

Epidemiology and Outcomes of Health-care–Associated Pneumonia*

Results From a Large US Database of Culture-Positive Pneumonia

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Context: Traditionally, pneumonia developing in patients outside the hospital is categorized as community acquired, even if these patients have been receiving health care in an outpatient facility. Accumulating evidence suggests that health-care–associated infections are distinct from those that are truly community acquired.

Objective: To characterize the microbiology and outcomes among patients with culture-positive community-acquired pneumonia (CAP), health-care–associated pneumonia (HCAP), hospital-acquired pneumonia (HAP), and ventilator-associated pneumonia (VAP).

Design and setting: A retrospective cohort study based on a large US inpatient database.

Patients: A total of 4,543 patients with culture-positive pneumonia admitted into 59 US hospitals between January 1, 2002, and December 31, 2003, and recorded in a large, multi-institutional database of US acute-care hospitals (Cardinal Health-Atlas Research Database; Cardinal Health Clinical Knowledge Services; Marlborough, MA).

Main measures: Culture data (respiratory and blood), in-hospital mortality, length of hospital stay (LOS), and billed hospital charges.

Results: Approximately one half of hospitalized patients with pneumonia had CAP, and > 20% had HCAP. *Staphylococcus aureus* was a major pathogen in all pneumonia types, with its occurrence markedly higher in the non-CAP groups than in the CAP group. Mortality rates associated with HCAP (19.8%) and HAP (18.8%) were comparable ($p > 0.05$), and both were significantly higher than that for CAP (10%, all $p < 0.0001$) and lower than that for VAP (29.3%, all $p < 0.0001$). Mean LOS varied significantly with pneumonia category (in order of ascending values: CAP, HCAP, HAP, and VAP; all $p < 0.0001$). Similarly, mean hospital charge varied significantly with pneumonia category (in order of ascending value: CAP, HCAP, HAP, and VAP; all $p < 0.0001$).

Conclusions: The present analysis justified HCAP as a new category of pneumonia. *S aureus* was a major pathogen of all pneumonias with higher rates in non-CAP pneumonias. Compared with CAP, non-CAP was associated with more severe disease, higher mortality rate, greater LOS, and increased cost. (CHEST 2005; 128:3854–3862)

Key words: community acquired; epidemiology; health care; mechanical ventilation; mortality; nosocomial; outcomes; pneumonia; resource use

Abbreviations: ASG = admission severity group; CAP = community-acquired pneumonia; CI = confidence interval; HAP = hospital-acquired pneumonia; HCAP = health-care–associated pneumonia; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification; LOS = length of hospital stay; MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-susceptible *Staphylococcus aureus*; NP = nosocomial pneumonia; OR = odds ratio; VAP = ventilator-assisted pneumonia

Pneumonia is often classified as either community acquired or nosocomial, depending on whether the infection developed while the patient was in an outpatient setting or in an inpatient setting.¹ Nosocomial pneumonia (NP) is further differentiated into ventilator-associated pneumonia (VAP) if the process arose after the patient had been receiving at least 24 h of mechanical ventilation.^{2,3} This classification

scheme reflects differences in the pathogens responsible for these infections and forms the basis for treatment decisions and antibiotic selections. For example, *Streptococcus pneumoniae* is a common cause of community-acquired pneumonia (CAP)^{4,5} but is infrequently implicated in VAP.^{3,6} Similarly, many empiric regimens for VAP include antimicrobials active against *Pseudomonas aeruginosa*, as this

is regularly recovered from patients with VAP⁷ but is rarely seen in outpatients with CAP.

Despite the popularity of this dichotomous classification scheme for pneumonia, recent evidence⁸⁻¹⁰

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indicates that this system may have significant limitations. Specifically, health care now reflects a continuum of care with many traditional inpatient services provided in outpatient settings. Invasive medical therapies are now routinely administered in nursing homes and rehabilitation hospitals, and many surgeries are performed in outpatient-based surgical centers. Additionally, some patients regularly utilize significant medical resources and transition from the hospital to a subacute care facility but are then soon thereafter return to the hospital, never truly residing in the "community." In each of these instances and despite the close link to traditional inpatient care, physicians often categorize new infections in such subjects as "community acquired."¹¹ Data indicate, however, that these health-care-associated infections have a unique epidemiology and that the pathogens causing and the outcomes related to these infections more closely resemble those seen with nosocomial processes.^{8,11-13} Some experts^{8,11,14} advocate creating a new class of "health-care-associated" infection. Clarifying the epidemiology of these health-care-associated infections generally, and of health-care-associated pneumonia (HCAP) specifically, is crucial to efforts to design appropriate empiric antimicrobial treatment guidelines.

Accumulating evidence pointing to the potentially significant impact of HCAP results in the very recent recognition of HCAP by the American Thoracic Society and the Infectious Diseases Society of America.^{15,16} However, to date, no multi-institutional data exist describing the epidemiology and microbiology of HCAP. Additionally, prior work on this topic has been limited to observations coming from mainly large, academic teaching hospitals. Therefore, to

better characterize HCAP and to compare it with CAP, hospital-acquired pneumonia (HAP), and VAP, we retrospectively analyzed the records of patients with culture-positive pneumonia registered in a large US database between January 1, 2002, and December 31, 2003. We hypothesized that HCAP would represent a distinct clinical entity, with the pathogens recovered more closely resembling those seen in HAP and VAP. We also sought to determine if HCAP was clinically distinct from these other types of pneumonia and to assess the economic impact of HCAP.

MATERIALS AND METHODS

Study Design

A retrospective cohort analysis was performed to characterize the epidemiology, microbiology, and clinical/economic outcomes of patients with culture-positive CAP, HCAP, HAP, and VAP in the first 5 days of hospital admission. Data were obtained for all patients with pneumonia admitted to 59 US hospitals between January 1, 2002, and December 31, 2003.

Data Source

Data for the present analysis were obtained from a large, multi-institutional database of US acute-care hospitals, the Atlas database (Cardinal Health-Atlas Research Database; Cardinal Health Clinical Knowledge Services; formerly MedisGroup; Marlborough, MA).² Details of this database were published previously.^{2,17-19} Briefly, Cardinal Health Clinical Knowledge Services develops the Atlas software and distributes it to acute-care hospitals in the United States for the collection and analysis of detailed clinical and administrative data. As the largest database of its kind, the Atlas database collects information on approximately 950,000 inpatient admissions to > 200 US acute-care hospitals annually. Hospitals included in the database are similar in bed size to American Hospital Association-member hospitals.

The Atlas database registers patient demographics, admission source, type of ICU, all documented procedure and diagnosis codes (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM]), admission and discharge dates for each stay in the ICU, total length of hospital stay (LOS) in hospital, billed total and ancillary hospital charges, discharge disposition, specific interventions received, and information on > 400 key clinical findings,^{2,20} including clinical history and pathophysiologic findings, such as vital signs, laboratory test results, culture findings, and physician assessments. During the study period from January 1, 2002, to December 31, 2003, a total of 162 hospitals in the Atlas database met the data quality criteria for inclusion, of which 59 hospitals (16 teaching hospitals and 43 nonteaching hospitals) collected clinical and culture data for the first 5 days of patient hospitalization and were included for the present study.

Sample Populations

Pneumonia was defined by the presence of either primary or secondary ICD-9-CM codes indicative of pneumonia and a concomitant positive respiratory bacterial culture. The study

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samples were then constructed stepwise according to definitions for different pneumonia types defined in Table 1. First, patients who were receiving mechanical ventilation for at least 24 h with a first positive bacterial respiratory culture result after ventilator start time were classified into the VAP group. Second, patients with a first positive bacterial respiratory culture result > 2 days from hospital admission who did not meet VAP definition were classified into the HAP group. Third, patients with a first positive bacterial respiratory culture result within 2 days of hospital admission and who were transferred from another health-care facility, had been receiving long-term hemodialysis, or had prior hospitalization within 30 days were classified into the HCAP group, which served as the control group. All remaining patients constituted the CAP group.

Data Analysis

For univariate analyses, the χ^2 test was used for mortality; the Wilcoxon rank-sum nonparametric test was used for LOS and total charge analyses when appropriate. For multivariate analyses, logistic regression models were used for mortality analysis to adjust for potential confounders. Potential candidate variables were identified based on review of the literature and clinical relevance. The risk factors included demographic variables, coexisting conditions (eg, cancer, cerebrovascular disease, liver disease, renal disease), physical examination findings (eg, vital signs, altered mental status), laboratory findings (eg, BUN, glucose), culture findings, radiologic findings (eg, pleural effusion), and other clinical findings. It also included subtype of pneumonia classified by the timing and relation to ventilator use. Severity of illness was measured by use of the admission severity group (ASG) classification system, which was specifically devised for use with the Atlas database and was described previously.²

Table 1—Definitions of Pneumonia Categories

Pneumonia Category*	Definition
VAP	Patients receiving mechanical ventilation for at least 24 h with a first positive bacterial† respiratory culture finding after ventilator start date
HAP	Patients with a first positive bacterial† respiratory culture finding > 2 days from admission who do not meet VAP definition
HCAP	Patients with a first positive bacterial† respiratory culture finding within 2 days of admission and any of the following: (1) admission source indicates a transfer from another health-care facility; (2) receiving long-term hemodialysis (ICD-9-CM codes); and (3) prior hospitalization within 30 days who do not meet VAP definition
CAP	Patients with a first positive bacterial† respiratory culture finding who do not meet VAP or HCAP definition

*All pneumonia cases with primary or secondary ICD-9-CM codes for pneumonia and positive respiratory culture finding treated in a hospital that collected at least 5 days of culture data.

†Eligible bacteria include: Acinetobacter, Bacillus, Bacteroides, Bordetella, Brucella, Chlamydia, Enterobacter, Escherichia, Haemophilus, Klebsiella, Legionella, Listeria, MRSA, Mycoplasma, Proteus, Pseudomonas, Salmonella, Serratia, Shigella, *S aureus*, Streptobacillus, Streptococcus A, Streptococcus B, Streptococcus C, Streptococcus D, Streptococcus F, Streptococcus G, Streptococcus nongroup, *S pneumoniae*, Yersinia.

Candidate variables that were associated with outcome of the interest at the univariate level ($p < 0.05$) were included as candidate covariates in a multiple logistic regression model for mortality. Variable selection in multivariable modeling was based on clinical and statistical significance. The crafting of continuous variables (laboratory, vital signs, and altered mental status) was based on a validated mortality predictive model using approximately 100,000 pneumonia admissions. Discrimination and calibration of the logistic model were assessed by the c-statistic and the Hosmer-Lemeshow χ^2 statistic. Models were examined for possible overfit using bootstrap validation with 200 iterations. Variables that never changed signs and retained statistical significance > 70% of the iterations were selected for the model. Finally, all the models were reviewed for consistency with literature, clinical plausibility, and statistical validity. Hospital charges were calculated by each specific institution, and the results were aggregated.

RESULTS

Patient Characteristics

A total of 4,543 patients met the inclusion criteria and were analyzed in the present study. Among these patients, there were 2,221 patients with CAP (48.9%), 988 patients with HCAP (21.7%), 835 patients with HAP (18.4%), and 499 patients with VAP (11%) [Table 2]. Gender differences were statistically nonsignificant among the four pneumonia types. HCAP patients (78.1%) were more likely to be white than were patients with VAP (71.7%). A significantly lower proportion of patients with HCAP were black (4.6%) compared with patients with HAP (6.8%) and VAP (12.2%). Patients with HCAP (median age, 77 years) were significantly older than those who had CAP (73 years) or VAP (65 years) but were comparable to those with HAP (76 years). A significantly higher percentage of patients with HCAP (71%) were receiving Medicare than were patients with CAP (62.5%), HAP (62.6%), or VAP (50.3%). Nearly one half of patients with HCAP (49.6%) were admitted from skilled nursing facilities, a rate markedly higher than for patients with CAP (0%), HAP (10.3%), or VAP (9.4%). Fewer patients with HCAP were admitted based on lower to moderate ASG scores of 1 to 2 than were patients with CAP or HAP. In contrast, a higher proportion of patients with HCAP were admitted on high ASG scores of 3 to 4 than were patients with CAP or HAP. A significantly lower proportion of patients with HCAP were admitted on ASG score 4 than were patients with VAP. Other clinical characteristics, including comorbidities and disease group description, were also different among the four pneumonia types (Table 2).

Pathogen Distribution

The distribution of pathogens varied among the four pneumonia categories (Table 3). *Staphylococcus*

Table 2—Patient Demographic and Clinical Characteristics (n = 4,543)

Variables	CAP (n = 2,221)	HCAP (n = 988)	HAP (n = 835)	VAP (n = 499)	Total (n = 4,543)
Male gender, %	57.5	58.7	57.5	61.3	58.2
Race, %					
American Indian-Eskimo	0	0	0.1	0	0
Asian-Pacific Islander	0.1	0	0.2	0.4	0.2
Black	6.0	4.6	6.8*	12.2†	6.5
White	76.6	78.1	77.3	71.7†	76.5
Other	0.7	0.4	0.4	1.6*	0.7
Unknown	3.0†	7.3	2.3†	5.6	4.1
Not specified	13.5†	9.6	12.9*	8.4	12.0
Median age (interquartile range), yr	73 (60–80)†	77 (66–83)	76 (64–82)	65 (50–77)†	74 (60–81)
Insurance, %					
Managed care	12.3†	9.1	17.1†	15.0†	12.8
Medicaid	8.0	6.2	5.4	6.8	7.0
Medicare	62.5†	71.0	62.6†	50.3†	63.0
Other	3.7	4.5	4.4	7.4*	4.4
Paid insurance	10.3*	8.1	7.8	15.2†	9.9
Self pay	3.1†	1.0	2.0	4.4†	2.6
Unknown	0.2	0.2	0.6	0.8	0.3
Admitted from skilled nursing facilities, %	0 0†	49.6	10.3†	9.4†	13.7
Comorbidities, %					
History of any cancer	22.7	22.3	23.6	13.0†	21.7
Current cancer metastatic diagnosis	4.5	3.7	4.7	1.6*	4.0
Current medical immunosuppression	15.1†	23.2	19.0†	11.8†	17.0
History of peripheral vascular disease	8.8*	11.2	13.8	10.0	10.4
History of diabetes	23.4†	32.2	28.6	26.5*	26.6
History of chronic liver disease	2.0	2.4	3.2	3.6	2.5
History of chronic lung disease	55.5	54.8	51.6	34.1†	52.3
History of chronic renal disease	8.5†	11.6	14.4	12.2	10.7
Cardiovascular disease	41.1†	52.2	47.4*	44.7†	45.1
Immunocompromised	2.3	1.5	2.9*	1.0	2.1
HIV positive	0.9	0.5	0.6	0.4	0.7
Diagnosis or history of cystic fibrosis	0	0.5	0	0	0.1
Previous stroke	11.7†	22.1	15.6†	11.6†	14.6
Previous amputation	2.2†	4.2	4.9	3.0	3.3
Previous CABG	11.1†	7.7	9.9	8.6	9.9
History of CHF	21.8†	36.5	27.8†	23.5†	26.3
Previous PTCA	5.5	4.8	6.8	4.0	5.4
Current medication insulin	7.7†	13.9	10.4†	10.6	9.9
Previous TIA	3.7†	6.4	5.3	1.0†	4.3
History of respiratory distress syndrome	0.2†	0.9	0.2	0.6	0.4
Previous AICD	0.5	0.1	0.6	0	0.4
Median comorbidities (interquartile range), No.	2 (1–4)†	3 (2–4)	3 (1–4)†	2 (0–4)†	2 (1–4)
Ventilator support during admission, %	16.9†	24.1	22.4	100.0†	28.6
≥ 99 Ventilator hours during admission, %	6.7†	10.4	13.1	75.2†	16.2
≥ 99 Ventilator hours during admission out of those with ventilator support, %	39.7	43.3	58.3†	75.2†	56.7
Surgery‡, %					
General or spinal anesthesia within first 2 days of admission	1.8	1.5	10.1†	23.7†	5.6
Primary discharge diagnosis of pneumonia, %	72.2	70.5	47.0†	15.8†	61.0
Secondary discharge diagnosis of pneumonia, %	35.5†	41.3	59.8†	88.2†	47.0
Risk-adjusted severity on admission§, %					
ASG 0	0.5	0.3	0.8	0.6	0.6
ASG 1	15.2†	5.7	13.4†	7.0	11.9
ASG 2	45.1†	28.9	42.2†	24.9	38.8
ASG 3	35.8†	59.2	42.2†	54.3	44.1
ASG 4	3.3†	6.0	1.3†	13.2†	4.6

*CABG = coronary artery bypass graft surgery; CHF = congestive heart failure; TIA = transient ischemic attack; PTCA = percutaneous transluminal coronary angioplasty; AICD = automatic implantable cardioverter defibrillator.

*p < 0.05 when compared with HCAP.

†p < 0.01 when compared with HCAP.

‡Surgery defined as general, spinal, or “convert to general” anesthesia codes within the first 2 days of admission.

§Predicted mortality on admission: ASG 0 = < 0.2%; ASG 1 = 0.2 to 1.1%; ASG 2 = 1.2 to 5.7%; ASG 3 = 5.8 to 49.9%; ASG 4 = > 50%.

Table 3—Frequency of Occurrence of Bacterial Pathogens Associated With CAP, HCAP, HAP, and VAP (n = 4,543)

Bacterial Pathogens*	CAP (n = 2,221)	HCAP (n = 988)	HAP (n = 835)	VAP (n = 499)
Gram-positive pathogens, %				
S aureus				
S aureus (all)	25.5†	46.7	47.1	42.5
MSSA (all)	17.2†	21.1	26.2†	28.5†
MSSA only	12.0	14.3	19.3†	19.0‡
MRSA (all)	8.9†	26.5	22.9	14.6†
MRSA only	6.2†	18.3	16.8	11.8†
All MRSA as percentage of all S aureus	34.8†	56.8	48.6‡	34.4†
Streptococcus nongroup	13.4†	7.8	13.9†	7.0
S pneumoniae	16.6†	5.5	3.1‡	5.8
Other Gram positive	7.1	7.7	8.1	8.6
Gram-negative pathogens, %				
Pseudomonas sp	17.1†	25.3	18.4†	21.2
Haemophilus sp	16.6†	5.8	5.6	12.2†
Klebsiella sp	9.5	7.6	7.1	8.4
Escherichia sp	4.8	5.2	4.7	6.4
Enterobacter sp	2.9	3.5	4.3	5.6
Acinetobacter sp	1.6‡	2.6	2.0	3.0
Other Gram negative	4.1†	9.5	3.7†	6.2‡

*Eligible bacteria include Acinetobacter, Bacillus, Bacteroides, Bordetella, Brucella, Chlamydia, Enterobacter, Escherichia, Haemophilus, Klebsiella, Legionella, Listeria, MRSA, Mycoplasma, Proteus, Pseudomonas, Salmonella, Serratia, Shigella, S aureus, Streptobacillus, Streptococcus A, Streptococcus B, Streptococcus C, Streptococcus D, Streptococcus F, Streptococcus G, Streptococcus nongroup, S pneumoniae, Yersinia.

†p < 0.01 when compared with HCAP.

‡p < 0.05 when compared with HCAP.

aureus was the dominant pathogen, and its subtypes (methicillin-susceptible S aureus [MSSA] and methicillin-resistant S aureus [MRSA]) were identified in large proportions of patients for all types of pneumonia. The occurrences of S aureus in the HCAP, HAP, and VAP groups were comparable and significantly higher than in the CAP group. Patients with HCAP and HAP were not statistically different from each other in terms of occurrences of S aureus or MRSA. The rate of MRSA infection (56.8%) in HCAP patients with S aureus infection was significantly higher than in patients with all other pneumonia types. Pathogens having an occurrence in > 10% of the patients in the CAP group included S aureus (25.5%), Pseudomonas sp (17.1%), Haemophilus sp (16.6%), S pneumoniae (16.6%), and nongroup Streptococcus (13.4%). For patients with HCAP, only S aureus (46.7%) and Pseudomonas sp (25.3%) had a presence in > 10% of the patients. In the HAP group, S aureus (47.1%), Pseudomonas sp (18.4%), and nongroup Streptococcus (13.9%), and in the VAP group, S aureus (42.5%), Pseudomonas sp (21.2%), and Haemophilus sp (12.2%) were identified in > 10% of the patients, respectively.

Clinical and Economic Outcomes

Mortality: For univariate analysis, mortality rates associated with HCAP (19.8%) and HAP (18.8%) were not significantly different from each other

(p > 0.05). Both were significantly higher than that of CAP (10.0%, both p < 0.0001) and lower than that of VAP (29.3%, both p < 0.0001; Fig 1).

Multiple logistic regression analysis results (Table 4) showed that patient demographics (age), physiologic derangement (vital signs, laboratory test results, neurologic function), chronic conditions (only metastatic cancer remained in the model), pathology, and subtype of pneumonia were independently associated with mortality risk. After controlling for age, acute physiologic severity, and comorbidity, S aureus

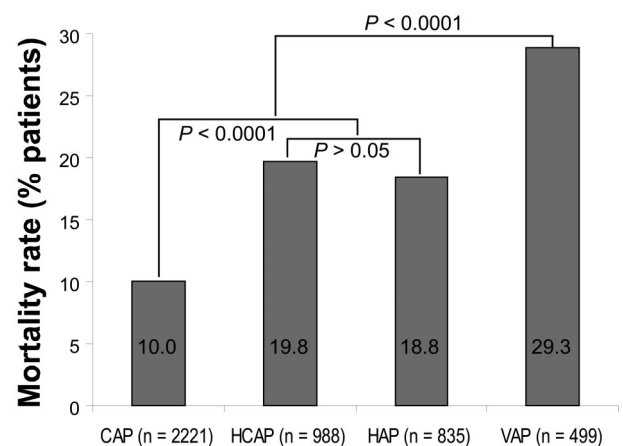


FIGURE 1. Mean mortality rates in patients with CAP, HCAP, HAP, and VAP.

Table 4—Results of Logistic Regression Analysis for Risk Factors Associated With Mortality in Patients (n = 4,543) With Pneumonia

Predictors	OR	95% CI	p Value
Age	1.02	1.01–1.03	< 0.0001
Coma	1.58	1.32–1.89	< 0.0001
<i>S aureus</i>	1.58	1.32–1.89	< 0.0001
Pneumonia sepsis*	1.77	1.35–2.32	< 0.0001
Albumin < 2.4 g/dL	1.68	1.32–2.14	< 0.0001
pH arterial < 7.3	2.40	1.87–3.08	< 0.0001
Creatinine > 1.5 mg/dL	1.38	1.10–1.73	< 0.0001
WBC < 4.3 or > 19.8 × 10 ³ /μL	1.50	1.22–1.84	0.0057
Platelets < 115,000/μL	2.10	1.57–2.82	0.0001
Bands > 32%	1.64	1.18–2.27	< 0.0001
BUN > 55 mg/dL	1.54	1.16–2.05	0.0034
BUN 40 to 55 mg/dL	1.47	1.10–1.96	0.0033
Temperature < 35.6°C	1.37	1.09–1.70	0.0092
Respiration > 39 breaths/min	1.55	1.15–2.08	0.0058
Metastatic cancer	3.45	2.41–4.92	0.0039
HCAP	1.65	1.31–2.08	< 0.0001
HAP	2.07	1.63–2.64	< 0.0001
VAP	3.24	2.48–4.25	< 0.0001

*Same pathogen found in the respiratory culture was also found in the blood culture.

was the only pathogen associated with significantly increased mortality for this patient population (odds ratio [OR], 1.58; confidence interval [CI], 1.32 to 1.89; $p < 0.0001$). Compared with CAP, the mortality risk was significantly higher if pneumonia was acquired after mechanical ventilation for at least 24 h (VAP: OR, 3.24; CI, 2.48 to 4.25; $p < 0.0001$), acquired 48 h after hospital admission (HAP: OR, 2.07; CI, 1.63 to 2.64; $p < 0.0001$), or associated with previous health-care exposure (HCAP: OR, 1.65; CI, 1.31 to 2.08; $p < 0.0001$), while other risk factors were controlled.

LOS: LOS values for CAP, HCAP, HAP, and VAP were significantly different from each other (all $p < 0.0001$; Table 5). Patients with CAP had the shortest mean LOS (7.5 days), and those with VAP had the longest mean LOS (23.0 days). Mean LOS for patients with HCAP was 8.8 days and 15.2 for patients with HAP.

Hospital Charges: Mean total hospital charge for patients with HCAP was significantly lower than in

patients with HAP or VAP but was significantly higher than that for patients with CAP (Table 5). The mean hospital charge for CAP, \$25,218, was the lowest among the four groups; the next lowest was in patients with HCAP (\$27,647). The mean hospital charge jumped to \$65,292 for patients with HAP, and peaked at \$150,841 for patients with VAP.

COMMENT

To our knowledge, this is the first multi-institutional study defining HCAP as a distinct type of pneumonia. The unique microbiology, epidemiology, and outcomes for patients with CAP, HCAP, HAP, and VAP demonstrated in the present study support a new, refined classification scheme categorizing pneumonias into these four subtypes. Compared with CAP, non-CAP, including HCAP, was associated with more severe disease, higher mortality rate, greater LOS, and increased cost. Our study also suggests that *S aureus* is a major pathogen with high occurrence among all types of pneumonias.

Pneumonia is one of the leading causes for hospitalization and mortality in the United States.²¹ Effective empiric treatment involves selection of an antibiotic with a spectrum of activity that includes the causative pathogen(s).²¹ In the absence of culture data, empiric antimicrobial treatment should be initiated within 4 h of a pneumonia diagnosis to optimize outcomes.^{22,23} Therefore, an evidence-based classification scheme that differentiates different types of pneumonia according to their most likely causative organism(s) will help clinicians maximize the likelihood of achieving a favorable patient outcome.

Due to the different etiologic pathogens underlying CAP and NP, initial empiric therapies differ. Major national^{21,24–26} and international^{27,28} guidelines recommend the combination of a macrolide and doxycycline, β -lactam, or fluoroquinolone, depending on the severity of illness at initial presentation and the presence of coexisting illness or advanced age, for the initial empiric antimicrobial treatment for CAP. In contrast, advanced-generation cephalosporins, β -lactam/ β -lactamase inhibitors, fluoroquinolones, clindamycin, certain carbapenems,

Table 5—Mean LOS in Hospital and Mean Hospital Total Charges for Patients With CAP, HCAP, HAP, and VAP*

Variables	CAP (n = 2,221)	HCAP (n = 988)	HAP (n = 835)	VAP (n = 499)
LOS, d	7.5 ± 7.2 (5.0)†	8.8 ± 7.8 (7.0)	15.2 ± 13.6 (11.0)†	23.0 ± 20.3 (17.0)†
Total charges, \$	25,218 ± 40,577 (13,358)†	27,647 ± 37,974 (17,508)	65,292 ± 101,886 (31,220)†	150,841 ± 151,155 (98,192)†

*Data are presented as mean ± SD (median).

† $p < 0.0001$ vs HCAP.

vancomycin, linezolid, aminoglycosides, and aztreonam, alone or in combination, are recommended for the treatment of NP.²⁹

Health-care services, such as dialysis, chemotherapy, and same-day surgery, are increasingly being provided in the outpatient environment.¹¹ At present, pneumonia related to these health-care-associated interventions may be classified as CAP and is treated as such. However, given the frequent transfer of patients and health-care workers between these facilities and hospitals, an outpatient facility is likely to be distinct from the true community and may more closely resemble the nosocomial setting in terms of the pathogens it might house. For example, MRSA strains isolated from patients with health-care-associated infections are distinct from those that are truly community acquired and have different susceptibility to antibiotics.¹³ In addition to the complexity introduced by evolving health-care practices, the causative pathogens associated with CAP have also changed in prevalence in recent years. Although *S pneumoniae* remains the most common causative pathogen, other potential pathogens (eg, *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, and *Legionella* spp) exist, and their prevalence changes over time and varies by geographic location.²¹ Furthermore, the emerging antimicrobial resistance of respiratory pathogens has complicated the management of these infections.³⁰ These changes necessitate an evolving treatment strategy based on the most recent findings regarding microbiology and epidemiology.³¹

The results of this study justify the separation of a new type of pneumonia, HCAP, from the traditionally defined CAP domain. HCAP is distinct from CAP in terms of patient characteristics, pathogen distribution patterns, and outcomes. HCAP is also different from HAP and VAP along the above-mentioned dimensions; however, in general, HCAP differs from HAP or VAP to a lesser degree than from CAP (eg, more comparable *S aureus* occurrences and mortality rates). Results of this study revealed that one half of hospitalized patients with culture-positive pneumonia had CAP and >20% had HCAP. Had the patients with HCAP been included in the CAP category according to the traditional classification scheme, they would have accounted for 31% of CAP patients who needed hospitalization. Given that data in this study were derived from a consortium of hospitals typical of acute-care US hospitals, it is reasonable to expect that at the present time, a large proportion of patients hospitalized in acute-care facilities are being treated for CAP but in fact should be treated for HCAP, resulting in potentially poor clinical outcomes.

We also observed that *S aureus* was a dominant pathogen in all types of pneumonia, including CAP. There is a consensus in the literature^{5,21} that the most common pathogen for CAP is *S pneumoniae*. Our results that fewer patients admitted for CAP had *S pneumoniae* infection than had *S aureus* infection probably reflected the effects of various forms of bias. Because only approximately one third of CAP patients require hospitalization,^{32,33} the CAP group in this analysis was more likely a sample of CAP patients who require hospitalization, rather than a representative sample for all patients with CAP. Additionally, the high prevalence of *S aureus* in the CAP group might be attributable to the relationship between *S aureus* and higher severity of illness, a major factor influencing the decision to hospitalize subjects with CAP treatment.²¹ Finally, since information regarding serologic diagnoses was limited and because of our express focus on culture results, we likely underestimated the incidence of certain pathogens, such as *Legionella pneumophila*.

The occurrence of *S aureus* in patients with HCAP was markedly higher than that in patients with CAP. Compared with the HAP group, a greater proportion of patients in the HCAP group had *Pseudomonas* sp and *S pneumoniae* and a lower proportion had nongroup Streptococcus. Compared with the VAP group, patients with HCAP were more likely to be infected by *S pneumoniae* and less likely to have *Haemophilus* sp infection. Thus, HCAP is microbiologically different from CAP, HAP, and VAP.

Multivariate analysis further indicated that *S aureus* was the only pathogen that correlated with mortality. It was possible that *S aureus* was the underlying reason for the increased mortality, LOS, and treatment costs observed in patients with HCAP, HAP, and VAP. The clinical outcomes in patients with HCAP and HAP were comparable in terms of raw mortality. However, the mean LOS and treatment costs for patients were significantly lower in these groups of patients than in those with HAP. This might reflect a general undertreatment for HCAP among clinicians who do not distinguish HCAP from CAP at present. Moreover, since treatment guidelines often do not recommend coverage for *S aureus* in CAP, the association between the presence of *S aureus* and mortality may reflect that subjects with such infections were more likely to have received antibiotics not effective against MSSA or, in particular, MRSA. In other words, recovery of *S aureus* may be a surrogate marker for the prescription of inappropriate antimicrobial therapy, a known predictor of poor outcomes in pneumonia.

The major strength of the present study was the use of a large, multicenter database that contained information allowing us to examine clinical and

economic variables. The availability of patient-specific outcomes data additionally allowed us to assess the clinical and economic burden associated with each type of pneumonia. Due to the way the patient-specific variables were coded in the database, patients with HCAP could also be identified. Furthermore, the continuous, ongoing data collection characteristic of the database enables us to collect similar data in the future in order to identify temporal trends of the epidemiology of these pneumonias for surveillance purposes.

Our study has several significant limitations. First, only hospitalized patients were included in the Atlas database. Data derived from such a database could have introduced bias for the CAP and HCAP groups in the present analysis, as not all patients with CAP or HCAP are necessarily admitted to an acute-care medical center. Second, we only included subjects with early onset (5 days on hospital admission) pneumonia; this approach may have introduced selection bias in the HAP and VAP groups by excluding late-onset HAP and VAP. Third, our definition of pneumonia based on the presence of ICD-9-CM codes indicative of pneumonia and a concomitant positive respiratory bacterial culture could have introduced misclassification biases. However, since diagnostic testing that involves sputum culture cannot always distinguish between colonization and true infection,²¹ it was impossible to causatively relate the isolated pathogen to pneumonia. Furthermore, our method excluded patients with pneumonia despite false-negative culture findings. Similarly, as noted earlier, the use of serologic studies was not uniformly prescribed. Hence, we likely undercounted events due to atypical organisms. Finally, we could not evaluate the appropriateness of initial empiric antimicrobial therapy. Without the therapy data, we were unable to determine the cost components of therapy and compare the cost-effectiveness of the new classification scheme with the traditional one.

Despite the limitations discussed above, the present analysis supports a new pneumonia classification scheme distinguishing CAP, HCAP, HAP, and VAP. It suggests that HCAP, traditionally classified into the CAP category, is clinically more similar to HAP and should be treated as such until culture data become available. In terms of pathogen distribution pattern, HCAP shares more similarity with HAP and VAP than with CAP. The results from the present analysis imply that the next generation of national treatment guidelines and local critical pathways aimed at optimizing and streamlining initial empiric antibiotic treatment for pneumonia would benefit by differentiating HCAP from CAP.

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