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Prognostic value of the lymphocyte-albumin index combined with PSI score in predicting mortality in severe community-acquired pneumonia

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Abstract

Aim: Severe community-acquired pneumonia (SCAP) is a leading cause of sepsis, septic shock, and mortality. Various prognostic scoring systems are used for evaluation, but their use and availability may be complex. Our objective was to evaluate the prognostic significance of LAI, which is easy and inexpensive to perform, and the importance of its combination with PSI score in predicting the mortality of patients with SCAP.

Materials and Methods: This is a retrospective, single-center, cross-sectional study. The patients aged ≥18 with SCAP in tertiary intensive care units were analyzed. Data from patient files and the hospital database include demographic data, PSI score, SOFA, GCS, APACHE II, laboratory parameters, and clinical variables. Cut-off values were used to assess the predictive accuracy of each predictor, measured by the area under the ROC curve (AUC) with a 95% confidence interval (CI). Additionally, we developed combined models for PSI+LAI utilizing various logistic regression analyses. Factors associated with mortality were analyzed using multivariate logistic regression analysis.

Results: The cut-off value of 110 for PSI was a good predictor with 97.8% sensitivity and 98.7% specificity. The cut-off value of 3379 for LAI was observed to be a good predictor of mortality with 92.5% sensitivity and 90.7% specificity. The AUC value for PSI was 0.987 and the AUC value for LAI was 0.933. The AUC value obtained when PSI and LAI values were evaluated together was 0.997. In multivariate analysis, high PSI score, low pulse rate, and LAI value constitute a risk for mortality.

Conclusion: Although PSI or LAI have a high predictive accuracy, their combined use may improve this accuracy and allow for more reliable management of SCAP patients. The PSI score offers a comprehensive assessment. This, combined with the faster and easier application of LAI, provides great advantages to clinicians.

Introduction

Severe Community-Acquired Pneumonia (SCAP) can be lethal by progressing to sepsis, septic shock, and then mortality [1]. Mortality remains high despite rapid diagnostic tests, advanced vaccination strategies, and all modern approaches and treatments [2]. Mortality rates reach 30% in the intensive care units (ICU) [3]. *Streptococcus pneumoniae*, *gram-negative bacteria*, and *Methicillin-Resistant Staphylococcus Aureus* are the pathogens causing SCAP [4,5].

Patients who do not respond to standard oxygen and fluid therapy and require mechanical ventilation (MV) or vasopressor support are considered to have SCAP [6]. Severe CAP is diagnosed with clinical findings, radiological imaging, and laboratory tests. Pneumonia severity index (PSI), CURB-65, and A-DROP Score are used to predict prognosis [7]. However, their use and availability are complex. The utility of various biochemical tests to predict the prognosis and optimize the treatment plan in this patient group is gradually gaining importance. These tests are crucial for identifying high-risk patients, ensuring appropriate and timely treatment, and ultimately reducing morbidity and mortality.

Until now, many biomolecules have been studied to predict the prognosis of SCAP. For example, procalcitonin is associated with morbidity and mortality in bacterial pneumonia [8]. In combination with the clinical parameters, procalcitonin is also used to guide altering the antibiotic treatment for SCAP. However, biomarkers including C-reactive protein (CRP), copeptin, adrenomedullin, and D-Dimer have been used, but their advantage over one an-

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other has not been confirmed [9]. A complete blood count is a cheap and simple test that is easy to perform. To date, ratios of various parameters in complete blood count have been studied in the course of pneumonia as in many other diseases [10,11]. An elevated neutrophil count and lymphopenia are frequently observed in bacterial pneumonia [12]. In addition, lymphopenia was shown to increase the mortality rate in SCAP [13]. However, serum albumin is a negative acute-phase reactant that decreases with increasing severity of inflammation. It also provides insight into the patient's nutritional status. Studies have shown that low albumin value is related to increased mortality in patients with SCAP as well as in various inflammatory diseases [14].

A negative correlation between the severity of inflammation and both lymphocyte count and albumin concentration has been observed [15]. The Lymphocyte Albumin Index (LAI), calculated by multiplying lymphocyte count by albumin concentration, was initially identified as a reliable prognostic marker in stage II/III rectal cancer [16].

This research focuses on evaluating the prognostic role of LAI, which is an easily applicable and low-cost parameter, and the importance of its combination with PSI score predicting mortality of patients with SCAP.

Materials and Methods

Study design and patients

This research is a single-center, retrospective cross-sectional study. The patients aged ≥18 years with SCAP hospitalized in tertiary intensive care units between January 2018 and October 2024 were retrospectively analyzed. Ethical approval was granted with the date and number 27.12.2024-29971. Our study was conducted according to the Helsinki Declarations and Standards for Reporting Diagnostic Accuracy Studies (STARD) guidelines. Informed consent was not obtained due to the study's retrospective design.

Exclusion criteria

Exclusion criteria included age under 18 years, ICU stay less than 48 hours with COVID-19 pneumonia, hematological disorders, extrapulmonary infections, infections occurring ≥48 hours post-hospitalization or intubation (including referred patients), and incomplete data.

Data collection

Demographic data, PSI score, Glasgow Coma Score (GCS), Sequential Organ Failure Assessment Score (SOFA), Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, laboratory parameters (CRP, Procalcitonin, Albumin, Platelet, Neutrophil, Lymphocyte, pH, pCO_2, pO_2, Lactate) in the first 24 hours of intensive care admission, were recorded from the hospital database. Clinical variables (pulse rate, respiratory rate, systolic and diastolic blood pressure, intubation/mechanical ventilation, vasopressor requirement, and mortality) were retrieved from the electronic database of the hospital. Comorbidities were recorded from patient files according to the Charlson Comorbidity Index.

LA index was calculated as lymphocyte count (10^3/μL) x serum albumin (g/dL) level.

Diagnosis of severe community-acquired pneumonia

The 2007 guidelines from the Infectious Diseases Society of America and the American Thoracic Society (IDSA/ATS) state that diagnosing severe community-acquired pneumonia and determining the need for ICU admission of the patient requires either one major criterion or at least three minor criteria.

Minor criteria

- Respiratory rate ≥30/min. - PaO_2/FIO_2 ≤250 - Multilobar infiltration - Confusion/disorientation - Uremia (BUN ≥20 mg/dL) - Leukopenia (Leukocyte <4.000/μl) - Hypothermia (<36 C^o) - Hypotension requiring intensive fluid administration.

Major criteria

- Respiratory failure necessitating invasive mechanical ventilation - Sepsis that requires vasopressor support.

The diagnosis of SCAP was made by an experienced intensive care specialist working in our intensive care unit.

PSI score

The Pneumonia Severity Index (PSI) score is a comprehensive assessment tool that incorporates demographic data, comorbidities, clinical findings, laboratory results, and radiological imaging. In our study, the PSI score was calculated and documented in line with the literature by an experienced specialist in the intensive care unit on the first day of admission. This data was sourced from the hospital database. Patients without physical examination findings, accompanying diseases, or laboratory results are classified as class I; those scoring ≤70 points are class II; 71-90 points are class III; 91-130 points are class IV; and scores >130 points are class V [17]. In this study, classes I-III were deemed low risk, while classes IV-V were regarded as high risk.

Endpoints

Primary endpoint: the significance of the LAI in predicting 30-day mortality. Secondary endpoints: a comparison of the importance of LAI, PSI, and LAI+PSI measurements in predicting mortality.

Statistical analysis

The sample size was calculated using the G*Power 3.1.9.2 software for logistic regression analysis. In this calculation, the odds ratio (OR) value was determined as 2.87, the significance level (α) as 0.05, and power (1 - β) as 0.95. As a result of the analysis, the minimum number of subjects that needed to be included in the study was determined as 86.

Statistical analyses were performed using Statistical software Package for Social Sciences version 22 (SPSSv22, Armonk, NY: IBM Corp.). The Kolmogorov-Smirnov test was used to evaluate the normal distribution of continuous variables. Categorical variables are expressed as frequencies (n) and percentages (%), whereas continuous data are reported as mean ± standard deviation (Mean ±

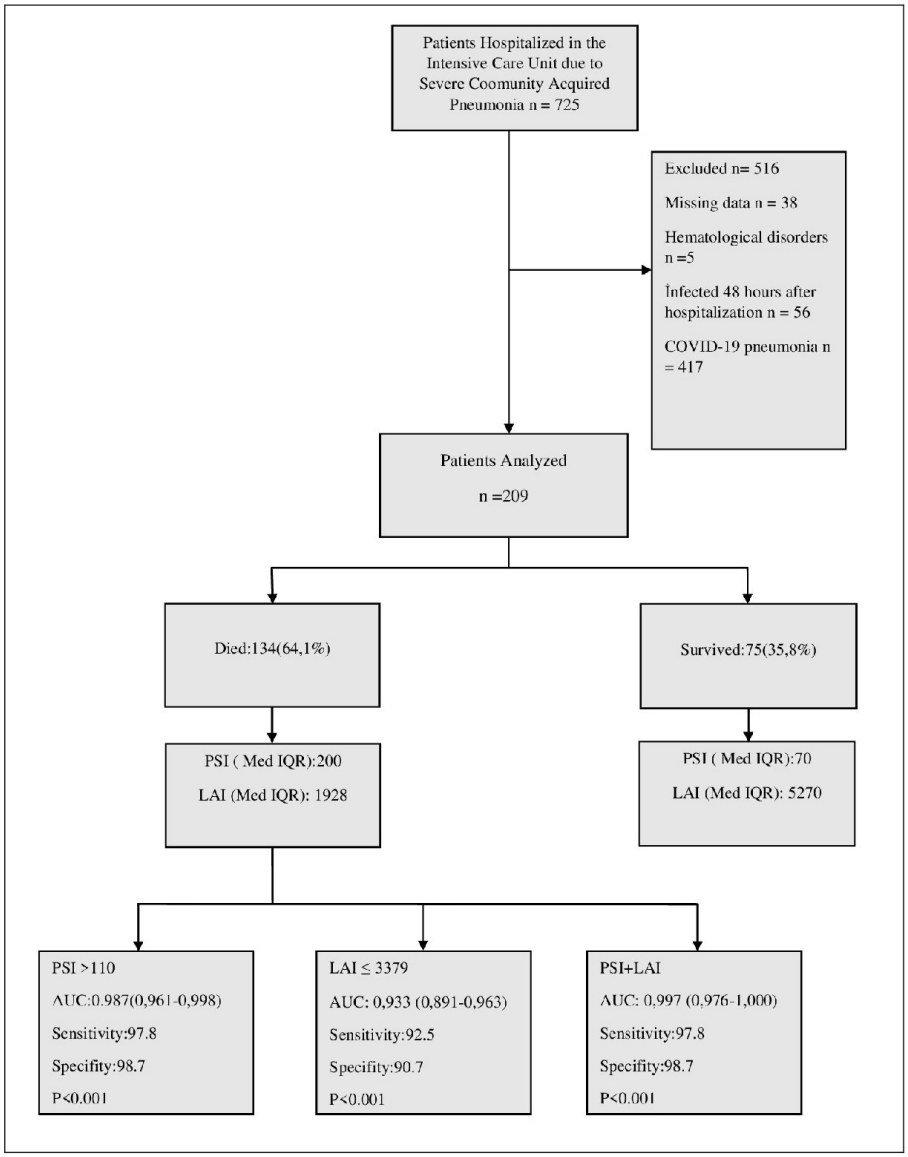

Figure 1. Flow-chart for the process of patient selection.

SD) or median with interquartile range (IQR) (25^{th}-75^{th} percentiles). Differences in categorical variables between groups were evaluated using Pearson's Chi-square test. T and the Mann-Whitney U-test were utilized for comparisons of variables between two independent groups.

Receiver operating characteristic (ROC) curve analysis was conducted to assess mortality, with specific cut-off values determined for each predictive continuous parameter. The area under the ROC curve (AUC) and the corresponding 95% confidence interval (CI) were used to determine the predictive performance of each variable. Additionally, logistic regression models integrating PSI and LAI were developed to enhance prediction accuracy.

Mortality risk factors were identified using multivariate logistic regression. This process began with univariate logistic regression to screen for potential associations between risk factors and mortality. Variables exhibiting a p-value <0.05 in the univariate analysis were included in a preliminary multivariate model, which was refined through backward stepwise selection. Spearman's correlation analysis was also employed to examine inter-variable relationships, with statistical significance defined as $p<0.05$.

Results

In this study, a total of 725 patients were admitted to our tertiary intensive care units between January 2018 and October 2024 due to SCAP. Of the patients, 38 were excluded due to lack of data, five due to hematological disease, 417 due to COVID-19 pneumonia diagnosis, and 56 due to the development of pneumonia 48 hours after hospitalization (patients referred from other centers) (Figure 1). A total of 209 patients were included. Eighty-five (40.7%) were female, with an average age of 69.0 ± 16.8 years.

Comparison of mortality of patients

Hundred and thirty-four (64.1%) patients died due to SCAP. Charlson ($p<0.001$), APACHE II ($p<0.001$), SOFA ($p<0.001$), and PSI ($p<0.001$) scores of the deceased patients were significantly higher, and the GCS score

Table 1. Comparison of all parameters in patients with and without mortality.

		Deceased		Survived	
		n	%	n	%
Gender	Female	54	40.3	31	41.3
	Male	80	59.7	44	58.7
PSI Group	Low Group	2	1.5	69	92.0
	High Group	132	98.5	6	8.0
Vasopressor	Needed	75	56.0	10	13.3
	Not needed	59	44.0	65	86.7
Mechanical Ventilation	Needed	96	71.6	24	32.0
	Not needed	38	28.4	51	68.0
Age (years) Median (IQR)		72.0 (62.0-81.0)		71.0 (53.0-83.0)	
Charlson Index Median (IQR)		5.5 (3.0-8.0)		4.0 (3.0-6.0)	
GCS Median (IQR)		8.0 (5.0-12.0)		11.0 (8.0-14.0)	
APACHE II Median (IQR)		27.0 (21.0-32.0)		18.0 (14.0-24.0)	
SOFA Median (IQR)		11.0 (8.0-13.0)		7.0 (4.0-9.0)	
PSI Score Median (IQR)		200.0 (170.0-220.0)		70.0 (60.0-80.0)	
Pulse rate (Beats/minute) Median (IQR)		123.5 (103.0-140.0)		107.0 (95.0-120.0)	
Systolic Pressure (mmHg) Median (IQR)		89.5 (72.0-114.0)		120.0 (103.0-141.0)	
Diastolic Pressure (mmHg) Median (IQR)		52.0 (42.0-64.0)		68.0 (58.0-81.0)	
Respiratory Rate (Breaths/minute) Median (IQR)		36.0 (31-41)		32.0 (29-39)	0.002**
Platelet (10^3/μL) Median (IQR)		204 (115-294)		242 (194-317)	0.047**
Neutrophil (10^3/μL) Median (IQR)		10.93 (6.52-16.68)		11.07 (6.73-16.77)	0.944**
Lymphocyte (10^3/μL) Median (IQR)		0.74 (0.48-0.88)		1.5 (1.25-1.76)	<0.001**
Albumin (g/dL) Median (IQR)		2.8 (2.5-3.1)		3.5 (3.1-3.9)	<0.001**
C-Reactive Protein (mg/L) Median (IQR)		131 (65-186)		106 (38-166)	0.044**
Procalcitonin (mg/mL) Median (IQR)		2.1 (.6-7.6)		1. (.4-4.2)	0.040**
pH Median (IQR)		7.28 (7.2-7.38)		7.34 (7.29-7.42)	<0.001**
PCO_2 (mmHg) Median (IQR)		48.6 (33.5-64)		44.5 (32.6-55)	0.059**
PaO_2 (mmHg) Median (IQR)		52.2 (42-67)		56.2 (48-68.4)	0.087**
Lactate (mmoL/L) Median (IQR)		3.6 (2.2-5.6)		2.6 (1.6-4.2)	<0.001**
LAI Median (IQR)		1928 (1323-2484)		5270 (4257-6435)	<0.001**

*Square analysis, **Mann Whitney U test was applied. PSI: pneumonia severity index; GCS: Glasgow Coma Score; APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment Score; LAI: Lymphocyte-Albumin Index.

Table 2. Area under the curve, sensitivity, and specificity of the optimal cut-off value of various predictors for mortality.

	AUC (95% CI)	p	Cut-off value	Sensitivity (95% CI)	Specificity (95% CI)
APACHE	0.766 (0.702-0.821)	**<0.001**	>24	64.9 (56.2-73.0)	78.7 (67.7-87.3)
SOFA	0.789 (0.727-0.842)	**<0.001**	>9	61.9 (53.2-70.2)	81.3 (70.7-89.4)
PSI	0.987 (0.961-0.998)	**<0.001**	>110	97.8 (93.6-99.5)	98.7 (92.8-100.0)
LA	0.933 (0.891-0.963)	**<0.001**	≤3379	92.5 (86.7-96.4)	90.7 (81.7-96.2)
PSI+LA	0.997 (0.976-1.000)	**<0.001**	-	97.8 (93.6-99.5)	98.7 (92.8-100.0)

AUC: Area Under Curve; APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment Score; LAI: Lymphocyte-Albumin Index; PSI: Pneumonia Severity Index.

Table 3. Logistic regression analysis regarding the risk factors of mortality.

	B	p	OR	%95 CI
PSI Score	0.125	**0.001**	1.133	1.052-1.219
Pulse Rate (Beats/minute)	-0.060	**0.047**	0.942	0.887-0.999
LAI	-0.001	**0.006**	0.999	0.998-0.999

LAI: Lymphocyte-Albumin Index; PSI: pneumonia severity index.

(p<0.001) was significantly lower. The rate of high PSI scores in the patients with mortality (98.5%) was significantly higher than the rate in the patients who were alive (p<0.001). The need for vasopressors (p<0.001)

Table 4. Correlation analyses of the scores.

		PSI Score	LAI	Charlson	APACHE II	SOFA
LAI	r	**-0.696**				
	p	**<0.001**				
Charlson	r	**0.256**	**-0.158**			
	p	**<0.001**	**0.022**			
APACHE II	r	**0.555**	**-0.379**	**0.292**		
	p	**<0.001**	**<0.001**	**<0.001**		
SOFA	r	**0.556**	**-0.362**	**0.292**	**0.842**	
	p	**<0.001**	**<0.001**	**<0.001**	**<0.001**	
Age (Years)	r	**0.181**	**-0.160**	0.061	**0.148**	0.070
	p	**0.009**	**0.021**	0.384	**0.032**	0.314
Pulse Rate (Beats/minute)	r	**0.309**	**-0.171**	0.090	**0.398**	**0.350**
	p	**<0.001**	**-0.014**	0.194	**<0.001**	**<0.001**
Systolic Pressure (mmHg)	r	**-0.426**	**0.300**	-0.129	**-0.545**	**-0.463**
	p	**<0.001**	**<0.001**	0.063	**<0.001**	**<0.001**
Diastoilic Pressure (mmHg)	r	**-0.442**	**0.297**	**-0.151**	**-0.522**	**-0.478**
	p	**<0.001**	**<0.001**	**0.029**	**<0.001**	**<0.001**
Respiratory Rate (Breaths/minute)	r	**0.253**	-0.083	0.006	**0.301**	**0.243**
	p	**<0.001**	0.231	0.932	**<0.001**	**<0.001**
Albumin (g/dL)	r	**-0.624**	**0.662**	**-0.168**	**-0.398**	**-0.395**
	p	**<0.001**	**<0.001**	**0.015**	**<0.001**	**<0.001**
C-Reactive Protein (mg/L)	r	**0.138**	**-0.192**	0.012	-0.002	-0.008
	p	**0.047**	**0.005**	0.863	0.973	0.903
Procalcitonin (mg/mL)	r	**0.200**	**-0.197**	0.093	**0.156**	**0.145**
	p	**0.004**	**0.004**	0.180	**0.024**	**0.037**

APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment Score; LAI: Lymphocyte-Albumin Index; PSI: Pneumonia Severity Index.

and MV ($p<0.001$) were significantly higher in the deceased than in the non-deceased. Pulse rate ($p<0.001$), respiratory rate ($p=0.002$), CRP ($p=0.044$), procalcitonin ($p=0.040$) and lactate ($p<0.001$) values of those who died were significantly higher than those who did not die; systolic blood pressure ($p<0.001$), diastolic blood pressure ($p<0.001$), PLT ($p=0.047$), lymphocyte ($p<0.001$), albumin ($p<0.001$), pH ($p<0.001$) and LAI ($p<0.001$) values were significantly lower (Table 1).

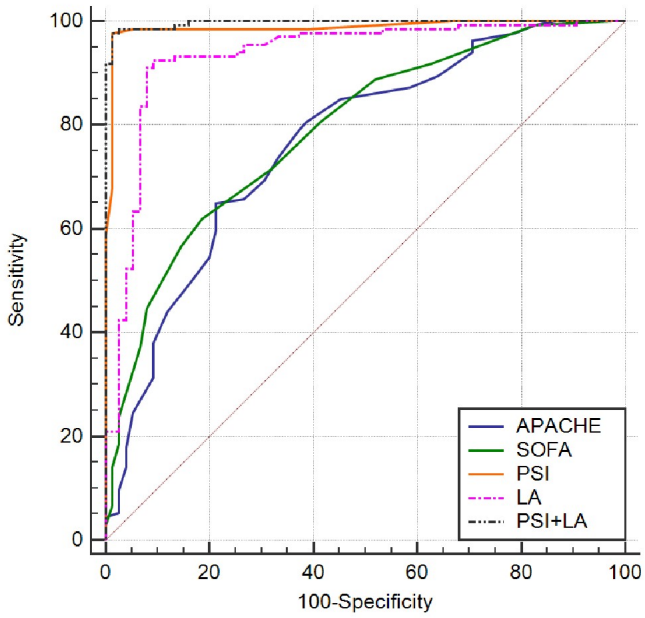

Figure 2. ROC curve analysis of various parameters for mortality

Receiver Operating Characteristic (ROC) curves and cut-off points

ROC analysis investigated the predictive ability of various parameters for mortality in SCAP patients, and cut-off values were determined. For APACHE II (cut-off ≥24), sensitivity and specificity were 64.9% and 78.7%, respectively, indicating good predictive ability. SOFA (cut-off ≥9) also showed good predictive ability with 61.9% sensitivity and 81.3% specificity. PSI (cut-off ≥110) demonstrated excellent predictive power with 97.8% sensitivity and 98.7% specificity. Similarly, LAI (cut-off ≥3379) was a good predictor of mortality, exhibiting 92.5% sensitivity and 90.7% specificity. The AUC values were 0.987 for PSI, 0.933 for LAI, and 0.997 when PSI and LAI were combined (Table 2, Figure 2).

Logistic regression analysis

The logistic regression analysis was performed to evaluate factors that contributed to mortality. Multivariate analysis identified high PSI score, low pulse rate, and LAI value as factors associated with increased mortality risk (Table 3).

Correlation analysis of various parameters

PSI score showed significant positive correlations with APACHE II, SOFA, age, pulse and respiratory rates, CRP, and procalcitonin, and negative correlations with LAI, blood pressure, and albumin. LAI was positively correlated with blood pressure and albumin but negatively with APACHE II, SOFA, age, pulse rate, CRP, and procalcitonin. A positive correlation was observed between APACHE II scores and SOFA scores, age, pulse rate, respiratory rate, and procalcitonin levels. Conversely, APACHE II scores exhibited a negative correlation with systolic blood pressure, diastolic blood pressure, and albumin levels. SOFA was positively correlated with pulse and respiratory rates and procalcitonin and negatively with systolic and diastolic blood pressures and albumin (Table 4).

Discussion

Severe community-acquired pneumonia is a critical infection that often necessitates hospitalization and intensive care support. Early prognosis determination and early management are of lifesaving importance in these patients. This study investigated the importance of both individual and combined use of PSI and LAI in determining patient mortality in the ICU due to SCAP. Our findings suggest that both are highly important in predicting the mortality of SCAP patients and provide a higher success rate when combined.

The PSI score is a comprehensive scoring system including age, comorbidities, vital signs, and laboratory values. Therefore, it provides a broad perspective in assessing the overall condition of patients. Koçak et al. [18] reported that high PSI was associated with low treatment response, prolonged hospital and ICU stay, prolonged treatment duration, and increased mortality rate. In our ROC analysis, we found that a PSI score >110 had a high specificity (98.7%) and sensitivity (97.8%) for predicting mortality in SCAP patients (AUC: 0.987). In particular, the moderate and advanced age groups and comorbidities of the patients may have increased the sensitivity and specificity of the PSI score. However, since the PSI score requires a complex calculation, it may be difficult to use this score in intensive care units due to the high workload of healthcare professionals.

In contrast, the LAI is based on two simple laboratory parameters: lymphocyte count and serum albumin levels. Studies have indicated that lymphopenia is linked to a worse prognosis in infections. Fernandez et al. [19] reported that a lymphocyte count $<724/mm^3$ increased the mortality risk 1.93-fold in patients with SCAP. Albumin levels can serve as an indicator of inflammation severity. Research has shown that serum albumin levels can predict the prognosis of SCAP patients admitted to ICUs [20]. LAI, which is formulated as the product of lymphocyte count and albumin level, is a biomarker that is easier to use in clinical practice to evaluate the severity of inflammatory response. In our study, LAI showed 92.5% sensitivity and 90.7% specificity in predicting mortality with a cut-off value of 3379. These findings reflect previous studies evaluating the prognostic value of LAI, which has been previously reported in different diseases [16, 21-23].

Woo Kim et al. [24] combined procalcitonin or CRP with PSI and IDSA/ATS guidelines in their modeling and observed an increase in the AUC value of adding CRP to PSI and IDAS/ATS in predicting mortality. The primary highlight of our study is that the combination of PSI score and LAI has a significant advantage in predicting mortality. The AUC value of 0.997 was obtained in the ROC analysis. This shows that these two parameters can predict mortality with high accuracy when combined. The PSI score covers a wider range of clinical parameters, whereas the LAI reflects inflammatory status and immune response in a simple but effective way. This situation shows the complementary features of PSI and LAI.

Especially in ICUs, rapid and accurate prognostic evaluation may reduce mortality by providing efficient treatment strategies. Although PSI or LAI alone have a high predictive accuracy, their combined use may improve this accuracy and allow for more reliable management of SCAP patients. The ability of the PSI score to provide a comprehensive assessment, combined with the faster and easier application of the LAI, provides great advantages to clinicians.

The mortality rate was 64.1% in SCAP patients included in our study. This rate is high compared to the literature, and we think that this is due to the high Charlson Comorbidity Index, APACHE II, SOFA, and PSI scores of the patients. We observed that inflammatory parameters such as procalcitonin and CRP were higher in deceased patients, whereas parameters such as lymphocytes and albumin were significantly lower. The need for vasopressors and mechanical ventilation was also significantly higher in these patients. These findings indicate the rapid impairment of organ function in SCAP patients and emphasize the necessity of invasive treatment modalities. We believe that the combination of the LAI and PSI scores may guide the physicians in optimizing the timing of such critical interventions.

Our correlation analysis revealed positive correlations between the PSI score and the Charlson Comorbidity Index, APACHE II, SOFA, age, pulse rate, respiratory rate, CRP, and procalcitonin. This suggests that higher PSI scores are associated with increased disease severity, aligning with these factors. Conversely, LAI showed negative correlations with the Charlson Comorbidity Index, APACHE II, SOFA, age, pulse rate, CRP, and procalcitonin, but a positive correlation with blood pressure. This pattern indicates that this combination of LAI and blood pressure is associated with a poorer prognosis.

Limitations

A notable limitation of this study is that it is retrospective, being conducted at a single center, and limited to

a low sample size, which limits the generalizability of the results. Another limitation is that the data consisted of the initial hospitalization of the patients in intensive care units. Dynamic measurements will provide more reliable data. Our other limitation is that subgroup analysis of microorganisms causing pneumonia was not analyzed. The use of these two scoring systems in different pneumonia subtypes should also be investigated.

Conclusion

This study showed that combining LAI and PSI scores serves as an effective tool for predicting the prognosis of SCAP patients. This combination has the potential to predict mortality early, especially in resource-limited centers or intensive care units with heavy workloads. In intensive care practice, it can both reduce mortality rates by improving clinical decision-making and allow more effective and timely management interventions.

Disclosures

Ethics Committee Approval: Ethical approval was obtained for this study from the Fırat University Non-Interventional Clinical Research Ethics Committee (Document date and number: 27.12.2024-29971).

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