Antimicrobial Management of CAP and HCAP

January 15, 2016

Evaluation of Initial Antimicrobial Management in Patients with Community-Acquired and Healthcare-Associated Pneumonia at a Tertiary, Teaching Hospital

Jennifer Set, Pharm.D.[a], Elizabeth O'Gara, Pharm.D.[a], Philip Grgurich, MBA, Pharm.D.[a,b], Jason Lancaster, MEd, Pharm.D.[a,c], Yuxiu Lei, Ph.D.[a], Donald E. Craven, M.D.[a,d]

Institutions:

[a]Lahey Hospital & Medical Center, 41 Mall Rd., Burlington, MA, 01805

[b]MCPHS University, 179 Longwood Ave., Boston, MA, 02115

[c]Northeastern University, 360 Huntington Ave., Boston, MA, 02115

[d]Tufts University School of Medicine, 145 Harrison Ave., Boston, MA, 02111

Corresponding Author:

Jennifer Set, PharmD

Lahey Hospital and Medical Center, Department of Pharmacy

Burlington, MA 01805

Email: jennifer.set@lahey.org

Citation: Set J, O'Gara E, Grgurich P, Lancaster J, Lei Y, Craven D. Evaluation of Initial Antimicrobial Management in Patients with Community-Acquired and Healthcare-Associated Pneumonia at a Tertiary, Teaching Hospital. *Journal of Academic Hospital Medicine*. 2016, Volume 8, Issue 1.

Abstract

BACKGROUND: Limited and conflicting data exist for risk factors to predict pneumonia caused by multi-drug resistant (MDR) pathogens requiring empiric broad-spectrum antibiotics in patients presenting from the community.

METHODS: Three-hundred and forty-two patients with community-acquired pneumonia (CAP) or healthcare-associated pneumonia (HCAP) admitted to a tertiary teaching hospital were retrospectively reviewed. Clinical outcomes were compared between patients initially treated

with antibiotic regimens that were concordant and non-concordant with evidence-based guidelines. Risk factors for pneumonia caused by MDR pathogens were evaluated by multivariate logistic regression analysis.

RESULTS: No differences in mortality, length of stay, antibiotic duration, 30-day all-cause readmission, or *Clostridium difficile* infection in-hospital or within 30 days post-discharge were noted between the concordant and non-concordant groups. However, a higher rate of outpatient or emergency department visits for clinical failure within 30 days post-discharge was noted in the non-concordant group (14.8% vs. 7.5%; $p < 0.05$). Risk factors independently associated with presence of MDR pathogens included: residence in a long-term care facility (odds ratio [OR], 5.64; 95% confidence interval [CI], 1.54 – 20.73), a history of methicillin-resistant *Staphylococcus aureus* (OR, 5.71; 95% CI, 1.46 – 22.32), and presence of severe chronic obstructive or structural lung disease (OR, 7.11; 95% CI, 2.2 – 22.95).

CONCLUSIONS: Antibiotic management for HCAP patients was not consistent with 2005 IDSA/ATS guidelines, but did not affect clinical outcomes. Using specific risk factors for MDR pathogens to identify HCAP patients that require broader spectrum coverage may reduce unnecessary antibiotic use.

KEY WORDS: community-acquired and nosocomial pneumonia; antimicrobial resistance; readmissions

Introduction

The 2005 Infectious Diseases Society of America and American Thoracic Society (IDSA/ATS) guidelines have categorized several types of pneumonia, including community-acquired (CAP) and healthcare-associated (HCAP).[1,2] Patient-specific factors may increase the risk of multi-drug resistant (MDR) pathogens in those residing within the community.[1] The IDSA/ATS guidelines recommend empiric treatment with broad-spectrum antibiotics targeted against MDR pathogens in patients suspected of having pneumonia. Previous literature has demonstrated that adherence to these guidelines in patients treated for CAP was associated with lower 30-day and in-hospital mortality rates, shorter time to clinical stability, time to change in therapy, and hospital length of stay (LOS).[3-6] However, in patients diagnosed with HCAP, adherence to clinical guidelines has not yielded similar clinical outcomes.[7,8] Furthermore, recent studies suggest that HCAP risk factors do not consistently predict the presence of MDR pathogens, leading to unnecessary use of empiric broad-spectrum antibiotic therapy.[9] Overuse of broad-spectrum antibiotics has increased antimicrobial resistance and adverse drug events, such as the development of *Clostridium difficile* infection.[10]

Despite the existence of guidelines, variability and controversy surrounding the need for broad-spectrum antibiotics remains.[9] Our study compares clinical outcomes in patients with pneumonia presenting from the community and initially treated with institution-specific, guideline-concordant regimens versus those receiving guideline non-concordant regimens. We also examined risk factors independently associated with infection due to MDR pathogens requiring initial broad-spectrum antibiotics.

Methods

Study Design

This institution review board approved study is a single-center, retrospective chart review of patients admitted and received treatment for pneumonia in a 341-bed tertiary care, community-based teaching hospital. Eligible subjects included adults ≥ 18 years of age, hospitalized from November 2012 – March 2013 with a primary diagnosis of pneumonia as identified by International Classification of Diseases, 9th Revision (ICD-9) codes (480-487.0). Additionally, patients with a primary diagnosis of respiratory failure (ICD-9 code 518.8) or septicemia (ICD-9 code 0.38) combined with ICD-9 code 480-487.0 (pneumonia) as the secondary diagnosis were also screened for inclusion.[11] Exclusion criteria included the presence of one, or more, of the following: pregnancy, residence at a correctional facility, comfort measures only care within 48 hours of admission, missing or miscoded records, transfer from, or to another acute care institution, presence of co-infection on admission, pneumonitis, aspiration pneumonia, non-bacterial pneumonia, HAP, VAP, pulmonary abscess, empyema, or post-obstructive pneumonia.

Study Definitions

HCAP is defined as pneumonia in a non-hospitalized patient with healthcare contact and at least one of the following risk factors: home infusion therapy or wound care within the prior 30 days, residence in a nursing home or other long-term care facility (LTCF), hospitalization in an acute care hospital for two or more days within the prior 90 days, chronic hemodialysis (HD) within the prior 30 days, immunosuppression, and/or receipt of intravenous or oral antibiotics in the last 90 days.[1] CAP is defined as pneumonia acquired from the community, not associated with HCAP risk factors.[2] Classification of patients for use of broad-spectrum antibiotics was based on the presence of MDR risk factors shown in **Table 1.** An MDR pathogen is defined as an organism with resistance to three or more different classes of antibiotics, including but not limited to methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa*.[12]

Table 1. Risk factors for MDR pathogens[1]

MDR Pathogens	MRSA	*Pseudomonas aeruginosa*

Antibiotics in preceding 90 days Immunosuppression Presence of HCAP risk factors: Hospitalization for ≥ 2 days within past 90 days Presented from nursing home or extended care facility Home infusion therapy Chronic dialysis within 30 days Home wound care	Close contact with someone with skin infection within past month History of MRSA infection/colonization Necrotizing/cavitary or multiple infiltrates Lung abscess, empyema Hemodialysis Intravenous drug users MDR pathogen risk factors	Structural lung disease COPD exacerbation with frequent steroid/antibiotic use Hemodynamically unstable MDR pathogen risk factors

MDR – multi-drug resistant, MRSA – methicillin-resistant *Staphylococcus aureus*, COPD – chronic obstructive pulmonary disease, HCAP – healthcare-associated pneumonia

For patients admitted with a diagnosis of CAP to a non-intensive care unit, concordance with institution-specific guidelines consisted primarily of empiric treatment with either ceftriaxone plus azithromycin or levofloxacin monotherapy. For patients with a diagnosis of CAP admitted to an intensive care unit (ICU) without pre-disposing risk factors for *P. aeruginosa,* or other MDR Gram-negative rods, empiric use of ceftriaxone with azithromycin was considered guideline-concordant. If patients had risk factors for *P. aeruginosa,* or other MDR Gram-negative rods, empiric use of cefepime, with or without vancomycin, depending on patients' risk factor(s) for MRSA, was considered guideline-concordant. Based on local resistance data and hospital formulary considerations, the preferred empiric, guideline-concordant, antibiotic regimen for HCAP included cefepime plus vancomycin. Alternatively, an antipseudomonal carbapenem plus vancomycin or linezolid was considered guideline-concordant.

Immunosuppression was defined as the presence, or suspicion, of febrile neutropenia with an absolute neutrophil count of < 1000/mcL, non-neutropenic active cancer or hematologic malignancy undergoing chemotherapy, human immunodeficiency virus with cluster of differentiation 4 count < 200 cells/mm3, inherited immunodeficiency, taking ≥ 10 mg prednisone, or equivalent, per day for > 30 days, or use of other immunomodulating drugs (e.g. calcineurin inhibitors, mycophenolate, methotrexate, tumor-necrosis factor-α inhibitors).[13]

Outpatient or emergency department (ED) visit for clinical failure was defined as a visit within 30 days post-discharge with signs or symptoms of recurrence of pulmonary infection that required re-initiation of antibiotics after completion of initial therapy.

Study Endpoints

The primary endpoint was in-hospital mortality for patients with diagnoses of either CAP, or HCAP, receiving empiric antibiotics that were concordant versus non-concordant with institution-specific guidelines. Secondary endpoints included LOS, antibiotic duration, 30-day

all-cause readmission, development of *C. difficile* infection during admission or within 30 days post-discharge, outpatient or ED visit for clinical failure within 30 days post discharge and independent risk factors associated with MDR pathogens.

Statistical Analysis

Statistical analysis was conducted utilizing Statistical Analysis Software, version 9.2 (SAS Institute Inc., Cary, North Carolina). A convenience sample size of 342 subjects was chosen. Normally distributed continuous variables were compared with the Student *t* test. Non-normally distributed continuous variables were compared with the Wilcoxon rank sum test. Categorical variables were compared using χ^2 or Fisher's exact test. All tests were 2-tailed with a *p*-value of <0.05 considered as statistically significant. Variables in the univariate analysis having a *p*-value <0.1 were included in the multivariate analysis. In multivariate analysis, logistic regression was used to determine risk factors independently associated with MDR pathogens.

Results

Based on the inclusion criteria, 510 subjects were screened and, of those screened, 168 subjects were excluded. Of the 342 subjects included, 200 were in the concordant group and 142 were in the non-concordant group. Baseline characteristics were similar between each group, with the exception of a higher percentage of males in the concordant group and a higher percentage of HCAP patients in the non-concordant group (**Table 2**). Patients with CAP had a lower Charlson comorbidity index (median, 1; interquartile range 1 – 3) vs. HCAP patients (2; 1 – 4), p < 0.001.

Table 2 – Baseline Characteristics between concordant and non-concordant group

Baseline Characteristics	Concordant (N=200)	Non-concordant (N=142)	P value
Age, year, median (IQR)	79 (68 – 85)	80 (69 – 86)	0.35
Male, number (%)	109 (54.5)	57 (40.1)	<0.05
ICU admission, n (%)	36 (18)	17 (12)	0.13
HCAP, number (%)	80 (40)	94 (66.2)	<0.05
CCI, median (IQR)	2 (1 – 4)	2 (1 – 4)	0.76

IQR – interquartile range, ICU – intensive care unit, HCAP – healthcare-associated pneumonia, CCI – Charlson Comorbidity Index

In the non-concordant group, 23 subjects (16.2%) were treated with empiric broad-spectrum antibiotics when a risk factor for an MDR pathogen was not present. Three patients with CAP were treated with a macrolide without ceftriaxone. When a risk factor for an MDR pathogen was present, the empiric antibiotic regimen for 116 subjects (81.7%) of the non-concordant group did not have appropriate broad-spectrum coverage for the predicted presence of a

resistant pathogen based on the 2005 IDSA guidelines. Of the patients who did not receive antibiotics to target potential MDR pathogens based on the guidelines, 81 (69.8%) were HCAP patients treated with a regimen recommended to manage a patient diagnosed with CAP. Also, 19 subjects (16.4%) lacked coverage for MRSA, and 16 subjects (13.8%) lacked coverage for *P. aeruginosa*, despite having risk factors for one, or both, pathogens. The risk factors present in the HCAP patients treated with a CAP regimen were identified as antibiotics within the preceding 90 days (N=46), recent hospitalization within the preceding 90 days (N=41), immunosuppression (N=16), residence in a LTCF (N=7), and chronic hemodialysis within the past 30 days (N=1). Fifty-two patients had one risk factor, twenty-seven patients had two risk factors, and two patients had three risk factors.

Clinical Outcomes

There was no difference between in-hospital mortality rate between the concordant and non-concordant groups (4% vs. 3.5%, p = 0.82). However, there was a significantly higher rate of outpatient or ED visits for clinical failure within 30 days post-discharge in the non-concordant group versus the concordant group (14.8% vs. 7.5%, p < 0.05). Although there was no difference in LOS, duration of antibiotics, and 30-day all-cause readmission, there was a trend toward higher development of *C. difficile* infection in-hospital or within 30 days post-discharge in the concordant versus non-concordant group (5.2% vs. 1.5%, p=0.07) (**Table 3**).

In the CAP subgroup, there was a significantly shorter median LOS in the concordant group versus the non-concordant group (4 vs. 5.5 days, p < 0.01) (**Table 3**). In the HCAP subgroup, there was a shorter median LOS (7 vs. 5 days, p < 0.001) and duration of antibiotics (9 vs. 8 days, p < 0.05) in the non-concordant group.

Table 3. Clinical outcomes between concordant versus non-concordant regimens of the entire cohort, patients with CAP, and patients with HCAP

Outcome	Concordant (N=200)	Non-concordant (N=142)	*P* value
In-hospital mortality, n (%)	8 (4)	5 (3.5)	0.82
LOS, days, median (IQR)	5 (4-8)	5 (4-7)	0.34
Duration of antibiotics, days, median (IQR)	8 (6 – 10)	8 (7 – 10)	0.89
30-day all-cause readmission, n (%)	36 (18)	28 (19.7)	0.70
***C. difficile* in-hospital or within 30 days post-discharge, n (%)**	10 (5.2)	2 (1.5)	0.07
Outpatient/ED visit for clinical failure within 30 days post-discharge, n (%)	15 (7.5)	21 (14.8)	<0.05
Subgroup Analysis in CAP patients (N=168)			

Outcome	Concordant (N=120)	Non-concordant (N=48)	*P* value
In-hospital mortality, n (%)	3 (2.5)	2 (4.2)	0.63
LOS, days, median (IQR)	4 (3 – 6)	5.5 (4 – 7.75)	<0.01
Duration of antibiotics, days, median (IQR)	8 (6 – 9)	7.5 (7 – 9)	0.54
30-day all-cause readmission, n (%)	16 (13.7)	7 (15.2)	0.80
***C. difficile* in-hospital or within 30 days post-discharge, n (%)**	3 (2.6)	0 (0)	0.56
Outpatient/ED visit for clinical failure within 30 days post-discharge, n (%)	9 (7.7)	6 (13.0)	0.29
Subgroup Analysis in HCAP patients (N=174)			
Outcome	**Concordant (N=80)**	**Non-concordant (N=94)**	***P* value**
In-hospital mortality, n (%)	5 (6.3)	3 (3.2)	0.47
LOS, days, median (IQR)	7 (5 – 11)	5 (3.5 – 6.5)	<0.001
Duration of antibiotics, days, median (IQR)	9 (7 – 12.5)	8 (7 – 10)	<0.05
30-day all-cause readmission, n (%)	20 (26.7)	21 (23.1)	0.59
***C. difficile* in-hospital or within 30 days post-discharge, n (%)**	7 (9.3)	2 (2.2)	0.08
Outpatient/ED visit for clinical failure within 30 days post-discharge, n (%)	6 (8)	15 (16.5)	0.10

IQR – interquartile range, ED – emergency department, HCAP – healthcare-associated pneumonia

Microbiologic Pathogens

In the total cohort, 46 patients (13.5%) had positive cultures with available susceptibilities from which 51 pathogens were isolated. HCAP patients had 38 pathogens isolated versus 13 pathogens in the CAP group. The prevalence of patients with MDR pathogens isolated from the entire cohort was 23 (6.7%), with 12.1% of HCAP patients having at least one MDR pathogen versus 1.2% of CAP patients. Of note, 100% (N=11) of MRSA isolates and 90% (N=9) of *P. aeruginosa* isolates were identified in patients with HCAP. Bacteremia occurred in four patients with CAP and six patients with HCAP.

Patients with positive microbial cultures were included in a logistic regression analysis. Variables entered in the univariate analysis that were significant for the presence of MDR organisms included hospitalization in the preceding 90 days, antibiotic use within the last 90 days, residence in a LTCF, history of MRSA, and severe chronic obstructive pulmonary

disease (COPD) or structural lung disease **(Table 4)**. The post-hoc power analysis indicated 99% statistical power to detect a difference in MDR rate.

Multivariate logistic regression analysis of independent risk factors for infection associated with MDR pathogens shown in **Table 4,** identified severe COPD or structural lung disease (odds ratio [OR] = 7.1), history of MRSA (OR = 5.7), and residence in a LTCF (OR = 5.6) as factors independently associated with acquiring potential MDR pathogens.

Table 4. Univariate and multivariate logistic regression analysis of individual risk factors for multi-drug resistant (MDR) pathogens

	Univariate Analysis			**Multivariate Analysis**
Risk Factor	**Patients with MDR Pathogen (N=23)**	**Patients without MDR Pathogen (N=319)**	***P* value**	**Odds Ratio (95% CI)**
Age, years, median (IQR)	72 (58-80)	80 (69-86)	0.013	0.96 (0.93 – 0.99)
ICU admission, n (%)	7 (30.4)	46 (14.4)	0.07	2.31 (0.77 – 6.97)
CCI, median (IQR)	2 (1-4)	2 (1-4)	0.30	–
Recent hospitalization, n(%)	14 (60.9)	96 (30.1)	0.004	1.33 (0.41 – 4.30)
Prior antibiotic use, n (%)	16 (69.6)	92 (28.8)	<.0001	3.25 (0.96 – 10.47)
LTCF, n (%)	6 (26.1)	22 (6.9)	0.006	5.64 (1.54 – 20.73)
Chronic HD, n (%)	1 (4.4)	8 (2.5)	0.477	–
Immunosuppression, n (%)	5 (21.7)	31 (9.7)	0.08	3.20 (0.91 – 11.28)
History of MRSA, n (%)	5(21.7)	10 (3.1)	0.002	5.71 (1.46 – 22.32)
Multiple infiltrates, n (%)	2 (8.7)	47 (14.7)	0.55	–
History of PSA, n (%)	1 (4.4)	5 (1.6)	0.34	–
Severe COPD/structural lung disease, n (%)	9 (39.1)	27 (8.5)	<0.001	7.11 (2.20 – 22.95)

IQR – Interquartile range, ICU – intensive care unit, CCI – Charlson comorbidity index, LTCF – long-term care facility, HD – hemodialysis, MRSA – methicillin-resistant *S. aureus*, PSA – *Pseudomonas aeruginosa*, COPD – chronic obstructive pulmonary disease

Discussion

We compared outcomes in patients presenting from the community with CAP or HCAP based on whether their empiric antibiotic treatment was concordant or non-concordant with institution-specific guidelines. Additionally, the presence of risk factors for acquiring MDR pathogens were evaluated. In the entire cohort, our study did not find a difference in in-hospital mortality, length of stay, antibiotic duration, 30-day all-cause readmission, or *Clostridium difficile* infection in-hospital or within 30 days post-discharge between the concordant and non-concordant groups, with the exception of a greater incidence of outpatient or ED visits for clinical failure in the guideline non-concordant group.

When analyzing the CAP and HCAP subgroups, we found that HCAP patients treated with guideline non-concordant therapy had a shorter LOS, and duration of antibiotic therapy, which was driven by the use of narrower-spectrum intravenous antibiotics that can be given orally upon discharge. While the 2005 IDSA/ATS guidelines recommend treating patients who have risk factors for MDR pathogens, including the HCAP criteria, with broad-spectrum antibiotics, our study, and a growing number of recently published studies, suggest that the use of empiric broad-spectrum antibiotics for all HCAP patients is not necessary. Reduction of broad-spectrum antibiotic use may reduce length of stay, antibiotic duration, and decrease rates of *C. difficile* infection.[9]

The similarity in clinical outcomes between the guideline-concordant versus non-concordant cohorts can be explained if the HCAP definition generally overestimates a patient's likelihood of having pneumonia due to an MDR pathogen. Chalmers and colleagues conducted a systematic review and meta-analysis of 24 studies involving 22,456 HCAP patients.[9] The authors found the discriminatory ability of the HCAP criteria to detect resistant pathogens was poor. Several other studies have reported similar findings, and identified models that are more accurate at predicting MDR pathogens.[14-18] In addition, Chalmers and colleagues concluded that mortality in HCAP patients was not associated with a higher frequency of resistant pathogens, but was associated with increased age and co-morbidities, after adjusting for these covariates.

A prospective study by Maruyama and colleagues[18] used an algorithm, based on presence of MDR risk factors and severity of pneumonia, to select narrow-spectrum versus broad-spectrum empiric therapy for 321 HCAP patients. Patients deemed to be low risk based on the presence of 0-1 MDR risk factor and/or diagnosed with non-severe pneumonia were treated with narrow-spectrum, empiric antibiotics. Patients deemed to be high risk based on the presence of two or more MDR risk factors, or diagnosed with severe pneumonia were treated with broad-spectrum, empiric antibiotics. From this study it was found that HCAP patients with two or more MDR risk factors were more likely to have a higher frequency of MDR pathogens than HCAP patients with 0-1 MDR risk factor, 27% vs. 2%, respectively, $p < 0.001$. Using this algorithm, only 53% of HCAP patients received broad-spectrum antibiotics with 93% of HCAP patients receiving appropriate therapy based on microbiologic data. The authors concluded that if patients are risk stratified, narrow-spectrum antibiotics for selected HCAP patients achieved good outcomes while limiting excessive use of broad-spectrum antibiotics.

Chen and colleagues,[20] had similar conclusions in their retrospective study of 228 patients with HCAP treated with either a CAP or HCAP regimen. There was no difference in clinical cure at 30 days post-discharge between these two regimens. Webb and colleagues[8] noted that patients had a higher risk of developing MDR pathogens when they had multiple HCAP risk factors. Furthermore, patients with ≥ 3 HCAP risk factors were ten times more likely to acquire drug-resistant pathogens than those without HCAP risk factors.

Our study identified several independent risk factors associated with presence of MDR pathogens, which are residence at a LTCF, history of MRSA infection, diagnosis of severe COPD, or structural lung disease. These results are consistent with other studies, which also demonstrated residence at a LTCF as an independent risk factor for acquiring MDR pathogens.[14,17,21-25] Madaras-Kelly and colleagues[14] demonstrated previous MRSA history in the last 90 days was associated with presence of MRSA pneumonia. Gross and colleagues[21] reported that *P. aeruginosa* colonization, or infection within the previous year, was associated with an increased rate of MDR pathogens. Severe COPD and structural lung disease were associated with acquiring MDR pathogens, in particular *P. aeruginosa* in our study, which is consistent with previous findings.[22,26]

While other studies identified recent antibiotic use as an independent risk factor for presence of MDR pathogens, our study did not.[12,16,17,21,22,24,27] Previous studies described patients exposed to prior antibiotic treatment as use of broad-spectrum intravenous antibiotic therapy; however, our study used a broader criteria for prior antibiotic use, which included both intravenous and oral therapy, which may explain the differences in our results. In addition, recent hospitalization was not found to be a significant risk factor for MDR pathogens in our study which is in contrast to prior studies.[14,16,17,22,23,25,27,28]

Our data demonstrate significant opportunities for improvement in the empiric management of HCAP based on the 2005 IDSA/ATS guidelines. This retrospective analysis demonstrated that many providers often chose narrower spectrum antibiotics in patients who, based on the presence of risk factors suggested in the guidelines, should have received empiric, broad-spectrum, antibiotics. Our study also showed no difference in clinical outcomes, except clinical failure in the outpatient setting post-discharge, suggesting that CAP therapy may be effective for treating pneumonia in select patients with MDR risk factors but that patients may require careful outpatient monitoring. Multivariate logistic regression analysis identified specific risk factors independently associated with MDR organisms that may improve clinical decisions regarding initial antibiotic therapy.

Limitations of this study include reliance on ICD-9 codes for diagnosis of pneumonia. There may have been missing or vague information in the medical record, which precluded accurate assessment of the patient's MDR risk factor history. Our study was conducted in a community-based teaching hospital with a low rate of MDR pathogens. Our findings may not be generalizable to other institutions with higher rates of MDR pathogens. There are limitations to assessing outpatient visits for clinical failure, as the data analyzed were only available for patients who stayed within our health system for their follow-up care, and

confounders such as socioeconomic factors may have affected the outcome. Finally, there was a low prevalence of patients with positive respiratory cultures isolated from the entire cohort attributed to less routine collection of cultures for CAP patients and invasive specimens for HCAP patients.

Early, appropriate antibiotic treatment can be improved with rapid collection of culture specimens and examination with matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF-MS) that are becoming available in many hospitals.[29] The rapid identification of respiratory pathogens within hours may help reduce inappropriate antibiotic use and improve clinical outcomes. Improved pathogen prediction models are warranted until this method is widely available.

Conclusion

Our study demonstrated no difference in clinical outcomes between patients treated with guideline-concordant therapy versus guideline non-concordant therapy in the management of community or healthcare-associated pneumonia. Our data underscore the importance of reassessing the HCAP guidelines to identify evidence-based risk factors for MDR pathogens in patients admitted with pneumonia and to decrease complications related to excessive antibiotic use.

References

1. American Thoracic Society; Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med*. 2005;171(4):388-416.
2. Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis.* 2007; 44 Suppl 2:S27-72.
3. Mortensen EM, Restrepo M, Anzueto A, Pugh J. Effects of guideline concordant antimicrobial therapy on mortality among patients with community-acquired pneumonia. *Am J Med.* 2004;117:726–731.
4. Frei CR, Restrepo MI, Mortensen EM, Burgess DS. Impact of guideline-concordant empiric antibiotic therapy in community-acquired pneumonia. *Am J Med*. 2006;119(10):865-871.
5. Dambrava PG, Torres A, Vallès X, et al. Adherence to guidelines' empirical antibiotic recommendations and community-acquired pneumonia outcome. *Eur Respir J*. 2008;32(4):892-901.
6. McCabe C, Kirchner C, Zhang H, Daley J, Fisman DN. Guideline-concordant therapy and reduced mortality and length of stay in adults with community-acquired pneumonia: playing by the rules. *Arch Intern Med.* 2009:169(16):1525-1531.
7. Grenier C, Pépin J, Nault V, et al. Impact of guideline-consistent therapy on outcome of patients with healthcare-associated and community-acquired pneumonia. *J Antimicrob Chemother*. 2011;66(7):1617-1624.
8. Webb BJ, Dangerfield BS, Pasha JS, Agrwal N, Vikram HR. Guideline-concordant

antibiotic therapy and clinical outcomes in healthcare-associated pneumonia. *Respir Med*. 2012;106(11):1606-1612.
9. Chalmers JD, Rother C, Salih W, Ewig S. Healthcare-associated pneumonia does not accurately identify potentially resistant pathogens: a systematic review and meta-analysis. *Clin Infect Dis*. 2014;58(3):330-339.
10. Boucher HW, Talbot GH, Bradley JS, et al. Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. *Clin Infect Dis*. 2009;48(1):1-12.
11. Aronsky D, Haug PJ, Lagor C, Dean NC. Accuracy of administrative data for identifying patients with pneumonia. *Am J Med Qual*. 2005;20(6):319-328.
12. Shindo Y, Sato S, Maruyama E, et al. Health-care-associated pneumonia among hospitalized patients in a Japanese community hospital. *Chest*. 2009;135(3):633-640.
13. Shorr AF, Zilberberg MD, Reichley R, et al. Readmission following hospitalization for pneumonia: the impact of pneumonia type and its implication for hospitals. *Clin Infect Dis*. 2013;57(3):362-367.
14. Madaras-Kelly KJ, Remington RE, Fan VS, Sloan KL. Predicting antibiotic resistance to community-acquired pneumonia antibiotics in culture-positive patients with healthcare-associated pneumonia. *J Hosp Med*. 2012;7(3):195-202.
15. Shorr AF, Zilberberg MD, Reichley R, et al. Validation of a clinical score for assessing the risk of resistant pathogens in patients with pneumonia presenting to the emergency department. *Clin Infect Dis*. 2012. 15;54(2):193-198.
16. Park SC, Kang YA, Park BH, et al. Poor prediction of potentially drug-resistant pathogens using current criteria of health care-associated pneumonia. *Respir Med*. 2012;106(9):1311-1319.
17. Park SC, Kim EY, Kang YA, et al. Validation of a scoring tool to predict drug-resistant pathogens in hospitalised pneumonia patients. *Int J Tuberc Lung Dis*. 2013;17(5):704-709.
18. Aliberti S, Cilloniz C, Chalmers JD, et al. Multidrug-resistant pathogens in hospitalised patients coming from the community with pneumonia: a European perspective. *Thorax*. 2013;68(11):997-999.
19. Maruyama T, Fujisawa T, Okuno M, et al. A new strategy for healthcare-associated pneumonia: a 2-year prospective multicenter cohort study using risk factors for multidrug-resistant pathogens to select initial empiric therapy. *Clin Infect Dis*. 2013 ;57(10):1373-1383.
20. Chen JI, Slater LN, Kurdgelashvili G, Husain KO, Gentry CA. Outcomes of health care-associated pneumonia empirically treated with guideline-concordant regimens versus community-acquired pneumonia guideline-concordant regimens for patients admitted to acute care wards from home. *Ann Pharmacother*. 2013;47(1):9-19.
21. Gross AE, Van Schooneveld TC, Olsen KM, et al. Epidemiology and predictors of multidrug-resistant community-acquired and health care-associated pneumonia. *Antimicrob Agents Chemother*. 2014;58(9):5262-5268.
22. Jeong BH, Koh WJ, Yoo H, et al. Risk factors for acquiring potentially drug-resistant pathogens in immunocompetent patients with pneumonia developed out of hospital. *Respiration*. 2014;88:190–198.

23. Aliberti S, Pasquale MD, Zanaboni AM, et al. Stratifying risk factors for multidrug-resistant pathogens in hospitalized patients coming from the community with pneumonia. *Clin Infect Dis*. 2012.15;54(4):470-478.
24. Schreiber MP, Chan CM, Shorr AF. Resistant pathogens in nonnosocomial pneumonia and respiratory failure: is it time to refine the definition of health-care-associated pneumonia? *Chest*. 2010;137(6):1283-1288.
25. Shorr AF, Zilberberg MD, Micek ST, Kollef MH. Prediction of infection due to antibiotic-resistant bacteria by select risk factors for health care-associated pneumonia. *Arch Intern Med*. 2008;168(20):2205-2210.
26. Chalmers JD, Taylor JK, Singanayagam A, et al. Epidemiology, antibiotic therapy, and clinical outcomes in health care-associated pneumonia: a UK cohort study. *Clin Infect Dis*. 2011. 15;53(2):107-113.
27. Shindo Y, Ito R, Kobayashi D, et al. Risk factors for drug-resistant pathogens in community-acquired and healthcare-associated pneumonia. *Am J Respir Crit Care Med*. 2013 15;188(8):985-995.
28. Brito V, Niederman MS. Healthcare-associated pneumonia is a heterogeneous disease, and all patients do not need the same broad-spectrum antibiotic therapy as complex nosocomial pneumonia. *Curr Opin Infect Dis*. 2009;22(3):316-325.
29. Wang YF, Fu Jianfeng. Rapid laboratory diagnosis for respiratory infectious diseases by using MALDI-TOF mass spectrometry. *J Thorac Dis*. 2014;6(5):507-511.