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ORIGINAL RESEARCH

# Assessment of Pneumonia Severity Indices as Mortality Predictors

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## Abstract

**Background:** The leading cause of infectious disease death in the United States is community-acquired pneumonia (CAP). Several pneumonia severity indices exist and are widely used as tools to assist physicians regarding site of care based on risk of death. However, limited data exists that discerns which of the most commonly used severity scores is the best predictor of mortality across multiple time points. The objective of this study is to determine the best mortality predictor at different time points between four of the most commonly used pneumonia severity scores.

**Methods:** This was a secondary analysis of a prospective, multicenter, population-based, observational study of patients hospitalized with CAP in the city of Louisville, KY. The severity indices used were the American Thoracic Society (ATS) criteria, the Pneumonia Severity Index (PSI), the British Thoracic Society criteria (CURB-65), Quick Sepsis-Related Organ Failure Assessment (QSOFA), and direct ICU admission to represent physician discretion. The accuracy, kappa statistic, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for the ability to predict in-hospital, 30-day, 6-month, and 1-year mortality. 95% confidence intervals for each variable were generated by bootstrapping with random sampling and resampling of the subjects 1000 times. In addition, the area under the curve (AUC) was calculated for each severity score and mortality time point.

**Results:** There were 6013 eligible patients included in this analysis with data collected between the years 2014 and 2016. At each time point, the QSOFA had the highest sensitivity and NPV, while the PSI had the highest specificity and PPV. QSOFA had the highest accuracy for in-hospital mortality, 30-day mortality, and 6-month mortality, and the CURB-65 had highest mortality for 1-year mortality. The QSOFA had the highest kappa statistic for in-hospital mortality, the CURB-65 had the highest kappa statistic for 30-day mortality, and the PSI had the highest kappa statistic for 6-month and 1-year mortality. The AUC was highest for the ATS criteria for in-hospital mortality, and was highest for the PSI at the remaining time points.

**Conclusions:** The results of this study show that QSOFA and the PSI are the most reliable severity indices for mortality predictions based on these measures. QSOFA was found, on average, to have the highest accuracy, sensitivity, and NPV. Additionally, PSI was found, on average, to have the highest kappa statistic, specificity, and PPV. The AUC, on average, was best with PSI as the predictor. QSOFA is most capable of making true negative predictions and the PSI is the most capable of making true positive predictions across the four time points.

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## Introduction

The leading cause of infectious disease death in the United States is community-acquired pneumonia (CAP) [1]. Therefore, understanding the severity of a specific pneumonia case is necessary to best direct life-saving treatment. Several indices have been created to categorize pneumonia cases by their severity in an ordinal manner. Validation of these severity indices have been conducted previously by assessing their discriminatory ability to measure the risk of death in a given population [2]. However, limited data exists that compares multiple severity indices as tests for mortality prediction. Previous validations could be the result of confounders for mortality related to the severity measurements within a given index.

The primary objective of this study is to conduct assessments of four of the most commonly used pneumonia severity indices to evaluate their use as mortality predictors at different time points. The secondary objective of this study is to determine, which of the four tests is best for making mortality predictions in a clinical setting before treatment is delivered.

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**Table 1** Measurements required for each severity index.

| | ATS | PSI | CURB-65 | QSOFA |
|---|---|---|---|---|
| Age | | x | x | |
| Altered Mental Status | x | x | x | x |
| Arterial pH | | x | | |
| Blood Pressure | x | x | x | x |
| Body Temperature | x | x | | |
| BUN | x | x | x | |
| Cerebrovascular disease | | x | | |
| Congestive Heart Failure | | x | | |
| Glucose | | x | | |
| Heart Rate | | x | | |
| Hematocrit | | x | | |
| Leukopenia | x | | | |
| Liver Disease | | x | | |
| Mechanical Ventilation | x | | | |
| Multilobar Infiltrate | x | | | |
| Neoplastic Disease | | x | | |
| Nursing Home | | x | | |
| Oxygen Saturation | | x | | |
| PaO2/FiO2 | x | | | |
| Pleural Effusion | | x | | |
| Renal Disease | | x | | |
| Respiratory Rate | x | x | x | x |
| Septic Shock | x | | | |
| Sex | | x | | |
| Sodium | | x | | |
| Thrombocytopenia | x | | | |
| Vasopressors | x | | | |

## Methods

*Study design*

This was a secondary analysis of a prospective, multicenter, population-based, observational study of patients hospitalized with CAP in the city of Louisville, KY from June 1, 2014 to May 31, 2016 [3].

*Subjects*

Patients were only eligible for inclusion in this analysis if
1) they were hospitalized for CAP during the study period,
2) pneumonia severity could be assessed for each index, and
3) mortality at each time point was known.

*Study Definitions and Measurements*

**Community-acquired pneumonia:** Screenings were conducted for the primary analysis participation for all hospitalized adult patients at participating hospitals. Individuals were asked to participate in the study if they met the following 3 criteria: (1) presence of a new pulmonary infiltrate on chest radiograph and/or chest computed tomography scan at the time of hospitalization, defined by a board-certified radiologist's reading; (2) at least 1 of the following: (a) new cough or increased cough or sputum production, (b) fever >37.8°C (100.0°F) or hypothermia <35.6°C (96.0°F), (c) changes in leukocyte count (leukocytosis: >11000 cells/μL; left shift: >10% band forms/mL; or leukopenia: <4000 cells/μL); and (3) no alternative diagnosis at the time of hospital discharge that justified the presence of criteria 1 and 2.

**Table 2** Patient characteristics

| Variable | Value |
|---|---|
| Total n | 6013 |
| Demographics | |
| Age, mean (standard deviation) | 67 (17) |
| Male sex, frequency (%) | 2762 (46) |
| African American race, frequency (%) | 1205 (20) |
| Severity, frequency (%) | |
| Direct ICU admission | 1060 (18) |
| One major and/or three minor ATS criteria | 2415 (40) |
| PSI risk class IV or V | 3711 (62) |
| Curb-65 score 4 or 5 | 975 (16) |
| QSOFA score 3 | 475 (8) |
| Mortality, frequency (%) | |
| In-hospital mortality | 426 (7) |
| 30-day mortality | 835 (14) |
| 6-month mortality | 1521 (25) |
| 1-year mortality | 1943 (32) |

**American Thoracic Society (ATS) Guidelines**
List of major and minor criteria for ICU admission intended primarily for use by emergency medicine physicians, hospitalists, and primary care practitioners in response to confusion regarding differences between guidelines for the ATS and the Infectious Diseases Society of America [4].

**Pneumonia Severity Index (PSI)**
A clinical prediction rule that considers patient demographics, comorbidities, physical examination findings, vital signs, and essential laboratory findings to categorize pneumonia severity into five risk classes, with categories IV and V having the highest probability of mortality [5].

**British Thoracic Society criteria (CURB-65)**
Severity assessment tool that identifies severe CAP and high risk mortality in the presence of two or more of the following features: mental confusion, respiratory rate > 30/min, diastolic blood pressure < 60 mmHg, and blood urea > 7 mmol/l [6].

**Quick Sepsis-Related Organ Failure Assessment (QSOFA)**
Identifies patients with a suspected infection at high risk for in-hospital mortality outside of the ICU, based on the following criteria: Respiratory rate ≥ 22/min, mental confusion, and systolic blood pressure < 100 mm Hg [7].

*Definition of Pneumonia Severity*

Pneumonia severity was then assessed using 4 severity indices: American Thoracic Society (ATS) criteria [3], the Pneumonia Severity Index (PSI) [4], the British Thoracic Society criteria (CURB-65) [5], Quick Sepsis-Related Organ Failure Assessment (QSOFA) [6], and direct ICU admission to represent physician discretion. The measurements associated with each index can be found in **Table 1**.

Severity for the ATS criteria was defined as the presence one major criteria and/or three minor criteria as defined in the guidelines [3]. Severity for the PSI was defined as risk class IV or V. Severity for the CURB-65 was defined as a score of 4 or 5. Severity for the QSOFA was defined as a score of 3.

*Human Subjects Protection*

The study was approved by the Institutional Review Board (IRB) at the University of Louisville Human Subjects Research Protection Program Office (IRB number 11.0613) and by the research offices at each participating hospital. The study was exempt from informed consent.

*Statistical Analysis*

Descriptive statistics were performed. For each severity index, severity as defined was used to determine accuracy, the kappa statistic, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for the ability to predict in-hospital, 30-day, 6-month, and 1-year mortality. To obtain 95% confidence intervals for each variable, bootstrapping with random sampling and resampling of the subjects 1000 times was performed. In addition, the area under the curve (AUC) was calculated for each severity score using the severity as defined and each mortality time point.

## Results

There were 6013 patients eligible for this analysis. Patient characteristics, including the number of patients who met severity as defined, and mortality, are shown in **Table 2**. For in-hospital mortality, the accuracy (0.888), kappa statistic (0.190), sensitivity (0.238), and NPV (0.935) were highest for QSOFA, while specificity (0.989) and positive predictive value (0.941) were highest for the PSI. For 30-day mortality, the accuracy (0.840), sensitivity (0.274), and NPV (0.943) were highest for QSOFA, while specificity (0.975) and positive predictive value (0.932) were highest for the PSI and the kappa statistic (0.237) was highest for CURB-65. For 6-month mortality, the accuracy (0.747), sensitivity (0.501), and NPV (0.947) were highest for QSOFA, while the kappa statistic (0.246), specificity (0.926) and positive predictive value (0.888) were highest for the PSI. For 1-year mortality, the sensitivity (0.577) and NPV (0.951) were highest for QSOFA, while the kappa statistic (0.299), specificity (0.888) and positive predictive value (0.868) were highest for the PSI and the accuracy (0.700) was highest for CURB-65. Across the 4 time points, QSOFA was found to most frequently have the highest accuracy (75%), sensitivity (100%), and NPV (100%); PSI was found to most frequently have the highest kappa statistic (50%), specificity (100%), and PPV (100%). The AUC yielded by severity scores for in-hospital mortality ranged from 0.600 to 0.693; at one year ranged from 0.546 to 0.685. The ATS yielded the highest AUC for in-hospital mortality, and the PSI yielded the highest AUC for mortality at all other time points. All calculated values can be found in **Tables 3-7 and Figures 1-5**.

## Discussion

This study indicates that QSOFA and the PSI are the most reliable severity indices for mortality predictions over the short and long-term. QSOFA is the most reliable severity index for accuracy, sensitivity, and NPV whereas the PSI is the most reliable severity index for the kappa statistic, specificity, and PPV. QSOFA is most capable of making true negative predictions and PSI is most capable of making true positive predictions. From the AUC values, we can see that the PSI is the most consistent, while QSOFA was always the poorest performer in predicting outcomes at every time point.

One important clinical implication is that these severity indices consistently outperform a physician's discretion when severity is determined. However, these indices are used almost exclusively in research settings and not in a clinical setting. This shows a need for an index that can predict mortality during the course of a patient's hospital stay to better direct medical interventions and improve health outcomes related to pneumonia.

This data supports the study and creation of these indices. However, the agreement between severity and mortality is poor across all indices at each time point, as evidenced by the low Kappa statistics and AUC values. No AUC went above 0.7, indicating that alone these severity indexes at a dichotomous cut-point do not exhibit strong predictive power for predicting mortality. Also, accuracy decreases as the time increases. This shows a need for an index that can better predict long-term mortality with higher accuracy.

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**Conflict of Interest:** All authors declared no conflict of interest in relation to the main objective of this work.

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**Table 3** Statistical measures for severity indices with in-hospital mortality as the outcome.

| In Hospital | | | | | |
|---|---|---|---|---|---|
| | ATS | PSI | CURB65 | QSOFA | Direct ICU |
| Accuracy | 0.635 (0.623, 0.646) | 0.445 (0.433, 0.458) | 0.828 (0.818, 0.837) | 0.888 (0.880, 0.895) | 0.819 (0.809, 0.829) |
| Kappa | 0.122 (0.106, 0.139) | 0.076 (0.068, 0.085) | 0.179 (0.149, 0.211) | 0.190 (0.154, 0.226) | 0.187 (0.156, 0.216) |
| Sensitivity | 0.134 (0.121, 0.148) | 0.108 (0.099, 0.118) | 0.187 (0.161, 0.212) | 0.238 (0.199, 0.278) | 0.189 (0.167, 0.212) |
| Specificity | 0.972 (0.966, 0.977) | 0.989 (0.985, 0.993) | 0.952 (0.946, 0.958) | 0.943 (0.938, 0.949) | 0.954 (0.949, 0.960) |
| PPV | 0.761 (0.720, 0.801) | 0.941 (0.917, 0.962) | 0.427 (0.381, 0.476) | 0.265 (0.221, 0.307) | 0.469 (0.428, 0.515) |
| NPV | 0.626 (0.613, 0.639) | 0.408 (0.395, 0.420) | 0.858 (0.849, 0.867) | 0.935 (0.929, 0.941) | 0.846 (0.836, 0.856) |

**Table 4** Statistical measures for severity indices with 30-day mortality as the outcome.

| 30 Days | | | | | |
|---|---|---|---|---|---|
| | ATS | PSI | CURB65 | QSOFA | Direct ICU |
| Accuracy | 0.654 (0.641, 0.666) | 0.504 (0.491, 0.517) | 0.804 (0.796, 0.815) | 0.840 (0.831, 0.849) | 0.785 (0.774, 0.796) |
| Kappa Stat | 0.194 (0.172, 0.215) | 0.151 (0.139, 0.164) | 0.237 (0.207, 0.269) | 0.188 (0.152, 0.220) | 0.195 (0.165, 0.229) |
| Sensitivity | 0.244 (0.227, 0.261) | 0.211 (0.199, 0.224) | 0.327 (0.296, 0.358) | 0.374 (0.328, 0.420) | 0.287 (0.262, 0.314) |
| Specificity | 0.930 (0.921, 0.938) | 0.975 (0.969, 0.981) | 0.896 (0.888, 0.904) | 0.880 (0.871, 0.888) | 0.892 (0.883, 0.900) |
| PPV | 0.699 (0.667, 0.731) | 0.932 (0.915, 0.948) | 0.378 (0.343, 0.413) | 0.211 (0.183, 0.238) | 0.363 (0.331, 0.395) |
| NPV | 0.647 (0.634, 0.660) | 0.434 (0.420, 0.447) | 0.874 (0.864, 0.883) | 0.943 (0.936, 0.949) | 0.854 (0.844, 0.864) |

**Table 5** Statistical measures for severity indices with 6-month mortality as the outcome.

| 6 Months | | | | | |
|---|---|---|---|---|---|
| | ATS | PSI | CURB65 | QSOFA | Direct ICU |
| Accuracy | 0.653 (0.642, 0.665) | 0.579 (0.567, 0.592) | 0.745 (0.734, 0.757) | 0.747 (0.736, 0.758) | 0.717 (0.705, 0.729) |
| Kappa Stat | 0.231 (0.207, 0.256) | 0.246 (0.228, 0.263) | 0.236 (0.206, 0.265) | 0.134 (0.109, 0.160) | 0.168 (0.139, 0.198) |
| Sensitivity | 0.383 (0.363, 0.401) | 0.364 (0.349, 0.379) | 0.496 (0.465, 0.527) | 0.501 (0.455, 0.546) | 0.415 (0.385, 0.444) |
| Specificity | 0.834 (0.823, 0.846) | 0.926 (0.915, 0.937) | 0.794 (0.784, 0.805) | 0.768 (0.757, 0.779) | 0.781 (0.771, 0.793) |
| PPV | 0.608 (0.584, 0.634) | 0.888 (0.871, 0.904) | 0.318 (0.296, 0.341) | 0.156 (0.139, 0.176) | 0.289 (0.269, 0.312) |
| NPV | 0.668 (0.654, 0.682) | 0.475 (0.460, 0.489) | 0.890 (0.881, 0.899) | 0.947 (0.941, 0.954) | 0.862 (0.851, 0.872) |

**Table 6** Statistical measures for severity indices with 1-year mortality as the outcome.

| 1 Year | | | | | |
|---|---|---|---|---|---|
| | ATS | PSI | CURB65 | QSOFA | Direct ICU |
| Accuracy | 0.645 (0.633, 0.657) | 0.620 (0.609, 0.633) | 0.700 (0.690, 0.712) | 0.689 (0.679, 0.701) | 0.673 (0.661, 0.685) |
| Kappa Stat | 0.238 (0.213, 0.261) | 0.299 (0.281, 0.320) | 0.212 (0.189, 0.238) | 0.114 (0.093, 0.134) | 0.151 (0.125, 0.176) |
| Sensitivity | 0.461 (0.443, 0.481) | 0.454 (0.439, 0.470) | 0.572 (0.542, 0.604) | 0.577 (0.532, 0.623) | 0.489 (0.460, 0.517) |
| Specificity | 0.769 (0.756, 0.783) | 0.888 (0.875, 0.901) | 0.725 (0.713, 0.738) | 0.699 (0.687, 0.711) | 0.712 (0.701, 0.725) |
| PPV | 0.573 (0.551, 0.595) | 0.868 (0.853, 0.883) | 0.287 (0.267, 0.308) | 0.141 (0.125, 0.156) | 0.267 (0.247, 0.286) |
| NPV | 0.680 (0.666, 0.695) | 0.502 (0.487, 0.518) | 0.898 (0.888, 0.907) | 0.951 (0.944, 0.957) | 0.867 (0.856, 0.877) |

**Table 7** Area under the curve (AUC) for mortality outcomes with severity indices as the predictor.

| Area Under the Curve (AUC) | | | | | |
|---|---|---|---|---|---|
| | ATS | PSI | CURB65 | QSOFA | Direct ICU |
| In-Hospital | 0.693 | 0.674 | 0.643 | 0.600 | 0.658 |
| 30 Day | 0.673 | 0.683 | 0.626 | 0.577 | 0.608 |
| 6 Month | 0.638 | 0.681 | 0.604 | 0.552 | 0.576 |
| 1 Year | 0.626 | 0.685 | 0.592 | 0.546 | 0.567 |

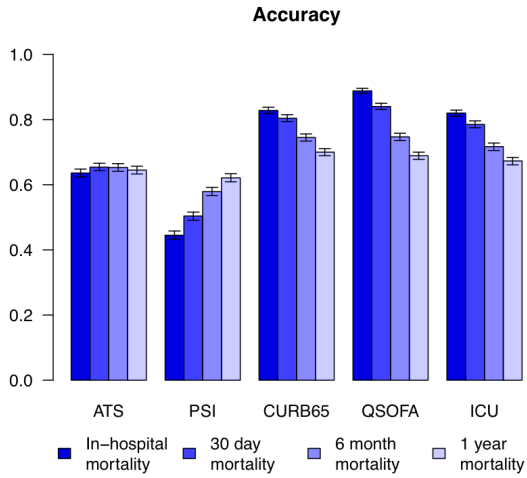


**Figure 1** Accuracy of severity models

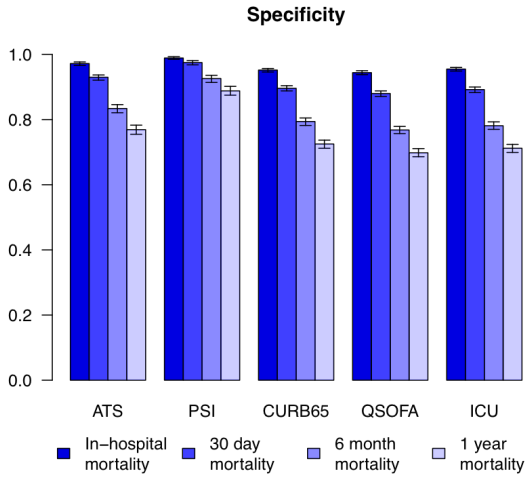


**Figure 4** Specificity of severity models

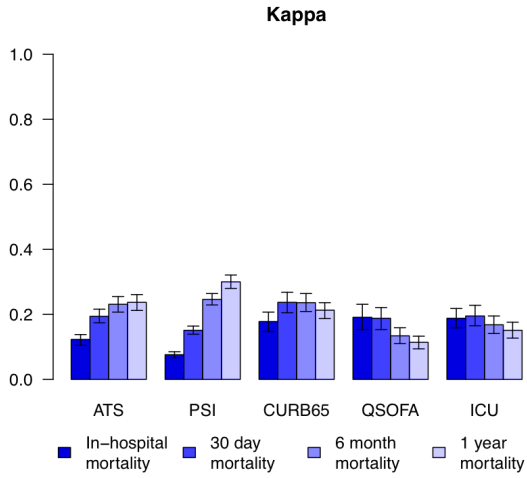


**Figure 2** Kappa statistic of severity models

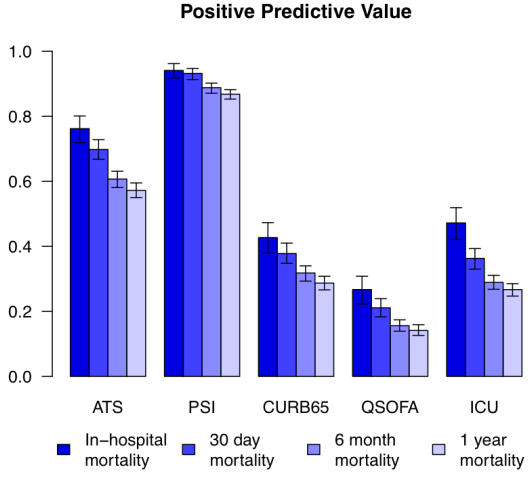


**Figure 5** Positive predictive value of severity models

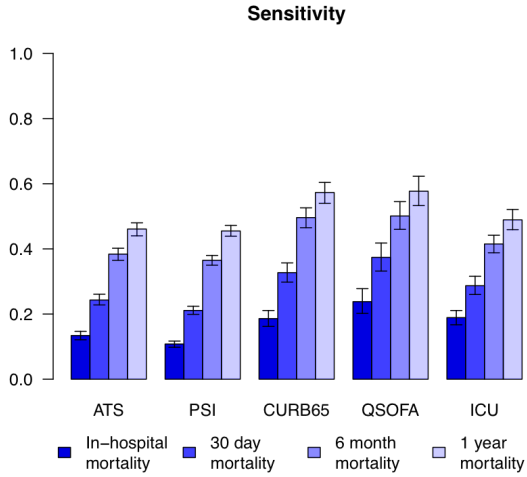


**Figure 3** Sensitivity of severity models

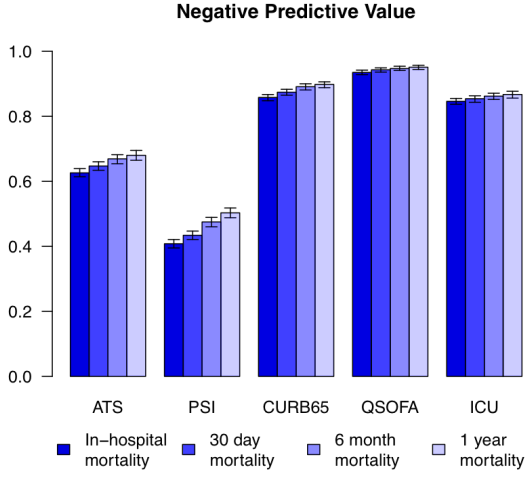


**Figure 6** Negative predictive value of severity models