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# Expanded A-DROP Score: A New Scoring System for the Prediction of Mortality in Hospitalized Patients with Community-acquired Pneumonia

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There are several established prognostic scoring systems for community-acquired pneumonia (CAP). The Pneumonia Severity Index (PSI) is a prediction rule consisting of 20 variables to identify low-risk patients with CAP. Although PSI had high discrimination ability, it is complex to calculate and difficult to use in busy hospital settings. The CURB-65 score is much simpler to use than is PSI, but it has lower sensitivity for predicting mortality compared with PSI. The A-DROP score is a modified version of the CURB-65 score and provides similar predictive power to that of CURB-65. This study was performed to determine whether a simpler score (CURB-65, A-DROP), expanded with a small number of additional variables, can predict mortality more accurately than PSI. We conducted a retrospective observational study of 1,031 patients with CAP who were hospitalized at a tertiary teaching hospital. We used age, sex, comorbidities, vital signs, and laboratory findings as prognostic variables. We compared the PSI, CURB-65, and A-DROP scores using receiver operating characteristic curve analysis. The areas under the curves (AUCs) of PSI, CURB-65, and A-DROP were 0.735, 0.701, and 0.730, respectively. Multivariable analysis identified malignancy [odds ratio (OR): 2.17, 95% confidence interval (CI): 1.13–4.17], respiration rate $\geq$ 24/min [OR: 2.18, 95% CI: 1.24–3.82], heart rate $\geq$ 100/min [OR: 2.92, 95% CI: 1.68–5.08], albumin $\leq$ 3.09 g/dL [OR: 3.85, 95% CI: 2.09–7.07], lactate $>$ 1.7 mmol/L [OR: 2.59, 95% CI: 1.53–4.38], and N-terminal prohormone brain natriuretic peptide $>$ 500 pg/mL [OR: 2.23, 95% CI: 1.26–3.95] as prognostic factors. Using the prognostic variables identified in the multivariable analysis, we assembled a new scoring system, the expanded A-DROP score. The AUC of this score for the prediction of 28-day mortality was 0.834 (95% CI: 0.794–0.874). Bootstrap validation yielded an estimated AUC of 0.833, indicating negligible overfitting of the model. The expanded A-DROP score is a relatively simple and effective scoring system, and its predictive value was superior to those of other scoring systems.

Community-acquired pneumonia (CAP) is a significant cause of morbidity and mortality throughout the world. It is the seventh-leading cause of death in the United States, where about 910,000 episodes of CAP occur annually in adults aged >65 years[1]. In Korea, CAP ranked tenth (7.1 deaths per 100,000 population) among all causes of death in 2004 and fifth (21.4 deaths per 100,000 population) in 2013, which was the highest mortality rate among causes of death due to infection[2]. In the management of CAP, initial assessment of disease severity is essential because it determines the therapeutic approach, including decisions about the need for hospitalization or intensive care unit admission, the extent of diagnostic testing, and the type of antibiotic treatment[1].

Several established severity scores and multiple biomarkers have been used to assess the severity of CAP. The Pneumonia Severity Index (PSI) is a predictive tool used to identify low-risk patients with CAP. Proposed in 1997, the PSI consists of 20 variables, including demographic characteristics, comorbidities, and physical examination, laboratory, and radiographic findings. Although the PSI has high discriminatory value, its calculation is complex, it is difficult to use in busy hospital settings, and it underestimates disease severity in young patients with no comorbidity[3].

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The CURB-65 score, consisting of confusion, urea >7 mmol/L, respiratory rate ≥30 breaths/min, blood pressure (systolic <90 mmHg or diastolic ≤60 mmHg), and age ≥65 years was proposed in 2003. It is simple to use, but was developed to identify patients with severe CAP at high risk of mortality. Thus, it does not identify patients at low risk of mortality, for whom home treatment might be suitable[4].

The A-DROP score, consisting of age ≥70 years in males or ≥75 years in females, blood urea nitrogen ≥21 mg/dL or dehydration, oxyhemoglobin saturation measured by pulse oximetry ≤90% or partial oxygen pressure in arterial blood ≤60 mmHg, confusion, and systolic blood pressure ≤90 mmHg, is a modified version of the CURB-65 score proposed by the Japanese Respiratory Society in 2006[5]. Its predictive power is similar to that of the CURB-65 and PSI[6,7].

This study was conducted to identify prognostic factors for 28-day mortality in patients with CAP, and to compare the predictive value of three pneumonia severity scores. Following these analyses, we developed a simpler and more accurate scoring system by expanding the A-DROP score, and evaluated its efficacy compared with that of preexisting scores for severity assessment.

## Methods

**Study design.** We performed a retrospective observational study of 1,031 patients with CAP who were hospitalized at Yeungnam University Hospital (a 930-bed, university-affiliated, tertiary referral hospital in Daegu, South Korea) between March 2012 and February 2014.

During the study period, all consecutive CAP patients admitted to the hospital via the emergency or outpatient department were considered to be eligible for inclusion. Pneumonia was defined as the presence of new radiographic infiltrate and at least two of the following criteria: fever (>38 °C) or hypothermia (≤35 °C), new cough with or without sputum production, pleuritic chest pain, dyspnea, and altered breath sounds on auscultation[8]. This study included some patients previously defined as having healthcare-associated pneumonia (HCAP), because the 2016 American Thoracic Society and Infectious Diseases Society of America (ATS/IDSA) guidelines removed the concept of HCAP[9]. Therefore, we considered previously defined HCAP as CAP in this study. This study excluded patients with hospital-acquired pneumonia that developed after >48 h hospitalization, those aged <18 years, immunocompromised patients (such as those with neutropenia after chemotherapy, human immunodeficiency virus infection, solid organ transplant recipients, and those receiving corticosteroids or other immunosuppressive agents), and patients with active *Mycobacteria tuberculosis* infection. This study only included the first admission in the case of multiple admissions for a same patient. The primary endpoint was 28-day mortality, and several clinical variables were compared between the survival and non-survival groups.

Antibiotic therapy was initiated according to the 2007 ATS/IDSA guidelines[1], according to the attending physicians' decisions and taking into consideration the severity of the disease and patients' underlying conditions. When a pathogen was identified, antibiotic therapy was modulated according to the susceptibility test results.

As reported previously[10], identified pathogens that were not susceptible to β-lactams, macrolides, and fluoroquinolones were defined as multidrug-resistant (MDR) pathogens.

This study was conducted in accordance with the Declaration of Helsinki. It was reviewed and approved by the institutional review board of our hospital (YUMC IRB 2017-11-013), and the requirement for informed consent was waived because of the retrospective design.

**Data collection.** Data on patients' age, sex, comorbidities, and vital signs were collected. The severity of pneumonia was assessed in all patients on admission using the PSI[3], CURB-65 score [confusion, urea >7 mmol/L, respiratory rate ≥30 breaths/min, blood pressure (systolic <90 mmHg or diastolic ≤60 mmHg), and age ≥65 years][4], and A-DROP score [age ≥70 years for males and ≥75 years for females, blood urea nitrogen (BUN) ≥21 mg/dL or dehydration, oxyhemoglobin saturation measured by pulse oximetry ≤90% or partial pressure of oxygen in arterial blood ($PaO_2$) ≤60 mmHg, confusion, and systolic blood pressure ≤90 mmHg][5].

Laboratory results, including complete blood counts with differentials and C-reactive protein (CRP), procalcitonin, lactate, N-terminal prohormone brain natriuretic peptide (NT-ProBNP), BUN, creatinine, albumin, glucose, sodium, and alkaline phosphatase (ALP) levels, were reviewed. $PaO_2$, partial pressure of carbon dioxide in arterial blood ($PaCO_2$), fraction of inspired oxygen ($FiO_2$) and $PaO_2/FiO_2$ values were obtained from the patients' arterial blood samples. The laboratory findings were analyzed within 24 hours after admission.

Two investigators (JHA and EYC) independently reviewed the baseline data using electronic medical records.

**Statistical analysis.** Continuous variables are expressed as means ± standard deviation and were compared using Student's *t*-test or the Mann–Whitney *U* test. Categorical variables were compared using the chi-squared test or Fisher's exact test. Receiver operating characteristic (ROC) curve analyses were performed to assess the effectiveness of pneumonia severity scores for predicting CAP prognosis. When continuous variables were converted to categorical variables, cut-off values were determined using ROC curves. Multivariable logistic regression analyses were performed to identify independent prognostic factors for mortality using variables with *p* values < 0.05 in univariable analyses, with odds ratios (ORs) and 95% confidence intervals (CIs). In all analyses, two-tailed *p* values < 0.05 were considered to indicate significance.

We conducted internal validation of the expanded A-DROP model to address the possibility of overfitting causing optimism regarding the model's performance. Among several internal validation methods, bootstrapping is known to provide more stable estimates with lower bias than other methods[11]. We used the bootstrap resampling method whereby our derived model was repeatedly fit in 1,000 bootstrap samples. The AUC estimates of these bootstrap models in the original study sample were then computed. We took the mean AUC for these 1,000 bootstrap models to represent the estimate of model performance. All statistical procedures were performed using SPSS software (ver. 21.0; SPSS Inc., Chicago, IL, USA) and R statistical software (version 3.4.3, Vienna, Austria).

| | Survival (n = 935) | Non-survival (n = 96) | P value | Whole population |
|---|---|---|---|---|
| 28-day mortality | | | | 9.3% |
| Mean age (years) | 68.7 ± 14.5 | 73.7 ± 11.2 | 0.001 | 69.2 ± 14.3 |
| Male, n (%) | 617 (66.0%) | 71 (74.0%) | 0.115 | 688 (66.7%) |
| **Smoking status, n (%)** | | | | |
| Current | 150 (16.0%) | 16 (16.7%) | 0.349 | 166 (16.1%) |
| Ex-smoker | 163 (17.4%) | 19 (19.8%) | | 182 (17.7%) |
| Never-smoker | 622 (66.5%) | 61 (63.5%) | | 683 (66.2%) |
| Pack-years | 12.0 ± 20.9 | 16.1 ± 32.4 | 0.390 | 12.4 ± 22.2 |
| **Comorbidities, n (%)** | | | | |
| Myocardial infarction | 33 (3.5%) | 3 (3.1%) | 1.000 | 36 (3.5%) |
| Congestive heart failure | 66 (7.1%) | 14 (14.6%) | 0.009 | 80 (7.8%) |
| Peripheral vascular disease | 74 (7.9%) | 13 (13.5%) | 0.059 | 87 (8.4%) |
| Cerebrovascular disease | 179 (19.1%) | 25 (26.0%) | 0.106 | 204 (19.8%) |
| Dementia | 67 (7.2%) | 13 (13.5%) | 0.026 | 80 (7.8%) |
| Chronic pulmonary disease[a] | 291 (31.1%) | 29 (30.2%) | 0.854 | 320 (31.0%) |
| Connective tissue disease | 17 (1.8%) | 3 (3.1%) | 0.422 | 20 (1.9%) |
| Mild liver disease | 14 (1.5%) | 1 (1.0%) | 1.000 | 15 (1.5%) |
| Diabetes mellitus | 198 (21.2%) | 23 (24.0%) | 0.527 | 221(21.4%) |
| Renal disease | 35 (3.7%) | 5 (5.2%) | 0.411 | 40 (3.9%) |
| Malignancy[b] | 97 (10.4%) | 19 (19.8%) | 0.005 | 116 (11.3%) |
| Moderate to severe liver disease | 16 (1.7%) | 3 (3.1%) | 0.327 | 19 (1.8%) |
| Mechanical ventilator, n (%) | 51 (5.5%) | 18 (18.8%) | <0.001 | 69 (6.7%) |
| ICU admission, n (%) | 43 (4.6%) | 15 (15.6%) | <0.001 | 58 (5.6%) |
| LOS | 12.7 ± 13.7 | 8.9 ± 10.3 | 0.008 | 12.3 ± 13.2 |
| MDR pathogen, n (%) | 87 (9.3%) | 17 (17.7%) | 0.009 | 104 (10.1%) |
| CURB-65 | 1.5 ± 1.1 | 2.3 ± 1.1 | <0.001 | 1.6 ± 1.1 |
| CURB-65 (≥3) | 165 (17.6%) | 40 (41.7%) | <0.001 | 205 (19.9%) |
| PSI class | 3.5 ± 1.1 | 4.2 ± 0.9 | <0.001 | 3.6 ± 1.1 |
| PSI class V | 139 (14.9%) | 38 (39.6%) | <0.001 | 177 (17.2%) |

**Table 1.** Baseline characteristics of the study patients. Data are expressed as mean ± SD for continuous variables. [a]Chronic lung disease includes chronic obstructive pulmonary disease, asthma, bronchiectasis, and interstitial lung disease. [b]Malignancy includes cancer that was active at the time of admission or was diagnosed within one year of admission. ICU: intensive care unit; LOS: length of stay; MDR: multidrug-resistant; PSI: Pneumonia Severity Index.

## Results

**Baseline characteristics.** During the study period, 1,046 patients with CAP were hospitalized. After application of the exclusion criteria, 1,031 patients were enrolled in the study. Enrolled patients were divided into two groups: 935 (90.7%) survivors and 96 (9.3%) non-survivors.

The demographic and baseline clinical characteristics of the patients with CAP are presented in Table 1. The non-survival group was significantly older than the survival group (mean age: 73.7 ± 11.2 vs. 68.7 ± 14.5 years, $p < 0.001$). The non-survival group was significantly more likely to have comorbidities, such as congestive heart failure (14.6% vs. 7.1%, $p = 0.009$), dementia (13.5% vs. 7.2%, $p = 0.026$) and malignancy (19.8% vs. 10.4%, $p = 0.005$).

CURB-65, PSI, and A-DROP scores differed significantly between the survival and non-survival groups. Table 2 presents 28-day mortality rates according to these three scores. A significant increase in mortality was observed with higher CURB-65, PSI, and A-DROP scores.

The clinical and laboratory findings are shown in Table 3. Of the vital signs, systolic blood pressure was significantly lower in the non-survival group (114.4 ± 26.8 mmHg vs. 120.5 ± 23.4 mmHg, p = 0.047). Respiration rate and heart rate were significantly higher in the non-survival group (26.6 ± 5.7vs. 22.7 ± 4.6, p < 0.001; and 107.6 ± 22.2 vs. 93.0 ± 19.4, p < 0.001).

With regard to the laboratory findings, arterial pH, $PaO_2$, $PaO_2/FiO_2$, lactate, BUN, creatinine, albumin, sodium, hemoglobin, hematocrit, platelet, ALP, procalcitonin, CRP, and NT-ProBNP differed significantly between the two groups. $PaCO_2$, glucose level, and white blood cell count were not significantly different between the two groups.

**Prognostic factors for 28-day mortality in patients with CAP.** In univariable analysis, age, pleural effusion, comorbidities (including congestive heart failure, dementia, and malignancy), vital signs (including systolic blood pressure, respiratory and heart rates), and laboratory findings (including arterial pH, hematocrit, platelet count, and $PaO_2$, $PaO_2/FiO_2$, BUN, creatinine, albumin, hemoglobin, ALP, CRP, lactate, procalcitonin,

| | Survival (n = 935) | Non-survival (n = 96) | Mortality rate | Subgroup mortality | Pvalue |
|---|---|---|---|---|---|
| **CURB-65, n (%)** | | | | | |
| 0 | 153 (16.4%) | 4 (4.2%) | 2.5% | 3.8% (0–1) | |
| 1 | 349 (37.3%) | 16 (16.7%) | 4.4% | | |
| 2 | 268 (28.7%) | 36 (37.5%) | 11.8% | 11.8% (2) | <0.001 |
| 3 | 128 (13.7%) | 27 (28.1%) | 17.4% | 19.5% (3–5) | |
| 4 | 33 (3.5%) | 10 (10.4%) | 23.3% | | |
| 5 | 4 (0.4%) | 3 (3.1%) | 42.9% | | |
| **PSI grade, n (%)** | | | | | |
| I | 78 (8.3%) | 3 (3.1%) | 3.7% | 2.6% (I–III) | |
| II | 77 (8.2%) | 1 (1.0%) | 1.3% | | |
| III | 176 (18.8%) | 5 (5.2%) | 2.8% | | <0.001 |
| IV | 465 (49.7%) | 49 (51.0%) | 9.5% | 9.5% (IV) | |
| V | 139 (14.9%) | 38 (39.6%) | 21.5% | 21.5% (V) | |
| **A-DROP, n (%)** | | | | | |
| 0 | 248 (26.5%) | 6 (6.3%) | 2.4% | 3.9% (0–1) | |
| 1 | 342 (36.6%) | 18 (18.8%) | 5.0% | | |
| 2 | 232 (24.8%) | 37 (38.5%) | 13.8% | 13.8% (2) | <0.001 |
| 3 | 85 (9.1%) | 20 (20.8%) | 19.0% | 23.6% (3–5) | |
| 4 | 26 (2.8%) | 14 (14.6%) | 35.0% | | |
| 5 | 2 (0.2%) | 1 (1.0%) | 33.3% | | |

**Table 2.** Severity risk classification of the study patients. PSI: Pneumonia Severity Index.

and NT-ProBNP levels) were significant prognostic factors for mortality in patients with CAP. In multivariable analysis, malignancy (OR: 1.99, 95% CI: 1.04–3.81, $p = 0.039$), respiratory rate (OR: 1.06, 95% CI: 1.02–1.10, $p = 0.008$), heart rate (OR: 1.02, 95% CI: 1.01–1.03, $p < 0.001$), albumin level (OR: 0.27, 95% CI: 0.18–0.41, $p < 0.001$), platelet count (OR: 0.998, 95% CI 0.996–1.00, $p = 0.03$), lactate level (OR: 1.28, 95% CI: 1.10–1.49, $p = 0.002$) and NT-ProBNP level (OR: 1.00, 95% CI: 1.00–1.00, $p = 0.001$) were significant prognostic factors (Table 4).

When the above-listed significant variables were converted to categorical variables using cut-off values, malignancy (OR: 2.17, 95% CI: 1.13–4.17, $p = 0.021$), respiratory rate $\geq 24$ breaths/min (OR: 2.18, 95% CI: 1.24–3.82, $p = 0.007$), heart rate $\geq 100$ beats/min (OR: 2.92, 95% CI: 1.68–5.08, $p < 0.001$), albumin $\leq 3.09$ g/dL (OR: 3.85, 95% CI: 2.09–7.07, $p < 0.001$), lactate $>1.7$ mmol/L (OR: 2.59, 95% CI: 1.53–4.38, $p < 0.001$) and NT-ProBNP $>500$ pg/mL (OR: 2.23, 95% CI: 1.26–3.95, $p = 0.006$) were significant prognostic factors in patients with CAP (Table 5). Table 6 shows the prevalence of these risk factors in different classes of the CURB-65 score, PSI, and A-DROP scores.

**ROC curves for mortality prediction with the three preexisting pneumonia severity scoring systems.** ROC analysis generated areas under the curve (AUCs) for the prediction of 28-day mortality of 0.735 (95% CI: 0.686–0.784), 0.701 (95% CI: 0.648–0.754), and 0.730 (95% CI: 0.678–0.782) for the PSI, CURB-65, and A-DROP scores, respectively (Fig. 1).

**New scoring system developed for assessment of pneumonia severity.** We developed four new score models using newly found significant prognostic variables,which expanded CURB-65 and A-DROP scores. As NT-proBNP and albumin are not available on admission in some hospitals, we constructed two models for each score. Model 1 consists of eight parameters, i.e., confusion, urea $>7$ mmol/L, respiration rate $\geq 30$ breaths/min, blood pressure (systolic $<90$ mmHg or diastolic $\leq 60$ mmHg), age $\geq 65$ years, malignancy, heart rate $\geq 100$/min, and lactate $>1.7$ mmol/L. Model 2 consists of 10 parameters, i.e., confusion, urea $>7$ mmol/L, respiratory rate $\geq 30$ breaths/min, blood pressure (systolic $<90$ mmHg or diastolic $\leq 60$ mmHg), age $\geq 65$ years, malignancy, heart rate $\geq 100$/min, albumin $\leq 3.09$ g/dL, lactate $>1.7$ mmol/L, and NT-ProBNP $>500$ pg/mL. Model 3 consists of eight parameters, i.e., age $\geq 70$ years for males or $\geq 75$ years for females, blood urea nitrogen $\geq 21$ mg/dL or dehydration, oxyhemoglobin saturation measured by pulse oximetry $\leq 90\%$ or partial pressure of oxygen in arterial blood $\leq 60$ mmHg, confusion, systolic blood pressure $\leq 90$ mmHg, malignancy, heart rate $\geq 100$/min, and lactate $>1.7$ mmol/L. Model 4 is composed of 10 parameters, i.e., age $\geq 70$ years for males or $\geq 75$ years for females, blood urea nitrogen $\geq 21$ mg/dL or dehydration, oxyhemoglobin saturation measured by pulse oximetry $\leq 90\%$ or partial pressure of oxygen in arterial blood $\leq 60$ mmHg, confusion, systolic blood pressure $\leq 90$ mmHg, malignancy, heart rate $\geq 100$/min, albumin $\leq 3.09$ g/dL, lactate $>1.7$ mmol/L, and NT-ProBNP $>500$ pg/mL. Respiratory rate $\geq 24$/min was not added in the new score because CURB-65 and A-DROP scores already included respiratory parameters.

The predictive value of expanded CURB-65 score for prediction of 28-day mortality was superior (Model 1 AUC = 0.784, 95% CI: 0.740–0.828, Model 2 AUC = 0.821, 95% CI: 0.781–0.861) to PSI (AUC = 0.735, 95% CI: 0.686–0.784). The predictive value of expanded A-DROP score for prediction of 28-day mortality was also

| | Survival (n = 935) | n | Non-survival (n = 96) | n | P value |
|---|---|---|---|---|---|
| Systolic BP (mmHg) | 120.5 ± 23.4 | 934 | 114.4 ± 26.8 | 96 | 0.047 |
| Diastolic BP (mmHg) | 72.9 ± 14.5 | 934 | 68.9 ± 16.6 | 96 | 0.083 |
| Body temperature (°C) | 37.4 ± 0.8 | 935 | 37.5 ± 1.0 | 96 | 0.737 |
| Respiratory rate (breaths/min) | 22.7 ± 4.6 | 935 | 26.6 ± 5.7 | 96 | <0.001 |
| Heart rate (beats/min) | 93.0 ± 19.4 | 935 | 107.6 ± 22.2 | 96 | <0.001 |
| PH | 7.43 ± 0.7 | 932 | 7.39 ± 0.1 | 96 | 0.001 |
| $PaCO_2$ (mmHg) | 36.9 ± 20.6 | 932 | 35.9 ± 12.3 | 95 | 0.642 |
| $PaO_2$ (mmHg) | 70.8 ± 21.9 | 935 | 65.3 ± 22.2 | 96 | 0.020 |
| $PaO_2/FiO_2$ ratio | 318.2 ± 88.4 | 935 | 268.4 ± 77.1 | 96 | <0.001 |
| Lactate (mmol/L) | 1.6 ± 1.1 | 915 | 2.9 ± 2.2 | 94 | <0.001 |
| BUN (mg/dL) | 17.6 ± 12.2 | 935 | 28.5 ± 20.8 | 96 | <0.001 |
| Creatinine (mg/dL) | 1.2 ± 0.8 | 935 | 1.6 ± 1.2 | 96 | <0.001 |
| Albumin (g/dL) | 3.3 ± 0.7 | 935 | 2.7 ± 0.6 | 96 | <0.001 |
| Sodium (mEq/L) | 136.8 ± 5.0 | 935 | 136.0 ± 7.5 | 96 | 0.041 |
| Glucose (mg/dL) | 158.0 ± 74.6 | 736 | 183.8 ± 141.7 | 91 | 0.262 |
| White blood cells ($\times 10^3/\mu L$) | 11.5 ± 6.2 | 935 | 11.8 ± 7.3 | 96 | 0.928 |
| Hemoglobin (g/dL) | 12.3 ± 2.0 | 935 | 11.3 ± 2.1 | 96 | <0.001 |
| Hematocrit (%) | 36.1 ± 5.9 | 931 | 33.6 ± 6.0 | 96 | <0.001 |
| Platelet ($\times 10^3/\mu L$) | 283.1 ± 118.7 | 934 | 257.4 ± 125.2 | 96 | 0.045 |
| Alkaline phosphatase (IU/L) | 210.6 ± 114.6 | 902 | 251.1 ± 170.8 | 92 | 0.010 |
| Procalcitonin (ng/mL) | 3.4 ± 16.4 | 917 | 10.9 ± 34.0 | 95 | <0.001 |
| C-reactive protein (mg/dL) | 10.9 ± 10.1 | 932 | 16.7 ± 11.5 | 95 | <0.001 |
| NT-ProBNP (pg/mL) | 1152.2 ± 2959 | 902 | 4857.5 ± 7771 | 90 | <0.001 |
| Pleural effusion | 152 (16.3%) | 935 | 24 (25.0%) | 96 | 0.030 |

**Table 3.** Initial clinical and laboratory parameters. Data are expressed as mean ± SD for continuous variables. BP: blood pressure; $PaCO_2$: partial pressure of arterial carbon dioxide; $PaO_2$: partial pressure of arterial oxygen; $FiO_2$: fraction of inspired oxygen; BUN: blood urea nitrogen; NT-ProBNP: N-terminal pro-brain natriuretic peptide.

superior (Model 3 AUC = 0.805, 95% CI: 0.761–0.848, Model 4 AUC = 0.834, 95% CI: 0.794–0.874) to other scoring systems, such as PSI (AUC = 0.735, 95% CI: 0.686–0.784), CURB-65 score (AUC = 0.701, 95% CI: 0.648–0.754), and A-DROP score (AUC = 0.730, 95% CI: 0.678–0.782). Expanded A-DROP score (model 4) showed the highest predictive value among the four models. Validation of the expanded A-DROP score (model 4) using bootstrap resampling methods yielded an AUC of 0.833.

## Discussion

Among 1,031 patients with CAP, the 28-day mortality rate was 9.3% in this study. AUCs from the ROC analysis for the prediction of 28-day mortality were 0.735 (95% CI: 0.686–0.784), 0.701 (95% CI: 0.648–0.754), and 0.730 (95% CI: 0.678–0.782) for the PSI, CURB-65, and A-DROP scores, respectively. We showed that the presence of malignancy as a comorbidity, tachypnea, tachycardia, low albumin level, high lactate level, and high NT-ProBNP level were independent predictors of poor prognosis in patients with CAP. In addition, we proposed a new pneumonia severity score using newly identified prognostic variables. The expanded A-DROP score, based on one comorbidity (malignancy), tachycardia, and three laboratory findings (albumin, lactate, and NT-ProBNP levels), predicted mortality with a larger AUC (0.834) than that for the PSI. To our knowledge, this is the largest study to evaluate the usefulness of pneumonia severity score systems for the prediction of mortality in South Korean populations.

| Prognostic factors | Univariable | | | Multivariable | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | P value | OR | 95% CI | P value |
| Age | 1.03 | 1.01–1.05 | 0.001 | | | |
| Pleural effusion | 1.72 | 1.05–2.81 | 0.032 | | | |
| Congestive heart failure | 2.25 | 1.21–4.18 | 0.010 | | | |
| Dementia | 2.03 | 1.08–3.83 | 0.029 | | | |
| Malignancy | 2.13 | 1.24–3.67 | 0.006 | 1.99 | 1.04–3.81 | 0.039 |
| Systolic BP | 0.99 | 0.98–1.00 | 0.016 | | | |
| Respiratory rate (beats/min) | 1.13 | 1.09–1.17 | <0.001 | 1.06 | 1.02–1.10 | 0.008 |
| Heart rate (beats/min) | 1.03 | 1.02–1.04 | <0.001 | 1.02 | 1.01–1.03 | <0.001 |
| PH | 0.008 | 0.001–0.07 | <0.001 | | | |
| $PaO_2$ (mmHg) | 0.99 | 0.98–1.00 | 0.017 | | | |
| $PaO_2/FiO_2$ ratio | 0.99 | 0.99–1.00 | <0.001 | | | |
| BUN (mg/dL) | 1.04 | 1.03–1.05 | <0.001 | | | |
| Creatinine (mg/dL) | 1.44 | 1.20–1.73 | <0.001 | | | |
| Albumin (g/dL) | 0.27 | 0.19–0.38 | <0.001 | 0.27 | 0.18–0.41 | <0.001 |
| Hemoglobin (g/dL) | 0.78 | 0.70–0.87 | <0.001 | | | |
| Hematocrit (%) | 0.93 | 0.89–0.96 | <0.001 | | | |
| Platelet ($\times 10^3$/μL) | 0.998 | 0.996–1.00 | 0.046 | 0.998 | 0.996–1.00 | 0.030 |
| Alkaline phosphatase (IU/L) | 1.002 | 1.001–1.003 | 0.004 | | | |
| C-reactive protein (mg/dL) | 1.05 | 1.03–1.07 | <0.001 | | | |
| Lactate (mmol/L) | 1.52 | 1.35–1.71 | <0.001 | 1.28 | 1.10–1.49 | 0.002 |
| Procalcitonin (ng/mL) | 1.01 | 1.00–1.02 | 0.001 | | | |
| NT-ProBNP (pg/mL) | 1.00 | 1.00–1.00 | <0.001 | 1.00 | 1.00–1.00 | 0.001 |

**Table 4.** Univariable and multivariable analysis of prognostic factors for 28-day mortality. OR: odds ratio; CI: confidence interval; BP: blood pressure; $PaO_2$: partial pressure of arterial oxygen; $FiO_2$: fraction of inspired oxygen; BUN: blood urea nitrogen; NT-ProBNP: N-terminal pro-brain natriuretic peptide.

| | OR | 95% CI | P value |
|---|---|---|---|
| Malignancy | 2.17 | 1.13–4.17 | 0.021 |
| Respiratory rate ≥24 breaths/min | 2.18 | 1.24–3.82 | 0.007 |
| Heart rate ≥100 beats/min | 2.92 | 1.68–5.08 | <0.001 |
| Albumin ≤3.09 g/dL | 3.85 | 2.09–7.07 | <0.001 |
| Lactate >1.7 mmol/L | 2.59 | 1.53–4.38 | <0.001 |
| NT-ProBNP >500 pg/mL | 2.23 | 1.26–3.95 | 0.006 |

**Table 5.** Multivariable analysis of prognostic factors for 28-day mortality using categorical variables. OR: odds ratio; CI: confidence interval; NT-ProBNP: N-terminal pro-brain natriuretic peptide.

The mortality rate in our study was higher than in previous studies performed in the USA and Europe[12]. The number of patients with PSI risk class IV–V was higher in our study compared to those performed in the USA and Europe, which can explain the higher mortality in our cohort.

The ROC scores for CURB-65 and A-DROP in this study were lower than in some previous studies[7,13]. However, many studies showed lower ROC scores for CURB-65 and A-DROP than in our study[14–17]. The reasons for this difference are not clear. Further multicenter studies in larger numbers of patients are needed to improve the efficacy of these scores.

Five important factors improved the performance of the A-DROP score: the presence of malignancy, tachycardia, hypoalbuminemia, increased blood lactate level, and increased NT-ProBNP level. Malignancy is a well-established prognostic factor for CAP, worth 30 points in the PSI[3]. Ito et al.[18] reported that the presence of malignancy was a prognostic factor for hospitalized patients with CAP aged >15 years. Similarly, we found that malignancy was a poor prognostic factor for hospitalized patients with CAP aged >18 years.

Tachycardia is a known prognostic factor for CAP. It is included in the PSI (heart rate ≥125 beats/min, 10 points)[3] and in the Acute Physiology and Chronic Health Evaluation II score[19]. Several studies have shown that tachycardia is a prognostic factor for CAP[20,21]. However, as heart rate cut-off values have varied among studies, further studies are needed to confirm the usefulness of this factor.

Among laboratory parameters, we found that the albumin, lactate, and NT-ProBNP levels were significant prognostic factors for CAP. Albumin is synthesized in the liver using the amino acids in hepatocytes. Thus, decreased liver function and malnutrition may result in hypoalbuminemia. An imbalance between intravascular and extravascular albumin levels may also result in hypoalbuminemia. Kim et al.[22] reported that patients aged >18 years with debilitating conditions and aspiration pneumonia were assigned more frequently to the

| Subgroup | Patients | Malignancy | Respiratory rate ≥24/min | Heart rate ≥100/min | Albumin ≤3.09 g/dL | Lactate >1.7 mmol/L | NT-ProBNP >500 pg/mL |
|---|---|---|---|---|---|---|---|
| **CURB-65**, n (%) | | | | | | | |
| 0–1 | 522 (50.6%) | 49 (9.4%) | 125 (23.9%) | 164 (31.4%) | 158 (30.3%) | 126 (24.1%) | 99 (19.0%) |
| 2 | 304 (29.5%) | 43 (14.1%) | 119 (39.1%) | 101 (33.2%) | 156 (51.3%) | 90 (29.6%) | 139 (45.7%) |
| 3–5 | 205 (19.9%) | 24 (11.7%) | 137 (66.8%) | 118 (57.6%) | 124 (60.5%) | 112 (54.6%) | 134 (65.4%) |
| **PSI grade**, n (%) | | | | | | | |
| I-III | 340 (33.0%) | 19 (5.6%) | 73 (21.5%) | 95 (27.9%) | 72 (21.2%) | 58 (17.1%) | 42 (12.4%) |
| IV | 514 (49.9%) | 70 (7.8%) | 203 (39.5%) | 193 (37.5%) | 248 (48.2%) | 178 (34.6%) | 206 (40.1%) |
| V | 177 (17.2%) | 27 (15.3%) | 105 (59.3%) | 95 (53.7%) | 118 (66.7%) | 92 (52.0%) | 124 (70.1%) |
| **A-DROP**, n (%) | | | | | | | |
| 0–1 | 614 (59.6%) | 58 (9.4%) | 181 (29.5%) | 192 (31.2%) | 205 (33.4%) | 146 (23.8%) | 133 (21.7%) |
| 2 | 269 (26.1%) | 42 (15.6%) | 118 (43.9%) | 112 (41.6%) | 129 (48.0%) | 102 (37.9%) | 138 (51.3%) |
| 3–5 | 148 (14.4%) | 16 (10.8%) | 82 (55.4%) | 79 (53.4%) | 104 (70.3%) | 80 (54.1%) | 101 (68.2%) |

**Table 6.** The prevalence of risk factors detected in the different classes of CURB-65 score, PSI and A-DROP scores in CAP patients. PSI: Pneumonia Severity Index; CAP: community-acquired pneumonia.
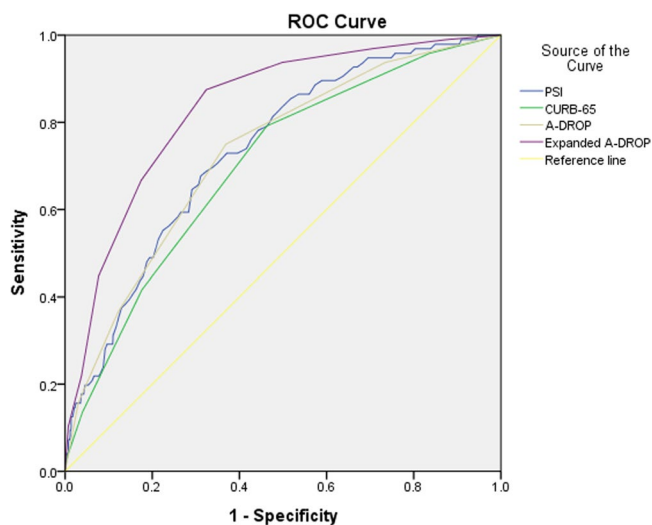


**Figure 1.** ROC curves for scoring systems in the study patients. ROC: Receiver operating characteristic.

hypoalbuminemia group than to the non-hypoalbuminemia group. Previous studies have shown that a low initial serum albumin concentration is an independent risk factor for mortality in patients with CAP[13,18,22]. In our study, hypoalbuminemia had the highest OR for mortality prediction. Malnutrition or underlying disease might influence the mortality of CAP.

The lactate level has been used widely in critically ill patients to assess perfusion status, organ dysfunction, treatment response, and prognosis[23]. In patients with pneumonia, hyperlactatemia is associated with mortality, hospitalization, and intensive care unit admission. The addition of the lactate level significantly improved the prognostic value of the CURB-65 score for CAP mortality prediction in previous studies[15,24]. NT-ProBNP is used in the assessment of cardiac dysfunction. It is secreted in response to excessive stretching of cardiomyocytes and regulates natriuresis, body fluid volume, vascular pressure, and electrolyte balance[25,26]. Some studies have suggested that increased BNP levels in patients with CAP are related to the inflammatory response and local hypoxia in the pulmonary circulatory system[27]. NT-ProBNP was a strong predictor of mortality in hospitalized patients with CAP, with a performance in predicting mortality comparable to that of the PSI and CURB-65 scores[28,29].

The expanded A-DROP score, which employs 10 significant risk factors to predict CAP severity, has greater predictive value than do preexisting severity scores. As NT-proBNP and albumin are not available on admission in some hospitals, we constructed two models. Not only model 4 (10 parameters) but also model 3 (8 parameters) showed higher predictive value compared to pre-existing severity scores. This finding has several significant implications. First, the score decreased the relative effects of age and comorbidities and removed the need for use
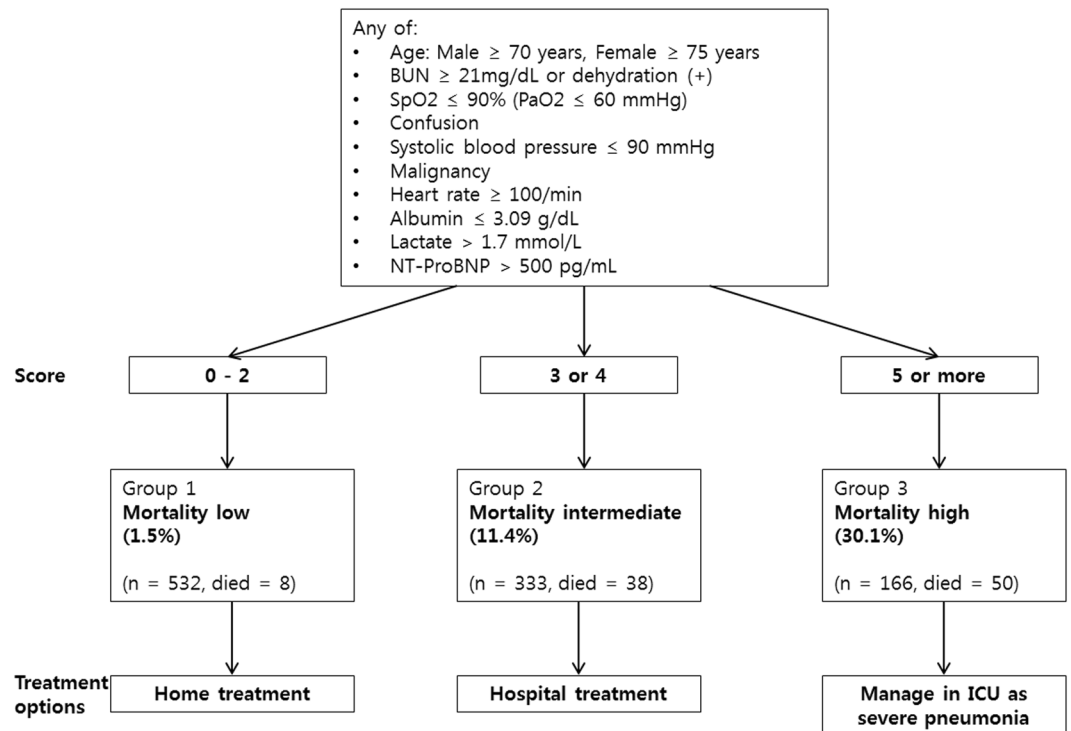
**Figure 2.** Clinical severity assessment in a patient with CAP. CAP: community-acquired pneumonia; BUN: blood urea nitrogen; SpO$_2$: oxygen saturation; PaO$_2$: partial pressure of arterial oxygen; NT-ProBNP: N-terminal pro-brain natriuretic peptide; ICU: intensive care unit.

radiographic findings in the calculation, as compared to PSI. PSI tends to weight age and comorbidities heavily. The expanded A-DROP score significantly improved prediction of high-risk patients by alleviating the weight of age and comorbidities in the calculation. In addition, the score includes several significant biomarkers that are not included in other severity scores. After addressing weaknesses in the preexisting score, the expanded A-DROP score showed greatly improved predictive value (AUC = 0.834). We found similar results (AUC = 0.833) with bootstrap validation. Second, the score can be used in real practice; it is a simpler (10-variable) alternative to the PSI (20-variable) for the prediction of short-term mortality in patients with CAP. The results for the expanded A-DROP score were superior to those for the PSI. In this study, patients with scores of 0, 1, and 2 were considered to be at low risk (1.5%) of mortality, with the possibility of management on a hospital outpatient basis. Patients with scores of 3 and 4 were regarded to be at intermediate risk (11.4%) of mortality, such that hospitalization should be considered. Patients with scores ≥5 were considered to be at high risk (30.1%) of mortality, and initial care in an intensive care unit should be considered (Fig. 2). However, we emphasize that the applicability of the expanded A-DROP score can only be determined by external validation in different cohorts of CAP patients. We hope that other groups will validate the accuracy of this score for predicting mortality in other patient populations.

This study had several limitations. First, as no external validation was conducted in this study, the applicability of the expanded A-DROP score in clinical practice requires further study. Second, it was retrospective and conducted at a single center in South Korea, which had only hospitalized patients. Thus, this new scoring system cannot be applied to outpatients. Third, medical records regarding restriction of treatment escalation, such as do-not-resuscitate orders, were insufficient. Thus, the influence of such restriction on mortality was not considered. Fourth, selection bias could not be avoided as we did not use population-based data and the severity of patients' conditions may differ among tertiary care hospitals in the same area.

In conclusion, five clinical factors – the presence of malignancy, tachycardia, hypoalbuminemia, increased blood lactate level, and increased NT-ProBNP level – are independent predictors of 28-day mortality in patients with CAP. By adding these predictors to the original A-DROP score, we developed a simpler and more accurate scoring system for the prediction of CAP severity in hospitalized patients.

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## Author Contributions

J.H.A. and E.Y.C. conceived and designed the study. J.H.A. and E.Y.C. collected samples. J.H.A. analyzed the data. J.H.A. and E.Y.C. wrote and edited the paper.

## Additional Information

**Competing Interests:** The authors declare no competing interests.

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