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ORIGINAL RESEARCH

Clinical and Economic Outcomes in Patients With Community-Acquired *Staphylococcus aureus* Pneumonia

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BACKGROUND: While the clinical and economic consequences of *S. aureus* pneumonia in healthcare settings have been well documented, much less is known about community-acquired *S. aureus* pneumonia (CAP).
METHODS: We retrospectively identified all patients admitted to a large US urban teaching hospital between January 2005 and May 2008 with pneumonia and positive blood or respiratory cultures for *S. aureus* within 48 hours of admission. Patients with suspected healthcare-associated pneumonia (HCAP) were excluded from the study sample, using established criteria (eg, recent hospitalization, admission from nursing home, hemodialysis). Patients were designated as having methicillin-resistant (MRSA) or methicillin-susceptible (MSSA) CAP based on initial *S. aureus* isolates. Initial therapy was designated "appropriate" vs. "inappropriate" based on expected susceptibility of the organism to the regimen received.
RESULTS: We identified a total of 128 CAP patients with *S. aureus* isolates; mean (standard deviation [SD]) age was 60 (17) years. A total of 55 patients (43%) had initial cultures positive for MRSA. Patients with MRSA CAP were more likely to receive inappropriate initial therapy (24 [44%] vs. 13 [18%] for MSSA; $P = 0.002$). Approximately 25% of all patients underwent surgery for pneumonia, 69% received mechanical ventilation, 79% were admitted to intensive care unit (ICU), and 24% died in hospital. Mean (SD) length of stay was 17.0 (15.7) days, and total hospital charges averaged $127,922 ($154,605) per patient; there were no significant differences between patients with MRSA vs. MSSA CAP.
CONCLUSION: Outcomes are poor, hospital stays are long, and costs of care are high in patients with *S. aureus* CAP, and do not differ between those with MRSA vs. MSSA. ***Journal of Hospital Medicine*** **2010;5:528–534.** © *2010 Society of Hospital Medicine.*

KEYWORDS: ***staphylococcus aureus*** **pneumonia, community-acquired, clinical-acquired, methicillin-resistant, methicillin-susceptible.**

Staphylococcus aureus (*S. aureus*) is well recognized as a major cause of nosocomial and healthcare-associated pneumonia (HCAP). These infections are associated with substantial morbidity and mortality, and generate high medical costs.[1–4] The significance of *S. aureus* in community-acquired pneumonia (CAP) is less clear. Historically, *S. aureus* has not been considered a common pathogen in CAP, usually arising in association with or following influenza or an influenza-like syndrome.[5–8] However, with the increasing prevalence of methicillin-resistant *S. aureus* (MRSA) as a cause of HCAP—and most recently, serious community-acquired non-pulmonary infections—interest in this pathogen and its impact beyond the hospital have been expanding. During the 2003 to 2004 influenza season, 15 cases of influenza-associated MRSA CAP were identified.[6] In January 2007, the US Centers for Disease Control and Prevention (CDC) received reports of an additional 10 cases of severe MRSA CAP, resulting in six deaths, among previously healthy children and adults in Louisiana and Georgia.[7] Kallen et al.[9] recently reported 51 cases from 19 states between November 2006 and April 2007. To the best of our knowledge, these reports represent the largest case series describing MRSA in CAP.

Earlier studies have suggested a relationship between the outcome of *S. aureus* infection and the presence of various patient and strain characteristics.[10–13] Most observations regarding the adverse impact of MRSA on patient outcomes have arisen from analyses of cohorts of patients with either mixed infections, bacteremias, or nosocomial infection. There is little information on outcomes in patients with *S. aureus* CAP. To address this issue, we conducted a retrospective study of patients with culture-proven *S. aureus* pneumonia admitted to a large urban hospital.

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Materials and Methods

Data Source

This retrospective study was conducted at Henry Ford Hospital in Detroit, MI, a 903-bed tertiary care center. (Preliminary findings from the study have been presented at annual meetings of the Infectious Diseases Society of America [IDSA], the American College of Chest Physicians [ACCP], and the Interscience Conference on Antimicrobial Agents and Chemotherapy [ICAAC].) Data were obtained from the Henry Ford CarePlus Electronic Medical Record database, the Henry Ford Infectious Diseases Research Laboratory database, and the cost component of the Corporate Data Store, which is a central repository of data on patient encounters at Henry Ford Hospital and all Henry Ford Health System (HFHS) ambulatory care sites.

Sample Selection

The source population for the study consisted of all admissions to Henry Ford Hospital between January 2005 and May 2008 ("study period") Patients were included in the study sample if they had: (1) a discharge diagnosis (principal or secondary) of pneumonia (International Classification of Diseases 9th Edition, Clinical Modification [ICD-9-CM] diagnosis codes 481.X – 486.X) on their discharge summary or in their medical record; (2) a positive chest x-ray (ie, infiltrate, consolidation, pleural effusion) within 48 hours of hospital admission; (3) an abnormal temperature (>38.3°C [101.0°F] or <36°C [96.8°F]), an abnormal white blood count (WBC) (>12,000/mm^3 or <4,000/mm^3), or increased sputum production on their day of hospital admission; and (4) a positive blood or respiratory culture for *S. aureus* within 48 hours of hospital admission.

Among these identified patients, those with probable HCAP were excluded from the study sample, based on evidence of: (1) hospitalization for ≥2 days during the 90-day period preceding the index hospitalization; (2) admission to hospital from a nursing home or long-term care facility; (3) hemodialysis ≤30 days prior to hospital admission; (4) receipt of cancer chemotherapy, IV antibiotic therapy, or wound care ≤30 days prior to hospital admission; or (5) receipt of an immunosuppressant at the time of hospital admission. All remaining patients were assumed to have CAP.

Data Extraction

For each admission in the study sample, selected demographic and clinical information was extracted from inpatient and outpatient medical records, beginning 1 year prior to the date of hospital admission and ending 30 days subsequent to the date of hospital discharge or the date of discontinuation of antibiotic therapy, whichever occurred later. All data were extracted by trained medical abstractors, using a set of case-report forms developed specifically for this study.

Study Measures

Baseline demographic and clinical characteristics of study subjects were examined, including age, sex, race, evidence of positive *S. aureus* culture during the 1-year period prior to hospital admission, history of selected disease conditions, and clinical status at admission (eg, comorbidities, vital signs, WBC, platelet count). A Confusion, Urea nitrogen, Respiratory rate, Blood pressure, 65 years of age and older score (CURB-65) was calculated for each patient, based on clinical information at hospital admission.[14] (A CURB-65 score of 0 indicates a low [<1%] risk of death from pneumonia, while a score of 5 indicates a very high [57%] risk of death.)

Patients were designated as having MRSA or MSSA CAP based on the results of blood or respiratory cultures obtained within 48 hours of hospital admission. MRSA isolates were initially identified using automated dilution testing, in accordance with guidelines of the Clinical and Laboratory Standards Institute.[15] The genotypic and phenotypic characteristics of MRSA isolates were examined, including susceptibility to vancomycin and presence of the Panton-Valentine leukocidin (PVL) gene. Minimum inhibitory concentrations (MICs) for vancomycin were ascertained using the E-test (AB BIODISK, Solna, Sweden).[16] The PVL gene was detected using pulse field gel electrophoresis patterns (PFGE) and polymerase chain reaction. PFGE was performed using the restriction endonuclease *Sma*I. All *S. aureus* isolates were entered into a database using Gel Doc 2000 (BioRad) gel documentation system, and PFGE patterns were analyzed using BioNumerics Version 3.5, and grouped into Pulse-field types using DICE coefficients and 80% relatedness.[17]

Initial antibiotic therapy was defined to consist of all antibiotics received within the first 48 hours in the hospital, regardless of sequence. Appropriateness of initial antibiotic therapy was ascertained based on susceptibility of the organism to the initial regimen received. Patients with MRSA isolates were designated as having received appropriate initial therapy if they were given vancomycin, linezolid or tigecycline. Those with MSSA isolates were designated as having received appropriate initial therapy if they were given a beta-lactam, vancomycin, linezolid, or tigecycline. For patients with MRSA or MSSA that received doxycycline, clindamycin, or sulfamethoxazole/trimethoprim, each culture was evaluated individually to determine appropriateness, defined as in vitro susceptibility of the antimicrobial received to the organism. Clinical and economic outcomes of interest included: (1) thoracic surgery for pneumonia any time prior to hospital discharge; (2) receipt of mechanical ventilation any time prior to hospital discharge; (3) admission to an intensive care unit (ICU), irrespective of reason, anytime prior to hospital discharge; (4) length of stay in hospital; (5) total hospital charges for all services provided between hospital admission and hospital discharge; and (6) in-hospital death ("case-fatality")

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Statistical Analyses

We examined the baseline demographic and clinical characteristics of patients in the study sample, on an overall basis and for those with MRSA vs. MSSA isolates respectively. Categorical measures were summarized using frequency distributions and percentages; means, standard deviations (SDs) and medians were employed for continuous measures.

Clinical and economic outcomes were similarly examined, on an overall basis and for patients with MSSA vs. MRSA isolates. For patients with MRSA, we also examined outcomes in relation to selected genotypic and phenotypic characteristics of MRSA isolates, including MIC to vancomycin (1.00 μg/mL, 1.50 μg/mL, and 2.00 μg/mL) and presence of the gene for PVL toxin.

Statistical significance of differences between patients with MRSA vs. MSSA isolates was assessed using *t*-tests for continuous measures, and chi-square tests for categorical measures; statistical significance was similarly assessed for patients with the PVL toxin gene vs. those without it. Because the distribution of vancomycin MICs was highly skewed, statistical significance of differences in outcomes was not assessed in relation to this measure.

All analyses were conducted using SAS® Proprietary Software, Release 9.1 (SAS Institute Inc., Cary, NC). Missing and/or incomplete case-report form data were not imputed, as observations were presumed not to be missing at random.

Results

There were 282 admissions to Henry Ford Hospital between January 2005 and May 2008 of patients with pneumonia who had positive blood or respiratory cultures for *S. aureus* within 48 hours of admission. (The total number of admissions over this period of patients with a principal diagnosis of pneumonia was 3894). Twelve patients had a negative chest x-ray or negative clinical findings for pneumonia on the day of hospital admission and were excluded from the analysis. An additional 142 (53%) patients had evidence of HCAP and were excluded from the analysis. The final study sample therefore consisted of 128 patients with *S. aureus* CAP; their demographic and clinical characteristics are presented in Table 1.

Mean (SD) age of study subjects was 60 (17.0) years; 72% were nonwhite, and 58% were males. Prevalence of selected comorbidities, including acute renal failure, coronary artery disease, congestive heart failure, chronic obstructive pulmonary disease, diabetes, myocardial infarction, and peripheral vascular disease was high (>20%). Mean (SD) CURB score at admission was 1.8 (1.1); scores did not differ significantly between MRSA vs. MSSA patients. Eight patients (6%) had evidence of positive *S. aureus* cultures in the year prior to admission.

A total of 55 (43%) patients had positive MRSA cultures within the first 48 hours of admission, while the remainder (n = 73 [57%]) had cultures positive for MSSA. Among the 55 patients with MRSA, 23 (42%) had USA300 MRSA strains that produced PVL toxin. Only 18% of MRSA patients had MICs to vancomycin of 1 μg/mL; most remaining patients (73%) had 1.5 μg/mL MIC values. Thirty-one patients (24%) died prior to hospital discharge (Table 2). Eighty-eight (69%) patients received mechanical ventilation, and 79% were admitted to ICU; 25% of patients underwent thoracic surgery for pneumonia. Mean (SD) length of stay in hospital was 17.0 (15.7) days, and mean (SD) total charges per hospitalization were $127,922 ($154,605). (Mean length of stay in hospital was 5.8 days for all 3894 patients with a principal discharge diagnosis of pneumonia, and mean total charges were $29,448).

Notwithstanding the fact that patients with MRSA were more than twice as likely to receive inappropriate initial therapy (44% for MRSA vs. 18% for MSSA; odds ratio [OR], 3.57; 95% confidence interval [CI], 1.60–7.97; $P = 0.0015$), there were no statistically significant differences in in-hospital mortality (26% for MSSA vs. 22% for MRSA; $P = 0.678$), surgery for pneumonia (26% vs. 24%; $P = 0.838$), or admission to ICU (82% vs. 74%; $P = 0.382$). Patients with MSSA CAP were more likely to receive mechanical ventilation (77% vs. 58%; $P = 0.034$). Mean (SD) total charges per admission did not differ between patients with MSSA vs. MRSA CAP ($135,784 [$170,046] vs $117,489 [$132,164], respectively [$P = 0.510$]). (30-day mortality following hospital discharge was 24% for MRSA CAP patients and 30% for MSSA CAP patients.)

Among patients with MRSA CAP, there were no notable differences in outcomes between those with strains with the PVL toxin vs. those without it (Table 2). Mean (SD) length of stay in hospital, however, was significantly longer among the former patients (25 [22.6] days vs. 13 [7.7] days for those without PVL toxin; $P = 0.020$). Reflecting this difference, mean (SD) total charges per admission were $76,909 higher among MRSA patients with PVL-positive strains vs. those with PVL-negative strains ($162,124 [$186,923] vs. $85,215 [$57,957] respectively; $P = 0.066$).

Among MRSA patients with MICs to vancomycin of 1.5 μg/mL, 17% died in hospital, 20% underwent surgery for pneumonia, 60% received mechanical ventilation, and 75% were admitted to ICU. Mean (SD) total charges per admission were $104,514 ($112,606) (Table 2).

Discussion

To the best of our knowledge, this is the largest observational study to date of outcomes in patients with *S. aureus* CAP. Our results indicate that MRSA represents almost one-half of all such infections, with USA300 strains accounting for a substantial proportion of these cases. In addition, for most outcome measures, there were no significant differences between patients with MSSA vs. MRSA CAP. In patients with MRSA CAP, however, those with PVL-positive strains had longer stays in the hospital and had higher total costs of hospitalization.

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TABLE 1. Characteristics of Patients With Community-Acquired *S. Aureus* Pneumonia

Characteristic	Overall (n = 128)	MSSA (n = 73)	MRSA (n = 55)	MSSA vs. MRSA *P* Value
Age, years				
17–34	10 (7.8)	6 (8.2)	4 (7.3)	1.000
35–49	22 (17.2)	12 (16.4)	10 (18.2)	0.817
50–64	47 (36.7)	26 (35.6)	21 (38.2)	0.854
≥65	49 (38.3)	29 (39.7)	20 (36.4)	0.717
Mean (SD)	59.8 (17.0)	59.8 (16.6)	59.8 (17.8)	0.999
Sex				
Male	74 (57.8)	35 (47.9)	39 (70.9)	0.011
Female	54 (42.2)	38 (52.1)	16 (29.1)	
Race				
African American	86 (67.2)	46 (63.0)	40 (72.7)	0.261
Caucasian	36 (28.1)	24 (32.9)	12 (21.8)	0.233
Other/unknown	6 (4.7)	3 (4.1)	3 (5.5)	1.000
Prior positive *S. aureus* culture*				
MSSA	4 (3.1)	4 (5.5)	0 (0.0)	0.134
MRSA	4 (3.1)	1 (1.4)	3 (5.5)	0.314
Both	0 (0.0)	0 (0.0)	0 (0.0)	–
Comorbidities†				
Active malignancy	11 (8.6)	6 (8.2)	5 (9.1)	1.000
Acute renal failure	60 (46.9)	31 (42.5)	29 (52.7)	0.285
Coronary artery bypass grafting	7 (5.5)	5 (6.8)	2 (3.6)	0.698
Coronary artery disease	39 (30.5)	21 (28.8)	18 (32.7)	0.700
Cerebrovascular disease	23 (18.0)	15 (20.5)	8 (14.5)	0.487
Congestive heart failure	40 (31.3)	22 (30.1)	18 (32.7)	0.848
Chronic renal failure	23 (18.0)	12 (16.4)	11 (20.0)	0.647
Chronic obstructive pulmonary disease	31 (24.2)	14 (19.2)	17 (30.9)	0.147
Diabetes	38 (29.7)	19 (26.0)	19 (34.5)	0.332
Diabetes mellitus with organ damage	4 (3.1)	2 (2.7)	2 (3.6)	1.000
End-stage renal disease with receipt of dialysis	1 (0.8)	1 (1.4)	0 (0.0)	1.000
HIV/AIDS	7 (5.5)	2 (2.7)	5 (9.1)	0.138
Myocardial infarction	27 (21.1)	15 (20.5)	12 (21.8)	1.000
Peripheral vascular disease	26 (20.3)	10 (13.7)	16 (29.1)	0.045
CURB-65				
0	15 (11.7)	6 (8.2)	9 (16.4)	0.175
1	36 (28.1)	21 (28.8)	15 (27.3)	1.000
2	48 (37.5)	28 (38.4)	20 (36.4)	0.855
3	20 (15.6)	14 (19.2)	6 (10.9)	0.229
4	8 (6.3)	3 (4.1)	5 (9.1)	0.288
5	1 (0.8)	1 (1.4)	0 (0.0)	1.000
Mean(SD)	1.8 (1.1)	2 (1.0)	2 (1.2)	0.379

NOTE: Values are No.(%) unless otherwise indicated.

*During 1 year prior to admission.

†History, or at clinical presentation.

Abbreviations: CURB-65, Confusion, urea nitrogen, respiratory rate, blood pressure, age ≥65 years; HIV/AIDS, human immunodeficiency virus/acquired immune deficiency syndrome; MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-sensitive *S. aureus; S. aureus, Staphylococcus aureus*; SD, standard deviation.

Our study highlights the significant clinical and economic burden of *S. aureus* CAP. In the US, the mortality rate in patients hospitalized with CAP is about 8%, while mean length of stay is approximately 5 days (it was 5.8 days in our institution among all patients with CAP). In contrast, we found that most patients with *S. aureus* CAP were admitted to ICU, and that nearly one in four died during hospitalization. One possible explanation for these findings is that patients with *S. aureus* CAP may often receive inappropriate initial antibiotic therapy, a major predictor of adverse outcome in infection. The overall rate of inappropriate treatment, however, was low in our study (although we note that optimal antibiotic treatment is not clearly defined for the USA300 strain, and as a result, we assumed that vancomycin would be appropriate for all MRSA infections). A more likely explanation for our findings is the severity of CAP associated with *S. aureus*, whether MRSA or MSSA. Given the nature of *S. aureus* infections, the need for prevention (and potentially, development of a vaccine) remains crucial.

While MRSA has been studied extensively as a cause of bacteremia, as well as HCAP and VAP, it has not been well studied in CAP. Patients with MRSA bacteremia have been

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TABLE 2. Clinical and Economic Outcomes Among Patients With Community-Acquired *S. Aureus* Pneumonia

Study Outcomes	Overall (n = 128)	MSSA (n = 73)	MRSA (n = 55)	*P* Value	PVL Toxin* (n = 23)	No PVL Toxin* (n = 28)	*P* Value
Case fatality	31 (24.2)	19 (26.0)	12 (21.8)	0.678	4 (17.4)	6 (21.4)	1.000
Surgery for pneumonia	32 (25.0)	19 (26.0)	13 (23.6)	0.838	7 (30.4)	5 (17.9)	0.329
Receipt of mechanical ventilation	88 (68.8)	56 (76.7)	32 (58.2)	0.034	12 (52.2)	18 (64.3)	0.576
ICU admission	101 (78.9)	60 (82.2)	41 (74.5)	0.382	15 (65.2)	22 (78.6)	0.348
Length of stay, days							
Mean (SD)	17.2 (15.7)	16.4 (15.0)	18.2 (16.6)	0.525	25.3 (22.6)	13.2 (7.7)	0.020
Median	13.0	13.0	13.0		16.0	12.0	
Total charges, $							
Mean (SD)	127,922 (154,605)	135,784 (170,046)	117,489 (132,164)	0.510	162,124 (186,923)	85,215 (57,957)	0.066
Median	81,374	84,593	71,868		106,599	67,328	

NOTE: Values are No.(%) unless otherwise indicated.

*Four patients were excluded from this analysis—2 patients had USA 300 strains but did not have a gene for PVL toxin, 1 patient had the PVL toxin gene but did not have the USA 300 strain, and in 1 patient the PVL toxin gene could not be characterized.

Abbreviations: ICU, intensive care unit; MRSA, methicillin-resistant S. aureus; MSSA, methicillin-sensitive *S. aureus*; PVL, Panton-Valentine leukocidin; *S. aureus*, *Staphylococcus aureus*; SD, standard deviation.

shown to have a higher mortality risk and higher healthcare costs than those with MSSA infections, and a meta-analysis of 31 studies of patients with *S. aureus* bloodstream infections demonstrated a significant increase in mortality among patients with MRSA vs. MSSA bacteremia.[18–20] Outcomes when comparing MRSA and MSSA in VAP are slightly more variable. A higher rate of mortality has been reported in patients with pneumonia caused by MRSA vs. MSSA, but others found no difference after controlling for potential confounders.[21,22] We found that case fatality, surgery for pneumonia, ICU admission, length of stay, and total hospital charges do not differ significantly between patients with MRSA vs. MSSA CAP. This suggests that appreciation of the burden of MRSA can only be done in the context of the syndrome in question, and that conclusions from analyses of bacteremia and VAP may not be generalizable to CAP.

In the US, an increasing number of community-associated infections are due to MRSA. Skin and skin structure infections comprise the majority of community-associated MRSA infections and are caused by a single pulsed field type, termed USA300. These strains are believed to have distinctive virulence and epidemiologic characteristics. USA300 isolates typically are resistant only to beta-lactam and macrolide antimicrobial agents and contain genes for the PVL toxin, which typically are not present in strains of healthcare-associated MRSA.[23] Recent studies of acute pneumonia with animal models and in humans have suggested that the PVL toxin—alone or in combination with other virulence factors—is associated with the development of necrotizing pneumonia.[24–30] In our study, 23 patients with MRSA CAP had strains that contained PVL toxin, and these patients had longer stays in hospital and higher total hospital charges than those with MRSA CAP not containing the PVL toxin. This is an important finding, as length of stay is an important proxy for morbidity and case severity. This also extends the finding of previous case studies reporting that MRSA CAP with PVL toxin is associated with worse outcomes.[24–30] Moreover, we clearly document that PVL-positive strains are emerging as a cause of pulmonary infection in broader clinical scenarios. As such, physicians must remain vigilant for this toxin-producing strain. The full extent of the impact of PVL-positive strains in our study is unknown, as we cannot ascertain whether morbidity was worse because of the PVL toxin itself, or because most patients were not treated with clindamycin or linezolid, which inhibit toxin production.

We failed to observe a correlation between MICs to vancomycin and the outcomes we studied. The clinical significance of reduced susceptibility of *S. aureus* to vancomycin remains a controversial issue. In our study, there was no significant association between MICs to vancomycin and mortality, need for surgery, ICU admission, length of stay, or total hospital charges. Sakoulas et al.[11] reported that as vancomycin MICs for MRSA isolates rose within the susceptible range from 0.5 mcg/mL to 2.0 mcg/mL, so too did the number of clinical failures among bacteremic patients receiving vancomycin. Moise-Broder et al.[31] reported a similar finding in a study of 63 patients with MRSA bacteremia, of whom 45 failed or were intolerant of vancomycin therapy. In a more recent report, Soriano et al.[12] prospectively evaluated 414 episodes of bacteremia. The authors concluded that mortality in patients with MRSA bacteremia is significantly higher when the empiric antimicrobial agent is inappropriate and when vancomycin is used to treat infections involving strains with MICs >1.0 mcg/mL. In pneumonia, Hidayat et al.[13] reported that patients with infections due to pathogens with higher MICs to vancomycin had a higher rate of mortality than those with lower MICs. Our findings likely differ from this report because of the proportion of subjects with PVL-positive strains, and because of the skew in the distribution of vancomycin MICs. More specifically, the majority of patients had higher MIC strains, clustered around 1.5 mg/L, leaving us with few lower MIC strains and fewer strains with MICs of 2.0 mcg/mL for comparison, and therefore limited statistical power to assess the relationship between MICs and outcomes.

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There were no clinical features that clearly distinguished patients with MRSA vs. MSSA CAP. This suggests that if physicians hope to ensure that patients with MRSA CAP receive appropriate initial antibiotic therapy, they cannot base therapeutic decision-making (ie, use of an anti-MRSA treatment) on clinical criteria. Presently, national guidelines recommend diagnostic testing only if the results might affect clinical decisions (eg, antimicrobial management).[32] Furthermore, the IDSA/ATS guidelines recommend sputum cultures along with blood cultures and other diagnostic tests only in select cases (eg, those with severe disease). Since beginning optimal therapy quickly can reduce mortality in pneumonia,[33] our results indicate a need for both rapid diagnostic tests to identify patients with MRSA, and reevaluation of current recommendations for diagnostic testing in CAP.

Our study has several important limitations. First, its retrospective design exposes it to many forms of bias. Second, because the diagnosis of pneumonia can be challenging, we required that all patients have both clinical and radiologic evidence of the disease. However, we may have thereby excluded some admissions for *S. aureus* pneumonia among the over 3000 pneumonia admissions to our hospital during the study period.

Third, we only included patients with culture evidence of infection. This was necessary by design, but as a result we may have failed to identify some patients with *S. aureus* infections because of the limitations of respiratory culture technology. Patients on general practice units often do not get cultured, and accordingly we may have missed those with milder disease caused by *S. aureus*.

Fourth, we used only one method of MIC testing to determine vancomycin susceptibility. It would have been of interest to have used automated dilution testing also and to have compared both methods. Comparison of laboratory methods was not among our study objectives, and most of the earlier studies examining epidemiology and outcomes used a single laboratory testing method only.

Finally, since the study was conducted at a large urban teaching hospital in a city with a long history of issues with MRSA and resistance, the generalizability of our results may be limited.

In summary, our study provides further evidence that *S. aureus* is an important pathogen in CAP. MRSA CAP has few obvious characteristics that differentiate it from MSSA CAP. MRSA and MSSA CAP are both very serious infections that should be treated aggressively to avoid poor outcomes.

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