RESEARCH

THE PROGNOSTIC AND DIAGNOSTIC VALUE OF PLASMA D-DIMER LEVELS IN ELDERLY PATIENTS WITH COMMUNITY-ACQUIRED PNEUMONIA

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■ Sertan BULUT[2]
■ Deniz ÇELİK[1]
■ Harun KARAMANLI[2]

CORRESPONDANCE

[1] Deniz ÇELİK

Phone: +902425106135
e-mail: drdenizcelik@hotmail.com

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[1] Alanya Alaaddin Keykubat University, Faculty of Medicine, Department of Pulmonology, ANTALYA, Turkey

[2] University of Health Sciences Atatürk Chest Diseases and Thoracic Surgery Education and Research Hospital,, Department of Pulmonology, ANKARA, Turkey

Abstract

Introduction: This study aimed to investigate the relationship between community-acquired pneumonia severity and D-dimer levels in individuals older than 65. We also investigated the relationship between D-dimer levels and the adverse outcomes in patients with community-acquired pneumonia after excluding all other potential causes of high D-dimer levels.

Materials and Methods: Patients older than 65 who were admitted to the emergency service of a tertiary chest diseases training and research hospital between January 1, 2019, and October 1, 2020, were evaluated. Patients who met the diagnostic criteria for community-acquired pneumonia were included. In clinically questionable cases of coexistence of pulmonary embolism and community-acquired pneumonia, D-dimer levels and pulmonary computerize tomography angiography or ventilation-perfusion scintigraphy were examined. Confirmed pulmonary embolism patients were excluded. Of 4,608 patients evaluated, 82 had a diagnosis of community-acquired pneumonia with no comorbidity. The severity of these cases was determined with the CURB-65 score and pneumonia severity index score.

Results: The mean age of the cases was 73.83±6.67 years, while their gender was predominantly male (n=51, 62.2%). A statistically significant correlation was found between D-dimer levels and both the CURB-65 and pneumonia severity index high-risk groups (p=0.001 and p=0.001, respectively). The adverse outcomes were statistically higher in both the CURB-65 and pneumonia severity index high-risk groups (p<0.001).

Conclusions: D-Dimer is an easy-to-interpret, fast, inexpensive, highly sensitive, and simple test widely used in clinics. We found that high levels of D-dimer can predict the need for intensive care unit care, disease severity, and mortality of elderly community-acquired pneumonia patients.

Keywords: Pneumonia; Aged; Severity of Illness Index.

INTRODUCTION

The World Health Organization (WHO) has reported that lower respiratory tract infections are the most common cause of infection-related deaths and are responsible for 3.5 million deaths per year (1). Lower respiratory tract infections are the fifth most common cause of death in the world (2). At the same time, the elderly population is increasing steadily in all countries, and both the incidence and mortality of community-acquired pneumonia (CAP) also increase with age. These factors all intensify the importance of CAP as a public health problem (3).

The annual incidence of CAP in people aged 65 and over in the USA is an estimated 1.3 million new cases, and it is not only a major cause of morbidity and mortality but also a significant economic burden (4). The severity of pneumonia increases markedly with age (5). While mortality is 1-5% in patients receiving outpatient treatment for CAP, the mortality prediction for patients requiring hospitalization increases to 10-30% (6, 7). Cetin et al. found the mortality rate to be 74.4% in patients hospitalized in the ICU due to CAP (8). The studies conducted in Turkey about the costs of CAP revealed a significant relationship between pneumonia severity and costs (9, 10).

In this context, it is important to understand the mortality and adverse effects associated with this disease as well as to accurately diagnose CAP and initiate treatment. For this purpose, two scoring tools, CURB-65, and the pneumonia severity index (PSI), have been developed to predict CAP severity and mortality. PSI consists of 20 parameters, and the CURB-65 consists of 5 parameters (11, 12, 13).

In addition, the D-dimer test has become widely used because of the COVID-19 pandemic. D-dimer is a plasmin-derived soluble degradation product of cross-linked fibrin. D-dimer increases in many conditions, especially in venous and arterial thrombosis. Other health conditions in which it increases are cancer, chronic inflammatory diseases, pregnancy and puerperium, disseminated intravascular coagulation, trauma or previous surgery, chronic inflammation, liver and kidney diseases, thrombolytic therapy, atrial fibrillation, coronary artery disease, HIV infection, advanced age, and active infection (14).

In a study comparing D-dimer levels between CAP and pulmonary embolism (PE) patients, it was observed that the D-dimer levels in PE were significantly higher than in CAP (15). CAP and PE overlap is a condition that can be observed clinically (16). For this reason, we identified the cases who had pulmonary computerize tomography angiography (CTPA) or ventilation-perfusion (V/Q) scintigraphy performed to exclude cases of PE accompanying CAP. Our hospital is a tertiary hospital that specializes in pulmonary diseases and chest surgery. In our emergency service, we always have a pulmonology specialist and two residents. These cases were examined by the pulmonology specialist in the emergency service, and the patients who had CAP without PE were enrolled in our study.

Although previous studies have investigated D-dimer levels in CAP, the relationships between D-dimer levels and CAP severity and D-dimer levels and adverse effects have not yet been clarified (17, 18). For this reason, we defined our study groups to include a low-risk group and a high-risk group, according to CURB-65 and PSI parameters (18). We investigated the relationship between CAP disease severity and D-dimer in individuals over 65 years of age with increased D-dimer levels and CAP infection. We aimed to demonstrate the utility of the D-dimer level for the prediction of in-hospital clinical outcomes in CAP cases. We also evaluated the relationships between the levels of D-dimer and the need for a vasopressor, noninvasive mechanical ventilation, or invasive mechanical ventilation as well as 30-day mortality. We excluded all other possible causes of high D-dimer levels in the study group.

MATERIALS AND METHODS

Study Population

Patients over 65 years old who were admitted to the emergency service of our tertiary chest diseases training and research hospital between January 1, 2019, and October 1, 2020, were retrospectively evaluated and included in the study. Because of hospital rules, in the admission process, permission was routinely requested of all patients to use their anonymous medical data for clinical studies. As such, only patients who gave their informed consent were included in this study. No obligation for ethics committee approval is present in retrospective studies; nevertheless, we received our institution's education commission board approval for the study.

For the study group, patients with pulmonary infection symptoms, such as fever, cough, shortness of breath, chest pain, hemoptysis, and consolidation on posteroanterior chest radiography who met the diagnostic criteria for CAP were selected. In cases of clinical uncertainty regarding the coexistence of PE and CAP, D-dimer levels and CTPA or V/Q scintigraphy were examined. Patients with both PE and CAP were excluded from the study, leaving only patients with CAP alone in the study population. In addition, patients with a diagnosis of hospital-acquired pneumonia, neoplastic diseases, liver diseases, autoimmune diseases, any hematological diseases, diffuse intravascular coagulation, use of an anticoagulant, having had a thrombotic event in the previous month, undergoing immunosuppressive therapy, and HIV positivity were excluded from the study.

The number of patients admitted to our institution's emergency room with pneumonia was 4,608 within the 21 months of the study window. Of this group, 340 patients had both elevated D-dimer levels and CTPA and/or V/Q scintigraphy. A total of 52 patients who had overlapping CAP with PE or PE alone were excluded. Another 206 patients had at least one of the other exclusion criteria and were thus excluded from the study. Ultimately, 82 patients with a CAP diagnosis were included in this study.

Data Collection

Physical examinations and medical records of all patients who were admitted to the emergency department of our tertiary chest diseases hospital were conducted by a pulmonologist. All demographic and clinical data were obtained from hospital electronic records to conduct this study. These data comprised complete blood count (CBC), serum biochemistry tests, glucose tests, and tests of blood urea nitrogen (BUN), creatinine, glomerular filtration rate (GFR), sodium, D-dimer, arterial blood gas (ABG) analysis, chest X-ray (C-XR), and CTPA or V/Q scintigraphy.

D-dimer was taken from a puncture of the antecubital vein within the first three hours after admission to the emergency department. CBC and biochemical examinations were also conducted prior to antibiotic treatment.

Community-Acquired Pneumonia

The CAP is defined as "In the presence of appropriate symptoms and physical examination findings and—if possible—observation of infiltrates on chest radiograms is sufficient for diagnosis" in a national guideline (13).

D-Dimer

D-dimer plasma levels were measured with Sysmex® CS-2500 System (Siemens, Germany) using the coagulometric optical method.

Spiral CTPA

After intravenous contrast was administered to the patient in the supine position, 0.9mm thick sections were taken in the axial plane with a 128 multidetector CT device (Ingenuity CT, Philips Healthcare, Andover, MA, USA). Imaging parameters were Kv=120, mA=160, rotation time=0.5 seconds, collimation=64x0.625, and FOV=220mm. The window settings were W:350, C:60 for mediastinum, and W:-1600 C:-600 for parenchyma.

Severity Assessment

The severity of CAP cases was determined with the CURB-65 and PSI scores. CURB-65 is scored with 1 point for each variable (minimum=0 points, maximum=5 points). The variables are confusion, BUN > 20mg/dL, respiratory rate ≥ 30 breaths per minute, blood pressure (BP) < 90mmHg for systolic or <60mmHg for diastolic, and age ≥65 years. The PSI consists of 20 variables and is divided into five stages, according to their severity. These variables are age, neoplastic disease, liver disease, congestive heart failure, cardiovascular disease, renal disease, altered mental status, respiratory rate ≥30 breaths/minute, systolic BP< 9 mmHg, confusion, temperature <35˚C or >40˚C, pulse >125 beats/minute, BUN>20mg/dL, sodium < 130mmol/L, glucose >250mg/dL, hematocrit < 30%, PaO2<60mmHg, and pleural effusion. Accordingly, the CURB-65 scores were defined as 0–2 points=low-risk group and 3–5 points=high-risk group. The PSI scores were defined as 1–3 points=low-risk group and 4–5 points=high-risk group (11, 12, 13, 18, 19, 20).

Statistical Analysis

We divided our CAP sample group into the low-risk and high-risk groups using the CURB-65 and PSI scoring systems. The distributions of the values of all continuous variables were examined. Statistical analysis was performed by student's t-test or the Mann-Whitney U test. Categorical data were expressed as the total number and percentage. Categorical data, such as gender, smoking status, presence of confusion, cough, sputum, dyspnea, hemoptysis, and the presence of pleural effusion were evaluated using the chi-square test. The correlation of the CURB-65 and PSI scoring systems was examined.

In addition, 30-day mortality estimation and D-dimer levels were evaluated by receiver operating characteristic (ROC) analysis. The best sensitivity and specificity and cutoff value were found for D-dimer. Adverse effects, such as vasopressor support, noninvasive or invasive mechanical ventilation, and death within 30 days of hospital admission were evaluated separately with the chi-square test for the two scoring tools. The correlation between D-dimer levels and adverse effects was examined using Spearman's test. The possibility of D-dimer as an independent risk factor for adverse effects was evaluated by logistic regression analysis. In multivariate logistic regression analysis, multicollinearity was avoided. Confounding factors, especially age, gender, and data with statistical p<0.25 in univariate analyses were included in this multivariate model. The p-value of the Hosmer-Lemeshow test results of >0.05 was considered significant for a good model fit. The SPSS (Statistical Package for the Social Sciences) statistical software package (version 22) was used. A p-value of <0.05 was considered statistically significant.

RESULTS

Out of 4,608 patients admitted between January 1, 2019, and October 1, 2020, 82 patients remained after the exclusion criteria were applied. The demographic characteristics of these 82 patients are shown in Table 1 and basic clinical features in Table 2. The mean age of the total sample was 73.83±6.67 years, and the gender was predominantly male (n=51, 62.2%). PE diagnosis was excluded by CTPA in 80 patients and by V/Q scintigraphy in 2 patients.

The patients with CAP were classified using the CURB-65 scale. A total of 72 patients (88%) were considered low-risk and 10 patients (12%) high-risk. When PSI scores were used for classification, 43 patients (52%) were considered low-risk and 39 patients (48%) high-risk. In the evaluation of comorbidities in the study group, 21 patients had chronic obstructive pulmonary disease (COPD), and 13 patients had diabetes mellitus (DM). A significant relationship was found between COPD and CURB-65 scores (p=0.01), but no significant relationship was found with the PSI scoring system (p=0.617). When the relationship between comorbidity and 30-day mortality (from the date of hospital admission for

CAP) was evaluated, no significant relationship was found for either COPD or DM (p=0.687, and p=0.223, respectively).

The compatibility of the scoring tools for CAP severity was evaluated. CURB-65 (0–2 points=low-risk and 3–5 points=high-risk) and PSI (1–3 points=low-risk and 4–5 points=high-risk) were found to be compatible (k=0.27 and p<0.001). Likewise, the relationship between basic clinical features and low-risk/high-risk groups for both scoring tools was examined. Respiratory rate (p<0.001), systolic blood pressure (p=0.002), fever (p=0.003), heart rate (p<0.001), and confusion (p=0.001) were statistically significant between the CURB-65 low-risk and high-risk groups. Systolic blood pressure (p=0.021), heart rate (p=0.037), confusion (p=0.008), and hospitalization days (p=0.032) were statistically significant between the PSI low-risk and high-risk groups. No statistical significance was observed within any group in the presence of cough, sputum, dyspnea, hemoptysis, or pleural effusion (Table 2).

Table 4 shows the frequency of adverse outcomes in both CURB-65 and PSI both the low- and high-risk groups. The adverse outcomes experienced were as follows: 9.8% of patients with CAP required vasopressor support, 15.86% required noninvasive mechanical ventilation, 7.31% required invasive mechanical ventilation, and 7.3% of patients died within the first 30 days after hospital admission. The need for vasopressor support, noninvasive mechanical ventilation, or invasive mechanical ventilation, and 30-day mortality were statistically higher in the high-risk groups of both the CURB-65 and PSI scoring systems (p<0.001).

The mean D-dimer levels were 2.29±1.58 (mean±SD) in the entire study group. As seen in Figures 1a and 1b, elevated D-dimer levels were associated with increased disease severity and high CURB-65 and PSI scores (both p=0.001). In addition, as seen in Figure 1c, the D-dimer levels were higher in non-surviving patients (p=0.009). When the relationship between laboratory data and disease severity was examined, a statistically significant correlation was found between leukocytes and CURB-65 score, neutrophil/lymphocyte ratio (NLR) and creatinine and PSI score, and albumin and D-dimer levels, with both scoring systems indicating greater significance in the high-risk group (Table 3).

Figure 2 compares the ROC curves and Area under the ROC Curve (AUC) with the CURB-65 scores, PSI scores, and D-dimer levels to predict mortality within 30 days after admission. The ROC analysis indicated that the CURB-65 score showed the best AUC at 0.97 [confidence interval (CI) 95%, 0.941–1, p<0.001], followed by the D-dimer levels, with an AUC of 0.82 (CI 95%, 0.709–0.931, p=0.009), while the PSI score showed an AUC of 0.78 (CI 95%, 0.659–0.907, p=0.022).

We also found that the cutoff value for D-dimer level was 2660 mcg/L [sensitivity=83%, specificity=75%, positive predictive value=0.833, negative predictive value=0.737, odds ratio (OR) =14 (p<0.009)] for 30-day mortality. The D-dimer levels higher than 2660 mcg/L showed an OR of 14 (CI 95%, 1.541–127, p<0.019) for 30-day mortality, an OR of 14 (CI 95%, 1.541–127, p<0.019) for the need for vasopressor support, an OR of 12 (CI 95%, 2.926–49.217, p=0.001) for noninvasive mechanical ventilation, and an OR of 14 (CI 95%, 1.541–127, p<0.019) for invasive mechanical ventilation by logistic regression analysis.

Neither age nor gender showed any statistical differences between patients with and without adverse outcomes. Evaluation of death within 30 days by age and gender was not statistically significant (p=0.789 and p=0.814, respectively). When we examined the patients in terms of surviving and non-surviving, we found that white blood cell (WBC), sedimentation, albumin, D-dimer levels, and CURB-65 and PSI scores were statistically significant between the two groups (p=0.03, p=0.032, p=0.009, p=0.009, p<0.0001, and p=0.008, respec-

Table 1. Demographic characteristics at the admission of 82 patients with community-acquired pneumonia

Low-risk group n=72 (%88)		CURB-65 (n=82)		PSI (n=82)		CURB-65 p-value	PSI p-value
		High-risk group n=10 (12%)	Low-risk group n=43 (52%)	High-risk group n=39 (48%)			
Age, year, mean ± SD		74.06± 6.79	72.10±5.74	71.48±4.6	76.41±7.64	p=0.456	**p=0.003**
Male gender, n (%)		45(62.5)	6(60)	21 (41.2)	30(58.8)	p=0.879	**p=0.009**
Smoking status (%)	Never	25 (34.7)	3 (30)	18 (41.9	10 (25.6)	p=0.621	p=0.246
	Exsmoker	42 (58.3)	7 (70)	22 (51.2)	27 (69.2)		
	Current	5 (6.9)	0 (0)	3 (7)	2 (5.1)		
Comorbity (n)	COPD	14	7	12	9	**p=0.001**	p=0.617
	Diabetes Mellitus	10	3	5	8	p=0.191	p=0.271

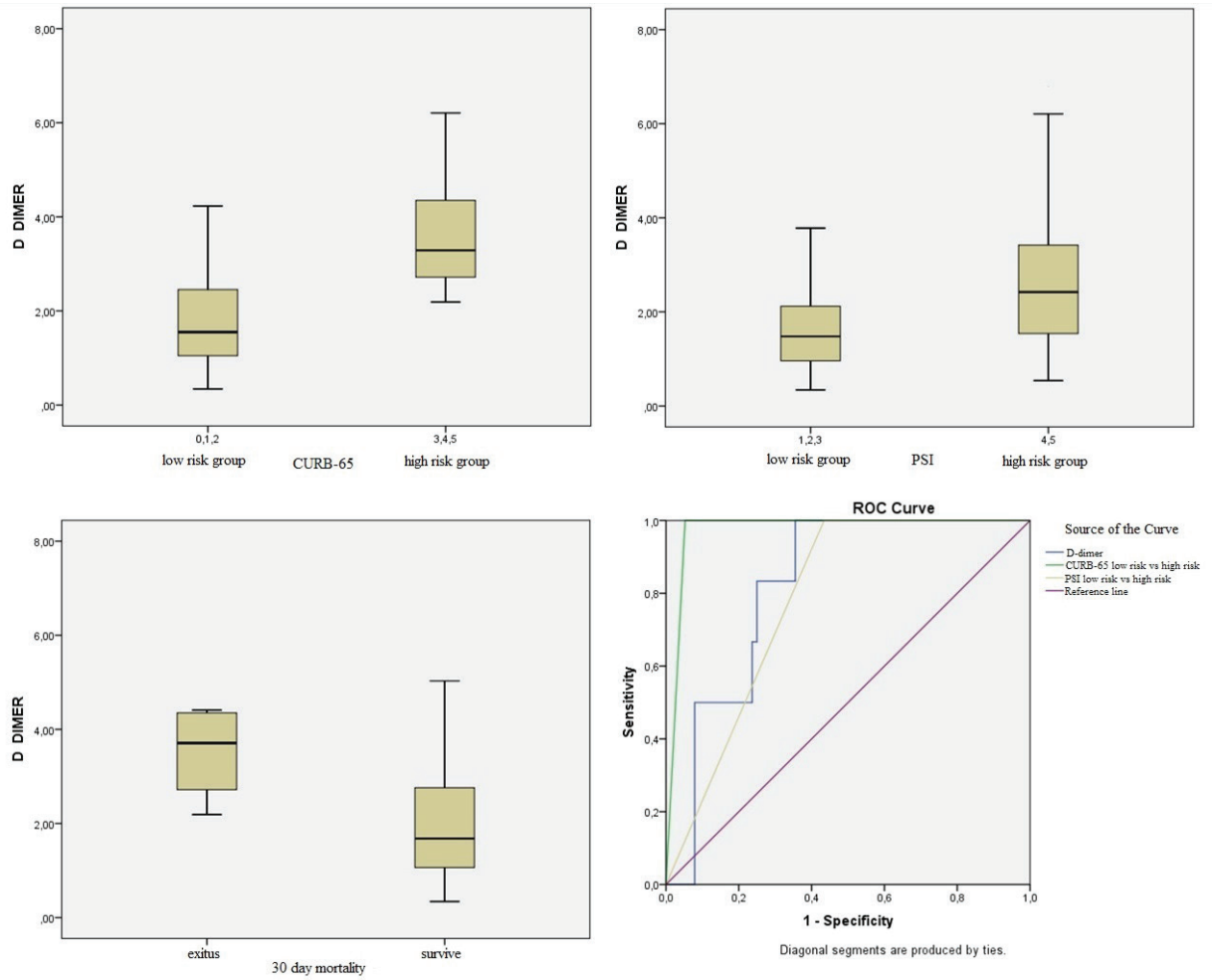
Table 2. Clinical characteristics at the admission of 82 patients in terms of CURB-65/PSI scores low-risk vs high-risk groups

Symptoms and findings	(Mean ± SD)	CURB-65 Low-risk vs high-risk groups p-value	PSI Low-risk vs high-risk groups p-value
Respiratory rate	21.24±0.62	**p<0.001**	p=0.11*
Systolic blood pressure	121.03±1.68	**p=0.002**	**p=0.021***
Fever	37.4±0.14	**p=0.003**	p=0.081*
Heart rate	97.35±1.76	**p<0.001**	**p=0.037***
Days of hospitalization	11.15±0.60	p=0.876	**p=0.032***
Confusion	Present (n=6) Nonpresent (n=76)	**p<0.001**	**p=0.008****
Cough	Present (n=73) Nonpresent (n=9)	p=0.916	p=0.107**
Sputum	Present (n=29) Nonpresent (n=53)	p=0.302	p=0.307**
Shortness of breath	Present (n=74) Nonpresent (n=8)	p=0.267	p=0.549**
Hemoptysis	Present (n=18) Nonpresent (n=64)	p=0.512	p=0.442**
Pleural effusion	Present (n=25) Nonpresent (n=57)	p=0.359	p=0.105**

*Mann Whitney test

**Chi-square test

Figure 1. The correlation between D-dimer levels and the high-risk group of CURB-65, the high-risk group of PSI, and 30 days in-hospital mortality were statistically significant (p=0.001, p=0.001 and p=0.001, respectively). Comparison of ROC curves and AUC between CURB-65 scores, PSI score, and D-dimer levels to predict mortality within 30 days after admission. CURB-65 score showed the best AUC=0.97 (CI 95%, 0.941-1, p<0.001), followed by the D-dimer levels with an AUC=0.82 (CI 95%, 0.709-0.931, p=0.009), while PSI scores showed an AUC=0.78 (CI 95%, 0.659-0.907, p=0.022).



tively). NRL and C reactive protein (CRP) levels were insignificant between the surviving and non-surviving groups (p=0.137 and p=0.054, respectively).

The adverse outcomes (vasopressor support, noninvasive mechanical ventilation, invasive mechanical ventilation, and 30 days in-hospital mortality) versus low-risk and high-risk groups (both CURB-65 score and PSI score) were analyzed by chi-square analysis and the results were significant for each variable (p<0.001) (Table 4).

Finally, we evaluated age, gender, smoking status, COPD and DM status, radiological features of lobar pneumonia or multilobar pneumonia, CRP, and D-dimer levels with multivariate logistic regression analysis. The model fit for logistic regression analysis was evaluated with the Hosmer-Leme-

Table 3. Laboratory parameters at the admission of 82 patients in terms of CURB-65/PSI low-risk vs high-risk groups

Parameters	(Mean ± SD)	CURB-65 Low-risk vs high-risk groups p-value	PSI Low-risk vs high-risk groups p-value
Leukocyte	11.21±4.70	p=0.005	p=0.981*
Neutrophil / lymphocyte ratio	7.56±6.74	p=0.399	p=0.005*
Platelet	270.80±106.98	p=0.245	p=0.519*
Sedimentation rate	45.11±24.99	p=0.144	p=0.411*
C reactive protein	84.35±65.37	p=0.174	p=0.845*
Creatinine	0.92±0.22	p=0.523	**p=0.003****
Uric acid	5.38±1.56	p=0.854	p=0.507**
Alanine aminotransferase	23.3±19.01	p=0.22	p=0.629*
Aspartate aminotransferase	27.88±15.79	p=0.268	p=0.348*
Glomerular filtration rate	75.32±17.24	p=0.766	p=0.114**
Albumin	32.63±5.22	**p=0.024**	**p=0.003***
Plasma D-Dimer	2.29 ±1.58	**p=0.001**	**p=0.001***

* Mann Whitney test
**ANOVA

Table 4. Adverse outcomes in 82 patients with community-acquired pneumonia

Adverse outcomes	Total (n=82) %	CURB-65 Low-risk group (n=72)	CURB-65 High-risk group (n=10)	PSI Low-risk group (n=43)	PSI High-risk group (n=39)	CURB-65 p-value	PSI p-value
The need for vasopressor therapy	8 (9.8%)	0	8	0	8	**p<0.001**	**p<0.001**
The need for noninvasive mechanical ventilation	13 (15.86%)	3	10	1	12	**p<0.001**	**p<0.001**
The need for invasive mechanical ventilation	6 (7.31%)	0	6	0	6	**p<0.001**	**p<0.001**
30 day inhospital mortality	6 (7.31%)	0	6	0	6	**p<0.001**	**p<0.001**

show test. A good model fit was confirmed by chi-square (0.944, p=0.999). As a result of multivariate logistic regression analysis, D-dimer and CRP values reached statistical significance. D-dimer significance was found to be p=0.047 (OR=2.11, CI: 1.011–4.405), and CRP significance was p=0.039 (OR=1.018, CI: 1.001–1.036).

DISCUSSION

In our study, the CAP patient group was divided into a low-risk group and a high-risk group according to the prognostic scoring tools CURB-65 and PSI, as in the study by Cerda-Mancillas et al. (18). We demonstrated a relationship between disease severity and D-dimer levels. In our study population, which was

formed by excluding patients with other conditions likely to cause high D-dimer levels, patients were 65 years old or older. We found that the increased D-dimer levels were correlated with an increase in the death rate within 30 days after admission to the hospital as well as an increase in the rate of other adverse outcomes.

D-dimer is a protein produced by the degradation of cross-linked fibrin by factor XIII (14). In his study, Abraham E. explained the pathophysiology of increased coagulation in lung injury or sepsis. He explained that in patients with pneumonia the coagulation system is activated and fibrinolysis is inhibited. Fibrin deposition in the alveolar space triggers inflammation (21).

It is important to note that PE and CAP present similarly. In the study conducted by Zhang et al., 139 patients whose diagnosis could not be clinically distinguished between CAP and PE at the time of the first diagnosis underwent CTPA. A total of 80 patients (58%) were diagnosed with PE, and PE was excluded from 59 (42%) patients who were diagnosed with CAP (22). In their study examining D-dimer values to differentiate between CAP and PE patients, Ateş et al. found that D-dimer level was an independent risk factor in patients with CAP. In their study, all 34 patients with PE were diagnosed by CTPA and the diagnosis of CAP was made by chest radiography (C-XR) (n=38), and CTPA was planned for only some patients who needed differential diagnosis (23). For their part, Varol et al. found that if D-dimer levels were over 1700µ/L, the diagnosis was commonly PE (AUC=0.820). Also, in their study, the diagnosis of CAP was made by C-XR (24).

Our study comprised 340 geriatric patients. They all had both D-dimer test and PCTA and/or V/Q scintigraphy. A total of 52 patients with the diagnosis of CAP overlapping with PE or PE only were excluded. Two hundred and six patients had at least one of the other exclusion criteria and were excluded from the study. In the final analysis, 82 patients with the CAP diagnosis were included in the study. This study contributes a unique insight to the literature in that it analyzed D-dimer levels in CAP cases after excluding all other possible causes of D-dimer elevation.

Snijders et al. found a correlation between D-dimer levels and disease severity in CAP, but they found no difference between D-dimer levels and clinical success or failure (25). Likewise, Cerda-Mancillas et al. found a relationship between D-dimer level and both disease severity and adverse events in 61 CAP patients. Their study found a positive correlation between D-dimer level and CURB-65 score ($p=0.001$) and PSI score ($p<0.0001$). In addition, PSI score, CURB-65 score, and D-dimer levels were evaluated by Cerda-Mancillas et al. with ROC analysis in terms of mortality within seven days after hospitalization. The ROC analysis showed that AUC was 0.93 ($p<0.001$) for PSI scores, 0.853 ($p=0.01$) for CURB-65 scores, and 0.789 ($p=0.001$) for D-dimer levels. In addition, if the D-dimer level was >2400mcg/L, the seven-day in-hospital mortality risk was OR 16.1 ($p=0.07$) (18).

Elbi et al. found that the best discriminatory power to predict the 28-day mortality rate was demonstrated by the CURB-65 score (26). In our ROC analyses, the CURB-65 scores showed the best AUC at 0.97 (CI 95%, 0.941–1, $p<0.001$), followed by the D-dimer levels, with an AUC of 0.82 (CI 95%, 0.709–0.931, $p=0.009$). The PSI scores showed an AUC of 0.78 (CI 95%, 0.659–0.907, $p=0.022$) to predict mortality within 30 days after admission in patients with CAP. We found that the cutoff value for D-dimer level was 2660 mcg/L (sensitivity=83%, specificity=75%, positive predictive value=0.833, negative predictive value=0.737, OR=14, $p<0.009$) for 30-day in-hospital mortality. The D-dimer levels higher than 2660 mcg/L showed an OR of 14 (CI 95%, 1.541-127, $p<0.019$) for 30-day mortality.

Borovac et al. analyzed CAP patients as surviving and non-surviving groups and found no statistically significant relationship between the two groups in terms of CRP or WBC. They did, however, find

a significant difference between the two groups in terms of PSI score and D-dimer level (p<0.001 for D-dimer) (27). Surme et al. found high CRP values in non-surviving groups in pneumonia patients (28). Yılmaz et al. found a positive correlation between high CRP levels and mortality rates in CAP patients hospitalized in the ICU (7). When we examined our patients in terms of surviving and non-surviving, we found that WBC, sedimentation, albumin, D-dimer levels, and CURB-65 and PSI scores were statistically significant between the two groups (p=0.03, p=0.032, p=0.009, p=0.009, p<0.0001, and p=0.008, respectively). On the other hand, NRL and CRP levels were insignificant between the groups (p=0.137 and p=0.054, respectively).

Among the adverse outcomes, vasopressor support, noninvasive mechanical ventilation, invasive mechanical ventilation, and 30-day in-hospital mortality were compared between the CURB-65 and PSI low- and high-risk groups. We found a statistically significant difference for each comparison (p<0.001). These results were in line with previous study results (18, 29, 30).

For pneumonia patients, disease severity, need for ICU care, and the expected mortality rate thereafter are expected to increase with comorbid conditions (31). Since our primary aim was to examine D-dimer levels in CAP patients and we excluded potential comorbid conditions and malignancy that may affect D-dimer levels and/or mortality rates. Due to this, our overall mortality rate is not very high.

Previous studies that evaluated the relationship between CAP and D-dimer levels, applied no limitations in terms of excluding patients with comorbidities. Because our primary aim was to evaluate D-dimer levels in CAP patients, we had patients with COPD and DM as comorbidities, and their frequency was consistent with the literature. Restrepo et al. found that both disease severity and mortality were higher in patients with COPD as an additional disease in all patients with CAP (29). Rello et al. reached similar conclusions (30). In our study, the prevalence of COPD was higher in the CURB-65 high-risk group (p=0.001), which was consistent with the literature. However, we did not find a statistically significant effect of COPD on mortality rates (p=0.155). In addition, we found no significant correlation between D-dimer levels and COPD (p=0.315). On the other hand, a positive correlation was observed between DM, CAP severity, and D-dimer levels (32). In our study, when all confounding factors, including DM and COPD, were analyzed with multivariate logistic regression, statistical significance was found between D-dimer levels and mortality within 30 days after admission in patients with CAP (p=0.047, OR=2,11 CI: 1.011–4.405).

CONCLUSION

The D-dimer level is an easy-to-interpret, fast, inexpensive, highly sensitive, and simple test widely used in clinics. This may be the first study in the literature that analyzes the D-dimer levels in the CAP cases after excluding all other possible causes of the D-dimer elevation. In conclusion, high levels of D-dimer can predict the need for ICU care, disease severity, and mortality of elderly CAP patients.

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