 days ($n = 6$), group 4 = >42 days ($n = 15$). While mean vancomycin MBC increases in patients exposed to >7 days of vancomycin, mean daptomycin MBC does not.

Table 1

(A) Demographics, clinical characteristics, and *S. aureus* nasal carriage rates among enrolled hemodialysis patients and controls; (B) number of hemodialysis and control patients who completed follow-up within each study period (1–4)

Characteristics	Controls (<i>n</i> = 159)	Hemodialysis (<i>n</i> = 157)	Total (<i>n</i> = 316)	
(A)				
Age (mean [SD])	55.5 (15.7)	58.7 (15.6)	57.1 (15.7)	
% Males/% females	38.9/61.6	58.6/41.4	48.4/51.6	
% subjects with:				
HIV	0.6	8.9	4.7	
IV drug use	0.6	0	0.3	
Diabetes	18.2	36.9	27.5	
Hypertension	48.4	83.4	65.8	
Chronic liver disease	6.2	16.5	11.4	
COPD ^a	3.1	1.3	2.2	
Known malignancy	12.6	3.8	8.2	
Prior transplantation	0	12.1	6.0	
Peripheral vascular disease	2.5	14.6	8.5	
Indwelling catheter/prosthesis	18.2	74.5	46.2	
Hospitalization:				
Within the prior year	17.6	50.9	34.2	
In the past 3 months	3.8	16.5	10.1	
Use of antibiotics in prior year	NA	60.5	NA	
Any positive culture	21.4	30.6	25.9	
>1 positive culture (<i>n</i> = 145) ^b	NA	15.2	NA	
Persistent colonization (<i>n</i> = 145) ^b	NA	15.9	NA	
Patient group Period number All study periods				
	1	2	3	4
(B)				
Control	159	0	0	0
Hemodialysis	157	135	126	103
				93

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Patient group	Period number				All study periods
	1	2	3	4	
Total (<i>n</i>)	316	135	126	103	93

^aChronic obstructive pulmonary disease.

^bNumber of patients available for follow-up in 2 study periods (not necessarily contiguous).

Table 2Patient characteristics associated with *S. aureus* nasal carriage

Characteristic (%)	<i>S. aureus</i> -positive (<i>n</i> = 60)	<i>S. aureus</i> -negative (<i>n</i> = 256)	<u>Univariate logistic regression</u>	
			OR (95% CI)	<i>P</i> value
Hemodialysis	26 (43%)	131 (51%)	0.73 (0.4–1.3)	0.27
Male sex	35 (58%)	118 (46%)	1.64 (0.9–2.9)	0.09
Age (years), mean (SD)	58 (15)	57 (16)	1.003 (0.98–1.02)	0.72
HIV+	4 (7%)	11 (4%)	1.59 (0.5–5.2)	0.49
IV drug use	1 (2%)	0 (0%)	NA	NA
Known diabetes	18 (30%)	69 (27%)	1.16 (0.6–2.2)	0.63
Hospitalizations/year, mean (SD)	0.62 (1.1)	0.66 (1.2)	0.98 (0.77–1.25)	0.89
Hospitalizations/3 months, mean (SD)	0.17 (0.5)	0.11 (0.4)	1.34 (0.71–2.52)	0.36

Table 3

Patient characteristics associated with MRSA nasal carriage

Characteristic	MRSA <i>n</i> = 12		No MRSA ^a <i>n</i> = 304		Univariate logistic regression		Multivariate logistic regression	
					OR (95% CI)	<i>P</i> value	OR (95% CI)	<i>P</i> value
Hemodialysis	10 (83%)		147 (58%)		5.3 (1.2–24.8)	0.03	4.1 (0.9–20.1)	0.08
Male sex	8 (67%)		145 (48%)		2.2 (0.6–7.4)	0.21		
Age (years), mean (SD)	65 (15)		57 (16)		1.03 (0.99–1.08)	0.08		
HIV +	1 (8%)		14 (5%)		1.9 (0.2–15.6)	0.56		
IV drug use	0 (0%)		1 (0.3%)		NA	NA		
Known diabetes	5 (42%)		82 (27%)		1.16 (0.6–2.2)	0.63		
Hospitalizations/year, mean (SD)	1.8 (1.8)		0.61 (1.2)		1.6 (1.2–2.1)	0.004		
Hospitalizations/3 months, mean (SD)	0.5 (0.8)		0.11 (0.4)		3.2 (1.4–7.1)	0.005	2.5 (1.1–5.6)	0.03

^aNo MRSA denotes either no *S. aureus* nasal colonization or colonization with MSSA.

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Summary of minimal inhibitory concentrations (MICs) to various anti-Staphylococcal antibiotics by time period and patient group, respectively

Table 4

MIC (µg/mL)	By period				All periods	Persistent	Transient
	1	2	3	4			
(A) MIC to vancomycin, daptomycin, and oxacillin by time period							
Vancomycin	0.5 (0.5–1.0)	0.5 (0.5–1)	0.5 (0.5)	0.5 (0.5–1)	0.5 (0.5–1.0)	0.5 (0.5–1.0)	0.5 (0.5–1.0)
Daptomycin	0.25 (0.125–0.25)	0.25 (0.25–0.5)	0.25 (0.125–0.5)	0.25 (0.125–2.0)	0.25 (0.125–2.0)	0.25 (0.125–2.0)	0.25 (0.125–0.25)
Oxacillin	0.25 (0.125–4.0)	0.125 (0.125–4.0)	0.125 (0.125–4.0)	0.25 (0.125–4.0)	0.25 (0.125–4.0)	0.25 (0.125–4.0)	0.25 (0.125–4.0)
Linezolid	2 (1–4)	2 (1–8)	2 (1–8)	2 (1–4)	2 (1–8)	2 (1–8)	2 (1–8)
Total observations (<i>n</i>)	60	19	25	17	121	66	20
MIC (µg/mL)	Hemodialysis		Controls		All patients		
(B) MIC of the same antibiotics by patient group							
Vancomycin	0.5 (0.5–1.0)	0.5 (0.5)	0.5 (0.5–1.0)				
Daptomycin	0.25 (0.125–2.0)	0.25 (0.25)	0.25 (0.125–2.0)				
Oxacillin	0.25 (0.125–4.0)	0.125(0.125–4.0)	0.25 (0.125–4.0)				
Linezolid	2 (1–8)	2 (1–4)	2 (1–8)				
Observations (<i>n</i>)	86	35	121				

In A, values shown are median MICs with the MIC range in parentheses. In B, the number of total observations (n) in each group is listed in the bottom row of each table.

Table 5

MBCs to vancomycin and daptomycin among MSSA and MRSA isolates within each patient group (hemodialysis cohort and normal controls)

MBC (µg/mL)	Dialysis cohort		Controls	
	No. of MSSA isolates (%)	No. of MRSA isolates (%)	No. of MSSA isolates (%)	No. of MRSA isolates (%)
Vancomycin				
2	47 (78)	19 (73)	23 (70)	0 (0)
4	8 (13)	5 (19)	1 (3)	0 (0)
8	2 (3)	1 (4)	3 (9)	1 (50)
16	3 (5)	1 (4)	6 (18)	1 (50)
Daptomycin				
0.25	17 (28)	5 (19)	0 (0)	0 (0)
0.5	35 (58)	14 (54)	17 (52)	1 (50)
1.0	3 (5)	5 (19)	12 (36)	0 (0)
2.0	4 (6)	2 (8)	4 (12)	1 (50)
4.0	1 (2)	0 (0)	0 (0)	0 (0)
Total no. of isolates	60 (100)	26 (100)	33 (100)	2 (100)

Values shown are the number of isolates within each MBC range with percentage shown in parentheses.