Severe Sepsis in Community-Acquired Pneumonia: When Does It Happen, and Do Systemic Inflammatory Response Syndrome Criteria Help Predict Course?

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Severe Sepsis in Community-Acquired Pneumonia*

When Does It Happen, and Do Systemic Inflammatory Response Syndrome Criteria Help Predict Course?

Tony Dremsizov, MBA; Gilles Clermont, MD, CM, FCCP; John A. Kellum, MD, FCCP; Kenneth G. Kalassian, MD, FCCP; Michael J. Fine, MD; and Derek C. Angus, MD, MPH, FCCP

Study objectives: Most natural history studies of severe sepsis are limited to ICU populations. We describe the onset and timing of severe sepsis during the hospital course for patients hospitalized with community-acquired pneumonia (CAP). We also determine the ability of the systemic inflammatory response syndrome (SIRS) and other proposed risk stratification scores measured at emergency department (ED) presentation to predict progression to severe sepsis, septic shock, or death.

Design: Retrospective analysis of a prospective observational outcome study from the Pneumonia Patient Outcomes Research Team (PORT).


Participants: The 1,339 patients hospitalized for CAP in the PORT study cohort, and a random subset of 686 patients for whom we had information for SIRS criteria.

Interventions: None.

Measurements and results: All subjects had infection (CAP). Severe sepsis was defined as new-onset acute organ dysfunction in this cohort, using consensus criteria. Severe sepsis developed in one half of the patients (n = 639, 48%), nonpulmonary organ dysfunction developed in 520 patients (39%), and septic shock developed in 61 subjects (4.5%). Severe sepsis and septic shock were present at ED presentation in 457 patients (71% of severe sepsis cases) and 27 patients (44% of septic shock cases), respectively. While SIRS was common at presentation (82% of the subset of 686 had two SIRS criteria), it was not associated with increased odds for progression to severe sepsis (odds ratios [ORs], 0.65 and 0.89 for two or more SIRS criteria and three or more SIRS criteria, respectively), septic shock (ORs, 0.80 and 0.55), or death (ORs, 0.65 and 0.39), with poor discrimination (all receiver operating characteristic [ROC] areas under the curve < 0.5). The pneumonia severity index was associated with severe sepsis (p < 0.001) with moderate discrimination (ROC, 0.63).

Conclusions: Severe sepsis is common in hospitalized CAP patients, occurring early in the hospital course. SIRS criteria do not appear to be useful predictors for progression to severe sepsis in CAP.

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Key words: community-acquired pneumonia; critical illness; organ dysfunction; organ failure; outcome; sepsis; systemic inflammatory response syndrome

Abbreviations: AOD = acute organ dysfunction; APACHE = acute physiology and chronic health evaluation; CAP = community-acquired pneumonia; CI = confidence interval; ED = emergency department; OR = odds ratio; PORT = Pneumonia Patient Outcomes Research Team; PPV = positive predictive value; PSI = pneumonia severity index; ROC = receiver operating characteristic; SIRS = systemic inflammatory response syndrome; SOFA = sequential organ failure assessment
Most studies of severe sepsis begin at the moment that the patient has already met diagnostic criteria, and usually focus on patients in the ICU. However, data suggest that many cases of sepsis occur outside the ICU and, further, that early intervention in subjects with incipient severe sepsis may improve outcome. Thus, future therapies for severe sepsis may attempt to target patients earlier and target patients outside the ICU. Yet, there are few data regarding the early course of sepsis. For example, in major sources of severe sepsis, such as community-acquired pneumonia (CAP), it is not even clear what proportion of patients acquire severe sepsis.

Historically, the presence of the systemic inflammatory response syndrome (SIRS) was suggested to be a precursor of severe sepsis. However, several investigators challenged the utility of the 1991 American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference definition of SIRS. There are empiric data in ICU patients showing that SIRS does not predict subsequent organ dysfunction. The latest International Sepsis Consensus Conference recommended abandoning the traditional “two out of four SIRS criteria” for the definition of sepsis. More recently, Alberti and coworkers analyzed a large European cohort and concluded that SIRS was not predictive of mortality during the ICU stay regardless of the timing of infection onset. This study was confined to the ICU and did not assess the possible connection of SIRS with subsequent development of severe sepsis and septic shock. The same research group later developed updated SIRS criteria that, when measured at the onset of infection in the ICU, may better predict subsequent severe sepsis or death.

The first objective of this study was to determine the timing of onset of severe sepsis, defined as infection plus acute organ dysfunction (AOD), in a large North American cohort of subjects hospitalized with CAP. Our second objective was to determine the ability of SIRS criteria, as measured at the time of presentation to the emergency department (ED), to predict the development of severe sepsis or subsequent adverse events. In addition, we explored the predictive ability of one disease-specific scoring instrument, the pneumonia severity index (PSI).

Materials and Methods

The Institutional Review Board of the University of Pittsburgh approved this research study. All participants signed an informed consent form.

Subjects

We studied the inpatients of the Pneumonia Patient Outcomes Research Team (PORT) cohort study (n = 1,339) recruited at four North American sites. Patients were ≥18 years old, had clinical and radiographic evidence of pneumonia within 24 h of presentation to the ED, and provided informed consent. We assessed characteristics through chart review, reviewing records from the time of presentation to the ED to hospital discharge or 30 days. We had information on SIRS criteria for a random subset of 686 patients (51% of the cohort) that allowed us to analyze the association of SIRS with subsequent adverse events and outcomes.

Definitions and Measurements

We defined severe sepsis as infection plus AOD, following the 2003 International Sepsis Definitions Conference criteria. Infection was present in all subjects as a criterion for study entry. AOD was measured across six organ systems as described previously. We defined septic shock as infection plus hypotension refractory to volume resuscitation and requiring vasopressor therapy. We defined SIRS criteria as follows: (1) body temperature >38°C or <36°C; (2) heart rate >90 beats/min; (3) respiratory rate >20 breaths/min; minute ventilation >10 L/min; or PaCO₂ <32 mm Hg; and (4) WBC count <12,000/μL or <4,000/μL (with >10% immature forms), following the 1991 American College of Chest Physicians/Society of Critical Care Medicine Sepsis Definitions Consensus criteria.

Although the consensus conference defined SIRS as the presence of at least two of the four criteria, researchers have also used a stricter rule requiring the presence of at least three of the four SIRS criteria, so we also considered this variant of the definition. We considered the possibility that our previously used definition of AOD may be “mild” compared to commonly used by other researchers levels of organ dysfunction. Specifically, we have previously dichotomized dysfunction in six systems into “base” and “more severe” definitions and used the base definition for analysis. The base definition loosely corresponds to sequential organ failure assessment (SOFA) scores of 1 to 2, while the more severe definition corresponds to SOFA scores of 3 to 4. The base definition was our default definition because we have used it before in published analyses from this cohort. However, to account for the difference in definitions, we repeated all analyses using both definitions of AOD.

Patients were stratified into PSI classes I to V according to published criteria and dichotomized into low-risk PSI (classes I to V).
III, expected mortality < 3%, expected ICU admission < 6%) and high-risk PSI (classes IV to V, expected mortality > 8.5%, expected ICU admission > 10%). This corresponds to the decision rule proposed by Fine et al15 to hospitalize patients who present to the ED with pneumonia in PSI classes IV to V. Because ICU admission is often required when severe sepsis develops in pneumonia patients, we considered high-risk PSI patients to have a higher chance of acquiring severe sepsis.

Study day 1 equals hospital day 1. The first day describes events and clinical characteristics assessed from the period of initial presentation to the ED until midnight. Subsequent days are the subsequent midnight-to-midnight 24-h periods. Whenever more than one episode of severe sepsis occurred during a patient’s hospital course, only the initial episode was included in the analysis.

Predictive Value of Scoring Instruments

We described the progression to severe sepsis, septic shock, and death in patients with and without SIRS at presentation. We calculated the discriminative power and the association of SIRS with these three events. Only patients free of the event of interest (eg, severe sepsis) on study day 1 were included in the analysis of the predictive value of SIRS. This allowed us to assess the utility of SIRS in predicting future events or progression of disease. The outcome of patients without severe sepsis at presentation was analyzed to determine the ability of PSI to predict subsequent severe sepsis.

Statistical Analysis

Categorical data are presented as counts and proportions. We determined the predictive utility of SIRS criteria and of the PSI using the receiver operating characteristic (ROC) area under the curve as a measure of discrimination. In addition, the positive predictive value (PPV) of the high-risk PSI category was calculated using the proportion of subjects in this group who went on to acquire severe sepsis. To test association, we used χ² tests of the proportion of patients with and without SIRS and with or without high PSI scores, as well as with differing numbers of SIRS criteria or differing PSI scores who developed the outcomes of interest. χ² tests were also used to determine the odds of dying. All ROC curves and odds ratios (ORs) are presented using 95% confidence intervals (CIs). We considered differences statistically significant when the p value was < 0.05. A database analysis was conducted (Visual FoxPro and Excel; Microsoft; Redmond, WA), as was statistical analysis (SPSS Version 10.1; SFSS; Chicago, IL, and EpiPak, Version 1; Centers for Disease Control and Prevention; Atlanta, GA).21

RESULTS

Of the 2,287 patients enrolled in the PORT cohort in the ED, 1,343 patients were admitted. Of the 1,343 patients, 1,339 patients had complete organ dysfunction data and formed the study population. Of these 1,339 patients, 170 patients (12.7%) were admitted to the ICU at some point. We described the baseline characteristics of the study population previously.22 One half of the patients (n = 669, 49.96%) had a PSI class of IV or V, conferring a 30-day mortality risk of ≥ 8.5%.15 We collected the requisite physiologic data to determine the SIRS criteria in a random subset of 686 patients. This subset was also described previously.14 Table 1 shows comparisons between the subset and the full cohort in terms of patient age, gender, prevalence of ICU care, ICU length of stay, and mortality. The subset of 686 subjects was younger and had a lower 30-day mortality but was otherwise statistically the same.

Incidence, Timing, and Outcome of Severe Sepsis and Septic Shock

More than one third (34.1%, n = 457) of the 1,339 patients presented to the ED with severe sepsis, and 2% (n = 27) were in septic shock. Nearly one half of the 1,339 patients (47.7%, n = 639) had severe sepsis (Fig 1), and 4.5% (n = 61) had septic shock at some point during their hospitalization. Of those who did not present with severe sepsis (n = 882), severe sepsis developed in 182 patients later in the hospital course (20.6%). These rates were not significantly different from the event rates in the subset of 686 patients with full physiologic data, of whom 52% acquired severe sepsis (n = 357, p = 0.07) and 3% had septic shock (n = 22, p = 0.15).

Using the more severe definition of AOD, 317 patients (23.7%) presented to the ED with severe sepsis, and 110 more patients acquired severe sepsis

### Table 1—Comparison of Patient Characteristics Between the Inpatient PORT Cohort and the Subcohort of 686 Subjects With Full Physiologic Data

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>PORT Inpatient Cohort (n = 1,339)</th>
<th>Subcohort With Full Physiologic Data (n = 686)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, yr</td>
<td>61.7</td>
<td>54.4</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Male gender, %</td>
<td>52.4</td>
<td>49.1</td>
<td>0.17†</td>
</tr>
<tr>
<td>ICU stay, %</td>
<td>12.7</td>
<td>9.3</td>
<td>0.05†</td>
</tr>
<tr>
<td>Mean ICU length of stay, d</td>
<td>7.1</td>
<td>8.5</td>
<td>0.99*</td>
</tr>
<tr>
<td>Mean 30-day mortality, %</td>
<td>8.0</td>
<td>2.9</td>
<td>&lt; 0.001†</td>
</tr>
</tbody>
</table>

*Independent-samples t test.
†χ² test.
later, for a total of 31.9% of the cohort. In the subset of 686 patients, these percentages were 19.2 and 27.7, respectively.

Most AOD (>60% of all AOD in each organ system) was either present on presentation to the ED or occurred on day 1, but the subsequent course varied by system, with most renal dysfunction occurring early, while cardiovascular and hematologic dysfunction tended to occur later (Fig 2). Nonpulmonary organ dysfunction was present in 28% of the cohort (n = 374) at presentation to the ED and 39% of the cohort (n = 520) at some point during their hospital stay (Fig 1). Of the 520 patients who had nonpulmonary AOD at some point, 15% acquired it after day 2 and 10% acquired it after day 5. Organ dysfunction in more than one organ system occurred in 19% of all patients.

Mortality at 30 days or hospital discharge among the patients with severe sepsis was 13.1% using the base AOD definition, and 15.5% using the severe definition. Mortality varied by type of organ system (Fig 3).

Predictive Power of SIRS and PSI for Severe Sepsis, Septic Shock, and Death

Of the 686 patients with full physiologic data, 562 patients (82%) had two of four SIRS criteria on day 1, and 94% met two of four SIRS criteria at some point during their hospitalization. SIRS at presentation was not associated with increased odds of subsequent development of severe sepsis, septic shock, or death (Table 2). Of the 99 patients in this subset who acquired severe sepsis after day 1, 24% (n = 24) did not meet the SIRS criteria at presentation. Similarly, 3 of the 14 patients (21%) who acquired septic shock after day 1 did not meet SIRS criteria at presentation (Table 2), while one quarter of nonsurvivors (n = 5, 25%) did not present with SIRS.

The ROC curves for the discriminative ability of the SIRS criteria to predict severe sepsis, septic shock, and mortality were all >0.5 (Table 2). Even when the more stringent definition of sepsis requiring three of four SIRS criteria was used, the ROC area under the curve remained very low (Table 2; Fig 4, 5). These results did not change when the more severe definition of AOD was used (Table 2; Fig 4). χ² analysis indicated that neither the presence of two nor three SIRS criteria at presentation were associated with subsequent severe sepsis, septic shock, or death. The only exception was that the presence of at least three SIRS criteria at presentation was weakly associated with a decreased odds of dying (OR, 0.39; 95% CI, 0.14 to 0.98; p = 0.04) [Table 2]. In fact, for all six tested associations, the raw proportions of patients with SIRS at baseline who went on to acquire severe sepsis, septic shock, or died were less...
Figure 3. Mortality with AOD in hospitalized patients with CAP. The gray bar represents mortality when the named organ dysfunction is present; this includes both single and multiple organ dysfunction. The patterned bars represent mortality only from occurrences of single organ dysfunction. Mortality in CAP patients is highest when neurologic organ dysfunction is present. By comparison, in CAP patients with single organ dysfunction, mortality is highest when cardiovascular and renal dysfunction are present. GI/hep = GI/hepatic; Resp = respiratory; Hem = hematologic; Cardio = cardiovascular; Neuro = neurologic; see Figure 2 legend for expansion of abbreviation.

Figure 2. Distribution of first-time AOD by organ system. Renal and GI/hepatic dysfunction were more common than respiratory dysfunction in patients with CAP but occurred later during the hospital course. OF = organ failure.
than the respective proportion of subjects who did not have SIRS at baseline (Table 2). The distributions of patients with none, one, two, three, or four SIRS criteria who acquired new severe sepsis were not different (Table 3). The same was true for those who acquired new septic shock or died (Table 3).

The PSI score at presentation was associated with the subsequent development of severe sepsis (p < 0.001). This held true after analyses both for all PSI strata (two-by-five \( \chi^2 \) for PSI scores of I, II, III, IV, or V), and when PSI was analyzed as a dichotomous variable (two-by-two \( \chi^2 \) for PSI scores of IV or V vs PSI scores of I, II, or III). However, the ROC area under the curve for the discriminative power of the PSI score to predict subsequent AOD was 0.629 (95% CI, 0.586 to 0.673). The ROC area under the curve worsened to 0.608 (95% CI, 0.564 to 0.652) when the PSI was analyzed as a dichotomous variable. A high PSI score (IV or V) had a low PPV (36.2%) for subsequent severe sepsis.

**Discussion**

We demonstrated that SIRS criteria measured as early as the patient’s presentation to the ED are poorly predictive of severe sepsis, shock, and death in pneumonia patients. Once the cornerstone of the sepsis definition, SIRS appears to be of very limited use in forecasting any of the adverse events in the sepsis cascade. Our results show for the first time that this holds true for a mixture of ICU and non-ICU patients even when SIRS is present very early during their hospital course. However, the PSI, which is a pneumonia-specific scoring instrument, was associated with subsequent development of severe sepsis although it had a weak predictive discrimination power. We also showed that severe sepsis is common in CAP, occurring in approximately one half of all hospitalized CAP patients. Most patients who acquire severe sepsis do so on the first day of hospital admission. Importantly, hospitalized pneumonia patients frequently acquire nonrespiratory AOD.

There are several implications of these findings. We believe we are the first to demonstrate that the SIRS criteria lack the ability to predict all of the subsequent events in the sepsis cascade, including organ dysfunction, septic shock, and death, for patients at the very early stages of hospital care. This has important implications for the delivery of care for the critically ill because of the growing body of evidence that early identification and treatment of severe sepsis, especially in the ED, saves lives.3

Even in the ICU, the utility of SIRS for predicting organ dysfunction has been disputed. There seems to be evidence that SIRS is associated with organ dysfunction in severe trauma,23 and investigators24 have shown that persistent SIRS may predict organ dysfunction.
dysfunction in postoperative patients. However, SIRS does not seem as helpful in evaluating the prognosis of the “average” ICU patient. Rangel-Frausto et al\(^4\) published data showing that the attack rates for ARDS, disseminated intravascular coagulation, and acute renal failure “increased directly” as more SIRS criteria were met (but did not show the attack rates for patients without SIRS), and the same group\(^8\) published an article demonstrating that SIRS did not predict subsequent severe sepsis in a surgical ICU. Salvo et al\(^9\) showed that ICU patients who acquired SIRS at any point and those who did not had similar rates of subsequent severe sepsis and septic shock.

More recently, investigators have demonstrated that when multivariate analysis is employed, SIRS loses significance as a risk factor for acute renal failure in the ICU\(^10\) or for death.\(^11\) Alberti et al\(^12\) showed that in a broad set of ICU patients who either presented with or went on to acquire infection in the ICU, SIRS criteria failed to select patients at higher risk of death. However, one half of the patients with severe sepsis are not treated in the ICU.\(^1\) Our findings support those of Alberti et al\(^12\) and broaden them to include the following: (1) both ICU and non-ICU patients; (2) all events in the sepsis cascade; and (3) identification of SIRS as early as in the ED.

Of note, we found that the PSI, a score that specifically assesses the risk of death for patients presenting with pneumonia, was associated with the subsequent development of severe sepsis. In other words, pneumonia patients who present with higher PSI scores are not only at a higher risk of death, they are also at a higher risk for organ dysfunction. There is mounting evidence that PSI scores could support the decision whether to hospitalize patients with pneumonia.\(^15,22,25–28\) PSI scores can be generated at or before hospital admission, early enough for use in prescribing proper hospital level of care at the time of hospital admission.

Our results, however, do not unequivocally endorse the use of the PSI. In ROC analysis, which is a better
indication of the ability of the instrument to predict individual patient outcomes, PSI showed weak (but still better than the SIRS) discriminative power. The low PPV of the PSI also means that high PSI scores often failed to select the patients at risk for subsequent severe sepsis. Therefore, its best use as a stratification tool may be as an adjunct to clinical judgment.

In addition to the PSI, there are other existing scores that incorporate information from multiple clinical variables, such as APACHE, but they were

![Figure 5. ROC areas under the curve that describe the discriminative ability of SIRS to predict subsequent septic shock and death. As the curve inside the box deviates farther away from the top left corner, the discrimination worsens. SIRS demonstrates poor discrimination in predicting septic shock and death.](image)

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**Table 3—Predictive Ability of Different Number of SIRS Criteria in Relevance to Severe Sepsis, Septic Shock, and Mortality**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients With 0 SIRS Criteria at Baseline</th>
<th>Patients With One SIRS Criterion at Baseline</th>
<th>Patients With Two SIRS Criteria at Baseline</th>
<th>Patients With Three SIRS Criteria at Baseline</th>
<th>Patients With Four SIRS Criteria at Baseline</th>
<th>p Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with severe sepsis (base definition for AOD)</td>
<td>6/20 (30)</td>
<td>18/71 (25)</td>
<td>21/120 (18)</td>
<td>36/174 (21)</td>
<td>18/105 (17)</td>
<td>0.47</td>
</tr>
<tr>
<td>Patients with severe sepsis (severe definition for AOD)</td>
<td>4/21 (19)</td>
<td>11/78 (14)</td>
<td>10/137 (7)</td>
<td>20/201 (10)</td>
<td>12/119 (10)</td>
<td>0.36</td>
</tr>
<tr>
<td>Patients with septic shock</td>
<td>0/23 (0)</td>
<td>3/99 (3)</td>
<td>5/167 (3)</td>
<td>5/245 (2)</td>
<td>1/144 (1)</td>
<td>0.68</td>
</tr>
<tr>
<td>Patients who die in the hospital by day 30</td>
<td>1/24 (4)</td>
<td>4/100 (4)</td>
<td>8/168 (5)</td>
<td>3/249 (1)</td>
<td>4/145 (3)</td>
<td>0.16</td>
</tr>
</tbody>
</table>

*Data are presented as No./total (%). All data exclude patients who present with the event from the first column. See “Materials and Methods” section for explanation of SIRS criteria.

†χ² test.
also developed to predict mortality rather than to predict subsequent organ dysfunction. In addition, APACHE only applies to subjects already in the ICU and requires 24 h to calculate. Alberti et al\textsuperscript{13} have modified the SIRS criteria to develop a score that predicts subsequent severe sepsis or shock in subjects presenting to the ICU with infection or acquiring infection in the ICU. This interesting “upgrade” of the SIRS criteria does not appear to predict death or the continuous progression of the sepsis cascade, and may have similar disadvantages to the APACHE.

Others\textsuperscript{29} have suggested that serum levels of proteins such as procalcitonin or C-reactive protein can help diagnose infection but, again, the development of organ dysfunction has not been a focus of these investigations. Perhaps a combination of clinical characteristics and biological markers might be more useful in predicting severe sepsis and death. In the meantime, we believe that we complement the data from previous investigators\textsuperscript{4,8,12,13} with the most comprehensive analysis to date of the predictive ability of SIRS, and that our results support the contention of the sepsis definitions conference\textsuperscript{7} that SIRS criteria alone are of little clinical utility.

In addition, our data reinforce the importance of CAP as a cause of severe sepsis. Estimates of the number of Americans hospitalized with CAP range from 600,000 to 1,000,000/yr.\textsuperscript{30–33} Extrapolating from our findings, several hundred thousand of cases of CAP-associated severe sepsis develop each year. This extrapolation is consistent with another study\textsuperscript{4} we conducted of the national incidence of severe sepsis and with the frequent observation that pneumonia is the most common source of severe sepsis.\textsuperscript{2,4}

Finally, hospitalized pneumonia patients frequently have additional organ dysfunction. Almost 40\% of the patients in our cohort acquired nonpulmonary AOD at some point in the hospital course.

There are limitations to our study. First, we focused only on CAP and therefore cannot be certain that our findings would extend to other infections. Second, our cohort was enrolled in the early 1990s at four hospitals. Hospital admission policies may have changed over time or may differ at other hospitals, potentially changing the spectrum of illness severity in subjects hospitalized with CAP. However, we do not believe that such differences would have had a large impact on our findings because we analyzed the progression of patients’ conditions during their hospitalization irrespective of the initial status. Furthermore, we do not believe that management of CAP has changed significantly. One study\textsuperscript{34} showed great disparity in the quality of care for patients with CAP, which is indicative of a lack of focused change in treatment practices. In fact, the latest American Thoracic Society guidelines admitted that there is a paucity of data that would allow firm recommendations in terms of antimicrobial choices, length of inpatient therapy, and even utility of diagnostic methods related to outcomes.\textsuperscript{35} Finally, the in-hospital mortality rate of CAP has been holding relatively steady over the last 20 years.\textsuperscript{31,36,37}

Another limitation is that the definition of severe sepsis is dependent on the choice of organ dysfunction measurement. The use of alternative measures might produce different results. However, we reinforced our measurements with a sensitivity analysis of more severe AOD, and our results did not change. Also, our base measures are similar to the SOFA\textsuperscript{20} scores of 1 or 2 widely used to define AOD. In addition, these measures were previously used by us in a study\textsuperscript{18} in which they were defined \textit{a priori}, and the mortality rates in this study are similar to the mortality rates in other studies\textsuperscript{15,31} of hospitalized pneumonia patients. Furthermore, we previously demonstrated in the same cohort that alternative definitions of organ failure had minimal impact on associations with other mortal and nonmortal outcomes.\textsuperscript{18} Finally, our sample size only allowed detection of moderate and large associations of SIRS criteria with subsequent outcomes. There may have been smaller associations that we were unable to detect.
### APPENDIX

#### HOW TO CALCULATE THE PSI SCORE

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Points Assigned</th>
<th>Patient's Points</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic Factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (in years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>age</td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>age – 10</td>
<td></td>
</tr>
<tr>
<td>Nursing home resident</td>
<td>+ 10</td>
<td></td>
</tr>
<tr>
<td><strong>Coexisting Conditions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neoplastic disease</td>
<td>+ 30</td>
<td></td>
</tr>
<tr>
<td>Liver disease</td>
<td>+ 20</td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>+ 10</td>
<td></td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>+ 10</td>
<td></td>
</tr>
<tr>
<td>Renal disease</td>
<td>+ 10</td>
<td></td>
</tr>
<tr>
<td><strong>INITIAL Physical Examination Findings</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Altered mental status (acute)*</td>
<td>+ 20</td>
<td></td>
</tr>
<tr>
<td>Respiratory rate ≥ 30/min</td>
<td>+ 20</td>
<td></td>
</tr>
<tr>
<td>Systolic BP &lt; 90 mm Hg</td>
<td>+ 20</td>
<td></td>
</tr>
<tr>
<td>Temperature &lt; 35 or &gt; 40°C</td>
<td>≥ 15</td>
<td></td>
</tr>
<tr>
<td>(≥ 95 F or &gt; 104 F)</td>
<td>+ 10</td>
<td></td>
</tr>
<tr>
<td>Pulse ≥ 125/min</td>
<td>+ 10</td>
<td></td>
</tr>
<tr>
<td><strong>INITIAL Diagnostic Test Findings</strong></td>
<td>(score zero if not tested)</td>
<td></td>
</tr>
<tr>
<td>pH &lt; 7.35</td>
<td>+ 30</td>
<td></td>
</tr>
<tr>
<td>BUN &gt; 50 mg/dL</td>
<td>+ 20</td>
<td></td>
</tr>
<tr>
<td>Sodium &lt; 130 mEq/L</td>
<td>+ 20</td>
<td></td>
</tr>
<tr>
<td>Glucose &gt; 250 mg/dL</td>
<td>+ 10</td>
<td></td>
</tr>
<tr>
<td>Hematocrit &lt; 30%</td>
<td>+ 10</td>
<td></td>
</tr>
<tr>
<td>pO2 &lt; 60 mmHg or O2 sat &lt; 90%</td>
<td>+ 10</td>
<td></td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>+ 10</td>
<td></td>
</tr>
</tbody>
</table>

### TOTAL SCORE (sum all patient's points):

* See right column for definitions

#### DEFINITIONS

**Coexisting Conditions**

- **Neoplastic Disease:** Any cancer, except basal- or squamous-cell cancer of the skin, that was active at the time of presentation or diagnosed within one year prior to presentation.
- **Liver Disease:** Prior clinical or histologic diagnosis of cirrhosis or another form of chronic liver disease, e.g., chronic active hepatitis.
- **Congestive Heart Failure:** Prior history of cardiomyopathy, congestive heart failure, or systolic or diastolic ventricular dysfunction, or ejection fraction < 40% documented by history, physical exam, chest radiograph, echocardiogram, multiple gated acquisition scan or left ventriculogram.
- **Cerebrovascular Disease:** Prior clinical diagnosis of hemorrhagic or non-hemorrhagic stroke, intracerebral bleed, or transient ischemic attack; or stroke documented by MRI or CT.
- **Renal Disease:** Prior history of chronic renal disease or prior documentation of abnormal BUN (≥ 40 mg/dL) or creatinine (≥ 2.0 mg/dL) concentrations.

**INITIAL Physical Exam Findings**

- Altered Mental Status: Stupor or coma; acute disorientation to person, place, or time. Must be an acute change.

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### REFERENCES


Severe Sepsis in Community-Acquired Pneumonia: When Does It Happen, and Do Systemic Inflammatory Response Syndrome Criteria Help Predict Course?
Tony Dremsizov, Gilles Clermont, John A. Kellum, Kenneth G. Kalassian, Michael J. Fine and Derek C. Angus
Chest 2006;129:968-978
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