The pneumonia severity index predicts time to clinical stability in patients with community-acquired pneumonia


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**SUMMARY**

**SETTING:** A total of 33 hospitals in 13 countries in North America, Europe, Africa, Asia and Latin America. **OBJECTIVE:** To investigate the relationship between the pneumonia severity index (PSI) and the time to clinical stability from intravenous to oral antibiotic therapy in hospitalized adult patients with community-acquired pneumonia (CAP). **DESIGN:** An international, retrospective, observational study of random adult patients meeting the definition of CAP between June 2001 and May 2004. **RESULTS:** The risk class (RC) according to the PSI was calculated for all patients. The criteria to define when a patient is clinically stable were evaluated daily during the first 7 days of hospitalization in all patients. The mean time to clinical stability for 254 patients in RC I was 4.2 days, for 233 patients in RC II it was 3.9 days, for 395 patients in RC III it was 4.6 days, for 644 patients in RC IV it was 5.0 days and for 296 patients in RC V it was 6.0 days. Significant positive correlations were observed between RC and time to clinical stability ($P < 0.0001$). **CONCLUSION:** The PSI is a tool that can be used to predict time to clinical stability (i.e., time to antimicrobial switch therapy) in hospitalized patients with CAP. **KEY WORDS:** community-acquired infection; pneumonia; length of stay

IN THE UNITED STATES alone, approximately 1.3 million patients are hospitalized for community-acquired pneumonia (CAP) each year.1 In 2001, 60,000 patients died from pneumonia,2 and physicians caring for patients with CAP have strived to reduce the mortality rate. An accurate tool to predict the mortality rate of patients with CAP was developed in 1997, in what has been referred to as the most important investigation for CAP in the last decade.3,4 This tool, known as the pneumonia severity index (PSI), was...
The association of the PSI with 30-day mortality has applications in the areas of patient care, quality improvement and clinical research. For decades, the fact that physicians tended to overestimate the risk of death during initial patient evaluation led to the admission of patients at low risk for mortality. Currently, in the area of patient care, the PSI is a useful tool for better defining mortality risk when the clinician makes the decision to admit a patient. In the area of quality improvement, a pneumonia performance improvement team reviewing local hospital mortality for a given time period may gauge how well their hospital is performing compared to the values predicted by patients’ PSI scores. In the area of clinical research, when comparing the 30-day mortality of populations of patients with CAP receiving different interventions, the PSI is a useful tool for adjusting for mortality based on the severity of disease at the time of hospitalization.

Besides mortality, two other important outcomes in hospitalized patients with CAP are the time required for the patient to show clinical improvement and thus switch from intravenous to oral therapy, and the length of hospital stay. The American Thoracic Society (ATS) considers the discharge date to be the same day that criteria for switch therapy occur, medical and social factors permitting. The ATS also considers the time to be a candidate for switch therapy equivalent to the time to clinical stability, defining it using four criteria that address clinical improvement, temperature, leukocyte count and oral toleration. Additional factors were used by other authors prior to the publication of the ATS CAP guidelines, which defined the time to switch therapy as the time to clinical stability.

The time required for a patient to achieve clinical stability is an important early outcome in hospitalized patients with CAP. During the evaluation of different antibiotics for therapy of CAP, differences in time to clinical stability among the study populations may be one of the best indicators of antibiotic activity. However, differences in time to clinical stability may be related to antibiotic activity as well as patient characteristics. To allow a comparison of populations with CAP, a tool is needed in clinical research to predict the time to clinical stability based on patient characteristics at the time of hospitalization.

There is currently no prediction score to estimate the time to clinical stability in hospitalized patients with CAP. The primary objective of our study was to determine whether a relationship exists between the PSI and the time to clinical stability in an international population of hospitalized patients with CAP. As secondary outcomes, we evaluated the relationship of PSI with length of stay and mortality in the same population.

### MATERIALS AND METHODS

**Study design and population**

This was an international, retrospective, observational study of adult patients hospitalized with CAP in 33 hospitals in 13 countries. Data were collected from 1 June 2001 to 17 May 2004 by members of the Community-Acquired Pneumonia Organization (CAPO), an international network created to facilitate clinical research. Medical records of hospitalized patients with a clinical diagnosis of CAP were randomly selected for review at each of the participating hospitals. Each investigator completed a case report form and transferred it electronically to a database at the University of Louisville in Louisville, KY, USA, where the internal review board evaluated the process. Each case was validated by a study coordinator and a group of investigators at the University of Louisville before being entered into the database. Patients >18 years of age who met the study criteria for CAP were included in the analysis. The risk class (RC) according to PSI was calculated as previously described.

**Study definitions**

CAP was defined as a new pulmonary infiltrate (within 24 h of admission), associated with at least one of the following factors: a new or increased cough, an abnormal temperature (<35.8°C or >37.8°C), an abnormal leukocyte count (leukocytosis, leukopenia or the presence of immature neutrophils). Pneumonia was considered as community-acquired if a patient had no history of hospitalization during the 2 weeks prior to admission.

Time to clinical stability was defined using the criteria below for candidacy for switch therapy. As in the ATS guidelines for the management of CAP, a patient was considered to reach clinical stability and be a candidate for switch therapy when the following four criteria were met: 1) improvement in cough and shortness of breath, 2) afebrile for ≥8 hours (<37.8°C), 3) normalizing leukocyte count by at least 10% from the previous day, and 4) adequate oral intake. The first day of hospitalization was defined as day 0. Criteria for time to clinical stability were recorded for 7 days. All patients who met criteria for time to clinical stability after 7 days were given a value of 8 days.

Time to be a candidate for clinical stability in days was calculated by subtracting the date of admission from the date when the patient met all four criteria, regardless of whether switch to oral therapy was performed. Length of stay (LOS) was calculated by subtracting the date of admission from the date of discharge.

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* A sample of the data collection form is available from the study website (www.caposite.com).
Statistical methods
Statistical analysis was performed using SPSS, version 11.5 (SPSS Inc, Chicago, IL, USA). Analysis of variance was performed between the outcomes, time to switch therapy, LOS, and the RC. Post-hoc comparison was also performed using Scheffe’s test. Spearman’s correlation analyses were performed to determine the strength of the associations. All hypothesis tests were evaluated using alpha < 0.05 (two-tailed).

RESULTS
A total of 1822 patients with time to clinical stability, LOS and mortality data were evaluated. There were 254 patients in RC I, 233 patients in RC II, 395 patients in RC III, 644 patients in RC IV, and 296 patients in RC V. A total of 159 patients met the criteria for clinical stability after day 0 on day 1, 313 patients on day 2, 275 patients on day 3, 190 patients on day 4, 139 patients on day 5, 84 patients on day 6, 68 patients on day 7, and 594 patients on day 8. The Table lists the patients’ demographic information and clinical characteristics.

Figure 1 shows the mean time to clinical stability for patients in each RC, according to the calculated PSI. Figure 2 compares the mean LOS for patients in each RC. A total of 1800 patients had complete case report forms and were evaluated for mortality. The relationship of mortality and RC was significant (P < 0.0001). Figure 3 shows the mortality of the 145 patients who died with respect to their RC.

Analyses of variance indicated that RC significantly influenced both time to clinical stability (P < 0.0001) and length of stay (P < 0.0001). Post-hoc comparisons indicated that patients in RCs IV and V had more days to switch, on average, and significantly longer hospital stays than did patients in RCs I, II and III. Using Spearman’s correlation, there was a signifi-

Table  Demographic factors and clinical characteristics of all patients

<table>
<thead>
<tr>
<th>CAPO cohort</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic factors</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1121 (62)</td>
</tr>
<tr>
<td>Female</td>
<td>701 (38)</td>
</tr>
<tr>
<td>Mean age, years</td>
<td>65.1</td>
</tr>
<tr>
<td>Coexisting conditions</td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td>503 (27.6)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>355 (19.5)</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>159 (8.7)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>356 (19.5)</td>
</tr>
<tr>
<td>Liver disease</td>
<td>72 (4.0)</td>
</tr>
<tr>
<td>Pneumonia CAP</td>
<td>175 (9.6)</td>
</tr>
<tr>
<td>Aspiration</td>
<td>131 (7.2)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>279 (15.3)</td>
</tr>
<tr>
<td>Neoplastic disease</td>
<td>170 (9.3)</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>165 (9.1)</td>
</tr>
<tr>
<td>Nursing home</td>
<td>138 (7.6)</td>
</tr>
</tbody>
</table>

CAPO = Community-Acquired Pneumonia Organization; COPD = chronic obstructive pulmonary disease; CAP = community-acquired pneumonia.
cant relationship between RC and days to switch ($P < 0.001$), and between RC and length of stay ($P < 0.001$).

**DISCUSSION**

This study indicates that the PSI can be used as a tool to predict time to clinical stability in hospitalized patients with CAP. Although this was an expected finding, we think that it is important to have a study supporting the association between time to clinical stability and PSI, because other studies have already been performed assuming that the association exists without the evidence we now provide. The association between time to clinical stability and the PSI was, until now, based on an extrapolation of the well-founded associations of RC with LOS and mortality. Establishing protocols based on extrapolated associations from the PSI may put patients at risk. For example, creating a protocol to prevent the admission of any patient with CAP with an RC of I or II may put patients at risk because studies published well after the PSI was established show that the admission of certain patients with a low RC was justified (e.g., patients with disease comorbidities or unmet social needs). Our data also reproduced the association between the PSI with length of hospitalization as previously reported in two studies, and the well-established association of PSI with patient mortality, originally established by Fine et al.

The finding that the PSI is a useful instrument for predicting late outcomes (e.g., mortality) as well as early outcomes (e.g., time to clinical stability and switch therapy) in hospitalized patients with CAP strengthens its current application in the area of clinical research. In the area of clinical practice, as with any other prediction rule, it will not establish the correct time to switch therapy for an individual patient at the time of hospitalization, but it can help the practicing physician estimate the number of days that the patient may take to be a candidate for switch therapy.

Although the association of PSI with early CAP outcomes has not been well established, and because no prediction rule is available, the PSI has been used in clinical research to adjust for the patient characteristics that may influence early outcomes. For example, a prospective study sought to determine the time to clinical stability in patients with moderate-to-severe CAP based upon how quickly they received antimicrobials. Three groups of patients were created depending on when antimicrobials were given: <4 h from emergency room triage, 4–8 h from triage, and >8 h from triage. They then reported the time to clinical stability and LOS for each group. To adjust for patient characteristics that may have influenced study outcomes, the mean PSI was reported for each group with statistical values that showed no significant difference.

Regarding LOS, an association with the PSI was actually shown as a secondary outcome with the introduction of the PSI in 1997; however, it did not share in the robust statistical power generated from the >50 000 patients used to generate the primary outcome of mortality; rather, it was calculated from only 1236 patients. Nevertheless, other studies have defined prolonged LOS based on a patient’s PSI at admission alone. Our study adds to the body of evidence indicating that the PSI score can be used to predict LOS in hospitalized patients with CAP. An implication of predicting LOS may lead to significant hospital cost savings.

The present study was strengthened by its multicenter, international nature, and the large cohort of patients evaluated. It more firmly established an association between clinical stability and the PSI by recognizing each RC as a separate category. A recent study based the association on findings from two categories of patients (RC I–III vs. RC IV–V). The present study also used the objective criteria defined by the 2001 ATS CAP guidelines to identify clinical stability and candidacy for switch therapy. As no exclusion criteria were used in the selection of patients, this study is a reflection of the current international population hospitalized with CAP. Our study was limited, however, by the observational design.

In summary, we found significant associations between a patient’s RC at time of hospitalization and time to switch therapy and length of hospitalization. The PSI should be considered an important clinical research tool which will allow an accurate comparison between patient populations when early outcomes are being evaluated in hospitalized patients with CAP.

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**References**


RÉSUMÉ
OBJECTIF : Investiguer les relations entre l’indice de gravité de la pneumonie (PSI) et le temps nécessaire à une stabilisation clinique, c’est-à-dire celui de la possibilité de passage du traitement antibiotique IV au traitement per os chez les patients adultes hospitalisés pour pneumonie acquis dans la collectivité (CAP).
RÉSULTATS : On a calculé la classe de risque (RC) en ce qui concerne le PSI chez tous les patients. Les critères pour définir la stabilisation clinique des patients ont été évalués chez tous les patients chaque jour durant les 7 premiers jours d’hospitalisation. La durée moyenne avant stabilisation clinique pour les 254 patients de la classe RC I a été de 4,2 jours, pour les 233 patients de la classe RC II de 3,9 jours, pour les 395 patients de la classe RC III de 4,6 jours, pour les 644 patients de la classe RC IV de 5,0 jours et pour les 296 patients de la classe RC V de 6,0 jours. Une corrélation positive et significative a été observée entre la durée avant stabilisation clinique (P<0,0001).
CONCLUSION : Le PSI est un outil qui peut être utilisé pour prévoir la durée avant stabilisation clinique (c’est à dire la durée avant la modification du traitement antimicrobien) chez les patients hospitalisés pour CAP.