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Poor Functional Status Is an Independent Predictor of Surgical Site Infections Due to Methicillin-Resistant *Staphylococcus aureus* in Older Adults

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Abstract

BACKGROUND—Methicillin-resistant *Staphylococcus aureus* (MRSA) has become a common surgical site infection (SSI) pathogen, particularly in older adults. Risk factors for MRSA SSI in elderly patients have not been described.

METHODS—A nested case–control study was conducted. Patients were enrolled from seven study hospitals (one medical center and six community hospitals) between January 1, 1998, and April 1, 2003. Risk factors for MRSA SSI were identified by comparing cases with two reference groups: uninfected surgical patients and patients with SSI due to methicillin-susceptible *S. aureus* (MSSA). Two separate multivariate models were created using logistic regression and then compared and contrasted.

RESULTS—Eighty-six patients with MRSA and 64 with MSSA SSI were identified. One hundred sixty-seven uninfected surgical patients were selected. In multivariate analysis using uninfected surgical patients as controls, requiring assistance in three or more activities of daily living (ADLs) was an independent risk factor for MRSA SSI (odds ratio (OR) = 2.73, 95% confidence interval (CI) = 1.16–6.46). Using patients with MSSA SSIs as a reference group, requiring assistance in three or more ADLs was also a significant predictor for MRSA SSI (OR = 3.78, 95% CI = 1.43–9.98) in multivariate analysis. Other independent predictors included Charlson score, wound class, and surgical duration. Lack of independence in ADLs was an independent risk factor for MRSA SSI in elderly patients in both models.

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CONCLUSION—Poor functional status (requiring assistance in ≥3 ADLs) was specifically associated with MRSA SSI. Functional status is an objective, readily available variable that can be used to stratify patients at risk for MRSA SSI.

Keywords

MRSA; surgical site infection; elderly

With the increasing age of the U.S. population, it is estimated that the number of older adults undergoing surgery will increase from 40 million in 2010 to 71 million by 2030.[1] Surgical site infection (SSI) accounts for 11% of all nosocomial infections in patients aged 65 and older.[2] As the number of older adults who undergo surgery increases, the frequency of SSI in this vulnerable population will probably increase as well. This greater frequency of SSI is particularly troubling, because SSI is associated with adverse outcomes in older adults. A recent study detailed how SSI in older adults was associated with adverse clinical outcomes; subjects with SSI had more than twice the mortality risk than uninfected operative controls, a more than 2-week longer hospitalization, and more than $40,000 higher hospital charges.[3]

The most common cause of SSI is *Staphylococcus aureus*. Methicillin-resistant *S. aureus* (MRSA) has emerged as the most common pathogen causing invasive SSI. The prevalence of MRSA SSI increased from less than 15% in 2000 to 20% by 2005.[4] MRSA SSI is associated with a significant adverse attributable effect on the patient and on the healthcare system. Identifying at-risk populations for MRSA SSI is particularly important, because routine preoperative antimicrobial prophylaxis does not cover MRSA, and specific interventions can be designed to prevent MRSA SSI.

Data pertaining to risk factors for MRSA SSI in the general population have been recently published; specific risk factors included lack of independence with activities of daily living (ADLs) and prolonged duration of surgery,[5] but to the authors' knowledge, no study has examined risk factors of SSI caused by MRSA exclusively in elderly patients. Thus, the objective of the current study was to identify risk factors for MRSA SSI specifically in older adults.

METHODS

Study Design and Study Population

This was a retrospective nested case–case–control study. The study population was a subset of patients from a larger cohort study that was designed to assess the epidemiological outcomes of patients with SSI due to *S. aureus*.[5] Study hospitals included Duke University Medical Center (a 750-bed tertiary care hospital) and six community hospitals that are members of the Duke Infection Control Outreach Network in North Carolina and Virginia (bed size range 102–305, mean 208). Patients were included in the study if they underwent surgery between January 1, 1998, and April 1, 2003. All study patients were aged 65 and older.

Cases were patients who developed MRSA SSI. Two groups of control patients were studied. Infection control practitioners prospectively identified case patients with MRSA SSI and control patients with SSI due to methicillin-susceptible *S. aureus* (MSSA) using standard criteria from the Centers for Disease Control and Prevention (CDC) and National Nosocomial Infection Surveillance System (NNIS).[6] Surveillance methods were the same in all study hospitals. SSI was identified through a combination of review of microbiology culture reports, screening of operative patients for readmission to the hospital after surgery, and clinical rounds by infection control practitioners. In addition, questionnaires were provided to surgeons to help identify SSIs that occurred after discharge.[5]

The first control group included uninfected patients who underwent surgery and did not develop SSIs, as confirmed by chart review and record of microbiology laboratories. Uninfected controls were frequency matched to cases according to procedure type, year, and hospital in a 1:1 ratio. The second control group included patients who developed MSSA SSI. Infection control practitioners prospectively identified control patients with MSSA SSI using the same standard CDC and NNIS criteria and procedures as used to identify MRSA SSI as noted above.[6]

Variables

Demographic, microbiological, and perioperative data were prospectively collected on all surgical patients and stored in Infection Control Operative databases. Perioperative data included duration of procedure, wound class, and American Society of Anesthesiologists (ASA) physical classification score.[7] Additional data retrospectively collected from the patient chart were sex, race, age, admission source, insurance type, body mass index, the presence of comorbid conditions or any catheter at the time of hospital admission or surgery, prior intensive care unit stay, and functional status, determined according to independence with ADLs (dressing, bathing, feeding, ambulation, bowel continence, and urinary continence).[8] Perioperative glucose levels and antimicrobial prophylaxis data were retrospectively collected from patients' medical records. Antimicrobial prophylaxis was deemed appropriate if an appropriate antimicrobial agent was given within 2 hours before the surgery, according to published guidelines.[9] McCabe Score[10] at the time of hospital admission (which reflects acute severity of illness) was retrospectively determined according to chart review, and Charlson score[11] (which reflects severity of underlying chronic illness) was calculated. Surgical duration was dichotomized using procedure-specific NNIS cut points.[12] A binary variable for functional status and an ordinal variable for Charlson score were created. Low functional status was defined as lack of independence in three or more ADLs. Charlson score was categorized into three groups: patients with a score of 0 in the first group; patients with a score of 1 to 2 in the second group; and patients with a score of 3 or greater in the third group. BMI greater than 30 was considered obese.

Statistical Analysis

The *t*-test or the Wilcoxon Rank Sum test was used to analyze continuous variables, and chi-square or Fisher exact test was used for dichotomous variables in baseline comparisons. Conditional logistic regression was performed when comparing MRSA SSI cases with matched uninfected controls. Traditional logistic regression was used when comparing patients with MRSA SSI with patients with MSSA SSI. For model building, variables with a $P < .20$ in bivariate analysis were included as candidate variables. Backward selection was used to select for variables in the final model. Final models included only variables with adjusted $P < .05$. All candidate variables were checked for confounding. Confounders were defined as variables that changed the beta coefficients of selected variables by more than 10% when removed from the model. Confounding variables were added back into the final model. Missing data were imputed by the mean for continuous variables or the mode for categorical variables when more than 5% of data was missing. Dummy variables were created if bias occurred after imputation to account for missing data. All analyses were performed using SAS (9.1, SAS Institute, Inc., Cary, NC).

RESULTS

Patients with MRSA SSI Compared with Uninfected Patients

Eighty-six patients with MRSA SSI were identified and matched with 167 uninfected surgical patients (Table 1). Mean ages of cases and controls were similar (case, 73.4 ± 5.7; control, 73.7 ± 6.1; $P = .85$). Thirty-seven percent of cases and 47% of controls were male ($P = .15$). The most common type of surgery was cardiothoracic surgery (case, 40%; control, 45%; *P* = .41), followed by orthopedic surgery (case, 40%; control; 37%; *P* = .64). Twenty-five patients (15%) in the control group and 11 (13%) in the case group had hip replacement. Compared to controls, cases had a higher frequency of congestive heart failure (case, 38%; control, 20%; *P* = .002), chronic obstructive pulmonary disease (case, 20%; control, 9%; *P* = .009) and renal disease (case, 13%; control, 5%; *P* = .02). Cases had poorer functional status than controls and more often lacked independence in ADLs, including ambulation (45% vs 28%; *P* = .009), bathing (37% vs 15%; *P* < .001), dressing (37% vs 15%; *P* < .001) and feeding (15% vs 6%; *P* = .02) Forty-two percent of cases and 30% of controls had surgical duration greater than the 75th percentile of the NNIS cut point duration (*P* = .05). There were also more patients with wound class greater than 1 (e.g., contaminated or dirty) in the case group (case, 22%; control, 10%; *P* = .007).

In multivariate analysis, independent predictors of MRSA SSI included lack of independence in ADLs, Charlson score, and wound class (Table 2). Patients who lacked independence with three or more ADLs had a greater risk for MRSA SSI than those who lacked independence in fewer than three ADLs (OR = 2.73, 95% confidence interval (CI) = 1.16–6.46). Using a Charlson score of 0 as the reference group, patients with a Charlson score of 1 or 2 had almost four times the risk of MRSA SSI (OR = 3.93, 95% CI = 1.48–10.43) and patients with a Charlson score of 3 or greater had approximately six times the risk of MRSA SSI (OR = 5.72, 95% CI = 1.48–16.86). Wound class greater than 1 was also a risk factor for MRSA SSI (OR = 9.12, 95% CI = 1.86–44.67). There were no confounders or significant interactions between variables in the final model.

MRSA SSI Compared with MSSA SSI

Sixty-four patients with MSSA SSI were identified (Table 1). They were similar in age, sex, and types of operative procedures to the 86 patients with MRSA SSI. The most common type of surgery was orthopedic surgery (case, 40%; MSSA controls, 44%; *P* = .61), followed by cardiothoracic surgery (case, 40%; MSSA controls, 34%; *P* = .20). Eleven patients (13%) in the MRSA case group and seven (11%) in the MSSA control group had hip replacement. Cases with MRSA SSI (38%) more frequently had congestive heart failure than did patients with MSSA SSI (19%; *P* = .01). Patients with MRSA SSI (33%) were more likely to be admitted from other institutions, including nursing homes and rehabilitation centers, than were patients with MSSA SSI (17%; *P* = .04). Moreover, MRSA cases more frequently had a lack of independence with ambulation (45% vs 23%; *P* = .009), bathing (37% vs 13%; *P* = .003), dressing (37% vs 13%; *P* = .003) and feeding (15% vs 2%; *P* = .03). Forty-two percent of patients in the case group and 25% of patients in the MSSA control group had surgical duration longer than the 75th percentile cut-point (*P* = .03).

In the multivariate logistic model, independent predictors of MRSA SSI included lack of independence with ADLs, Charlson score, wound class, and surgical duration (Table 2). Lack of independence with three or more ADLs increased risk for MRSA SSI (OR = 3.78, 95% CI = 1.43–9.98). Patients with a Charlson score of 1 or 2 had almost four times the risk of MRSA SSI as those with a Charlson score of 0 (OR = 3.93, 95% CI = 1.35–11.49), and patients with a Charlson score of 3 or greater had approximately six times the risk of MRSA SSI as did patients with a Charlson score of 0 (OR = 5.75, 95% CI = 1.86–17.78). A surgical duration longer than the 75th percentile of the NNIS cut-point resulted in a greater risk of MRSA SSI than of MSSA SSI (OR = 3.45, 95% CI = 1.53–7.80). There were no confounders or significant interactions between model variables in the final model.

Comparing and Contrasting the Two Models

Charlson score, lack of independence in three or more ADL, and a wound class greater than 1 were independent risk factors for MRSA SSI in both models, regardless of the type of control group used. This indicates that these variables were independently associated with MRSA SSI, as opposed to SSI due to *S. aureus* in general (MRSA or MSSA). Longer operative duration was associated with greater risk for MRSA SSI when patients with MSSA SSI were used as controls, but not when uninfected controls were used.

DISCUSSION

This is the first study to identify risk factors for MRSA SSI in older patients. The results encompassed 318 patients from seven hospitals over 5 years. Because two different types of control group were used, it was possible to differentiate between risk factors for MRSA SSI and SSI due to *S. aureus* in general and to identify risk factors specifically associated with MRSA SSI in older adults. Lack of independence in three or more ADLs was associated with approximately three times greater risk for MRSA SSI, regardless of the type of control group used.

Lack of independence with ADLs has been recognized as a risk factor for higher costs and 1-year mortality in older adults after hospitalization.[13,14] Previous studies have also shown immobility to be an independent risk factor for MRSA colonization in long-term care facilities.[15,16] A post hoc analysis to explore the effect of each individual ADL in this study (data not shown) indicated that requiring assistance in bathing or dressing put patients at highest risk of MRSA SSI. One possible explanation for these findings is that, because these patients require more-frequent and longer contact with caregivers during hospitalization or in long-term care facilities than individuals with independent function, they were at greater risk for preoperative MRSA colonization. This association between functional status and MRSA SSI represents a potential vicious circle; patients who lack independence with ADLs are prone to infection,[5] and infection in turn may worsen functional status. One might also hypothesize that lack of independence in ADLs is a surrogate or intermediate factor related to a long-term facility population, although in this study, the association between lack of independence in ADLs and MRSA SSI was independent and unaffected by the status of preoperative residence in a long-term care facility. Ultimately, the causal relationship between poor functional status and MRSA SSI needs to be studied further.

The association between risk for MRSA SSI and Charlson score and wound class are consistent with previous studies of risk factors for SSI due to various types of pathogens in the general population[17,18] and in older adults. One unexpected finding was the association between a lower risk for MRSA SSI and history of myocardial infarction when cases were compared with uninfected controls, but myocardial infarction was not a significant predictor of MRSA SSI in univariate analysis and was included only in multivariate analysis because the *P*-value for the association between myocardial infarction and MRSA SSI was less than .20. If a more stringent *P*-value, such as .05, had been used to select variables for multivariate modeling, myocardial infarction would not have been included in multivariate analyses. Caution should also be taken with regard to interpretation of the lack of protective effect of appropriate antibiotic prophylaxis on MRSA SSI. Appropriate antibiotic prophylaxis, as defined in this study and by current guidelines,[6] does not necessarily provide coverage for MRSA. Thus, it was not surprising in this study that appropriateness of antibiotic prophylaxis was not associated with a lower risk of MRSA SSI.

There are a few limitations to this study. First, much of the patient data was collected retrospectively, so it has the inherent weaknesses of a retrospective study. Nevertheless, it was attempted to minimize biases by using standard and clearly defined procedures for extracting data. Different infection control personnel conducted surveillance for SSI at each site. Thus, there might have been some differences in surveillance and case-finding methodology and accuracy, although because SSIs were identified prospectively using standard CDC criteria at all study sites for SSI diagnosis, and SSI was restricted to infections categorized as deep incision or organ–space, the specificity and accuracy of SSI case-finding was optimized. No molecular studies were performed in this study, so the contribution of community-acquired MRSA cannot be explored, although because the study was conducted during 1998 to 2003, it is likely that few pathogens were community-acquired MRSA.[19]

Functional status is a strong predictor of invasive MRSA SSI in older adults and is independently associated with MRSA SSI after controlling for admission from a long-term care facility, body mass index, and other severity-of-illness markers. Because MRSA has emerged as the primary pathogen causing SSI and because MRSA SSIs are particularly devastating in older adults, interventions such as screening patients for targeted interventions and changing antimicrobial prophylaxis to provide MRSA coverage should be considered. Functional status measures are readily available and easily calculated and should be used to target older adults for interventions to prevent MRSA SSI. Future studies on prevention of MRSA SSI in these high-risk older adults are warranted.

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Table 1

Comparison of Characteristics of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Cases with Uninfected Controls and Methicillin-Susceptible *S. aureus* (MSSA) Controls

Variable	MRSA (N = 86)	No Infection (N = 167)	OR (95% CI)	*P*-Value	MSSA (N = 64)	OR (95% CI)	*P*-Value
Demographic							
Age, mean ± SD (range)	73.4 ± 5.7 (65–94)	73.7 ± 6.0 (65–94)	–	.85	73.0 ± 5.3 (65–87)	–	.67
Aged ≥75, n (%)	25 (29.1)	63 (37.7)	0.59 (0.33–1.07)	.17	20 (31.2)	0.90 (0.45–1.82)	.08
Male, n (%)	32 (37.2)	78 (46.7)	0.72(0.41–1.25)	.15	33 (51.6)	0.56 (0.29–1.07)	.08
White, n (%)	63 (73.2)	139 (84.2)	0.55 (0.28–1.08)	.06	53 (82.8)	0.57 (0.25–1.27)	.17
Private insurance, n (%)	3 (3.6)	10 (6.0)	1.27 (0.33–4.88)	.55	0	–	–
Admission not from home, n (%)	25 (32.9)	50 (30.9)	0.92 (0.49–1.73)	.75	10 (17.0)	2.40 (1.05–5.52)	.04
Comorbidities, n (%)							
Obesity (body mass index, kg/m^2, >30.0)	26 (32.9)	36 (22.2)	1.58 (0.85–2.92)	.07	24(10.0)	0.72 (0.36–1.43)	.38
Diabetes mellitus	28 (32.6)	47 (28.1)	1.20 (0.67–2.16)	.47	13 (20.3)	1.89(0.88–4.04)	.09
Diabetes mellitus with end organ damage	4 (4.7)	6 (6.6)	1.09 (0.49–2.45)	.68	3 (4.7)	0.99 (0.46–2.14)	.99
Myocardial infarction	19 (22.1)	51 (30.5)	0.60 (0.31–1.73)	.15	15 (23.4)	0.93 (0.43–2.00)	.85
Congestive heart failure	33 (38.4)	34 (20.4)	3.21 (1.61–6.40)	.002	12 (18.8)	2.70 (1.26–5.79)	.01
Perivascular disease	16 (18.1)	30 (18.0)	0.86 (0.41–1.84)	.90	9 (14.1)	1.40 (0.57–3.40)	.46
Cerebrovascular accident	12 (13.9)	16 (9.6)	1.26 (0.55–2.87)	.29	5 (7.8)	1.91 (0.64–5.74)	.24
Chronic obstructive pulmonary disease	18 (20.9)	15 (9.0)	2.77 (2.30–5.90)	.009	15 (23.4)	0.87 (0.40–1.88)	.71
Renal disease	11 (12.8)	8 (4.8)	2.92 (1.02–8.36)	.02	4 (6.3)	2.20 (0.67–7.26)	.18
Charlson score							
0	8 (9.3)	42 (25.1)	1	—	18 (28.1)	1	—
1 or 2	40 (46.5)	59 (35.3)	3.22 (1.30–7.98)	.01	30 (46.9)	3.00 (1.15–7.82)	.02
≥3	38 (44.2)	29 (17.4)	4.71 (1.77–12.56)	.002	16 (25.0)	5.34 (1.93–14.77)	.002
Taking immunosuppressants	11 (13.4)	12 (7.4)	1.73 (0.72–4.13)	.13	4 (6.5)	2.04 (0.75–5.60)	.18
Preoperative functional status, n (%)							
Need assistance in							
Ambulation	37 (45.1)	46 (28.4)	2.08 (1.06–4.09)	.009	14 (23.3)	2.70 (1.29–5.66)	.009
Bathing	30 (36.6)	25 (15.4)	3.78 (1.72–8.34)	.001	8(13.3)	3.75 (1.57–8.95)	.003
Dressing	30 (36.6)	25 (15.4)	3.78 (1.72–8.34)	.001	8 (13.3)	3.75 (1.57–8.95)	.003
Feeding	12 (14.6)	9 (5.6)	2.71 (1.03–7.17)	.02	1 (1.7)	9.94 (1.26–78.74)	.03

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Variable	MRSA (N = 86)	No Infection (N = 167)	OR (95% CI)	*P*-Value	MSSA (N = 64)	OR (95% CI)	*P*-Value
Bowel incontinence	2 (2.4)	4 (2.5)	0.87 (0.14–5.32)	>.99	0 (0)	—	—
Urine incontinence	3 (3.7)	6 (3.7)	0.83 (0.18–3.79)	>.99	2 (3.4)	1.08 (0.18–6.69)	>.99
Lack of independence in >3 activities of daily living	30 (34.9)	25 (15.0)	3.26 (1.52–7.03)	.029	7 (10.9)	4.36 (1.77–10.75)	.01
Hospital and surgical variables							
Postoperative glucose > 200 mg/dL, n (%)	32 (39.5)	59 (37.6)	1.14 (0.52–2.07)	.77	17 (29.3)	1.58 (0.77–3.24)	.21
Preoperative length of stay, mean ± SD	2.4 ± 3.6	1.6 ± 2.6	1.10 (1.00–1.21)	.08	1.2 ± 2.4	1.15 (1.01–1.31)	.02
Orthopedic surgery, n (%)	34 (39.5)	61 (36.5)	—*	.64	28 (43.8)	0.84 (0.44–1.62)	.60
Cardiothoracic surgery, n (%)	34 (39.5)	75 (44.9)	—*	.41	19 (29.7)	1.55 (0.78–3.08)	.21
American Society of Anesthesiologists physical classification score >4, n (%)	33 (38.8)	67 (40.4)	1.12 (0.48–2.60)	.81	21 (33.3)	1.27 (0.64–2.51)	.49
Appropriate perioperative antibiotics, n (%)	59 (72.0)	122 (75.3)	1.02 (0.52–2.02)	.57	45 (76.3)	0.80 (0.37–1.72)	.57
Wound class >1 (not clean), n (%)	19 (22.1)	16 (19.7	7.58 (1.61–35.67)	.007	7 (10.9)	2.31 (0.91–5.89)	.07
Repeat surgery, n (%)	9 (10.5)	16 (9.6)	0.99 (0.42–2.38)	.82	8 (12.5)	0.81 (0.30–2.24)	.69
Surgical time >75% of cut point, n (%)	36 (41.9)	49 (29.3)	1.94 (1.04–3.61)	.05	16 (25.0)	2.20 (1.08–4.49)	.03

SD = standard deviation; OR = order ratio.

*Matched criteria, including procedure type, year, and hospital.

Table 2

Multivariate Analysis of Risk Factors for Surgical Site Infection in Cases with Methicillin-Resistant *Staphylococcus aureus* Versus Controls

	Multivariate Odds Ratio (95% Confidence Interval) *P*-Value	
Predictor	**No Infection**	**Methicillin-Susceptible *Staphylococcus aureus***
Charlson score		
0 (reference)	1.0	1.0
1 or 2	3.93 (1.48–10.43) .006	3.93 (1.35–11.49) .01
≥3	5.72 (1.94–16.86) .002	5.75 (1.86–17.78) .002
Needed assistance with ≥3 activities of daily living at admission	2.73 (1.16–6.46) .02	3.78 (1.43–9.98) .007
Wound class > 1	9.12 (1.86–44.67) .006	3.85 (1.28–11.54) .02
Surgical time >75th percentile of Centers for Disease Control and Prevention cut point	Not included in model	3.45 (1.53–7.80) .003
History of myocardial infarction	0.35 (0.17–0.75) .006	Not included in model