Annals of Clinical and Analytical Medicine
Original Research

Predictors of mortality in lung cancer patients hospitalized with community-acquired pneumonia

Kaan Kara[1], Eyyup Cavdar[2]
[1] Department of Chest Desease, Yedikule Chest Diseases and Chest Surgery Training and Research Hospital, İstanbul
[2] Department of Oncology, Adiyaman Training and Research Hospital, Adiyaman, Turkey

Abstract
Aim: Lung cancer is a common associated risk factor for pneumonia and increases the severity of pneumonia. In this study, we investigated predictive factors for mortality in patients with lung cancer hospitalized for pneumonia.
Material and Methods: In this retrospective study, 821 patients who were hospitalized between 2013-2018 were included. Clinic pathological patient information and laboratory data were obtained from the hospital archive. Evaluation of predictive factors for mortality was performed by logistic regression analysis and the area under the receiver operating characteristic curve (ROC-AUC).
Results: The 2-day mortality rate was 2.4% and the 30-day mortality rate was 14%. In the multivariate logistic regression analysis, hypotension status (OR=4.18, p=0.004), sodium level (OR=4.30, p=0.007), ALT level (OR=3.83, p=0.027) and calcium level (OR) =6.27, p<0.001) was found to be an independent predictive factor for 2-day mortality. In 30-day mortality analysis, hypotension (OR=1.59, p=0.045), albumin level (OR=0.39, p=0.003), LDH level (OR=2.91, p<0.001), sodium level (OR=1.72, p=0.016), eosinophil counts (OR=0.57, p=0.021) and CURB-65 (OR=2.44, p=0.003) score were independent predictive factors.
Discussion: Hypotension status, serum sodium level, serum ALT level and serum calcium level for 2-day mortality and hypotension status, serum albumin level, serum LDH level, serum sodium level, eosinophil counts, and CURB-65 score for 30-day mortality are potential predictive factors. These predictive factors which can be easily accessible in clinical practice, can be used in the identification of high-risk patients and follow-up of patients.

Keywords
Lung Cancer, Pneumonia, PSI, CURB-65, Mortality

DOI: 10.4328/ACAM.22068 Received: 2023-12-09 Accepted: 2024-01-22 Published Online: 2024-03-29 Printed: 2024-05-01 Ann Clin Anal Med 2024;15(5):318-323
Corresponding Author: Kaan Kara, Department of Chest Desease, Yedikule Chest Diseases and Chest Surgery Training and Research Hospital, İstanbul, Turkey.
E-mail: kaankara3643@yahoo.com P: +90 505 674 09 62
Corresponding Author ORCID ID: https://orcid.org/0000-0001-5896-2497
This study was approved by the Ethics Committee of Yedikule Chest Diseases and Chest Surgery Training and Research Hospital (Date: 2022-08-18, No: 2022-267)

Introduction

According to 2022 data, when skin cancers are excluded, lung cancer is one of the most common types of cancer and the most common cause of cancer-related deaths [1]. Despite the increase in treatment options, its high mortality continues because the vast majority of patients are diagnosed in advanced stage [2]. While the 5-year survival is 60% in early stages, it decreases to 6% in the metastatic stage [1]. Mortality may be directly related to lung cancer or may be due to different etiological reasons resulting from the systemic effects of lung cancer. Infections are one of the major causes of mortality. This is due to the immunosuppression caused by the cancer itself and the potential of the agents used for cancer treatment to weaken the immune system [3].

While pneumonia is the sixth-rate cause of death in the United State of America (USA), it is the first cause of death because of infection. Moreover, it is a disease that can cause high morbidity and increase mortality and health care costs. Most of the pneumonia cases are observed on the ambulatory. While the mortality in these patients is 1-5%, the average mortality is 12% in patients requiring hospitalization and 40% in patients who need intensive care support [4]. It is known that the comorbidities accompanying these patients change the mortality rates.

Lung cancer is one of the risk factors that significantly reduces the survival time of patients [5]. However, studies which involve only lung cancer patients are limited. Existing studies included either a small number of lung cancer patients or only a subgroup analysis of lung cancer analyses reported. In addition, studies have shown that scoring and risk factors such as CURB-65 and PSI, which are used to evaluate risky groups in community-acquired pneumonia, may be insufficient in patients with lung cancer, and that new scales and risk factor analysis are needed [6].

In this study, we investigated the predictive factors for mortality in the patients diagnosed with lung cancer and hospitalized for pneumonia in a pulmonology center. In this way, we aimed to identify risky groups and to find predictors that can help clinicians during treatment and patient monitoring.

Material and Methods

Study population

The study was designed as a single center and retrospective cohort analysis. Lung cancer patients, who were hospitalized and treated between January 2013-december 2018 in the pulmonary diseases service for community acquired pneumonia (CAP), were included.

The inclusion criteria of patients are:

1- Having pathologically confirmed diagnosis of lung cancer

2- To be over 18 years old.

3- Getting CAP diagnosis by a chest disease specialist

Those who were thought to have hospital-acquired pneumonia, those with history of brain metastases, those with a history of previous or concurrent secondary malignancies, those with missing clinical pathological data, those who were referred to the intensive care unit and those who were referred to a different hospital were excluded from the study.

Our hospital is one of the biggest pulmonology reference center in Turkey, and the definition of CAP and CAP treatment are carried out in accordance with national and international guidelines, especially ERS (European Respiratory Society) and ATS (American Thoracic Society). Patients included in the study were followed up and treated in accordance with the guidelines [7].

Data Collection

Patients' demographic information, comorbidities, the first day of hospitalization examination's vital findings (including fever, respiratory rate, blood pressure, oxygen saturation at rest, heart rate), clinicopathological features, pneumonia severity scores and serum laboratory parameters measured before hospitalization were recorded from the hospital archive. The most widely used validations were used for PSI and CURB-65 scoring, the original version was preserved and saved from the hospital archive [8].

In hypotension categorization, systolic blood pressure was used <100mmHg, but in CURB-65 and PSI scoring, systolic blood pressure <90mmHg and/or diastolic blood pressure ≤60mm/Hg was accepted in accordance with the original versions. As in previous studies, the severity index of pneumonia for CURB-65 ≥2 and PSI ≥4 points were accepted as severe disease and this categorization was used in analyzes.

Statistical Analysis

Statistical analyzes were performed by using SPSS Statistic software 24 (SPSS Inc., Chicago, III). Continuous variables were summarised as median and categorical variables as number and percentages. Normal distribution was evaluated by Kolmogorov-Smirnov test. The Mann-Whitney U test and Chi square (x^2) test were used in 2-day (early mortality) and 30-day (a month) mortality's dependent factor analysis. Univariate and multivariate logistic regression analyzes were used to identify predictive factors for mortality. Variables with significant differences between the survivors and non-survivor's groups were included in the logistic regression analysis. All continuous variables were categorized according to clinically used thresholds [9]. Odds Ratio (OR) was reported with the corresponding 95% confidence intervals (95% CI). The calibration of the models was evaluated using the Hosmer-Lemeshow goodness-of-fit test. The receiver operating characteristic curve (ROC curve) and the area under the ROC curve (ROC-AUC) were calculated to compare the independent prognostic factors. Statistical significance was accepted as $p< 0.05$.

Ethical Approval

This study was approved by the Ethics Committee of Yedikule Chest Diseases and Chest Surgery Training and Research Hospital (Date: 2022-08-18, No: 2022-267).

Results

Patient Characteristics

Total 821 patients who were suitable for the inclusion criteria were included in the study. The median age of patients was 65 (range:18-93) and 604 (73.6%) were male. 666 (81.1%) patients had non-small cell lung cancer histology. 751 (91.5%) patients were in the metastatic stage and most of them those included were patients receiving chemotherapy by oncology doctors. CURB-65 score of 70.3% and PSI score of 96.1% of patients were compatible with severe disease. (Table-1).

123 (15%) patients died during follow–up after hospitalization. While the 2-day mortality of the patients was determined as 2.4%, the 30-day mortality was determined as 14%.

Early Mortality (2-Days)

In our analysis of factors associated with early mortality hypotension status, albumin, Lactate dehydrogenase (LDH), sodium, aspartate transaminase (AST), alanine transaminase (ALT), calcium, neutrophil count, thrombocyte count, red cell distribution width (RDW), C Reactive protein (CRP), procalcitonin, and arterial blood gas pH levels were found as associated factors for 2-day mortality (p=0.014, p=0.001, p=0.004, p=0.002, p=0.002, p=0.006, p=0.003, p=0.047, p=0.037, p=0.001, p=0.007, p=0.017, and p=0.021, respectively) (Table 1).

To determine factors predicting 2-day mortality, univariate regression analysis was performed on the factors that had a statistically significant relationship with 2-day mortality. Hypotension, sodium, AST, ALT and calcium showed predictive feature (p=0.019, p=0.003, p=0.007, p<0.001, and p<0.001, respectively) (Table-2). A multivariate model was established to accurately assess the predictive factors for 2-day mortality with parameters found to be significant. Hypotension (OR=4.18, 95% CI: 1.56–11.23, p=0.004), low serum sodium (OR=4.30, 95% CI: 1.49–12.45, p=0.007), high serum ALT (OR=3.83, 95% CI: 1.16–12.62, p=0.027) and low serum calcium (OR=6.27, 95% CI: 2.41–16.28, p<0.001) found to be predictive factors associated with higher mortality. (Table-3). Hosmer-Lemeshow test showed that the model was well calibrated (p=0.764).

Table 1. The relationship between patient features and the 2-day and 30-day mortality [s] Significant values are indicated in bold. *Continuous variables are expressed as the mean (standart deviation), and categorical variables are described as numbers (percentages)

Variables	Total*	2-Day Mortality			30-Day Mortality		
		Survivors	Non-Survivors	P	Survivors	Non-Survivors	P
Total	821 (100)	801 (97.6)	20 (2.4)		706 (86.0)	115 (14.0)	
Clinicopathologic							
Age ≥ 65	425 (51.8)	416 (97.9)	9 (2.1)	0.540	371 (87.3)	54 (12.7)	0.266
Female-Yes	217 (26.4)	209 (96.3)	8 (3.7)	0.164	185 (85.3)	32 (14.7)	0.715
Non-Small Cell-Yes	666 (81.1)	652 (97.9)	14 (2.1)	0.242	571 (85.7)	95 (14.3)	0.660
Metastasis-Yes	751 (91.5)	735 (97.9)	16 (2.1)	0.083	647 (82.6)	104 (13.8)	0.667
Chemotherapy-Yes	750 (91.4)	733 (97.7)	17 (2.3)	0.246	650 (86.7)	100 (13.3)	0.071
Comorbidity							
Diabetes mellitus-Yes	62 (7.6)	62 (100.0)	0	0.391	59 (85.2)	3 (4.8)	0.031
Hypertension-Yes	97 (11.8)	96 (99.0)	1 (1.0)	0.497	90 (82.8)	7 (7.2)	0.040
Clinical presentation							
Initially Fever ≥ 38°C	350 (42.6)	340 (97.1)	10 (2.9)	0.500	292 (83.4)	58 (16.6)	0.068
Hypotension-Yes	317 (38.6)	304 (95.9)	13 (4.1)	0.014	260 (82.0)	57 (18.0)	0.009
Respiratory rate >20	443 (54.0)	436 (98.4)	7 (1.6)	0.085	386 (87.1)	57 (12.9)	0.308
Confusion-Yes	89 (10.8)	85 (95.5)	4 (4.5)	0.260	71 (79.8)	18 (20.2)	0.073
Laboratory							
Albumin (g/dl)	3.24±0.6	3.25±0.6	2.79±0.6	0.001	3.30±0.6	2.86±0.6	<0.001
Protein (g/dl)	5.96±2.1	6.0±2.1	5.7±1.6	0.051	6.0±2.1	5.5±2.1	<0.001
LDH (U/L)	354.5±422.3	336.8±321.4	1064±675.2	0.004	311.5±276.3	618.8±853.8	<0.001
Sodium (mmol/L)	135.1±4.5	135.1±4.4	131.8±5.4	0.002	135.3±4.2	134.2±5.5	0.010
AST (IU/L)	37.3±126.6	35.5±94.4	110.4±93.7	0.002	30.9±50.3	77±312.6	0.001
ALT (IU/L)	30±61.5	28.6±57.9	87.3±136.5	0.006	28.1±57.3	41.8±82.2	0.606
Calcium (mg/dl)	9.5±0.9	9.7±0.9	8.6±1.2	0.003	9.1±0.9	8.9±1.2	0.011
T.biluribine (mg/dl)	0.7±1.7	0.7±1.1	3.13±8.0	0.078	0.65±1.1	1.2±3.5	0.003
Creatinine (mg/dl)	1.38±1.8	1.38±1.8	1.47±1.6	0.472	1.36±1.7	1.57±2.2	0.148
Hemoglobin (g/dl)	11.3±2.1	11.3±2.1	10.5±1.7	0.135	11.3±2.1	10.7±2.2	0.002
Neutrophil (103/ul)	9.8±6.6	9.72±6.4	14.5±10.2	0.047	9.38±6.1	12.64±8.3	<0.001
Lymphocyte (103/ul)	1.4±0.9	1.41±0.9	1.15±1	0.090	1.43±0.9	1.25±1	0.004
Thrombocyte (103/ul)	306.2±152.9	308±152.4	230.9±157.6	0.037	311.7±153.8	272.2±143.4	0.015
Eosinophil (103/ul)	0.13±0.2	0.13±0.3	0.76±1.4	0.063	0.14±0.26	0.09±0.26	0.001
RDW (%)	16±2.5	16±2.5	18±2.7	0.001	15.9±2.5	17±2.6	<0.001
CRP (mg/L)	137.8±104.0	136.1±102.6	208.4±132.9	0.007	131.6±102.7	176.2±104.4	<0.001
Procalcitonin (ng/ml)	2.3±8.1	2.3±8.2	4.2±6.9	0.017	2.02±7.4	4.2±11.5	0.002
Severity Indices							
CURB-65 score ≥2	577 (70.3)	560 (97.2%)	17 (2.8%)	0.145	480 (82.9%)	99 (17.1%)	<0.001
PSI score ≥4	789 (96.1)	771 (97.7%)	18 (2.3%)	0.181	681 (86.3%)	108 (13.7%)	0.194

s Significant values are indicated in bold. *Continuous variables are expressed as the mean (standart deviation), and categorical variables are described as numbers (percentages).

The 2-day mortality rate of the independent predictive factors was 4.1% in hypotension, 1.4% in non-hypotension, 4.6% in hyponatremia, 1% in non-hyponatremia, 6.7% in patients with high ALT level, 1.4% in patients with non-high ALT level, 7.4% in patients with hypocalcemia, and 1.3% in patients with non-hypocalcemia, respectively.

30-Day Mortality

Diabetes mellitus (DM), hypertension(HT), hypotension examination finding, albumin, protein, LDH, sodium, AST, calcium, total bilirubin, hemoglobin, neutrophil count, lymphocyte count, thrombocyte count, eosinophil count, RDW, CRP, procalcitonin level and CURB-65 score were found factors associated with 30 days mortality in this analysis (p=0.031, p=0.040, p=0.009, p<0.001, p<0.001, p<0.001, p=0.010, p=0.001, p=0.011, p=0.003, p=0.002, p<0.001, p=0.004, p=0.015, p=0.001, p<0.001, p<0.001, p=0.002, and p<0.001, respectively) (Table-1).

Factors which have statistically significant relationship with 30-day mortality were evaluated with univariate regression analysis in order to determine the factors predicting 30-day mortality. DM, HT, sign of hypotension, albumin, protein, LDH, sodium, AST, calcium, total bilirubin, hemoglobin count, eosinophil count, RDW, CRP, and CURB-65 score were found predictive (p=0.041, p=0.045, p=0.010, p<0.001, p<0.001, p<0.001, p=0.002, p=0.007, p=0.001, p=0.004, p=0.018, p=0.001, p=0.004, p=0.033, and p=0.001, respectively) (Table-2).

In multivariate model established with predictors in univariate analysis, hypotension (OR=1.59, 95% CI: 1.01–2.49, p=0.045), low serum albumin (OR=0.39, 95% CI: 0.21–0.72, p=0.003), high serum LDH (OR=2.91, 95% CI: 1.82–4.63, p<0.001), hypontaremia (OR=1.72, 95% CI: 1.11–2.66, p=0.016), eosinopenia (OR=0.57, 95% CI: 0.35–0.92, p=0.021) and high CURB-65 score (OR=2.44, 95% CI: 1.37–4.34, p=0.003) showed independent predictive feature for 30 days mortality. (Table-3). The Hosmer-Lemeshow test confirmed the model (p=0.639).

Table 2. Univariate logistic regression models for predicting 2-day and 30-day mortality

	Referance	OR(95% CI)	P
2-Day Mortality			
Hypotension	No vs Yes	3.04(1.20-7.69)	0.019
Albumin (g/dl)	<3.5 vs ≥3.5	0.33(0.10-1.14)	0.079
LDH (U/L)	<250 vs ≥250	2.61(0.99-6.86)	0.052
Sodium (mmol/L)	<135 vs ≥135	4.68(1.68-13.00)	0.003
AST (IU/L)	≤33 vs >33	3.44(1.41-8.42)	0.007
ALT (IU/L)	≤32 vs >32	5.18(2.11-12.71)	<0.001
Calcium (mg/dl)	<8.8 vs ≥8.8	5.87(2.39-14.44)	<0.001
Neutrophil (103/ul)	<1.5 vs ≥1.5	0.72(0.16-3.16)	0.659
Thrombocyte (103/ul)	<150 vs ≥150	0.38(0.14-1.01)	0.052
RDW (%)	<14 vs ≥14	5.12(0.68-38.51)	0.113
CRP (mg/L)	<20 vs ≥20	1.01(0.23-4.44)	0.987
Procalcitonin (ng/ml)	<0.5 vs ≥0.5	3.34(0.97-11.49)	0.056
pH	<7.35 vs ≥7.35	1.28(0.52-3.15)	0.599
30-Day Mortality			
Comorbidity-Diabetes Mellitus	No vs Yes	0.29(0.09-0.95)	0.041
Comorbidity-Hypertension	No vs Yes	0.44(0.20-0.98)	0.045
Hypotension	No vs Yes	1.69(1.13-2.51)	0.010
Albumin (g/dl)	<3.5 vs ≥3.5	0.27(0.15-0.46)	<0.001
Protein (g/dl)	<6.4 vs ≥6.4	0.47(0.32-0.70)	<0.001
LDH (U/L)	<250 vs ≥250	3.33(2.16-5.14)	<0.001
Sodium (mmol/L)	<135 vs ≥135	1.86(1.25-2.76)	0.002
AST (IU/L)	≤33 vs >33	1.77(1.17-2.68)	0.007
Calcium (mg/dl)	<8.8 vs ≥8.8	2.16(1.38-3.38)	0.001
Total biluribine (mg/dl)	<1.2 vs ≥1.2	2.50(1.33-4.69)	0.004
Hemoglobin (g/dl)	<10 vs ≥10	0.61(0.40-0.92)	0.018
Neutrophil (103/ul)	<1.5 vs ≥1.5	1.54(0.65-3.65)	0.333
Lymphocyte (103/ul)	<1.5 vs ≥1.5	0.73(0.48-1.11)	0.142
Thrombocyte (103/ul)	<150 vs ≥150	0.62(0.38-1.03)	0.066
Eosinophil (103/ul)	<0.5 vs ≥0.5	0.47(0.30-0.73)	0.001
RDW (%)	<14 vs ≥14	2.50(1.34-4.65)	0.004
CRP (mg/L)	<20 vs ≥20	2.73(1.08-6.90)	0.033
Procalcitonin (ng/ml)	<0.5 vs ≥0.5	1.51(0.98-2.33)	0.061
CURB-65	<2 vs ≥2	2.54(1.50-4.30)	0.001

sSignificant values are indicated in bold.

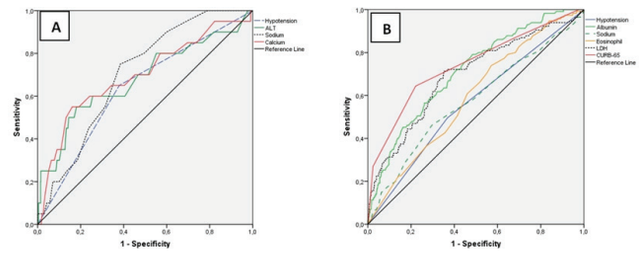

Figure 1. ROC-AUC curves were performed for factors predicting 2- day (A) and 30-day mortality (B)

Table 3. Multivariate logistic regression models for predicting 2-day and 30-day mortality

	Referance	OR(95% CI)	P
2-Day Mortality			
Hypotension	No vs Yes	4.18(1.56-11.23)	0.004
Sodium (mmol/L)	<135 vs ≥135	4.30(1.49-12.45)	0.007
AST (IU/L)	≤33 vs >33	1.40(0.43-4.61)	0.578
ALT (IU/L)	≤32 vs >32	3.83(1.16-12.62)	0.027
Calcium (mg/dl)	<8.8 vs ≥8.8	6.27(2.41-16.28)	<0.001
30-Day Mortality			
Comorbidity-Diabetes Mellitus	No vs Yes	0.39(0.11-1.38)	0.142
Comorbidity-Hypertension	No vs Yes	0.49(0.21-1.16)	0.105
Hypotension	No vs Yes	1.59(1.01-2.49)	0.045
Albumin (g/dl)	<3.5 vs ≥3.5	0.39(0.21-0.72)	0.003
Protein (g/dl)	<6.4 vs ≥6.4	0.72(0.45-1.13)	0.151
LDH (U/L)	<250 vs ≥250	2.91(1.82-4.63)	<0.001
Sodium (mmol/L)	<135 vs ≥135	1.72(1.11-2.66)	0.016
AST (IU/L)	≤33 vs >33	1.17(0.73-1.89)	0.513
Calcium (mg/dl)	<8.8 vs ≥8.8	1.38(0.83-2.30)	0.221
Total biluribine (mg/dl)	<1.2 vs ≥1.2	1.71(0.83-3.51)	0.144
Hemoglobin (g/dl)	<10 vs ≥10	0.98(0.61-1.57)	0.920
Eosinophil (103/ul)	<0.5 vs ≥0.5	0.57(0.35-0.92)	0.021
RDW (%)	<14 vs ≥14	1.61(0.82-3.19)	0.165
CRP (mg/L)	<20 vs ≥20	1.43(0.53-3.84)	0.483
CURB-65	<2 vs ≥2	2.44(1.37-4.34)	0.003

sSignificant values are indicated in bold. Hosmer-Lemeshow test for 2-Days p=0.764, for 30-Day p=0.639.

The 30-day mortality rate of the independent predictive factors were 18% in hypotension, 11.5% in non-hypotension, 18.4% in hypoalbuminemia, 5.7% in non-hypoalbuminemia, 21.2% in high serum LDH, 7.5% in non-high LDH levels, 18.6% in hyponatremia, 11% in non-hyponatremia, 17.4% in patients with eosinopenia, and 9% in patients with non-eosinopenia. Additionaly, the 30-day mortality rate was 16.8% for those with a CURB-65 score at high risk and 7.4% for those without a high risk.

Predictive performance of independent predictors

The comparison of independent predictive factors was evaluated with ROC-AUC analysis. Firstly, ROC-AUC curves were performed for factors predicting 2-day mortality. ROC-AUC value of hypotension status, serum sodium levels, serum ALT levels, and serum calcium levels were found to be 0.635 (95% CI: 0.51–0.76, p=0.039), 0.703 (95% CI: 0.61–0.79, p= 0.002), 0.680 (95% CI: 0.54–0.82, p= 0.006), and 0.696 (95% CI: 0.56–0.83, p= 0.003), respectively. And then ROC-AUC curves were performed for the evaluation of factors predicting 30-day mortality. ROC-AUC value of hypotension status, serum albumin levels, serum LDH levels, serum sodium levels, eosinophil count, and CURB-65 score were found to be 0.564 (95% CI: 0.51–0.62, p=0.028), 0.712 (95% CI: 0.66–0.76, p<0.001), 0.694 (95% CI: 0.64–0.75, p<0.001), 0.575 (95% CI: 0.52–0.64, p=0.010), 0.592 (95% CI: 0.54–0.65, p=0.002), and 0.741 (95% CI: 0.69–0.80, p<0.001), respectively (Figure).

Discussion

In this retrospective study, the prevalence and predictors of 2-day and 30-day mortality are evaluated with lung cancer patients hospitalized for pneumonia in a comprehensive pulmonology center in Turkey. In our study, 2-day mortality was 2.4% and 30-day mortality was 14%. Multivariate regression analysis showed that four variables were associated with 2-day mortality and six variables, including CURB-65, were associated with 30-day mortality, suggesting that these values have an important value in predicting mortality.

It is known that PSI and CURB-65 reveal predictive features for non-cancer patients with CAP [10]. However, in studies including cancer patients, there is no consensus for PSI and CURB-65. Aliberti et al. analyzed PSI and CURB-65's predictive feature in a large cohort study consisting of 2621 patients, 280 of whom had cancer. He reported that both scorings were not associated with mortality in cancer patients [11]. CURB-65 and PSI were not found to be predictive for CAP in a study established in a cancer center in Korea [12]. A study of Gonzales at al. that only included cancer patients, CURB-65 and PSI were found to be poor predictive for mortality [6]. In our study, while PSI was not revealed as predictive for mortality, CURB-65 was revealed an independent predictive factor for 30-day mortality. Moreover, we found that CURB-65 is one of the most important predictors in our ROC-AUC analysis which we compared with other predictive factors. These differences between the studies that are included cancer patients can be caused by being different types of cancer patients, having different anti-cancer treatment or having different locations of metastasis. In addition, the superiority of CUBR 65 to PSI is an acceptable result in our study. Because in our study, which consisted of all hospitalized patients, almost all patients got into high-risk group in this scoring because of giving additional points to malignancies in the PSI scoring system, and this situation affects the results.

In current studies, it has been reported that eosinophils play a defensive role against bacteria [13]. And also eosinopenia has been identified as an early predictor of sepsis and mortality [14, 15]. In our study eosinopenia was found as a poor predictor for 30 days mortality. Cancer and pneumonia are systemic diseases that can affect many organ systems. Their partnership can affect many other laboratory parameters besides eosinophilia. It is known from previous studies that LDH and albumin levels predicted 1- month mortality for CAP [16, 17]. In studies conducted on patients with CAP, Nair et al. hyponatremia, Ferreira et al. hypocalcemia has been shown to be poor predictive factors of survival in patients with CAP [18, 19]." Also in our study albumin, LHD and sodium levels were found compatibly as independent predictive for, 30-day mortality.

The first 48 hours are vital for CAP patients [7, 20]. Because starting antibiotic therapy for critical and high-risk patients in this time and invasive / non-invasive procedures are important for survival and in previous studies, this time period has been described as critical for patients [21]. According to the methodology of our study, all patients were hospitalized and given appropriate antibiotics. Necessary clinical interventions were applied to all patients. So, predictive factor analyses are needed to prevent death of hospitalized patients. For this purpose, we analyzed early mortality in our study. Hypotension, which is also included in the definition of shock, is a result expected to predict early mortality, and in our analysis, we found that it is one of the predictors of mortality, similar to the literature. On the other hand, it is known from previous studies that other independent predictors hyponatremia and liver function disorders are related with long-term mortality both for cancer patients and pneumonia [22]. And also in our study, hypocalcemia was found as a predictive factor for early mortality. There are many studies investigating hypercalcemia in cancer patients. However, studies of hypocalcemia are limited [23, 24]. Pneumonia and cancer can cause hypocalcemia in different ways [24]. In the case of hypocalcemia, its clinical manifestation may reach life- threatening levels. Early treatment is a must. Although it is a rare incidence, hypocalcemia's being detected as predictive in our study may be related with denosumab and bisphosphonate, which are among options of treatment of cancer, gaining importance and increasingly used in recent years. Because these treatments are frequently used in the treatment of paraneoplastic syndromes and/or direct bone metastases in lung cancer patients and one of their most important adverse events is hypocalcemia [25].

Limitations

Our study has some limitations. First, it is retrospective and has a single center design. Second, disease severity scoring could not be done prospectively. Third, although patients were selected carefully, various conditions can affect laboratory markers. Fourth, although microbial factors in the etiology of CAP have similar treatment, survival and laboratory effect, they can show different features. Analysis for the etiological factor

could not be performed in this study. Finally, previous studies were often done on patients whose immune system was not suppressed. This situation makes difficult to compare with the articles in the literature. Moreover, it is important that our study is the highest numbered predictive analysis and included comprehensive analysis, study on inpatient pneumonia patients, including only lung cancer patients.

Conclusion

In conclusion, in our comprehensive study with a large patient population, including only lung cancer patients, we found that hypotension, serum albumin level, serum LDH level and serum sodium level, eosinophil count and CURB-65 scoring are potentially predictive factors for 30-day mortality. These predictive factors, which are easily accessible in clinical practice, can be used in disease follow-up and in identifying high-risk patients. Moreover, these predictive factors can lead to further studies for potential therapeutic targets. Multicenter and prospective studies are needed to generalize the results.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or compareable ethical standards.

Funding: *None*

Conflict of Interest

The authors declare that there is no conflict of interest.

References

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. CA Cancer J Clin. 2022;72(1):7-33.

2. Youlden DR, Cramb SM, Baade PD. The international epidemiology of lung cancer: Geographical distribution and secular trends. J Thorac Oncol. 2008;3(8):819-31.

3. Murphy SL, Xu J. Kochanek KD. 2012. U.S. Department of health and human services, and national vital statistics reports deaths: Preliminary data for 2010. National Vital Statistics Reports. 2012;60(4):1-52.

4. Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al. Infectious diseases society of America; American thoracic society. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007;44(2):27-72.

5. Perlin E, Bang KM, Shah A, Hursey PD, Whittingham WL, Hashmi K, et al. The impact of pulmonary infections on the survival of lung cancer patients. Cancer. 1990;66(3):593-6.

6. Gonzalez C, Johnson T, Rolston K, Merriman K, Warneke C, Ewans S. Predicting pneumonia mortality using CURB-65, PSI, and patient characteristics in patients presenting to the emergency department of a comprehensive cancer center. Cancer Med. 2014;3(4):962-70.

7. Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, et al. Diagnosis and treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the american thoracic society and infectious diseases society of America. Am J Respir Crit Care Med. 2019;200(7):45-67.

8. Lim WS, van der Eerden MM, Laing R, Boersma WG, Karalus N, Town GI, et al. Defining community acquired pneumonia severity on presentation to hospital: An international derivation and validation study. Thorax. 2003;58(5):377-82.

9. Svaton M, Blazek J, Krakorova G, Buresova M, Teufelova Z, Vodicka J, et al. Laboratory parameters are possible prognostic markers in patients with advanced-stage NSCLC Treated with Bevacizumab plus Chemotherapy. J Cancer. 2021;12(19):5753-9.

10. Alavi-Moghaddam M, Bakhshi H, Rezaei B, Khashayar P. Pneumonia severity index compared to CURB-65 in predicting the outcome of community acquired pneumonia among patients referred to an Iranian emergency department: A prospective survey. Braz J Infect Dis. 2013;17(2):179-83.

11. Aliberti S, Brock GN, Peyrani P, Blasi F, Ramirez JA; Community-acquired pneumonia organization. The pneumonia severity index and the CRB-65 in cancer patients with community-acquired pneumonia. Int J Tuberc Lung Dis. 2009;13(12):1550-6.

12. Jeong BH, Koh WJ, Yoo H, Um SW, Suh GY, Chung MP, et al. Performances of prognostic scoring systems in patients with healthcare-associated pneumonia. Clin Infect Dis. 2013;56(5):625-32.

13. Ramirez GA, Yacoub MR, Ripa M, Mannina D, Cariddi A, Saporiti N, et al. Eosinophils from physiology to disease: A comprehensive review. Biomed Res Int. 2018;2018:9095275.

14. Lin Y, Rong J, Zhang Z. Silent existence of eosinopenia in sepsis: A systematic review and meta-analysis. BMC Infect Dis. 2021;21(1):471.

15. Mao Y, Qian Y, Sun X, Li N, Huang H. Eosinopenia predicting long-term mortality in hospitalized acute exacerbation of COPD patients with community-acquired pneumonia-a retrospective analysis. Int J Chron Obstruct Pulmon Dis. 2021;16:3551-9.

16. Liu JL, Xu F, Zhou H, Wu XJ, Shi LX, Lu R, et al. Corrigendum: Expanded CURB-65: A new score system predicts severity of community-acquired pneumonia with superior efficiency. Sci Rep. 2018;8:47005.

17. Viasus D, Garcia-Vidal C, Simonetti A, Manresa F, Dorca J, Gudiol F, et al. Prognostic value of serum albumin levels in hospitalized adults with community-acquired pneumonia. J Infect. 2013;66(5):415-23.

18. Nair V, Niederman MS, Masani N, Fishbane S. Hyponatremia in community-acquired pneumonia. Am J Nephrol. 2007;27(2):184-90.

19. Ferreira GF, Palma LC, Amaral ACKB, Brauer L, Nery B, Park M, et al. "What is the prevalence and clinical relevance of hypocalcemia in sepsis?" Critical Care. 2003;7(3):17.

20. Garcia-Vidal C, Fernández-Sabé N, Carratalà J, Díaz V, Verdaguer R, Dorca J, et al. Early mortality in patients with community-acquired pneumonia: causes and risk factors. Eur Respir J. 2008;32(3):733-9.

21. Rosón B, Carratalà J, Fernández-Sabé N, Tubau F, Manresa F, Gudiol F, et al. Causes and factors associated with early failure in hospitalized patients with community-acquired pneumonia. Arch Intern Med. 2004;164(5):502-8.

22. Albhaisi S, Qayyum R. The association between serum liver enzymes and cancer mortality. Clin Exp Med. 2022;22(1):75-81.

23. Zagzag J, Hu MI, Fisher SB, Perrier ND. Hypercalcemia and cancer: Differential diagnosis and treatment. CA Cancer J Clin. 2018;68(5):377-86.

24. Ferraz Gonçalves JA, Costa T, Rema J, Pinto C, Magalhães M, Esparança A, et al. Hypocalcemia in cancer patients: An exploratory study. Porto Biomed J. 2019;4(4):45.

25. Menshawy A, Mattar O, Abdulkarim A, Kasem S, Nasreldin N, Menshawy E, et al. Denosumab versus bisphosphonates in patients with advanced cancers-related bone metastasis: Systematic review and meta-analysis of randomized controlled trials. Support Care Cancer. 2018;26(4):1029-38.

How to cite this article:

Kaan Kara, Eyyup Cavdar. *Predictors of mortality in lung cancer patients hospitalized with community-acquired pneumonia. Ann Clin Anal Med 2024;15(5):318-323*

This study was approved by the Ethics Committee of Yedikule Chest Diseases and Chest Surgery Training and Research Hospital (Date: 2022-08-18, No: 2022-267)