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Original Article

The predictors of 3-month mortality in community-acquired pneumonia

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Abstract

Aim: The aim of the study was to compare the pneumonia severity scoring systems (PSI, CURB-65) and inflammatory markers (CRP, CAR, NLR and PLR) in predicting community-acquired pneumonia (CAP) patients' 3-month mortality.

Materials and Methods: This study included 113 patients (43 females, 70 males) diagnosed with CAP. Demographics, comorbidities, complete blood count, arterial blood gas, electrolytes, liver-renal functions and radiological findings were evaluated. PSI and CURB-65 were classified: PSI low risk (I-III, point ≤90); PSI moderate-high risk (IV-V, point 91≤); CURB-65; low risk (0-2) and high risk (3-5). All statistical calculations were performed with SPSS 23.0 for Windows.

Results: The mean age of the patients was 69.08 ± 16.58 and 3-month mortality rate among the patients hospitalized on admission was 22.4% (n=24). Albumin, hemoglobin, lymphocyte, PaO_2 were lower; NLR and lactate were higher in non-survivors. Albumin and lactate were higher in CURB-65 (0-2) and (3-5) groups, respectively. NLR was significantly higher in PSI group (IV-V). Red cell distribution width and lactate were lower in PSI (I-III); basophil and PaO_2 were significantly lower in PSI group (IV-V). CRP (AUC 0.744), PSI classification (AUC 0.72) and PSI scoring (AUC 0.746) showed higher mortality prediction.

Conclusion: Albumin, hemoglobin, lymphocyte, PaO_2 were lower; NLR and lactate were higher in non-survivors. CRP and PSI score are potent predictors of 3-month mortality.

Keywords: Community-acquired pneumonia; 3-month; mortality

INTRODUCTION

Community-acquired pneumonia (CAP) is one of the major reasons of mortality caused by infection with a rate of approximately 20-30% in developing countries and 3-4% in developed countries (1-3). The 30-day mortality rate associated with CAP is 10-12%, and the 5-year mortality rate is up to 50% (3). Long-term mortality rates due to CAP are higher than other hospitalized patients for other reasons (4). Advanced age and comorbidities may contribute to increased incidence and mortality of patients with CAP (5,6). Approximately 1/3 of CAP cases are inpatient and mortality rate is up to 50-55% in patients with pneumonia who need intensive care unit (ICU) admission (5). The incidence of pneumonia is 1.15% and this infectious disease is ranked 15th in all acute and chronic diseases in Turkey (5). It is estimated that 75% of CAP cases apply to emergency departments (EDs). It is substantial to predict risk factors for mortality, reduce economic burden and improve outcomes in patients with CAP require earlier intervention, hospitalization, ICU admission, optimal antibiotic treatment or discharge from the EDs (2). The diagnosis, treatment, prognosis and mortality data of CAP can vary depending on population structure of country, experience of physicians, resources and location of hospital, complementary tests, and social-sanitization qualifications.

Risk factors and causes of mortality associated with pneumonia may vary according to the time. In hospitalized patients with pneumonia, timing of mortality is divided into a) early period (the first 48 hours-7 days), b) short-term mortality (in the first 28-30 days after diagnosis or during hospitalization), c) long-term mortality (months or years after hospital discharge) (7).

Several algorithms based upon clinical findings and laboratory results including CURB-65, Pneumonia Severity

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Index (PSI) and well-known inflammatory markers such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and c-reactive protein (CRP)/ albumin ratio (CAR) have been used to predict severity, outcomes and short-long term mortality of patients with CAP (8-11).

The aim of the study was to compare the pneumonia severity scoring systems (PSI, CURB-65) and inflammatory markers (CRP, CAR, NLR and PLR) in predicting CAP patients' 3-month mortality in ED.

MATERIALS and METHODS

Study design and population

This cross-sectional study was conducted with approval of Kafkas University Medical Faculty Ethics Committee between February 2018 and November 2018. The study included 113 patients (43 females, 70 males) diagnosed with CAP admitted to the ED.

Patients aged 18 years or more, admitted to ED from the community, presenting with any opacity on chest x-ray in accordance with the diagnosis of acute pneumonia including two or more clinical signs and symptoms (cough, dyspnea, chest pain, crackles on auscultation and temperature >38°C) were enrolled in the study (12). The exclusion criteria were as follows: patients with human immunodefiency virus infection, active pulmonary tuberculosis, cystic fibrosis, receiving routine hemodialysis, homeless people, history of nursing at home or hospitalization longer than 24 hours in the last 90 days, history of chemotherapy or radiotherapy in the last 30 days, admission to the hospital or using any antibiotic in the last two weeks. Verbal consent was obtained from all patients.

Data collection

A questionnaire was designed for each patient, including demographic profile, comorbidities, physical examination, laboratory results and radiological findings. At admission to ED, the scores of PSI and CURB-65 were calculated and classified as follow: 1) PSI low risk group (classes I-III, total point value ≤90); and PSI moderate-high risk group (class IV-V total point value 91≤); 2) CURB-65; low risk group (scores 0-2) and high risk group (scores 3-5) (11).

The laboratory findings were analyzed within 3 hours after admission to ED including arterial blood gas analysis (partial oxygen pressure-PaO_2, lactate), serum electrolytes, liver and kidney function tests, complete blood count, NLR, PLR, CRP and CAR.

Statistical Reviews

SPSS (Statistical Package for Social Sciences) 16.0 program was used for Windows. It was evaluated with the Kolmogorov-Smirnov test. Mann-Whitney U test was used for parameters that did not show normal distribution. ROC Analysis was used to estimate the parameters. The results were evaluated as 95% confidence interval and significance p <0.05.

RESULTS

In Table 1, demographics, comorbidities and clinical findings of the cases were given. Accordingly, 70 (61.9%) of the cases were male and 43 (38.1%) were female. Their ages ranged from 24 to 98 years, with an average of 69.08±16.58. The frequency of comorbidities seen among the patients was: Hypertension (46%), diabetes mellitus (10.6%), coronary artery disease (12.4%), COPD (55.8%), asthma (8%), neoplastic disease (9.7%), congestive heart failure (12.4%), cerebrovascular diseases (5.3%) and chronic renal diseases (8%). Confusion was present in 10 (8.8%) of the cases and pleural effusion was positive 10 (8.8%) of them. The respiratory rate of the patients ranged between 14 and 44 per minute with an average of 22.89±9.81. The systolic blood pressure of cases varied between 80 and 160 mmHg, with an average of 118.60±12.61. The fever of the cases ranged from 35.9 to 40.1°C, with an average of 36.50±0.45. The heart rate of the cases varied between 20 and 144 per minute, with an average of 87.28±13.35. The 3-month mortality rate among the patients admitted to ICU on admission was 83.3% (n=6). The 3-month mortality rate among the patients hospitalized on admission was 22.4% (n=24).

CRP (p=0.459), CAR (p=0.080) and PLR (p=0.803) values between the survivors and non-survivors were not statistically significant (p>0.05). Albumin was significantly lower and NLR was higher in non-survivors, respectively (p <0.01, p<0.05) (Table 2).

White blood cell (WBC) (p=0.696), hematocrit (p=0.053), neutrophil (p=0.492), plateletcrit (p=0.402), mean platelet volume (MPV) (p=0.722), platelet (p=0.307), red cell distribution width (RDW) (p=0.214), basophil (p=0.674), eosinophil (p=0.885) and monocyte (p=0.585) values between the survivors and non-survivors were not statistically significant (p>0.05). Hemoglobin (p=0.014), lymphocyte (p=0.029) and PaO_2 (p=0.016) were lower and lactate was higher in non-survivors (p<0.05) (Table 3).

CRP (p=0.417), CAR (p=0.120), PLR (p=0.925) and NLR (p=0.405) were not statistically different between the CURB-65 score groups. Albumin was significantly higher in CURB-65 score (0-2) group (p=0.006) (Table 4). Lactate was significantly higher in CURB-65 score (3-5) group (p=0.002) (Table 5).

CRP (p=0.331), albumin (p=0.124), CAR (0.197) and PLR (0.727) were not statistically different between PSI groups (I-III and IV-V). NLR was significantly higher in PSI group (IV-V) (p=0.013) (Table 6). RDW and lactate were significantly lower (p<0.001) in PSI group (I-III); basophil and pO2 were significantly lower in PSI group (IV-V) (p<0.001) (Table 7).

CRP (AUC 0.744, 95% CI: 0.65-0.82) showed highest 3-month mortality estimation. Albumin (AUC 0.54, %95 CI: 0.45-0.64), CAR (AUC 0.81, %95 CI: 0.51-0.70), NLR (AUC 0.62, %95 CI: 0.53-0.71) and PLR (AUC 0.52, %95 CI: 0.42-0.61) indicated statistically significant lower 3-month mortality prediction (Table 8 and Figure 1). CURB-65

(AUC 0.61, 95% CI: 0.51-0.70) showed the lowest 3-month mortality prediction. PSI classification (AUC 0.72, 95% CI:0.63-0.80) and PSI scoring (AUC 0.746, 95% CI:0.65-0.82) indicated statistically higher 3-month mortality prediction (Table 9 and Figure 2).

Table 1. Demographic properties, comorbidities and clinical findings of the patients

		CAP patients (N=113)	
		No.	%
Gender	Male	70	61.9
	Female	43	38.1
Hypertension		52	46
Diabetes mellitus		12	10.6
Hyperlipidemia		5	4.4
Coronary artery disease		14	12.4
COPD		63	55.8
Asthma		9	8
Nursing home resident		-	-
Neoplastic disease		11	9.7
Chronic liver diseases		-	-
Congestive heart failure		14	12.4
Cerebrovascular diseases		6	5.3
Chronic renal diseases		9	8
Confusion		10	8.8
Pleural effusion		8	8.8
3-month mortality		30	26.5
	Min-Max	Mean	SD
Respiratory rate (min)	14-47	22.89	9.81
Systolic blood pressure (mmHg)	80-160	118.60	12.61
Fever (oC)	35.9-40.1	36.50	0.45
Heart rate (min)	20-144	87.28	13.35
Age (years)	24-98	69.08	16.58

CAP, community acquired pneumonia; COPD, chronic obstructive pulmonary disease; min-max; minimum and maximum values

Table 2. Comparison of inflammatory markers in survivors and non-survivors

	Groups	N	Mean rank	Sum of rank	U	z	p
CRP	Non-survivors	30	60.80	1824.00	1131.000	-.741	0.459
	Survivors	83	55.63	4617.00			
Albumin	Non-Survivors	30	36.47	1094.00	629.000	-4.010	.000**
	Survivors	83	64.42	5347.00			
CAR	Non-Survivors	30	65.98	1979.50	975.500	-1.752	0.080
	Survivors	83	53.75	4461.50			
PLR	Non-Survivors	30	57.77	1733.00	1192.000	-.250	0.803
	Survivors	82	56.04	4595.00			
NLR	Non-Survivors	30	66.70	2001.00	924.000	-2.011	.044*
	Survivors	82	52.77	4327.00			

**p<0.01 *p<0.05

Table 3. Comparison of complete blood count, lactate and PaO_2 in survivors and non-survivors

	Groups	N	Mean rank	Sum of rank	U	z	p
White blood cell	Non-Survivors	30	58.48	1754.50	1170.500	-.391	0.696
	Survivors	82	55.77	4573.50			
Hemoglobin	Non-Survivors	30	44.08	1322.50	857.500	-2.448	0.014*
	Survivors	82	61.04	5005.50			
Hematocrit	Non-Survivors	30	46.70	1401.00	936.000	-1.932	0.053
	Survivors	82	60.09	4927.00			
Neutrophil	Non-Survivors	30	59.98	1799.50	1125.500	-.687	0.492
	Survivors	82	55.23	4528.50			
Lymphocyte	Non-Survivors	30	45.45	1363.50	8898.500	-2.178	0.029*
	Survivors	82	60.54	4964.50			
Plateletcrit	Non-Survivors	30	60.75	1822.50	1102.500	-.838	0.402
	Survivors	82	54.95	4505.50			
Mean platelet volume	Non-Survivors	30	54.70	1641.00	1176.000	-.355	0.722
	Survivors	82	57.16	4687.00			
Platelet	Non-Survivors	30	61.68	1850.50	1074.500	-1.022	0.307
	Survivors	82	54.60	4477.50			
Red cell distribution width	Non-Survivors	30	62.80	1884.00	1041.000	-1.242	0.214
	Survivors	82	54.20	4444.00			
Basophil	Non-Survivors	30	54.43	1633.00	1168.000	-.420	0.674
	Survivors	82	57.26	4695.00			
Eosinophil	Non-Survivors	30	55.77	1673.00	1208.000	-.145	0.885
	Survivors	82	56.77	4655.00			
Monocyte	Non-Survivors	30	59.27	1778.00	1147.000	-.545	0.585
	Survivors	82	55.49	4550.00			
Lactate	Non-Survivors	30	65.52	1965.50	809.500	-2.400	0.016*
	Survivors	77	49.51	3812.50			
PaO_2	Non-Survivors	30	32.60	978.00	513.000	-4.507	.000**
	Survivors	78	62.92	4908.00			

**p<0.01 *p<0.0

Table 4. Comparison of inflammatory markers in CURB-65 score groups (0-2 and 3-5)

	Groups	N	Mean rank	Sum of rank	U	z	p
CRP	0-2	101	56.14	5670.00	519.000	-.811	0.417
	3-5	12	64.25	771.00			
Albumin	0-2	101	59.94	6054.00	309.000	-2.771	0.006*
	3-5	12	32.25	387.00			
CAR	0-2	101	55.35	5590.00	439.000	-1.556	0.120
	3-5	12	70.92	851.00			
PLR	0-2	100	56.60	5660.00	590.000	-.094	0.925
	3-5	12	55.67	668.00			
NLR	0-2	100	55.62	5561.50	511.500	-.833	0.405
	3-5	12	63.88	766.50			

*p<0.01

Table 5. Comparison of complete blood count, lactate and PaO_2 in CURB-65 score (0-2 and 3-5) groups

	Groups	N	Mean rank	Sum of rank	U	z	p
White blood cell	0-2	100	56.00	5599.50	549.500	-.475	0.635
	3-5	12	60.71	728.50			
Hemoglobin	0-2	100	56.30	5630.00	580.000	-.188	0.851
	3-5	12	58.17	698.00			
Hematocrit	0-2	100	56.51	5650.50	599.500	-.005	0.996
	3-5	12	56.46	677.50			
Neutrophil	0-2	100	55.78	5578.00	528.000	-.677	0.498
	3-5	12	62.50	750.00			
Lymphocyte	0-2	100	58.16	5816.00	434.000	-1.562	0.118
	3-5	12	42.67	512.00			
Plateletcrit	0-2	100	57.06	5705.50	544.500	-.522	0.602
	3-5	12	51.88	622.50			
Mean platelet volume	0-2	100	57.42	5741.50	508.500	-.862	0.389
	3-5	12	48.88	586.50			
Platelet	0-2	100	56.50	5649.50	599.500	-.005	0.996
	3-5	12	56.54	678.50			
Red cell distribution width	0-2	100	55.79	5579.00	529.000	-.668	0.504
	3-5	12	62.42	749.00			
Basophil	0-2	100	57.93	5792.50	457.500	-1.383	0.167
	3-5	12	44.63	535.50			
Eosinophil	0-2	100	56.06	5605.50	555.500	-.419	0.675
	3-5	12	60.21	722.50			
Monocyte	0-2	100	55.78	5577.50	527.500	-.682	0.495
	3-5	12	62.54	750.50			
Lactate	0-2	95	50.71	4817.00	257.000	-3.095	**.002****
	3-5	12	80.08	961.00			
PaO_2	0-2	96	55.49	5327.00	481.000	-.929	0.353
	3-5	12	46.58	559.00			

**p<0.01

Table 6. Comparison of inflammatory markers in PSI groups (I-III and IV-V)

	Groups	Mean rank	Sum of rank	Σ sira	U	z	p
CRP	I-III	50	53.64	2682.00	1407.000	-.971	0.331
	IV-V	63	59.67	3759.00			
Albumin	I-III	50	62.31	3115.50	1309.500	-1.537	0.124
	IV-V	63	52.79	3325.50			
CAR	I-III	50	52.54	2627.00	1352.000	-1.289	0.197
	IV-V	63	60.54	3814.00			
PLR	I-III	49	57.71	2828.00	1484.000	-.349	0.727
	IV-V	63	55.56	3500.00			
NLR	I-III	49	47.83	2343.50	1118.500	-2.493	**0.013***
	IV-V	63	63.25	3984.50			

*p<0.05

Table 7. Comparison of complete blood count, lactate and PaO_2 in PSI groups (I-III and IV-V)

	Groups	N	Mean rank	Sum of rank	U	z	p
White blood cell	I-III	49	51.06	2502.00	1277.000	-1.563	0.118
	IV-V	63	60.73	3826.00			
Hemoglobin	I-III	49	58.93	2887.50	1424.500	-.698	0.485
	IV-V	63	54.61	3440.50			
Hematocrit	I-III	49	58.97	2889.50	1422.500	-.710	0.478
	IV-V	63	54.58	3438.50			
Neutrophil	I-III	49	50.61	2480.00	1255.000	-1.692	0.091
	IV-V	63	61.08	3848.00			
Lymphocyte	I-III	49	60.98	2988.00	1324.000	-1.287	0.198
	IV-V	63	53.02	3340.00			
Plateletcrit	I-III	49	52.09	2552.50	1327.500	-1.267	0.205
	IV-V	63	59.93	3775.50			
Mean platelet volume	I-III	49	58.86	2884.00	1428.000	-.679	0.497
	IV-V	63	54.67	3444.00			
Platelet	I-III	49	50.53	2476.00	1251.000	-1.716	0.086
	IV-V	63	61.14	3852.00			
Red cell distribution width	I-III	49	46.83	2294.50	1069.500	-2.781	**.005****
	IV-V	63	64.02	4033.50			
Basophil	I-III	49	66.19	3243.50	1068.500	-2.873	**.004****
	IV-V	63	48.96	3084.50			
Eosinophil	I-III	49	56.26	2756.50	1531.500	-.070	0.944
	IV-V	63	56.69	3571.50			
Monocyte	I-III	49	51.08	2503.00	1278.000	-1.557	0.119
	IV-V	63	60.71	3825.00			
Lactate	I-III	49	44.81	2195.50	970.500	-2.822	**.005****
	IV-V	58	61.77	3582.50			
PaO_2	I-III	49	67.24	3295.00	821.000	-3.854	**.000****
	IV-V	59	43.92	2591.00			

**p<0.01

Table 8. Investigation of measurements effective in estimating mortality

	AUC	SE	95 % CI
CRP	**0.744**	0.0526	0.653 to 0.822
Albumin	**0.543**	0.0615	0.447 to 0.638
CAR	**0.605**	0.0631	0.508 to 0.696
PLR	**0.515**	0.0607	0.419 to 0.611
NLR	**0.624**	0.0585	0.528 to 0.714

Table 9. Investigation of measurements effective in estimating mortality

	AUC	SE	95 % CI
CURB-65	0.614	0.0553	0.518 to 0.704
PSI Classification	0.722	0.0503	0.630 to 0.802
PSI Scoring	0.746	0.0547	0.656 to 0.823

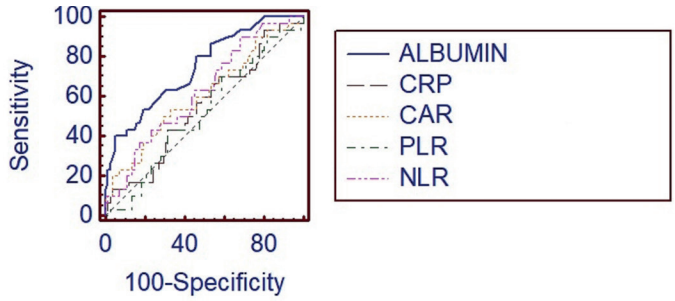

Figure 1. The ROC curves for prediction of 3-month mortality for CRP, albumin, CAR, PLR and NLR

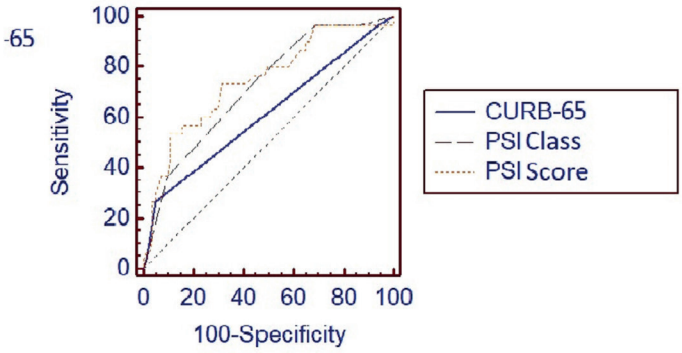

Figure 2. The ROC curves for prediction of 3-month mortality for CURB-65, PSI classification and PSI scoring

DISCUSSION

The prediction of mortality in a practical way in patients with CAP in ED is important in terms of time, cost, time and patient management. We found that 3-month mortality rate was 22.4% and this rate was higher compared to similar studies (11-15). Advanced age, increased number of comorbidities and late admission to the ED may lead to these poor results and may increase long-term mortality in patients with CAP (3).

The current study suggested that albumin was lower in non-survivors and higher in CURB-65 (0-2) score group. Increased CURB-65 score may indicate that in patients CAP, the severity of disease increases and serum albumin level starts to decrease. Hypoalbuminemia is an inevitable result of capillary leakage that caused by impaired endothelial permeability due to excessive release of pro-inflammatory and anti-inflammatory cytokines (secreted proteins and signal molecules) including interleukin (IL)-1, IL-2, IL-6, IL-10, interferon gamma and tumor necrosis factor-alpha during inflammatory reaction in critically ill patients such as CAP (16). Moreover, albumin is the main serum protein that binds approximately 40% of calcium in the human body circulation, which is responsible for cardiac contraction, coagulation cascade and platelet activation (17). In acute serious diseases such as pneumonia, the decrease of circulating albumin called hypoalbuminemia, an acute phase reactant, can predict poor outcomes including morbidity, ICU admission and mortality (16-18).

In recent studies, NLR has been reported as a cost-effective inflammatory marker that can be easily obtained from complete blood count, and predict prognosis and mortality in various clinical conditions including CAP (19). We realized that NLR was higher in non-survivors and PSI (IV-V) group. Increased PSI score indicates higher risk for mortality. It has been shown in similar studies that higher neutrophil count is associated with bacteremia and an increase in NLR predicts poor outcomes including mortality (9,19,20).

In the study, lactate was higher in non-survivors, CURB-65 score (5-9) and PSI group (IV-V); PaO_2 was lower in non-survivors and PSI group (IV-V). Lactate is the end product of the anaerobic glycolysis and it has been used for tissue perfusion status in critically ill patients including pneumonia and sepsis (21,22). A second cause of mortality in critically ill patients with CAP is hypoxemia, in which arterial blood oxygen saturation measured by pulse oximeter is <90% or PaO_2 is <60 mmHg (23). Alveolar congestion triggered by inflammatory reaction, prominent intrapulmonary shunting, enlarged dead space and ventilation/perfusion mismatch may result in disrupted gas exchange and lower PaO_2 (23).

Hemoglobin and lymphocyte were lower in non-survivors. RDW and basophil were lower in PSI (I-III) and PSI (IV-V) groups, respectively. Low hemoglobin level is generally seen in patients with septic shock with reduced red cell production secondary to systemic inflammation response (24). Low lymphocyte count is one of the physiological immune system adaptation mechanisms with increasing age and negative prognostic effect has been shown in coronary artery disease congestive heart failure and acute myocardial infarction (25). In addition, RDW is a routine laboratory test used to evaluate size, form and heterogeneity degree of erythrocyte volume that predicts diagnosis and prognosis of thrombotic and cardiovascular events, and it has been associated with increased mortality of patients with CAP (26). Basophil is the rarest granulocyte (<1% of peripheral blood leukocytes) and is expected to increase, such as neutrophils and eosinophils, especially in patients with sepsis (19,27). Basophil is one of the first leukocytes seen in the area of infection (27). The reason for being lower in clinically worse patients may be that we detect patients in the late period.

The outstanding result of this study was that CRP (AUC 0.744) showed highest 3-month mortality. Albumin (AUC 0.54), CAR (AUC 0.81), NLR (AUC 0.62) and PLR (AUC 0.52) indicated statistically significant lower 3-month mortality prediction. CURB-65 (AUC 0.61) showed the lowest 3-month mortality prediction. PSI classification (AUC 0.72) and PSI scoring (AUC 0.746) indicated statistically higher 3-month mortality prediction. Scoring systems (PSI, CURB-65) and inflammatory markers used in predicting severity, prognosis and mortality in critical diseases including pneumonia were compared in the study. Different results were obtained from several studies (1,8,9,11,15,20). Our results suggested that the strongest

predictor marker in long-term mortality estimation was CRP and PSI was more beneficial score about mortality compared to CURB-65.

This single center study had some limitations. Firstly, patient population size was relatively small and we didn't determine accurate etiology of microorganisms caused to CAP. Moreover, detailed effect of comorbidities to 3-month mortality was unknown. During the 3-month follow-up period after the ED, only mortality was recorded and the management of the treatment was not evaluated.

CONCLUSION

Albumins, hemoglobin, lymphocyte, PaO_2 were lower and NLR, lactate were higher in non-survivors. CRP and PSI score are potent predictors of 3-month mortality in patients with CAP.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: This cross-sectional study was conducted with approval of Kafkas University Medical Faculty Ethics Committee between February 2018 and November 2018.

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