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CHEST

Original Research

PNEUMONIA

A Comparative Study of Community-Acquired Pneumonia Patients Admitted to the Ward and the ICU*

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Background: **Limited information is available on the health-care utilization of hospitalized patients with community-acquired pneumonia (CAP) depending on the location of care. Our aim was to compare the clinical characteristics, etiologies, and outcomes of patients with CAP who were admitted to the ICU with those admitted who were to the ward service.**

Methods: **A retrospective cohort study, at two tertiary teaching hospitals, one of which was a Veterans Affairs hospital, and the other a county hospital. Eligible subjects had been admitted to the hospital with a diagnosis of CAP between January 1, 1999, and December 31, 2001, had a confirmatory chest radiograph, and a hospital discharge *International Classification of Diseases*, ninth revision, diagnosis of pneumonia. Subjects were excluded from the study if they had designated "comfort measures only" or had been transferred from another acute care hospital or were nursing home patients. Bivariate and multivariable analysis evaluated 30-day and 90-day mortality as the dependent measures.**

Results: **Data were abstracted on 730 patients (ICU, 145 patients; wards, 585 patients). Compared to ward patients, ICU patients were more likely to be male ($p = 0.001$), and to have congestive heart failure ($p = 0.01$) and COPD ($p = 0.01$). ICU patients also had higher mean pneumonia severity index scores (112 [SD, 35] vs 83 [SD, 30], respectively; $p = 0.02$). Patients admitted to the ICU had a longer mean length of hospital stay (12 days [SD, 10 days] vs 7 days [SD, 17 days], respectively; $p = 0.07$), and a higher 30-day mortality rate (23% vs 4%, respectively; $p < 0.001$) and 90-day mortality rate (28% vs 8%, respectively; $p < 0.001$) compared to ward patients.**

Conclusions: **ICU patients present with more severe disease and more comorbidities. ICU patients stay longer in the hospital and have a much higher mortality rate when compared to ward patients. Management strategies should be designed to improve clinical outcomes in ICU patients.**

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Key words: critical care; ICU; microbiology; mortality; outcome and process assessment; pneumonia

Abbreviations: CAP = community-acquired pneumonia; CHF = congestive heart failure; ICD-9 = *International Classification of Diseases*, ninth revision; LOS = length of stay; PSI = pneumonia severity index

Community-acquired pneumonia (CAP) affects > 5 million adults and accounts for > 1 million hospital admissions each year in the United States.[1,2] Pneumonia and influenza are the seventh leading cause of death in this country, and age-adjusted mortality attributable to these illnesses is increasing.[1] Up to 36% of patients admitted to the hospital with CAP are placed in the ICU.[3–6] Compared to outpatients and ward patients with CAP, ICU patients carry the highest morbidity, mortality, and cost of all patients with CAP.[7–9] Mortality rates in these patients have been reported to range from 21 to 58%.[7,9]

Multiple organizations around the world have developed clinical practice guidelines for the treatment of CAP.[9–17] All agree that CAP patients who are admitted to the hospital represent a major

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concern, and specific therapeutic approaches should be instituted as early as possible to improve clinical outcomes. Health-care costs have risen in the past decade, with significant efforts directed to shorten unnecessary hospital length of stay (LOS), to opti-

mize the initial decision to hospitalize, and to decrease mortality. However, most of these efforts have been concentrated on the group of patients who are at the lowest risk of death from CAP, and not in those patients who utilize significant health-care resources such as the severely ill. Several authors[8] have evaluated ICU cohort of patients with CAP in order to identify microbiology, in-hospital mortality, and hospital LOS, but a limited number have compared CAP patients admitted to the ICU vs those admitted to a ward.[4,6,8,18–23] The majority of the available literature is from Europe,[4,6,18–21] and only limited data are available on etiology, clinical presentation, and outcomes among patients with CAP who have been admitted to the ICU compared to ward patients.[8,22,23] Most of the available literature has described an isolated ICU cohort of patients, but only three studies[8,22,23] have compared these subjects with ward subjects to understand the clinical and microbiological differences that are important for clinical decision-making strategies. Our aims were to compare the clinical characteristics, etiologies, and outcomes of patients with CAP who were admitted to the ICU with those of patients admitted to ward service in order to understand how to design and implement strategies for improving the care of patients admitted to the ICU.

Materials and Methods

This a retrospective cohort study of patients hospitalized with CAP at two academic tertiary care hospitals in San Antonio, TX. The Institutional Review Board of the University Health Science Center at San Antonio classified this project as an exempt study.

Study Sites/Inclusion and Exclusion Criteria

We identified all patients who were admitted to the study hospitals between January 1, 1999, and December 1, 2002, with a primary discharge diagnosis of pneumonia (*International Classification of Diseases*, ninth revision [ICD-9] codes 480.0–483.99 or 485–487.0) or a secondary discharge diagnosis of pneumonia with a primary diagnosis of respiratory failure (ICD-9 code 518.81) or sepsis (ICD-9 code 038.xx). Subjects were included in the study if (1) they were > 18 years of age, (2) had received a hospital admission diagnosis of CAP, and (3) had a radiographically confirmed infiltrate or other finding consistent with CAP seen on a chest radiograph or CT scan of the chest obtained within 24 h of hospital admission.

Exclusion criteria included the following: (1) the patient had been discharged from an acute care facility within 14 days of hospital admission; (2) the patient had been transferred from another acute care hospital, long-term care facility, or nursing home[24]; and (3) the patient had designated that "comfort measures" only be provided on this hospital admission. If a patient was admitted to the hospital more than once during the study period, only the first hospitalization was abstracted.

Data Abstraction

Chart review data included demographics, comorbid conditions, physical examination findings, laboratory and microbiology data, and chest radiograph reports. Process measures previously reported that were associated with higher mortality were recorded, including therapy with antibiotics within 4 h of hospital admission, appropriate blood cultures collected before antibiotic therapy and within 24 h of hospital admission, and use of guideline-concordant antibiotics.[9,14,17]

Diagnostic Criteria

Microbiological data results were reviewed, and a microbiological cause was assigned independently by two of the investigators (M.I.R and E.M.M.). The cause of pneumonia was stratified as definitive or presumptive. The definitive diagnosis was considered if one of the following conditions were met: (1) blood cultures positive for bacterial pathogens (in the absence of an extrapulmonary source of infection); (2) pleural fluid cultures yielding a bacterial pathogen; (3) endotracheal aspirates with moderate or heavy growth of bacterial pathogens; (4) significant quantitative culture growth from bronchoscopic respiratory samples (protected specimen brush sample cultures of at least 10^3 cfu/mL, and in BAL fluid sample cultures of at least 10^4 cfu/mL); and (5) positive test result for the Legionella urinary antigen. A presumptive diagnosis was made if a qualitative valid sputum sample yielded one or more predominant bacterial pathogens. Definitive and presumptive causes were combined for reporting purposes. When two or more microbiological causes were present, the patient was considered to have a polymicrobial infection. A patient was considered to have CAP of unknown cause if microbiological studies were not performed or the findings were inconclusive.

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Clinical Outcomes

The primary outcomes were 30-day and 90-day mortality, and the secondary outcome was hospital LOS. Hospital LOS was calculated as the date of hospital discharge minus the date of hospital admission.

Statistical Analysis

For the statistical analyses, patients were stratified into either the medical ward service or the ICU service by whether a patient was admitted to the ICU within the first 24 h. Bivariate statistics were used to test the association of demographic and clinical characteristics with all-cause 30-day mortality. Categoric variables were analyzed using the χ^2 test, and continuous variables were analyzed using the Student *t* test. The pneumonia severity index (PSI) was used to assess severity of illness at presentation.[25] A multivariable Cox proportional hazard model was derived with time to death in the first 30 days and 90 days of hospital admission as the dependent variable, and PSI on hospital admission as the independent variable.[25,26] All analyses were performed using a statistical software package (SPSS, version 13.0 for Windows; SPSS; Chicago, IL).

Results

Initially, 730 patients with a diagnosis of CAP were identified. There were 145 patients admitted to the ICU, compared with 585 patients treated only on the medical ward services.

Patient Characteristics

Table 1 shows the characteristics of the patients by whether they were cared for in the ICU vs the medical wards. More ICU patients were male (88% vs 75%, respectively; p = 0.001), but there were no significant differences in mean age. Preexisting comorbid conditions including congestive heart failure (CHF) [21% vs 13%, respectively; p = 0.01] and COPD (35% vs 25%, respectively; p = 0.01) were more common in patients who were admitted to the ICU.

Physical examination, laboratory test, and radiologic data showed that ICU patients were significantly more likely to have altered mental status, tachypnea, hypotension, and tachycardia. In addition, ICU patients were significantly more likely to have acidemia, hypoxemia, elevation of BUN levels, hyperglycemia, hyponatremia, pleural effusion or multilobar infiltrates seen on a chest radiograph when compared to patients admitted to the ward service (Table 1). In general, ICU patients were more acutely ill than ward patients. Thirty percent of patients admitted to the ICU had low-risk PSI scores (*ie*, I to III) at the time of ICU admission compared to 61% of the patients admitted to the ward service. The mean PSI score was lower in ward patients (83; SD, 30) compared to ICU patients (112; SD, 35;

Table 1—*Comparison of Demographic and Clinical Characteristics Among CAP Patients Admitted to the ICU vs the Ward (n = 730)**

Variables	Ward Patients (n = 585)	ICU Patients (n = 145)	p Value
Age, yr	59.1 (SD, 16.2)	60.7 (SD, 15.5)	NS
Men	441 (75.4)	128 (88.3)	0.001
Preexisting comorbid conditions			
CHF	75 (12.8)	31 (21.4)	0.01
History of stroke	64 (10.9)	17 (11.7)	NS
Chronic liver disease	74 (12.6)	17 (11.7)	NS
History of malignancy	57 (9.7)	14 (9.7)	NS
Renal insufficiency	55 (9.4)	16 (11.0)	NS
Cigarette smoking	180 (30.8)	47 (32.4)	NS
Diabetes mellitus	164 (28.0)	44 (30.3)	NS
COPD	145 (24.8)	51 (35.2)	0.01
Alcoholism	59 (10.1)	21 (14.5)	NS
History, physical, laboratory, and radiographic data			
Altered mental status	30 (5.1)	38 (26.2)	< 0.001
Respiratory rate > 30 breaths/min	46 (7.9)	27 (18.6)	< 0.001
Systolic BP < 90 mm Hg	10 (1.7)	7 (4.8)	0.03
Heart rate > 125 beats/min	56 (9.6)	39 (26.9)	< 0.001
Temperature < 95°F or > 104°F	12 (2.1)	6 (4.1)	NS
Arterial pH < 7.35	11 (1.9)	35 (24.1)	< 0.001
Arterial oxygenation saturation < 90%	100 (17.1)	65 (44.8)	< 0.001
Hematocrit < 30%	47 (8.0)	18 (12.4)	NS
Serum BUN > 30 mg/dL	100 (17.1)	45 (31.0)	< 0.001
Serum glucose > 250 mg/dL	51 (8.7)	21 (14.5)	0.04
Serum sodium < 130 mEq/L	78 (13.3)	32 (22.1)	0.01
Pleural effusion	125 (21.4)	49 (33.8)	0.002
Multilobar infiltrates	173 (29.8)	82 (56.9)	< 0.001

*Values are given as No. (%), unless otherwise indicated. NS = not significant (*ie*, p > 0.05).

p = 0.02). In addition, more ICU patients had American Thoracic Society criteria for severe CAP compared to ward patients (79 patients [54.5%] vs 37 patients [6.3%], respectively; p < 0.001).

ICU patients were more likely to receive antibiotic therapy within 4 h of ICU admission (40% vs 25%, respectively; p = < 0.001) and to undergo appropriate blood culture collection (83% vs 74%, respectively; p = 0.03), but were less likely to receive guideline-concordant antibiotic therapy (67% vs 82%, respectively; p < 0.001). However, there were no statistically significant differences for these processes of care and 30-day mortality in the multivariate analysis (data not shown).

Pneumonia Etiology

An etiologic diagnosis was found in 177 patients (24%), and was found more commonly in ICU patients (57 of 145 patients; 39%) than in ward patients (120 of 585 patients; 20%) [Table 2]. Blood cultures were done in 553 patients (76%); more in ICU patients (83%) than in ward patients (74%; p = 0.03). Sputum samples were collected in 95 ICU patients (65%) and 301 ward patients (51%; p = 0.002). Of all the CAP patients in whom a microbiological diagnosis was reached, the most frequent pathogen isolated was *Streptococcus pneumoniae* (56%), followed by *Staphylococcus aureus* (15%), *Escherichia coli* (9%), and *Pseudomonas aeruginosa* (6%). However, ICU patients were more likely to have a microbiological diagnosis secondary to *S pneumoniae* and *P aeruginosa*, but were less likely to have *S aureus*, Klebsiella spp, and *E coli* than ward patients. Antibiotic resistance was not different among the most common pathogens whether the patients were in the ICU or on the ward service. Sixty-one Legionella urinary antigen tests were performed (ward patients, 35 tests [6.0%]; ICU patients, 26 tests [17.9%]; p < 0.001), but all of them yielded negative results.

Table 2—*Etiologic Diagnosis With an Identifiable Pathogen Causing CAP in Patients Admitted to the Ward and the ICU Service

Microorganisms	Ward Patients (n = 120)	ICU Patients (n = 57)
S pneumoniae	38 (31.7)	22 (38.6)
Penicillin-resistant *S pneumoniae*	3 (2.5)	2 (3.5)
Macrolide-resistant *S pneumoniae*	11 (9.2)	6 (10.5)
S aureus	25 (20.8)	12 (21.1)
Methicillin-resistant *S aureus*	7 (5.8)	3 (5.3)
P aeruginosa†	12 (10.0)	8 (14.0)
Haemophilus influenzae	16 (13.3)	3 (5.3)
E coli	8 (6.7)	1 (1.8)
Klebsiella pneumoniae	5 (4.2)	2 (3.5)
Proteus mirabilis	2 (1.7)	1 (1.8)
Miscellaneous‡	5 (0.8)	2 (1.3)
Other Gram-positive cocci§	3 (0.5)	1 (0.6)
Polymicrobial	6 (5.0)	7 (10.5)

*Values are given as No. (%). Percentages have been rounded and may not sum 100.
†Three *P aeruginosa* isolates were resistant to fluoroquinolones, and one of them was additionally resistant to piperacillin/tazobactam.
‡Consisting of Acinetobacter spp, Aspergillus spp, and *Haemophilus parainfluenzae*.
§Pathogens detected included Streptococcus spp.

Clinical Outcomes

The overall 30-day mortality rates (4% vs 23%, respectively; p < 0.001) and 90-day mortality rates (8% vs 28%, respectively; p < 0.001) were lower for ward patients compared to ICU patients (Fig 1). In addition, the mean hospital LOS was longer by 5 days for patients who were hospitalized in the ICU (11.9 days; SD, 10.1 days) compared to ward patients (6.6 days; SD, 16.6 days; p = 0.07). Seventy patients (48%) who were admitted to the ICU needed mechanical ventilation, and 33 patients (23%) required therapy with vasopressors.

Mortality at 30 and 90 days was significantly different when PSI class was divided in three categories or five classes, in which ICU patients had a much higher mortality in the low-to-moderate PSI classes, but not in the highest risk PSI class (Table 3). Patients in the lower risk groups had an increase in 90-day mortality rates compared to those observed at 30 days; however, this increase was not seen in patients who had a much higher severity-of-illness score despite their location in the hospital. In addition, a trend toward higher rates of mortality was observed among ICU patients vs ward patients at 30 days (22 patients [27.8%] vs 5 patients [13.5%], respectively; p = 0.089) and 90 days (24 patients [30.4%] vs 5 patients [13.5%], respectively; p = 0.051) if there were criteria for severe

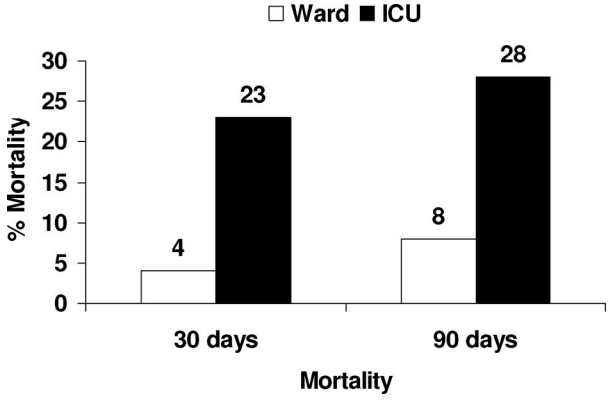

FIGURE 1. Mortality of CAP patients admitted to the ward and the ICU service.

Table 3—*Comparison of 30-Day and 90-Day Mortality Rates for ICU and Ward Patients With CAP***

Risk Class	Patients per Class, No.	Mortality at 30 d: Ward Patients (n = 585)	Mortality at 30 d: ICU Patients (n = 145)	Mortality at 30 d: p Value	Mortality at 90 d: Ward Patients (n = 585)	Mortality at 90 d: ICU Patients (n = 145)	Mortality at 90 d: p Value
I	186	2/169 (1.2)	3/17 (17.6)	< 0.0001	4/169 (2.4)	4/17 (23.5)	< 0.0001
II	78	1/72 (1.4)	1/6 (16.7)	0.023	2/72 (2.8)	1/6 (16.7)	0.089
III	139	6/119 (5.0)	2/20 (10.0)	0.378	10/119 (8.4)	3/20 (15.0)	0.349
I–III	403	9/360 (2.5)	6/43 (14.0)	< 0.0001	16/360 (4.4)	8/43 (18.6)	< 0.0001
IV	243	9/183 (4.9)	12/60 (20.0)	< 0.0001	21/183 (11.5)	17/60 (28.3)	0.002
V	84	8/42 (19.0)	15/42 (35.7)	0.09	12/42 (28.6)	15/42 (35.7)	0.4

*Values are given as No. of patients/total No. of patients (%), unless otherwise indicated. The percentages have been rounded and may not sum 100.

CAP to admit the patient to the ICU based on American Thoracic Society recommendations. Furthermore, higher 30-day mortality rates (11 patients [16.7%] vs 21 [3.8%], respectively; $p < 0.0001$) and 90-day mortality rates (16 patients [24.2%] vs 44 patients [8.0%], respectively; $p < 0.0001$) were observed among ICU vs ward patients in whom there were no criteria for severe CAP.

In the Cox proportional hazard model, after adjusting for potential confounders including severity of illness, ICU patients had an increase risk of dying within 30 days of ICU admission (hazard ratio, 3.4; 95% confidence interval, 1.9 to 6.0) and these findings persisted to 90-days post admission (hazard ratio, 2.3, 95% confidence interval, 1.4 to 3.7). Figure 2 shows the survival curves based on the Cox proportional hazard model and demonstrates that ICU patients have significantly increased mortality compared to ward patients, even when the groups are stratified by PSI categories.

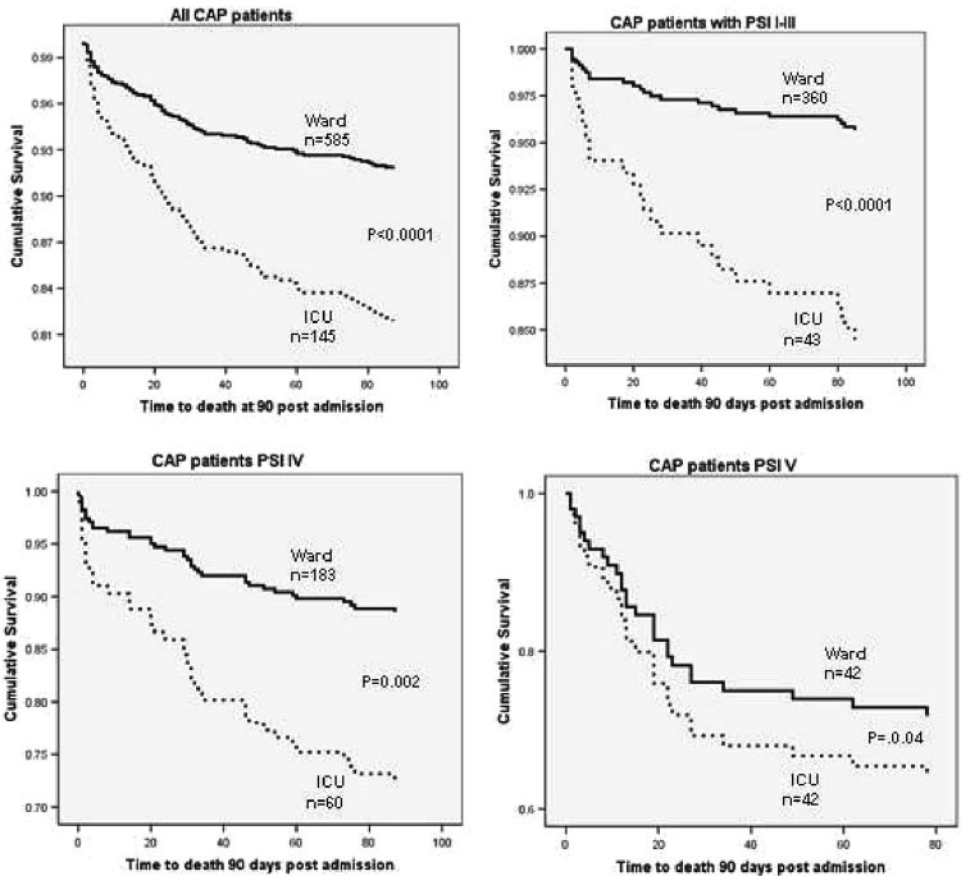

FIGURE 2. Cox survival curves of ICU vs ward CAP patients after adjusting for severity of illness (PSI classes).

Discussion

Our primary findings are that CAP patients admitted to the ICU had significantly higher 30-day and 90-day mortality rates compared to ward patients, as well as longer hospital LOSs, after adjusting for severity of illness. In addition, we identified several comorbid conditions, including COPD and CHF, which were much more common in patients requiring ICU care. Also, contrary to expectations, *P aeruginosa* was also found in ward patients with CAP.

Although there were important differences between ICU and ward patients, all of these clinical differences were included in the PSI score, which was the severity-of-illness instrument used in this study.[25] Contrary to what we had expected, however, the difference in mortality in CAP patients admitted to the ICU vs those admitted to a hospital ward was in those patients in the low and moderate PSI risk classes (*ie*, PSI classes I to III and IV) rather than the highest risk patients. We expected that almost all ICU patients who were hospitalized with CAP would be in the highest PSI classes (*ie*, IV and V). However, we found that in all PSI classes there was a large percentage of patients who required ICU admission. Therefore, it appears that the PSI does not completely adjust for all of the abnormalities that are present in ICU patients and are related to mortality. For example, ICU patients in the low-risk PSI class (I–III) had 30-day and 90-day mortality rates of 16% and 20%, respectively, which are much higher than those cited in prior reports in the literature.[8,25] Thus, the decision to admit a patient to the ICU despite the low severity-of-illness score determines which type of therapy the patient will receive, which may change patient outcomes.

In addition, it is concerning that the mortality rate continues to increase between 30 and 90 days after hospital admission. Previous research[27] has demonstrated that almost all CAP-related mortality occurs within 30 days of presentation, suggesting that medical conditions other than CAP are the source of this increased mortality. For example, in our study ICU patients with a moderate risk of death had a mortality rate of 20% at 30 days, which increased to 28% at 90 days. Therefore, this suggests that there should be close follow-up of other comorbid conditions, such as coronary artery disease, CHF, or COPD, after hospital discharge for patients hospitalized with CAP.[28,29]

In addition to increased mortality, ICU patients stay longer in the hospital, which results in increased health-care utilization. Other authors[30] have suggested strategies to reduce LOS in ward patients, such as switching to oral therapy as soon as the patient reaches clinical stability, but similar strategies in the ICU are lacking.

The choice of appropriate empiric antibiotic regimens will depend on several factors that include the etiology of CAP, clinical characteristics, severity of illness, and antimicrobial resistance. Our results showed that ICU and ward patients have similar rates of *S pneumoniae, S aureus*, and *P aeruginosa* infections. Several studies[21,28,29,31,32] have found that *P aeruginosa* is an important pathogen in patients with pulmonary comorbidities, especially those with bronchiectasis. In our study *P aeruginosa* was the third most common organism in ICU patients, which suggests that antipseudomonal antibiotic coverage should be considered in all ICU patients with structural lung disease, whether or not bronchiectasis is present. In addition, *P aeruginosa* was present in several ward patients, which suggests that physicians should consider it as a potential pathogen in ward patients, especially in those patients with COPD, as has been suggested by our own and other data.[28,29] Etiologic pathogens were more frequently found in CAP patients admitted to the ICU; therefore, we concur with the clinical practice guidelines[9–17] suggesting that there be extensive efforts to identify causative pathogens (*ie*, bacterial cultures, and Legionella and pneumococcal urinary antigen tests) in ICU patients. Appropriate identification of the pathogen may assist clinicians to appropriately target antimicrobial therapy.[9,17]

Our results question the current recommendations regarding empiric antibiotic use depending only on the site of care. For patients admitted to the ICU, the current recommendations[9,14,17] are to use combination therapy, which will include an antipneumococcal β-lactam agent and additional coverage for atypical pathogens (especially Legionella spp) with a respiratory fluoroquinolone or a macrolide (for those persons without risk factors for Pseudomonas infection). In contrast, the recommended therapies[9,14,17] for ward patients include monotherapy with a fluoroquinolone or combination therapy with a β-lactam antibiotic and a macrolide. However, our data suggest that not only the site of care, but also severity of illness and/or comorbid conditions, predict poor outcomes and should be part of the decision-making process for choosing antibiotic regimens.

We reviewed the literature and identified a great number of epidemiologic studies[4,6,8,18–23] of severe CAP in the ICU; however, only a limited number of studies[8,22,23] compared ICU patients with ward patients. However, we found that only Angus and colleagues[8] had reported similar results, which documented similar differences between groups depending on their severity of illness and their risk of death at 30 and 90 days after hospital admission.

Our study has limitations that are important to acknowledge. First, this study was a retrospective cohort study, and there are inherent problems related to this design, including selection bias. However, we do not feel that this study has significant problems with bias due either to our methods using hospital admission and discharge diagnosis ICD-9 codes to identify patients with CAP or to the fact that we encountered only a small amount of missing data. Moreover, we were able to verify that all of the patients had a radiologic diagnosis of CAP. Second, our sample was predominantly male since one of our sites was a Veterans Affairs hospital, and we are unable to exclude the hypothesis that female CAP patients admitted to the ICU may have had different clinical courses, or outcomes, compared to male CAP patients.

Conclusions

In conclusion, this study demonstrates that CAP patients admitted to the ICU have higher 30-day and 90-day mortality rates, and increased LOS compared to patients who are admitted to a ward setting. The PSI score does not completely adjust for all the abnormalities that are present in ICU patients, suggesting that there are variables not included in the PSI that are related to mortality. Additional clinical attention should be paid not only to ICU patients with CAP but also to those CAP patients who are at higher risk of dying, as indicated by the severity of illness or the presence of comorbid conditions.

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