Rapid Antibiotic Delivery and Appropriate Antibiotic Selection Reduce Length of Hospital Stay of Patients With Community-Acquired Pneumonia

Link Between Quality of Care and Resource Utilization

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Objectives: To measure quality-of-care variables relevant to the treatment of community-acquired pneumonia and to determine their relative contribution to variation in length of hospital stay (LOS).

Methods: One hundred cases of pneumonia requiring hospitalization from each of 7 institutions (2 community and 5 university teaching hospitals) were randomly selected (total sample, 700 cases). Demographic and clinical variables were abstracted using a standardized data instrument. Three quality-of-care measures were analyzed: (1) site of initial antibiotic treatment (emergency department vs floor), (2) door-to-needle time, and (3) appropriateness of antibiotic selection. Appropriate antibiotic selection was defined by the 1998 Infectious Disease Society of America guidelines for the treatment of hospitalized pneumonia cases. Regression modeling was used to determine associations between LOS and our quality-of-care (process) variables.

Results: The mean ± SD LOS for this sample was 7.0 ± 4.1 days. Prolonged LOS, defined as greater than or equal to the 75th percentile of the LOS distribution, was the dependent variable in our regression analysis and was greater than or equal to 9.0 days. After clinical and demographic variables were adjusted for, logistic regression modeling revealed that all 3 quality-of-care measures were associated with prolonged LOS: (1) initial antibiotic treatment in the emergency department (odds ratio [OR], 0.31; 95% confidence interval [CI], 0.19-0.48); (2) appropriate antibiotic selection (OR, 0.55; 95% CI, 0.35-0.88); and (3) door-to-needle time (OR, 1.75 per 8 hours; 95% CI, 1.34-2.29). In a secondary analysis, we examined the clinical and demographic characteristics of the patients who were treated more rapidly in the emergency department compared with those who were treated on the inpatient floor. No clinically meaningful differences were observed between these groups.

Conclusions: Unlike clinical and demographic variables, process-of-care variables are modifiable and amenable to quality improvement. We observed that rapid antibiotic initiation and appropriate antibiotic selection in the emergency department have a statistically significant association with shorter LOS. These findings suggest quality improvement targeted at these processes of care may improve resource utilization and reduce LOS for patients with community-acquired pneumonia.

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COMMUNITY-ACQUIRED pneumonia (CAP) is diagnosed in approximately 4 million adults each year, 25% of whom require hospitalization.1, 2 Pneumonia remains one of the most common reasons for adult hospitalization in the United States, and the overall incidence is on the rise. Between 1984 and 1995, discharge rates for CAP increased by more than 30%.3, 4 Mortality from pneumonia is also increasing. Community-acquired pneumonia is the number 1 infectious cause of death,5 and between 1979 and 1994, the age-adjusted mortality rate for patients with pneumonia increased by 22%.5 Also, the economic burden of CAP is substantial, with annual direct costs exceeding $9.7 billion.4

Despite the availability of well-established treatment guidelines,5-8 many studies have documented significant regional variation in length of hospital stay (LOS) among patients hospitalized with pneumonia.6, 12 Variation in LOS has been attributed to differences in patient, physician, and hospital-based factors.10, 14 However, much of the observed LOS variation in CAP remains poorly understood. These findings would suggest that LOS may be determined by other characteristics, such as physician judgment or variation in processes of care.
PATIENTS AND METHODS

SETTING

The setting for this study was the New York Presbyterian Healthcare (NYPH) system, a developing integrated health care delivery system in the New York metropolitan region. Patients for this study were identified from among 7 hospital sites in the NYPH system. Hospital sites were chosen because of a high annual incidence of pneumonia cases. Five institutions were university-based teaching hospitals; 2 were community-based nonteaching hospitals. Cases were identified between January 1998 through December 1998 using diagnosis related group (DRG) billing codes for pneumonia (DRG codes 89 and 90).

STUDY DESIGN

We performed a retrospective chart review. One hundred cases were randomly selected from each of 7 network institutions based on DRG discharge coding, representing between 4.9% and 21.1% of the total CAP admissions for the participating study sites. Adult cases of CAP were confirmed by physician record review and then screened using the following inclusion/exclusion criteria: (1) the patient had to be older than 18 years; (2) the admitting diagnosis by the admitting ED physician had to be pneumonia; (3) the patient had to be admitted from either his or her home or a nursing home; and (4) the patient had to be admitted through the ED (direct-to-the-floor admissions were excluded). Direct-to-the-floor admissions were excluded because accurate admission times could not consistently be determined for these patients, thereby invalidating the door-to-needle time calculation (see below).

Also, patients with known or suspected immunodeficiency (human immunodeficiency virus, acquired immunodeficiency syndrome, or concurrent immunosuppressive therapy) were excluded. Patients were also excluded if a diagnosis of Pneumocystis carinii pneumonia or tuberculosis was suspected based on a physician’s review of the medical record. Patients readmitted for pneumonia within 30 days of discharge were excluded, as were patients who had antibiotic therapy initiated prior to ED presentation. Finally, all in-hospital deaths and patients who left against medical advice were excluded. Because our primary outcome measure was LOS and because the combined death and against-medical-advice rates were low (3.9%), we chose to exclude these patients from the analysis. An institutional review board exemption was obtained for this study at each participating institution because the data collection was limited to retrospective chart review.

DATA INSTRUMENT

Each chart was reviewed and abstracted by a trained reviewer using a structured data instrument. Length of hospital stay, our dependent variable, was measured in days. Additionally, 13 independent variables were also collected. Data elements included 5 demographic and 5 clinical variables, as well as 3 process-of-care measures. Demographic variables included (1) age; (2) sex; (3) ethnicity (white vs nonwhite); (4) admission site (admitted from nursing home vs private home); and (5) payer status (Medicaid/self-pay vs Medicare/commercial insurance).

Clinical variables included (1) chronic obstructive pulmonary disease (history of chronic obstructive pulmonary disease on admission); (2) comorbid illness (history of active neoplastic disease, renal failure, cerebrovascular disease, liver failure, congestive heart failure, or altered mental status at admission); (3) white blood cell count (WBC) at admission; (4) respiratory rate (RR) at admission; and (5) chest x-ray film at admission (chest x-ray film consistent with pneumonia within 48 hours of admission). Co-morbid illness definitions were adopted from the pneumonia severity illness classification.15 Chest x-ray films were

Table 1 lists the demographic, clinical, and process variables that describe our patient population. Our initial sample consisted of 700 patients. Ninety-one patients, or 13% of the original sample, were excluded from analysis based on the criteria outlined above, resulting in a study sample of 609 patients. Eighteen patients were not admitted through the ED. Twenty-four patients did not have an ED physician’s admitting diagnosis of pneumonia. Twelve patients had human immunodeficiency virus, and another 8 patients had known or suspected immunodeficiency. Two patients were excluded because of a prior 30-day admission. Twenty-three deaths and 4 patients who were discharged against medical advice were also excluded.

Sixty-one (67%) of the 91 patients who were excluded were from university-based teaching hospitals, averaging 12.2 cases excluded per teaching hospital. Thirty (33%) of the 91 patients who were excluded were from the community-based nonteaching hospitals, averaging

Continued on next page
Process-of-care variables included (1) site of initial antibiotic administration (ED vs floor); (2) door-to-needle time (hours); and (3) appropriateness of antibiotic selection. The site of initial antibiotic administration (ED treatment vs floor treatment) was measured as percent ED (the percentage of patients who received their initial antibiotic therapy in the ED). Door-to-needle time was measured in hours and represents the difference between the triage time and the documented time of initial antibiotic administration. Appropriateness of initial antibiotic selection was scored based on the 1998 Infectious Disease Society of America (IDSA) guidelines, for the treatment of patients hospitalized with pneumonia. Antibiotic selection within the first 24 hours of admission was determined to be consistent or inconsistent with published guidelines based on independent physician review of the medical record and recorded as percent appropriate.

Ten percent of the records were randomly sampled and rescored. Reliability testing indicated moderate to excellent interrater reliability with a k statistic ranging from 0.68 to 0.98: for pneumonia confirmation (k=0.98); exclusion criteria (k=0.88); and abstraction of demographic (k=0.94), clinical (k=0.91), and process (k=0.68) variables.16

STATISTICAL METHODS

We used descriptive statistics (SPSS statistical software version 10.0; SPSS Inc, Chicago, Ill) to characterize our study population. For this analysis, our interest was prolonged LOS (pLOS). pLOS was defined as LOS beyond the upper bounds of the interquartile range (>75th percentile), and for our study sample it was 9.0 days. Univariate measures of association were then tested between our primary outcome variable, pLOS, and each of the demographic, clinical, and process variables listed above. Patients who died or left against medical advice were excluded from the analysis (see above).

Univariate measures of association for categorical variables were calculated using the Fisher exact test. Univariate measures of association for continuous variables were tested using either the t test (parametric) or the Wilcoxon rank sum test (nonparametric). We compared the unadjusted mean LOS between ED-treated patients and floor-treated patients using a base-10 logarithmic transformation of LOS because of the skewed distribution of this variable to aid in its statistical interpretation. All P values presented in the univariate analysis are 2-tailed.

A multivariate logistic regression model was then developed using pLOS as our dependent variable. We selected the best model by applying stepwise selection to any variable significant at P<.2 from the univariate analyses. There was no interaction between the site of initial antibiotic administration and appropriate antibiotic selection, nor between any of the statistically significant variables from the univariate analyses. Obviously correlated variables (site of antibiotic selection and door-to-needle time) were not included together in models. We did not find evidence of multicollinearity between other terms. Continuous variables were rescaled as follows to maintain comparability of regression coefficients: (1) age per 10-year increase; (2) WBC per 5-unit increase; (3) RR per 5-unit increase; and (4) door-to-needle time per 8-hour period.

To improve the efficiency of the statistical model, we used a power transformation to the process variable, door-to-needle time, to follow the implicit statistical assumptions of normality. All P values presented in the multivariate models are 2-tailed. We report the odds ratios (ORs) with 95% confidence intervals (CIs) such that an OR greater than 1.0 is more highly associated with a prolonged LOS and an OR less than 1.0 is associated with a shorter, nonprolonged LOS.

Dichotomization of LOS ANALYSIS

Univariate associations between pLOS and each of the independent demographic, clinical, and process variables are presented in Table 2. Of the demographic variables analyzed, older age (OR=1.28 per 10 years; 95% CI=1.15-1.44) and white race (OR=1.49; 95% CI=1.02-2.19) were significant univariate predictors of pLOS. Of the clinical variables analyzed, comorbid illness (OR=2.39; 95% CI=1.57-3.65) and RR at admission (OR=1.28 per 5 breaths/min; 95% CI=1.11-1.48) demonstrated significant associations with pLOS. Of the 2 process variables initially examined, only site of initial antibiotic administration demonstrated a strong statistical association with pLOS in the univariate analysis. In this population, the process of administering the initial dose of antibiot-

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ics in the ED was protective (OR=0.42; 95% CI=0.28-0.61), suggesting that initiating treatment in the ED could lead to a shorter LOS. The clinical significance of this effect is demonstrated in the mean difference in LOS between these 2 groups of patients. The LOS for patients treated initially in the ED was 6.3±3.5 days, while the LOS for patients receiving antibiotic therapy that was started when they reached the inpatient floor was 8.4±4.7 days (P<.001).

Multivariate logistic regression analysis was used to assess the independent associations between demographic, clinical, and process variables and the outcome pLOS. The results from this regression model are also shown in Table 2. In this analysis, age (OR=1.28 per 10 years; 95% CI=1.12-1.46), RR at admission (OR=1.23 per 5 breaths/min; 95% CI=1.04-1.45), and comorbid illness (OR=2.64; 95% CI=1.55-4.49) were the demographic and clinical variables that remained significant predictors of pLOS after multivariate adjustment. In terms of process measures, both initial antibiotic administration in the ED (OR=0.31; 95% CI=0.19-0.48) and appropriate antibiotic selection (OR=0.53; 95% CI=0.35-0.88) were significantly associated with pLOS. Both of these process-of-care variables demonstrated a protective effect with respect to pLOS, suggesting that administering antibiotics in the ED and selecting appropriate initial antibiotic therapy were independent predictors of shorter LOS. It is of interest to note that appropriate antibiotic selection was not associated with pLOS in the univariate analysis but was strongly associated with pLOS in the multivariate analysis (explained below).

**DOOR-TO-NEEDLE TIME ANALYSIS**

To further explore the relationship between site of initial antibiotic selection and pLOS, we collected data on the door-to-needle time as a possible root cause explanation for this association. The average door-to-needle time for the entire sample was 5.5±3.5 hours. Figure 2 is a clustered box plot depicting the distribution of the ED door-to-needle times vs the floor door-to-needle times. On average, patients who received their initial antibiotic treatment in the ED had a door-to-needle time of 3.5±1.4 hours, while patients who had their initial antibiotic treatment on the inpatient floor had a door-to-needle time of 9.5±3.0 hours (P<.001). Because door-to-needle time and site of initial antibiotic treatment were strongly related to each other (high degree of collinearity), a second regression model was constructed to test the association between door-to-needle time and pLOS. In this second multivariate model (data not shown), door-to-needle time demonstrated a significant independent association with pLOS (OR=1.75 per 8 hours; 95% CI=1.34-2.29; P<.001). Longer door-to-needle time was strongly associated with prolonged LOS.

**APPROPRIATE ANTIBIOTIC SELECTION ANALYSIS**

As mentioned above, appropriate antibiotic selection was not associated with pLOS in the univariate analysis but was strongly associated with pLOS in the multivariate analysis. This finding suggests that only after adjustment for other covariates does the appropriate antibiotic selection variable become significant. A correlation matrix was developed to identify potential suppressor covariates. The comorbid illness variable had the strongest correlation with appropriate antibiotic selection (R=0.33) and was selected for subgroup analysis. Table 3 demonstrates that within the subgroup of patients with significant comorbid illness (n=354), appropriate antibiotic selection is strongly associated with pLOS in both the univariate (OR=0.45; 95% CI=0.27-0.74) and the multivariate (OR=0.42; 95% CI=0.24-0.73) models. These data suggest that in patients with significant comorbid illness, correct antibiotic selection may hasten hospital discharge. The original univariate and multivariate associations between pLOS and appropriate antibiotic selection for all 609 patients are shown for comparison.

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**Table 1. Descriptive Statistics of the Study Population**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Demographic</td>
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<tr>
<td>Ethnicity, % white</td>
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<td>Admit site, % SNF</td>
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<tr>
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<td>Clinical</td>
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<tr>
<td>Other comorbid illness, %</td>
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<td>WBC at admission, mean ± SD, ×10³/µL</td>
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<tr>
<td>RR at admission, mean ± SD, beats/min</td>
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<td>Process</td>
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<td>Initial antibiotics, % ED</td>
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</tr>
<tr>
<td>Appropriate antibiotic, %</td>
<td>56</td>
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</tbody>
</table>

* N=609. SNF indicates skilled nursing facility; COPD, chronic obstructive pulmonary disease; WBC, white blood cell count; RR, respiratory rate; CXR, chest x-ray film; and ED, emergency department.

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**Figure 1.** Box plot demonstrating the distribution of the length of hospital stay (LOS) for the study sample (N=609). 25% LOS indicates the 25th percentile of the LOS distribution; 75% LOS, the 75th percentile of the LOS distribution.
To determine the patient characteristics that predicted which patients received antibiotics in the ED vs delayed antibiotic treatment on the inpatient floor, we performed a final multivariate analysis (Table 4). All 609 patients in this study were admitted through the ED; however, only 66% of the study population (406 patients) received antibiotic treatment in the ED. Thirty-four percent (203 patients) received their first dose of antibiotics on the inpatient floor. In this table, we compared demographic and clinical variables between these 2 subgroups. As shown, only increased WBC at admission (OR=1.27 per 5 units; 95% CI=1.08-1.49) and increased RR at admission (OR=1.20 per 5 breaths/min; 95% CI=1.03-1.41) predicted the rapid administration of antibiotics in the ED. However, the WBC was not an independent predictor of pLOS (Table 2) and, though statistically significant, the magnitude of the differences observed in both WBC and RR between these 2 groups is of little clinical significance. All the other clinical and demographic variables were similar between the 2 groups, suggesting that these clinical and demographic variables were not driving treatment decisions.

**PREDICTORS OF ED VS FLOOR ANTIBIOTIC THERAPY INITIATION**

To determine the patient characteristics that predicted which patients received antibiotics in the ED vs delayed antibiotic treatment on the inpatient floor, we performed a final multivariate analysis (Table 4). All 609 patients in this study were admitted through the ED; however, only 66% of the study population (406 patients) received antibiotic treatment in the ED. Thirty-four percent (203 patients) received their first dose of antibiotics on the inpatient floor. In this table, we compared demographic and clinical variables between these 2 subgroups. As shown, only increased WBC at admission (OR=1.27 per 5 units; 95% CI=1.08-1.49) and increased RR at admission (OR=1.20 per 5 breaths/min; 95% CI=1.03-1.41) predicted the rapid administration of antibiotics in the ED. However, the WBC was not an independent predictor of pLOS (Table 2) and, though statistically significant, the magnitude of the differences observed in both WBC and RR between these 2 groups is of little clinical significance. All the other clinical and demographic variables were similar between the 2 groups, suggesting that these clinical and demographic variables were not driving treatment decisions.

**COMMENT**

Variation in LOS has been well documented for many medical conditions, including CAP. In this study, we examined the relationship between quality-of-care variables (process measures) and LOS to further quantify determinants of variation in LOS.
We observed statistically significant and clinically important associations between our process-of-care measures and our outcome of interest, pLOS (LOS ≥9.0 days). After clinical and demographic factors were adjusted for, initial antibiotic therapy in the ED was shown to be associated with pLOS (multivariate OR = 0.31; 95% CI = 0.19-0.48). Subsequent analysis revealed that antibiotic treatment in the ED was associated with nearly a 3-fold reduction in door-to-needle time in comparison to initial treatment on the inpatient floor (3.5±1.4 hours vs 9.5±3.0 hours, respectively; \(P < .001\)). Door-to-needle time was also shown to be associated with pLOS after patient characteristics were adjusted for (multivariate OR = 1.75 per 8 hours; 95% CI = 1.09-2.84). Notably, in univariate analysis, appropriate antibiotic selection did not demonstrate this protective effect. Only after multivariate adjustment were we able to uncover this strong association between antibiotic selection and pLOS. Subgroup analysis revealed comorbid illness as a suppressor covariate (negative confounder) responsible for this effect. Three hundred fifty-four patients had significant comorbid illness as defined by the pneumonia severity illness classification.\textsuperscript{13} Within this subgroup, appropriate antibiotic selection was associated with a shorter LOS in both the univariate and multivariate models, suggesting that in this subgroup of sick patients, antibiotic selection is an important independent driver of LOS variation.

Finally, we analyzed the clinical and demographic characteristic of the patients who were treated initially in the ED (n=406) vs those treated initially on the inpatient floor (n=203). All clinical and demographic variables between these 2 groups were similar except for the initial WBC and the initial RR. Although patients who were treated in the ED had statistically higher WBCs (13±6.2 \(10^3/\mu L\) vs 11±5.3 \(10^3/\mu L\); \(P<.01\)) and RRs (24±6.5/min vs 22±5.4/min; \(P<.05\)), the magnitude of these differences was of little clinical significance. Furthermore, from these data, one might infer that the ED-treated patients were more significantly ill (higher initial WBCs and RRs) and would bias our results toward ED-treated patients having a longer LOS. In fact, ED-treated patients had a shorter LOS, demonstrating that these statistical differences were not clinically meaningful. It is possible, however, that our data set did not capture other important clinical differences between these 2 groups.

Our results build on those of previous studies by demonstrating the impact of process-of-care measures in CAP. Previous studies have examined the relationship between processes of care and 30-day mortality rates. In a retrospective multicenter study of more than 14000 Medicare beneficiaries, Meehan et al\textsuperscript{20} demonstrated that antibiotic delivery times of less than 8 hours were associated with a 15% lower odds of 30-day mortality (95% CI = 0.75-0.96). Similar findings with respect to timing of antibiotic administration and 30-day mortality rate have been found by other investigators as well.\textsuperscript{21,22}

Also, associations between initial antibiotic selection and 30-day mortality rates have also been reported. Gleason et al\textsuperscript{23} reviewed the medication records of 12945 Medicare inpatients with pneumonia. Using a Cox proportional hazards model and after adjusting for baseline patient characteristics, they found that 3 initial antibi-
otic regimens were independently associated with a lower 30-day mortality. Initial treatment with a second-generation cephalosporin plus a macrolide, a nonpseudomonal third-generation cephalosporin plus a macrolide, or a fluoroquinolone alone was associated with 26%, 29%, and 36% lower 30-day mortality rates, respectively. All these antibiotic regimens are consistent with the IDSA recommendations for the treatment of hospitalized patients with pneumonia.

McCormick et al24 recently analyzed differences in LOS among 4 hospital sites. After adjusting for comorbid illness, severity of disease, and sociodemographic variables, they found that a shorter LOS was not associated with differences in an important clinical outcome, 30-day mortality. The authors propose that one possible explanation for this observation was that hospitals with a shorter LOS may have more effective processes of care, permitting a faster resolution of the acute illness and earlier discharge. Our data support this hypothesis.

These data must be interpreted within the context of the study design. Medical record documentation and chart abstraction could have introduced errors; however, our interrater reliability was measured and found to be moderate to excellent. Our study was observational in design, and the association between our measured quality-of-care variables and LOS may be subject to unmeasured confounding factors, such as unmeasured patient, physician, or hospital characteristics. Also, we did not examine subsequent in-hospital processes of care that may also be important in determining LOS, such as the switch from parenteral to oral antibiotic therapy. However, the fact that our data on timing and appropriateness of antibiotic therapy are consistent with prior data suggests that the associations reported herein are likely to be valid. Also, we must caution that the findings in this study may not be generalizable because the study was conducted primarily at urban hospital sites, 5 of which were teaching hospitals. Therefore, these data may not be applicable to other settings. Finally, retrospective chart review is inherently subject to selection bias. Although we analyzed a random sample of medical records with DRG codes for CAP, it is possible that some patients initially admitted with pneumonia were not coded as such because of subsequent in-hospital events. To address this limitation, a prospective analysis would need to be performed.

In conclusion, we found rapid delivery of appropriate antibiotics in the ED was associated with a shorter LOS in patients with CAP. Given the clinical and economic importance of pneumonia, there is substantial interest in understanding and reducing the drivers of variation in LOS. Unlike clinical and demographic variables, process-of-care variables, such as door-to-needle time and antibiotic selection, are modifiable and lend themselves to quality improvement initiatives. In our study, only 66% of patients were treated rapidly in the ED and only 56% of patients were treated with appropriate antibiotics as defined by the IDSA, suggesting substantial opportunity for quality improvement. Future prospective clinical trials will be needed to determine if improvements in these quality-of-care measures can lead to improvements in the effectiveness of care of hospitalized patients with CAP.

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