Epidemiol. Infect. (2016), **144**, 647–651.
doi:10.1017/S0950268815001132

SHORT REPORT
Risk factors for methicillin-resistant *Staphylococcus aureus* skin and soft tissue infection in MRSA-colonized patients discharged from a Veterans Affairs hospital

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Received 4 February 2015; Final revision 6 May 2015; Accepted 7 May 2015; first published online 21 July 2015

SUMMARY

Currently, limited studies have quantified the risk of methicillin-resistant *Staphylococcus aureus* (MRSA) skin and soft tissue infections (SSTIs) for MRSA-colonized patients on discharge from hospital. Our retrospective, case-control study identified independent risk factors for the development of MRSA SSTIs among such patients detected by active MRSA nasal screening in an acute care hospital by PCR on admission, and bacteriological cultures on discharge. Cases were MRSA-colonized patients aged ⩾18 years who developed a MRSA SSTI post-discharge and controls were those who did not develop a MRSA SSTI post-discharge. Controls were matched to cases by length of follow-up (±10 days) for up to 18 months. Potential demographic and clinical risk factors for MRSA infection were identified using electronic queries and manual chart abstraction; data were compared by standard statistical tests and variables with P values ⩽0·05 in bivariable analysis were entered into a logistic regression model. Multivariable analysis demonstrated prior hospital admission within 12 months ($P = 0{\cdot}02$), prior MRSA infection ($P = 0{\cdot}05$), and previous myocardial infarction ($P = 0{\cdot}01$) were independently predictive of a MRSA SSTI post-discharge. Identification of MRSA colonization upon admission and recognition of risk factors could help identify a high-risk population that could benefit from MRSA SSTI prevention strategies.

Key words: Infection, MRSA, skin, soft tissue, surveillance.

Methicillin-resistant *Staphylococcus aureus* (MRSA) causes significant morbidity in the United States, especially in skin and soft tissue infections (SSTIs) for which the risk is increased by nasal MRSA colonization [1–3]. The Veterans Health Administration recently implemented the 'MRSA bundle' which has been shown to reduce the rate of healthcare-associated MRSA infections in the hospital but its impact post-discharge is unknown [4]. Limited data suggest that patients with MRSA carriage during their hospital stay have an increased risk of SSTIs post-discharge [3]. We sought to assess the risk factors for MRSA SSTIs among MRSA-colonized patients on the reasoning that identifying MRSA colonization upon admission might help to identify a high-risk population that could benefit from strategies to decrease the risk for subsequent MRSA SSTIs.

We included data from the Audie L. Murphy Division of the South Texas Veterans Health Care System from

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1 September 2009 to 31 August 2011 and performed a retrospective, case-control, matched study to evaluate the risk factors for MRSA SSTIs among patients found to be colonized during an acute care hospital admission. Patients were identified using electronic surveillance software (Theradoc® Clinical Surveillance System Hospira, USA). These patients underwent nasal screening for MRSA using PCR (Gene expert MRSA, Cepheid®, USA) on admission or transfer, and nasal cultures on discharge (BDL Chromagar® MRSA, Becton Dickinson and Co. USA).

Only MRSA-colonized patients aged ⩾18 years were included in this study and cases were those who developed a MRSA SSTI post-discharge. Cases were grouped as surgical site and non-surgical site infections for subgroup analysis. Controls were those patients who did not develop a MRSA SSTI post-discharge. Controls were matched to cases by length of follow-up (±10 days); end of follow-up was defined as the last evaluation within our system. Three controls were randomly selected for each case using the random number generator function in Microsoft Excel (Microsoft Corporation, USA) and both cases and controls were followed up to 18 months post-discharge. Patients with MRSA infection on admission, and those admitted to long-term care, spinal cord injury, or bone marrow transplantation units were excluded.

Patients' demographic and clinical characteristics were identified using electronic queries and manual chart abstraction from the electronic medical record. Index admission was the first admission during the study period when the patient was found to be colonized with MRSA. Patient comorbidities were used to calculate the Charlson comorbidity index [2, 5]. Risk factors were selected based on literature review and baseline characteristics and outcomes are listed in Table 1.

Statistical analyses were conducted using JMP 8.0® (SAS Institute Inc., USA). Characteristics of cases and controls were compared using χ^2, Fisher's exact, and Wilcoxon rank sum tests. All variables with $P \leqslant 0{\cdot}05$ in bivariable analysis were entered simultaneously into a logistic regression model to identify risk factors independently associated with MRSA SSTI. Variables with $P \leqslant 0{\cdot}05$ in the multivariable model were considered to be independent predictors of outcome. A sensitivity analysis was also conducted using a cut-off P value of $\leqslant 0{\cdot}20$ for inclusion in the multivariable model. A subgroup analysis was conducted for those patients with surgical site infections.

We identified 28 cases and 84 controls with similar demographic variables and clinical characteristics. Bivariable analysis of cases *vs.* controls identified prior hospital admission within 12 months (68% *vs.* 39%, $P < 0{\cdot}01$), MRSA infection prior to hospital admission (29% *vs.* 8%, $P = 0{\cdot}01$), history of myocardial infarction (MI) (29% *vs.* 5%, $P < 0{\cdot}01$), and peripheral vascular disease (PVD) (29% *vs.* 8%, $P = 0{\cdot}01$) as risk factors for MRSA SSTI post-discharge. Each of these risk factors, with the exception of PVD, was shown by multivariable analysis to be independently predictive of a MRSA SSTI post-discharge (Table 2). In a sensitivity analysis, using a cut-off P value of $\leqslant 0{\cdot}20$ for inclusion in the multivariable model, these same three characteristics remained independently predictive of infection post-discharge.

Twenty-one of the 28 cases were non-surgical-site cases and matched with 63 controls. Analysis of this subgroup identified MRSA infection prior to hospital admission [bivariable: 33% *vs.* 8%, $P < 0{\cdot}01$; multivariable: odds ratio (OR) 4·8, 95% confidence interval (CI) 1·2–20·6, $P = 0{\cdot}03$], history of MI (bivariable: 28% *vs.* 6%, $P < 0{\cdot}01$; multivariable: OR 6·4, 95% CI 1·5–31·4, $P = 0{\cdot}02$) and current alcohol abuse (bivariable: 25% *vs.* 12%, $P = 0{\cdot}05$; multivariable: OR 4·3, 95% CI 1·2–15.8, $P = 0{\cdot}03$) as risk factors for MRSA SSTI post-discharge.

MRSA is a frequent cause of SSTI, but literature regarding the risk of infection after MRSA colonization in the setting of active surveillance is scarce. Furthermore, MRSA colonization among veterans has been shown to be associated with increased risk of hospital readmission, increased mortality, and MRSA infections [2, 6, 7]. In this study, we found that risk factors for MRSA SSTI post-discharge included prior hospital admission within 12 months, MRSA infection prior to hospital admission, and a history of MI.

Patients known to be colonized by MRSA can develop an infection within weeks, or even months, after initial colonization. Davis *et al.* reported that adult patients found to be colonized with MRSA during active screening were 10 times more likely to develop MRSA infections; two of the patients in their cohort developed infections >250 days after colonization [8]. Furthermore, Huang *et al.* [7] demonstrated an increased risk for MRSA infection 18 months after colonization and Advani *et al.* [9] found 10% of MRSA-colonized children developed an infection within a year after hospital discharge. An additional study reported an increased risk of

. https://doi.org/10.1017/S0950268815001132

Table 1. *Comparison of baseline characteristics and outcomes between patient cases and controls as risk factors for MRSA skin and soft tissue infection*

Baseline characteristics	Cases ($N = 28$)	Controls ($N = 84$)	P value
Age (years), median (IQR)	60 (53–73)	64 (59–75)	0·11
Male sex	96	95	1·00
New acquisition MRSA colonization	32	17	0·08
Immunocompromised from time of admission	14	24	0·29
Central line from time of admission	21	26	0·61
Previous surgery in 12 months prior to colonization	14	20	0·48
Previous MRSA infection before admission	29	8	0·01
Previous admission to hospital in last 12 months prior to colonization	68	39	<0·01
Admission to long-term care facility with 12 months prior to colonization	18	25	0·44
Admission to ICU within 12 months prior to colonization	11	8	0·71
Comorbid conditions	93	99	0·15
Myocardial infarction	29	5	<0·01
Congestive heart failure	14	23	0·34
Coronary artery disease	39	33	0·57
Peripheral vascular disease	29	8	0·01
Cerebrovascular accident with mild or no residual or transient ischaemic attacks	11	12	1·00
Dementia	14	14	1·00
Chronic obstructive pulmonary disease	25	21	0·69
Connective tissue disease	4	1	0·44
Peptic ulcer disease	4	2	1·00
Diabetes mellitus no organ damage	18	21	0·69
Diabetes mellitus organ damage	39	27	0·24
Chronic kidney disease – moderate to severe	29	21	0·44
Hemiplegia	7	1	0·15
Active leukaemia (acute or chronic)	4	2	1·00
Active lymphoma	7	0	0·06
Active solid tumour	7	18	0·23
Metastasis	7	7	1·00
Liver disease – mild	14	8	0·46
Liver disease – moderate or severe	7	13	0·51
AIDS	0	1	1·00
Current intravenous substance abuse	0	1	1·00
Current alcohol abuse	25	12	0·13
Current smoker	39	21	0·06
Chronic skin condition	7	6	1·00
Homeless	4	6	1·00
Pressure ulcer	7	2	0·26
Steroid therapy	14	14	1·00
Gastrostomy tube	14	17	1·00
Outcomes			
Length of stay initial admission (days), median (IQR)	6 (2–12)	6 (2–9)	0·40
Time to infection for cases and length of follow-up for controls (days), median (IQR)	197 (28–437)	399 (115–638)	0·05
Readmission during follow-up period	43	52	0·38
Readmission within 90 days	29	30	0·90
Surgery from admission to infection	36	45	0·38
Admission to hospital from admission to infection	46	51	0·66
Admission to long-term care facility from admission to follow-up	21	31	0·33
Admission to ICU this hospital admission follow-up period	25	31	0·55
Dialysis from time of admission to follow-up	11	5	0·36

Values given are % unless stated otherwise.
MRSA, Methicillin-resistant *Staphylocccus aureus*; IQR, interquartile range; ICU, intensive care unit.

Table 2. *Independent risk factors for MRSA skin and soft tissue infection in MRSA-colonized patients discharged from a Veterans Affairs hospital*

Characteristic	OR	95% CI	*P* value
Previous MRSA infection before admission	4·0	1·0–15·5	0·05
Previous hospital admission in 12 months prior to colonization	3·2	1·2–9·2	0·02
Myocardial infarction	6·3	1·5–30·2	0·01
Peripheral vascular disease	2·8	0·7–10·5	0·13

MRSA, Methicillin-resistant *Staphylocccus aureus*; OR, odds ratio; CI, confidence interval;

MRSA infections and SSTIs in patients colonized by MRSA at the time of hospital admission compared to those colonized during admission, but that study was based on clinical cultures and SSTI diagnoses performed by physicians, with limited chart review to confirm significance of positive cultures, which may have overestimated the rate of infection [10]. However, they found a high rate of true infections in those with skin and soft tissue cultures in the subset of patients where chart review was performed (95%) [10]. In our study, we reviewed each case to ensure they were consistent with true infection.

Prior MRSA infection, infection with other multidrug-resistant organisms, and several comorbidities, are well-known risk factors for MRSA SSTI [5, 11]. Prior hospitalization is specifically a risk factor for antimicrobial resistance and may represent both previous exposure to antibiotics and more opportunities to be colonized with resistant organisms [11]. Subgroup analysis of non-surgical-site infections also identified a history of MI as an independent risk factor for MRSA SSTI. Previous MI could be associated with increased contact with healthcare settings, including previous admissions, which was also shown to be an independent risk factor for MRSA SSTI. Additionally, a history of MI may also be indicative of PVD, which is reported by recent literature to be a risk factor for MRSA SSTI [12]; a history of either of these characteristics were both associated with a greater likelihood of MRSA SSTI post-discharge in our cohort; but a statistically significant relationship for history of PVD was not identified here due to the limited sample size.

Our study is unique and has important strengths. It is one of very few studies that includes active surveillance for MRSA colonization of patients followed up to 18 months post-discharge combined with case review to confirm true infection. However, its limitations include the retrospective, observational study design, which is subject to various types of bias including selection bias and confounding by unmeasured variables. Additionally, our study included a limited number of predictor variables and did not gather data on behavioral or socioeconomic variables. While these may not have had a significant impact on our results, future studies may wish to explore their possible contribution to MRSA SSTIs.

In conclusion we have identified include prior hospital admission within 12 months, MRSA infection prior to admission, and a history of MI as independent risk factors for the development of MRSA SSTI in patients colonized with MRSA at hospital admission. Future studies should further examine the prevalence and risk factors for MRSA SSTI across various geographical locations.

ACKNOWLEDGEMENTS

This research received no specific grant from any funding agency, commercial or not-for-profit sectors. The views expressed herein are those of the authors and do not necessarily represent the views of the Department of Veterans Affairs or the US Government.

DECLARATION OF INTEREST

None.

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