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A comparison of clinical outcomes between healthcare-associated infections due to community-associated methicillin-resistant *Staphylococcus aureus* strains and healthcare-associated methicillin-resistant *S. aureus* strains

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SUMMARY

There are limited data examining whether outcomes of methicillin-resistant *Staphylococcus aureus* (MRSA) healthcare-associated infections (HAIs) are worse when caused by community-associated (CA) strains compared to HA strains. We reviewed all patients' charts at our institution from 1999 to 2009 that had MRSA first isolated only after 72 h of hospitalization ($n=724$). Of these, 384 patients had a MRSA-HAI according to CDC criteria. Treatment failure was similar in those infected with a phenotypically CA-MRSA strain compared to a phenotypically HA-MRSA strain (23% *vs.* 15%, $P=0{\cdot}10$) as was 30-day mortality (16% *vs.* 19%, $P=0{\cdot}57$). Independent risk factors associated with ($P<0{\cdot}05$) treatment failure were higher Charlson Comorbidity Index, higher APACHE II score, and no anti-MRSA treatment. These factors were also associated with 30-day mortality, as were female gender, older age, MRSA bloodstream infection, MRSA pneumonia, and HIV. Our findings suggest that clinical and host factors, not MRSA strain type, predict treatment failure and death in hospitalized patients with MRSA-HAIs.

Key words: Community-associated, genotype, healthcare-associated, MRSA, outcomes.

INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the most common healthcare-associated infections (HAIs) [1]. Over the last decade, the epidemiology of MRSA has rapidly changed. Previously, MRSA-HAIs were primarily caused by a limited amount of healthcare-associated MRSA strains (HA-MRSA), for example USA100 in the USA [2]. Community-associated strains (CA-MRSA), such as USA300, now cause an increasingly recognized proportion of HAIs, and are now reported to cause 20–60% of MRSA-HAIs [3–8]. In the USA, CA-MRSA strains are predominantly the USA300 pulse-field type [2], and are characterized by the presence of Panton–Valentine leukocidin (PVL) [9], SCC*mec* type IV [10], and/or susceptibility to

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clindamycin, trimethoprim-sulfamethoxazole, and gentamicin [11].

Some clinicians and investigators disagree on whether the presence of specific virulence factors such as PVL makes CA-MRSA strains intrinsically more virulent than HA-MRSA strains and that CA-MRSA strains result in more severe infection and worse clinical outcomes [12, 13]. While several studies have examined the molecular epidemiology of CA-MRSA and HA-MRSA, there are only limited data on the associations between strain type and the clinical outcomes of patients with HAIs. Investigation comparing outcomes between CA-MRSA and HA-MRSA strains have been limited by relatively small sample size [14, 15], or focus on a subset of HAIs (bacteraemia) [15]. Two reports of *S. aureus* bacteraemia found a decrease in all-cause mortality and infection with CA-MRSA strains [16,17], while another of MRSA bacteraemia found an increase in mortality in those infected with USA300 [18]. However, each of these investigations included patients with community-onset infections. Community-onset infections are frequently less severe than HAIs and may confound the ability to assess associations with clinical outcomes [19, 20]. Additionally, none of the three foregoing studies examined non-bloodstream MRSA-HAIs.

We set out to compare the clinical outcomes of patients with MRSA-HAIs. To test the hypothesis that CA-MRSA strains were associated with worse clinical outcomes compared to HA-MRSA strains, we conducted a retrospective cohort investigation at a large tertiary-care, urban, county hospital.

METHODS

Study design

A retrospective investigation of adult (aged $\geqslant 18$ years) patients with MRSA-HAI was performed at Harbor–UCLA Medical Center, a 400-bed tertiary-care county hospital. All cultures from the Clinical Microbiology Laboratory that grew MRSA and were collected $\geqslant 72$ h after patient admission between 1 January 1999 and 31 December 2009 were examined. Laboratory data from 1 January 2005 to 30 April 2006 were not available for review and thus patients admitted during this time period were not included in the cohort. For patients with >1 culture during admission, only the first MRSA culture associated with infection was used. Patients with MRSA-HAI from >1 admission were only included once (first episode).

Standardized definitions of HA and CA infection were used, according to CDC criteria [21]. Of note, this definition categorizes an infection as HA if the infection occurred >48 h after admission. However, we used a more conservative $\geqslant 72$ h cut-off to minimize the chance of bias in which community-associated infections would inadvertently be categorized as HAIs. Categorization of infection by infection site (e.g. skin and soft tissue, pneumonia, etc.) were made using CDC criteria [22]. A study physician reviewed the medical records of each patient to confirm that the MRSA culture represented an infection based on CDC criteria and not a colonization, contamination, or reflected an infection present on admission. Anti-MRSA antibiotics were defined as vancomycin, daptomycin, linezolid, clindamycin, trimethoprim-sulfamethoxazole, doxycycline, minocycline, tigecycline, and quinupristin/dalfopristin. Microbiologically active antibiotics were defined as antibiotics to which the infection isolate was susceptible according to antibiotic susceptibility test results.

The primary outcome was treatment failure at 14 days, which was defined as lack of resolution of infection and/or need for additional intervention or change in antibiotic therapy and the secondary outcome was all-cause mortality at 30 days. We did not attempt to analyse attributable mortality due to MRSA as the cohort had various underlying conditions that prohibited matching and distinguishing the cause of death due to MRSA *vs.* non-MRSA was considered too subjective [23]. This investigation was approved by the Los Angeles Biomedical Research Institute at Harbor–UCLA Medical Center Institutional Review Board.

Data collection

A standardized instrument based on previous surveys previously developed for investigations of MRSA epidemiology [4, 24–26] was used to abstract information from the medical records of each patient. Data were abstracted from paper and electronic medical records by physician investigators (A.A.W., N.L.G., D.W.). This included demographics, admission date and time, hospital location, comorbidities, laboratory values, Charlson Comorbidity Index [27], APACHE II score [28], antibiotic treatment, treatment failure at 14 days, and 30-day all-cause mortality.

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Definition of HA-MRSA and CA-MRSA strains and molecular analysis

Because all strains were not available for molecular typing, we used a phenotypic definition of a CA-MRSA or HA-MRSA strain, as described and used previously [4]. This method has been shown to correlate with molecular phenotypes in 92% of specimens at our institution [4]. MRSA strains were defined as CA-MRSA strain phenotype if the isolates were resistant to oxacillin and susceptible to gentamicin, clindamycin, and trimethoprim-sulfamethoxazole. All other isolates were considered to be phenotypically HA-MRSA strains.

A limited selection of MRSA isolates from sterile sites was saved for infection control purposes at Harbor–UCLA Medical Center. Available isolates were genotyped to validate the above phenotypic definitions of CA-MRSA and HA-MRSA strains using *spa* typing, multi-locus sequence typing and polymerase chain reaction for the presence of PVL as described elsewhere [29–31]. Strain types were classified as HA-MRSA or CA-MRSA strains based on accepted categorizations [2, 32].

Data analysis

Bivariate analysis was used to compare variables from the chart abstraction instrument hypothesized to be associated with treatment failure at 14 days or 30-day all-cause mortality. Bivariate analyses were assessed using odds ratios (ORs), 95% confidence intervals (CIs), and the associated P values. All variables with a P value $\leqslant 0{\cdot}20$ in the bivariate analysis were included in a multivariate logistic regression analysis predicting failure or mortality using standard modelling procedures [33]. Multi-collinearity for the logistic regression model was assessed by condition indices and variance decomposition proportions analysis. Backwards elimination was performed using the Likelihood ratio test to find the best model. Models were examined for goodness of fit using the Hosmer–Lemeshow statistic. All variables were considered statistically significant at the $\alpha = 0{\cdot}05$ level. Data analyses were performed using SAS version 9.3 (SAS Institute, USA).

RESULTS

We found 724 patients with MRSA-positive cultures during the study period. Of these, 384 (53%) were considered to reflect MRSA-HAI and were included in the final analysis. Of the 339 patients excluded from the infection cohort, 209 cultures were categorized as contamination or colonization cultures; 66 represented infections present at admission, 49 represented patients that did not fit the infection definition (e.g. cultures taken <72 h after admission), eight had charts that were unavailable for review; five patients were transferred to another facility on the day of culture collection; and three cultures were from autopsy.

Of the 384 patients, mean age was 51 years (median 50 years, range 19–97 years), 67% were male; 39% were Hispanic, 22% were African-American, 25% were Caucasian, and 14% were of other race/ethnicity. Site of infection was skin and soft tissue in 35% of cases (86/133 were surgical site infections), bacteraemia in 19%, pneumonia in 34%, and other in 12%. For our study outcomes, treatment failure at 14 days occurred in 20% and the 30-day mortality rate was 18%.

Among infection isolates, 30% were phenotypically classified as a CA-MRSA strain and 70% as HA-MRSA strain. Molecular typing of 43 bloodstream isolates, showed an 82% correlation between the genotype and the phenotypic definition of each strain. Twenty-three isolates were classified as HA-MRSA strains (12 ST5, 10 ST239, 1 ST840) and 20 were CA-MRSA strains (1 ST1, 19 ST8). Eight strains were discordant in genotype and phenotype with four ST8/t008/PVL-positive strains being resistant to clindamycin and four ST5/t242/PVL-negative strains being susceptible to gentamicin, clindamycin and trimethoprim-sulfamethoxazole.

The results for the bivariate analysis of failure at 14 days are summarized in Table 1. Treatment failure occurred in 23% (60/267) of those infected with a HA-MRSA strain and 15% (18/117) of those infected with a CA-MRSA strain (OR 0·63, 95% CI 0·35–1·12, $P = 0{\cdot}10$). Factors associated with treatment failure at 14 days ($P \leqslant 0{\cdot}05$) included Hispanic ethnicity (OR 0·51, 95% CI 0·27–0·95), older age (OR 1·02 for each year of age, 95% CI 1·01–1·04), MRSA pneumonia (OR 1·84, 95% CI 1·01–3·35), never having been treated with an anti-MRSA antibiotic (OR 6·26, 95% CI 3·11–12·61), higher Charlson Comorbidity score (OR 1·10, 95% CI 1·01–1·20), and higher APACHE II score (OR 1·03, 95% CI 1·01–1·06).

Of note, when examining predictors of failure at 14 days, we found no significant interaction between MRSA strain type (CA *vs*. HA) and type of infection

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Table 1. *Bivariate analysis of risk factors associated with failure at 14 days*

Variable	All patients, $n=384$ (%)	Treatment failure at 14 days, $n=78$ (%)	No treatment failure at 14 days, $n=306$ (%)	OR	95% CI	*P* value
Strain type*						
Healthcare associated	267 (70)	60 (23)	207 (77)	Ref.		
Community associated	117 (30)	18 (15)	99 (84)	0·63	0·35–1·12	0·10
Ethnicity						
Caucasian	95 (25)	26 (27)	69 (73)	Ref.		
Hispanic	150 (39)	24 (16)	126 (84)	**0·51**	**0·27–0·95**	**0·03**
African-American	86 (22)	14 (16)	72 (84)	0·52	0·25–1·07	0·08
Other	53 (14)	14 (26)	39 (74)	0·95	0·45–2·04	0·90
Gender						
Female	126 (33)	28 (22)	98 (78)	1·19	0·71–2·00	0·59
Male	258 (67)	50 (19)	208 (81)	Ref.		
Age						
Mean ± S.D.	51 ± 16	56 ± 16	50 ± 16	**1·02**	**1·01–1·04**	**0·004**
Median (range)	50 (19–97)	55 (24–97)	49 (19–92)			
Year of infection						
1999	29 (8)	3 (10)	26 (90)	0·42	0·10–1·66	0·21
2000	42 (11)	11 (26)	31 (74)	1·28	0·48–3·41	0·63
2001	32 (8)	6 (19)	26 (81)	0·83	0·27–2·57	0·75
2002	22 (6)	5 (23)	17 (77)	1·06	0·31–3·58	0·93
2003	32 (8)	4 (13)	28 (88)	0·51	0·15–1·81	0·30
2004	30 (8)	8 (27)	22 (73)	1·31	0·45–3·82	0·62
2005	1 (0)	0 (0)	1 (100)	—	—	0·99
2006	34 (9)	5 (15)	29 (85)	0·62	0·19–2·02	0·43
2007	65 (17)	14 (22)	51 (78)	0·99	0·40–2·47	0·98
2008	51 (13)	12 (24)	39 (77)	1·11	0·43–2·88	0·83
2009	46 (12)	10 (22)	36 (78)	Ref.		
Length of stay prior to culture collection						
Mean ± S.D.	20 ± 27	17 ± 15	21 ± 29	0·99	0·98–1·01	0·23
Median (range)	13 (3–400)	11 (3–77)	14 (3–400)			
Type of infection						
Skin/soft tissue	133 (35)	22 (17)	111 (83)	Ref.		
Bloodstream	74 (19)	14 (19)	60 (81)	1·18	0·56–2·47	0·67
Pneumonia	131 (34)	35 (27)	96 (73)	**1·84**	**1·01–3·35**	**0·046**
Other†	46 (12)	7 (15)	39 (85)	0·91	0·36–2·39	0·83
On empirical anti-MRSA antibiotic when culture obtained	65 (17)	17 (26)	48 (74)	1·50	0·81–2·78	0·24
Never treated with an anti-MRSA antibiotic	38 (10)	21 (55)	17 (45)	**6·26**	**3·11–12·61**	**<0·0001**
Charlson Comorbidity Index						
Mean ± S.D.	3 ± 3	3 ± 3	2 ± 2	**1·10**	**1·01–1·20**	**0·04**
Median (range)	2 (0–12)	2 (0–12)	2 (0–11)			
Cancer	61 (16)	11 (18)	50 (82)	0·84	0·42–1·70	0·73
HIV	9 (2)	3 (33)	6 (67)	2·00	0·49–8·18	0·40
Diabetes	116 (30)	25 (22)	91 (78)	1·11	0·65–1·90	0·68
APACHE II score						
Mean ± S.D.	17 ± 11	21 ± 11	17 ± 11	**1·03**	**1·01–1·06**	**0·005**
Median (range)	17 (0–55)	20 (0–55)	15 (0–50)			

OR, Odds ratio; CI, confidence interval; Ref., reference group.

* Based on antibiotic susceptibility phenotype (minimum inhibitory concentration susceptible to gentamicin, clindamycin, and trimethoprim-sulfamethoxazole).

† Other infection type ($n=46$) includes 21 urinary tract infections, 19 intra-abdominal infections, and six arterial or venous cardiovascular system infections.

Bold values indicate variables statistically significant at the alpha = 0·05 level.

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Table 2. *Multivariable analysis of risk factors associated with treatment failure at 14 days*

Variable	OR	95% CI	*P* value
Community-associated strain type*	0·78	0·42–1·44	0·43
Never treated with an anti-MRSA antibiotic†	9·89	4·55–21·50	<0·0001
Charlson Comorbidity Index‡	1·11	1·01–1·23	0·03
APACHE II score‡	1·05	1·02–1·07	0·0003

OR, Odds ratio; CI, confidence interval.

* Referent group is healthcare-associated strain type; community-associated strain type based on antibiotic susceptibility phenotype (minimum inhibitory concentration susceptible to gentamicin, clindamycin, and trimethoprim-sulfamethoxazole).

† Referent group is those treated with an anti-MRSA antibiotic.

‡ These items measured each as continuous variables where odds ratio reflects changes for a one point change in the score.

(skin/soft tissue, blood, pneumonia, or other). In the multivariate logistic regression model of treatment failure at 14 days (Table 2), independent predictors of failure included never having been treated with a microbiologically active antibiotic (OR 9·89, 95% CI 4·55–21·50, $P<0·0001$), higher Charlson Comorbidity score (OR 1·11, 95% CI 1·01–1·23, $P=0·033$), and higher APACHE II score (OR 1·05, 95% CI 1·02–1·07, $P=0·0003$). A subset analysis of treatment failure at 14 days in patients who received effective anti-MRSA therapy showed similar results (data not shown).

Bivariate analysis of 30-day mortality is summarized in Table 3. Seventy (18%) patients of the cohort died within 30 days of their MRSA infection. This includes 19% (51/267) of persons with a HA-MRSA strain and 16% (19/117) of persons with a CA-MRSA strain (OR 0·82, 95% CI 0·46–1·46, $P=0·57$). In the bivariate analysis, factors associated with 30-day mortality ($P\leqslant 0·05$) included female gender (OR 2·28, 95% CI 1·34–3·86), older age (OR 1·05, 95% CI 1·03–1·07), MRSA bloodstream infection (OR 5·37, 95% CI 2·11–13·66), MRSA pneumonia (OR 7·91, 95% CI 3·39–18·46), HIV infection (OR 6·0, 95% CI 1·56–22·81), higher Charlson Comorbidity score (OR 1·20, 95% CI 1·09–1·31), and higher APACHE II score (OR 1·07, 95% CI 1·04–1·09).

When examining predictors of 30-day mortality, we found no significant interaction between MRSA strain type (CA *vs.* HA) and type of infection (skin/soft tissue, blood, pneumonia, or other). In the multivariate logistic regression model of 30-day mortality (Table 4), predictors of mortality included female gender (OR 2·34, 95% CI 1·25–4·35, $P=0·008$), older age (OR 1·03, 95% CI 1·01–1·05, $P=0·006$), MRSA bloodstream infection (OR 4·00, 95% CI 1·42–11·02, $P=0·009$), MRSA pneumonia (OR 5·24, 95% CI 1·96–14·01, $P=0·001$), never having been treated with a microbiologically active antibiotic (OR 4·99, 95% CI 1·80–13·80, $P=0·002$), HIV infection (OR 9·46, 95% CI 1·71–52·21, $P=0·01$), higher Charlson Comorbidity score (OR 1·15, 95% CI 1·02–1·29, $P=0·02$), and higher APACHE II score (OR 1·05, 95% CI 1·02–1·09, $P=0·002$). A subset analysis of 30-day mortality in patients who received effective anti-MRSA therapy showed similar results.

Of note, our investigation found that 10% (39/385) of the cohort was never treated with a microbiologically active antibiotic, a finding associated with treatment failure and mortality. We examined the 39 cases in detail and found that most (15/39) of these patients were discharged or transferred before the results were available at our centre. These patients were managed at outside hospitals or in the outpatient setting. Thirteen of the 39 had died prior to or by the time culture results were available; 10 patients were treated only surgically (source control). The remaining patient was treated with clindamycin that was inactive against their MRSA strain. Our proportion is consistent with other investigations of *S. aureus* bacteraemia that have a similar percentage (10–21%) of patients not receiving appropriate therapy [14, 34].

DISCUSSION

MRSA-HAIs are common and often result in substantial clinical morbidity, mortality, and cost. There are increasing reports of CA-MRSA strains causing HAI and heightened concern about the implications CA-MRSA strains may have on patients' outcomes. In our retrospective cohort investigation, we did not find any significant difference in treatment failure or mortality based upon MRSA strain type. Treatment failure was, however, associated with factors that were expected to predict poor outcomes, such as higher Charlson Comorbidity score, higher APACHE II score, and never having been treated with an

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Table 3. *Bivariate analysis of risk factors associated with 30-day mortality*

Variable	All patients, $n=384$ (%)	Dead at 30 days, $n=70$ (%)	Alive at 30 days, $n=314$ (%)	OR	95% CI	*P* value
Strain type*						
Healthcare associated	267 (70)	51 (19)	216 (81)	Ref.		
Community associated	117 (30)	19 (16)	98 (84)	0·82	0·46–1·46	0·57
Ethnicity						
Caucasian	95 (25)	19 (20)	76 (80)	Ref.		
Hispanic	150 (39)	22 (15)	128 (85)	0·69	0·35–1·35	0·28
African-American	86 (22)	15 (17)	71 (83)	0·85	0·40–1·79	0·66
Other	53 (14)	14 (26)	39 (74)	1·44	0·65–3·17	0·37
Gender						
Female	126 (33)	34 (27)	92 (73)	**2·28**	**1·34–3·86**	**0·003**
Male	258 (67)	36 (14)	222 (86)	Ref.		
Age						
Mean ± S.D.	51 ± 16	61 ± 16	49 ± 15	**1·05**	**1·03–1·06**	**<0·0001**
Median (range)	50 (19–97)	62 (26–97)	48 (19–88)			
Year of infection						
1999	29 (8)	3 (10)	26 (90)	0·95	0·21–4·28	0·94
2000	42 (11)	12 (29)	30 (71)	3·28	1·04–10·30	0·04
2001	32 (8)	5 (16)	27 (84)	1·52	0·39–5·75	0·54
2002	22 (6)	3 (14)	19 (86)	1·30	0·28–5·99	0·74
2003	32 (8)	3 (9)	29 (91)	0·85	0·19–3·83	0·83
2004	30 (8)	8 (27)	22 (73)	2·90	0·87–10·22	0·08
2005	1 (0)	0 (0)	1 (100)	—	—	0·99
2006	34 (9)	5 (15)	29 (85)	1·41	0·38–5·33	0·61
2007	65 (17)	16 (25)	49 (75)	2·69	0·90–7·94	0·08
2008	51 (13)	10 (20)	41 (80)	2·00	0·63–6·36	0·24
2009	46 (12)	5 (11)	41 (89)	Ref.		
Length of stay prior to culture collection						
Mean ± S.D.	20 ± 27	18 ± 15	21 ± 29	0·99	0·98–1·008	0·40
Median (range)	13 (3–400)	14 (3–77)	13 (3–400)			
Type of infection						
Skin/soft tissue	133 (35)	7 (5)	126 (95)	Ref.		
Blood	74 (19)	17 (23)	57 (77)	**5·37**	**2·11–13·66**	**0·0004**
Pneumonia	131 (34)	40 (31)	91 (69)	**7·91**	**3·39–18·46**	**<0·0001**
Other†	46 (12)	6 (13)	40 (87)	2·70	0·86–8·50	0·09
On appropriate anti-MRSA antibiotic at culture	65 (17)	15 (23)	50 (77)	1·44	0·76–2·75	0·29
Never treated with an anti-MRSA antibiotic	38 (10)	11 (29)	27 (71)	1·98	0·93–4·21	0·08
Charlson Comorbidity Index						
Mean ± S.D.	3 ± 3	4 ± 3	2 ± 3	**1·20**	**1·09–1·31**	**<0·0001**
Median (range)	2 (0–12)	3 (0–12)	2 (0–11)			
Cancer	61 (16)	15 (25)	46 (75)	1·59	0·83–3·05	0·20
HIV	9 (2)	5 (56)	4 (44)	**6·00**	**1·59–22·81**	**0·01**
Diabetes	116 (30)	19 (16)	97 (84)	0·83	0·46–1·49	0·57
APACHE II score						
Mean ± S.D.	17 ± 11	24 ± 9	16 ± 11	**1·07**	**1·04–1·09**	**<0·0001**
Median (range)	17 (0–55)	24 (0–55)	14 (0–50)			

OR, Odds ratio; CI, confidence interval; Ref., reference group.

* Based on antibiotic susceptibility phenotype (minimum inhibitory concentration susceptible to gentamicin, clindamycin, and trimethoprim-sulfamethoxazole).

† Other infection type ($n=46$) includes 21 urinary tract infections, 19 intra-abdominal infections, and six arterial or venous cardiovascular system infections.

Bold values indicate variables statistically significant at the alpha = 0·05 level.

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Table 4. *Multivariable analysis of risk factors associated with 30-day all-cause mortality*

Variable	OR	95% CI	*P* value
Community strain type*	1·32	0·68–2·59	0·41
Female gender	2·34	1·25–4·35	0·008
Age	1·03	1·01–1·05	0·006
Type of infection			
Skin/soft tissue	Ref.		
Blood	4·00	1·42–11·02	0·009
Pneumonia	5·24	1·96–14·01	0·001
Other†	3·33	0·93–11·93	0·064
Never treated with an anti-MRSA antibiotic	9·46	1·71–52·21	0·01
Charlson Comorbidity Index‡	1·15	1·02–1·29	0·02
APACHE II score‡	1·05	1·02–1·09	0·002

OR, Odds ratio; CI, confidence interval; Ref., reference group.

* Based on antibiotic susceptibility phenotype (minimum inhibitory concentration susceptible to gentamicin, clindamycin, and trimethoprim-sulfamethoxazole).

† Other infection type ($n=46$) includes 21 urinary tract infections, 19 intra-abdominal infections, and six arterial or venous cardiovascular system infections.

‡ These items measured each as continuous variables where odds ratio reflects changes for a one point change in the score.

anti-MRSA antibiotic. We also could not find an association between mortality and MRSA strain type.

To our knowledge, this is the first investigation to look specifically at the role MRSA strain type plays in both clinical cure and mortality in patients with a HAI. Other studies comparing HA-MRSA and CA-MRSA strains have focused on bloodstream infections [15–18, 34–36], included community-onset infections [14, 16–18, 34, 36], or did not look at both clinical cure and mortality [14–16, 18, 35, 37]. Our findings suggest that host factors and severity of illness drive clinical outcome, not the MRSA strain type. Other investigations, although limited in power or scope, also failed to find an association with strain type and key clinical outcomes [15, 35, 36]. One study that did find an association between SCC*mec* type II (HA-MRSA strain) and higher mortality in bacteraemic patients [17] did not examine infections other than bacteraemia, included both MSSA and CA-onset infections, and did not examine the relationship between days of hospitalization prior to infection and strain type, which was associated with poor outcome in a previous investigation [4]. Similarly, another investigation found an association between USA300 and decreased mortality in MRSA bacteraemia [16], and did not examine other types of HAIs, included community-onset infections, and also did not examine the relationship between days of hospitalization prior to infection and strain type. Another report of MRSA bacteraemia found an increase in mortality in those infected with USA300 and again did not examine other types of HA-MRSA infection, and included CA-onset infections or the relationship of hospitalization [18].

Of note, there were 39 subjects who were not treated with anti-MRSA antibiotics, a factor associated with treatment failure and mortality. While this number was surprising, we found that the proportion of persons not being treated with effective antibiotics in our cohort (10%) is consistent with investigations of *S. aureus* bacteraemia where 10–21% of patients did not receive appropriate therapy [14, 34]. Moreover, a detailed analysis of the 39 subjects revealed that the majority classified as lack of treatment had a clinically understandable reason, such as transfer to another hospital (for which we had no records) or had died before results were available. Only one patient was treated with an antimicrobial that was not active against their MRSA strain.

There are limitations to our investigation. First, our phenotypic definition of HA-MRSA and CA-MRSA strains was accurate in only 82% of strains that could be typed, which was lower than the 92% that we anticipated, based on a prior, similar investigation at our institution [4]. The major discrepancy was clindamycin resistance which is known to be increasing in USA300 strains [38, 39]. To address this in a *post-hoc* analysis, we modified our phenotypic definition of CA-MRSA strains to include clindamycin-resistant isolates resulting in a 91% concordance between the phenotypic and genotypic definitions of CA-MRSA strains. Using the modified definition did not

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significantly change any of the results (data not shown) and would only be of relevance for more recent MRSA strains. Second, the patients in this cohort are from a single centre and the findings may not be generalizable to other populations although our patient population is similar to many tertiary and community hospitals and is ethnically diverse. Third, our investigation is retrospective and limited to the data recorded in the medical charts. Data on MRSA cultures from 1 January 2005 to 30 April 2006 were not available for inclusion in this analysis. Nevertheless, we had a robust sample size with which to analyse the data and no differences were found between clinical outcomes and year of infection.

There are strengths to our investigation. First, while almost all other studies of clinical outcomes in HAIs focus on bacteraemia and mortality, we have focused on the associations between all HAIs and included data on treatment failure. Second, several types of infections were included rather than limiting the scope to only bloodstream infections. Third, we used strict definitions of infection and excluded possible infections and MRSA colonization, which allowed us to eliminate 47% of patients with MRSA cultures during the study period and ensured that cases truly reflected infection.

In summary, we found that patients with MRSA-HAIs caused by CA-MRSA strains were not more likely to have treatment failure at 14 days or death at 30 days compared to patients with HAIs caused by traditional HA-MRSA strains. In fact, treatment outcomes of failure and death were heavily driven by host comorbidities and severity of illness, not strain factors. Although CA-MRSA strains have a variety of virulence factors that distinguish them from traditional HA-MRSA strains, in hospitalized patients these characteristics do not appear to have a significant association with key clinical outcomes.

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DECLARATION OF INTEREST

None.

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