Clinical research

Can neutrophil/lymphocyte ratio, C-reactive protein (CRP) and procalcitonin predict the hospitalization time in patients with lower tract respiratory infections?

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Abstract

Introduction: Lower respiratory tract infections (LTRI) are important hospitalization cause in pulmonary wards. The hospitalization time directly affects hospitalization costs. We aimed to find out whether the blood neutrophil/lymphocyte ratio (NLR), C-reactive protein (CRP) and procalcitonin (PCT) values predict the hospitalization time in patients with LTRI.

Material and methods: We evaluated patients retrospectively between January 2016 and December 2018 in a cross-sectional study. 1297 patients with the diagnosis of pneumonia, chronic obstructive pulmonary disease (COPD) exacerbation, bronchiectasis exacerbation, parapneumonic effusions, and empyema were included in the study according to ICD-10 and hospitalization criteria guidelines.

Results: Of 1297 patients, 762 (58.75%) were male and median age was 63 (interquartile range (IQR): 55–75). Median hospitalization time was 7 (IQR: 5–10) days. Median NLR was 6.28 (3.78–10.92), median CRP was 79.2 (IQR: 26.7–171.5) mg/l and median PCT was 0.23 (IQR: 0.08–0.51) ng/ml. Over 7 days' hospitalization time was accepted as long-term hospitalization time. Median NLR was 5.73 (IQR: 5.51–10.16) in < 7 days, 6.94 (IQR: 4.22–11.77) in > 7 days. The difference was statistically significant between the groups (p = 0.000). Median CRP value was 61.5 (IQR: 21.75–139.70) mg/l in ≤ 7 days, and 109.4 (IQR: 22.4–199.5) mg/l in > 7 days. The difference was significant between the groups (p < 0.001). Median PCT value was 0.20 (IQR: 0.07–0.45) mg/l ≤ 7 in days and 0.28 (IQR: 0.10–0.55) mg/l in > 7 days. The difference was not significant between the groups (p = 0.055). For the multivariate analysis, the possible factors identified with univariate analyses were further entered into a logistic regression analysis to determine independent predictors of long-term hospitalization. The odds ratio for CRP was OR = 0.004 (p < 0.001), but NLR and PCT was not significant (p = 0.777, p = 0.784, respectively). Sputum culture positivity and radiological infiltration were associated with the long-term hospitalization (p = 0.003 and p = 0.027, respectively).

Conclusions: CRP value was associated with the long-term hospitalization in patients with LTRI, but not with NLR and PCT. Sputum culture positivity and radiological infiltration might affect the long-term hospitalization.

Key words: C-reactive protein, length of stay, lower respiratory tract infections, neutrophil/lymphocyte ratio, procalcitonin.

Introduction

A lower respiratory tract infection is an acute event (onset in 21 days or less). It is a disease picture in which cough is accompanied by one of the other basic respiratory symptoms (sputum, dyspnea, chest pain, wheezing) and cannot be explained by any other diagnosis (such as sinusitis and asthma) [1]. Lower respiratory tract infections are specified as tracheitis, bronchitis, bronchiolitis, bronchiolitis, pneumonia, infectious exacerbations of chronic obstructive pulmonary disease (COPD), acute exacerbations of bronchiectasis, complicated parapneumonic pleurisy and empyema [2]. Even though there is such a large subgroup, the main published basic guidelines have focused on 3 main diseases. These are pneumonias, acute exacerbations of COPD and exacerbations of bronchiectasis. Biomarkers are structures that can be measured in body fluids, blood or urine that can be used to detect infectious, pathologic or biologic events and evaluate response to treatment. Procalcitonin (PCT) is a protein encoded by the CALC-I gene on chromosome 11 that produces calcitonin. C-reactive protein (CRP) has high sensitivity but low specificity in indicating inflammation. Neutrophil/lymphocyte ratio (NLR) is another marker recently used to evaluate inflammation. It is an inexpensive parameter that can be easily measured on complete blood count (CBC). The response of leukocytes to a stress in circulation is an increase in the number of neutrophils and is a decline in the number of lymphocytes. The ratio of these is used in many studies to indicate inflammation [3–5]. The length of stay of patients hospitalized for lower respiratory tract infections is important in centers with high hospitalization cycles. It also directly affects patient hospitalization costs. Efforts should be made for fast, effective and low-cost treatments. If we can find parameters that will provide us with predictions in this regard, we think that other methods can be tried in treatment approaches. The primary objective was to determine whether neutrophil/lymphocyte ratio, CRP, procalcitonin and other inflammation markers such as leukocyte, neutrophil and lymphocyte counts can predict the length of hospitalization in patients hospitalized in the chest diseases clinic due to lower respiratory tract infections (LTRI).

Material and methods

Our study was conducted in accordance with the Declaration of Helsinki with the approval of the Scientific Committee of the University of Health Sciences, Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital and the Ethics Committee of the Istanbul Training and Research Hospital (approval date: 14.09.2018, decision no. 2018/1409).

The study design is retrospective and cross-sectionally. All patients admitted to the 2nd Thoracic Diseases Clinic of the University of Health Sciences, Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital between January 1, 2016 and December 31, 2018 were examined. The date of admission, time of admission, demographic information (ID number, age, gender), hemogram, CRP and procalcitonin values at admission and during hospitalization (according to the date of admission), diagnoses (as ICD-10), and discharge status of all patients were obtained from the Hospital Information System (HIS) as an Excel file. The hospitalization diagnoses of the patients were then confirmed by examining their medical records, radiologic images and other laboratory tests were evaluated in detail and necessary corrections were made. There is no conflict of interest in our study.

Primary endpoint of the study: to determine in patients hospitalized in the chest diseases clinic for LTRI, whether neutrophil/lymphocyte ratio, CRP, procalcitonin and other markers of inflammation such as leukocyte, neutrophil and lymphocyte counts can predict the length of stay; and to determine in patients with longer than the clinical mean length of hospitalization considered as long-term hospitalized, whether neutrophil/lymphocyte ratio, CRP and procalcitonin values differed according to the length of stay and whether they predicted the length of stay,

Secondary endpoint: It was examined whether the duration of patient hospitalization differed with other parameters such as neutrophil/lymphocyte ratio, procalcitonin and CRP values and underlying diseases that may affect the duration of hospitalization (COPD, bronchiectasis, diabetes mellitus (DM), hypertetnsion (HT), chronic heart failure (CHF), cronik renal failure (CRF), microbiological agent detection and radiological infiltration.

1297 patients were evaluated in the study. The flow chart of our study is shown in Figure 1.

Pneumonia diagnosis was made based on clinical, laboratory and radiological infiltration according to generally accepted guidelines. Acute exacerbations of patients who were diagnosed with COPD by previous pulmonary function tests or who were diagnosed in the evaluation of their current hospitalization were evaluated. Among the causes of their exacerbation, non-infectious causes were identified. Acute exacerbation of bronchiectasis was determined by radiologic imaging and laboratory tests in addition to significant clinical findings. Complicated parapneumonic effusion and empyema were determined by evaluating liquid pH and liquid lactate dehydrogenase (LDH) in the biochemical evaluation of the fluid samples. Apart from this, the remaining group includes patients who have a clinic of lower respiratory tract

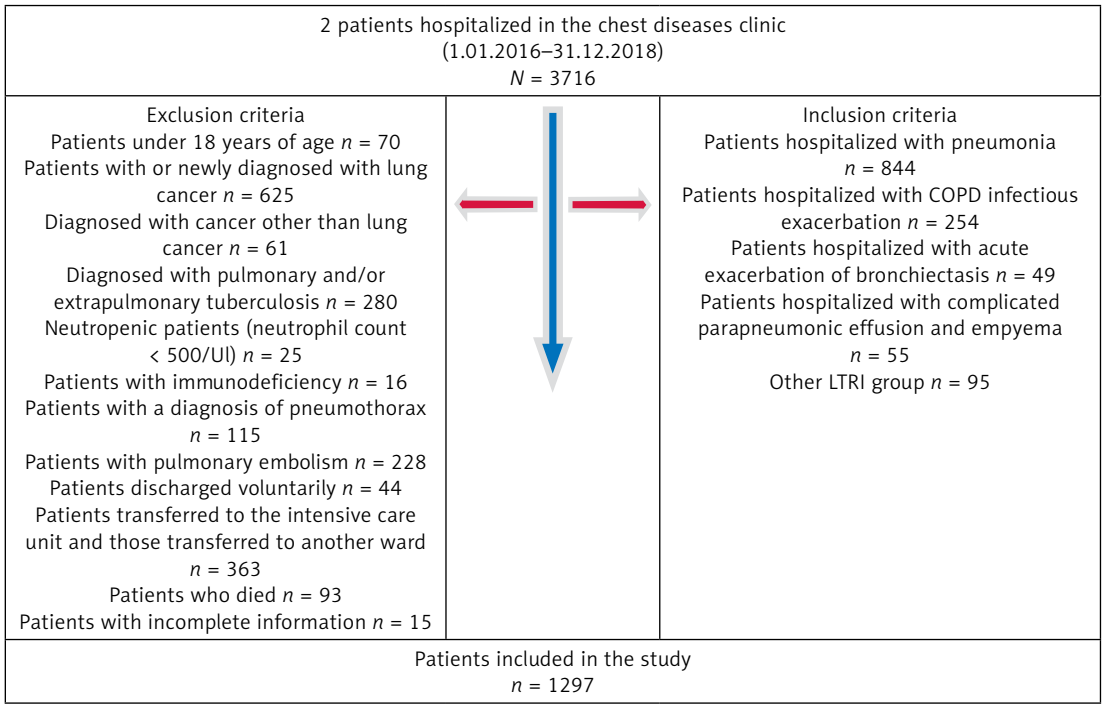

Figure 1. Flow chart

infection but do not have a significant pneumonic infiltration, bronchiectasis, pleural fluid or COPD diagnosis.

Laboratory evaluation method

Hemogram values were studied in the relevant laboratory with Mindray 6800 device. Serum CRP value was determined by immunoinhibition method on Beckman Coulter AU 2700 device. Normal CRP range is 0–5 mg/l. Procalcitonin was measured in a secondary biochemistry laboratory using lateral chromatography and immune turbidimetry.

Microbiology evaluation method

The patients' sputum, induced sputum, deep tracheal aspiration, bronchoscopic lavage samples and other upper and lower respiratory tract samples were collected and sent to the microbiology laboratory in a short time. For culture, 5% sheep blood medium, chocolate medium and MacConkey medium were used depending on the condition of the sample.

Statistical analysis

Statistical analyses were performed made using StataCopr 2015 Stata Statistical Software Release 15.1, College Station, TX StataCopr LP software. While evaluating the study data, mean and standard deviation values from measures of central tendency were given for numerical variables and frequency distributions (number, percentage) were given for categorical variables. The difference between the two groups was analyzed by independent sample *t* test for variables that conformed to normal distribution and Mann Whitney *U* test for variables that did not conform to normal distribution. Factors that may affect prolonged hospitalization were given using cross-tabulations. The difference between the groups in terms of frequency was compared using χ^2 tests.

In multivariate analysis to determine long-term hospitalization, independent predictors to predict long-term hospitalization were evaluated using logistic regression analysis using possible factors identified in previous analyses. The results were evaluated at a 95% confidence interval and a $p < 0.05$ significance level.

Results

Demographic data

The mean age of the 1297 patients included in our study was 63 ±15 years. 762 (58.75%) of the patients were male and 535 (41.25%) were female. When the subgroups of our patients were analyzed, 844 patients had pneumonia, 254 patients had acute infectious exacerbation of COPD, 49 patients had bronchiectasis exacerbation, 55 patients had complicated parapneumonic effusion and empyema, and 95 patients were disgeneral data tributed as the other group receiving treatment for a lower respiratory tract infection for which a differential diagnosis could not be made (Table I).

General data

The patients' median length of hospitalization was 7 (interquartile range (IQR 25-75: 5–10) days (Figure 2). The median leukocyte value was 11.80 × 10^3/mm^3 (IQR: 8.92–15.70), neutrophil 8.82 × 10^3/mm^3 (IQR: 6.15–12.56), lymphocyte 1.41 ×

Table I. Statistical evaluation of all parameters

Parameter	Inpatients *N* = 1297	≤ 7 days *N* = 736	> 7 days *N* = 561	*P*-value
Age Median (IQR)	63 (55–75)	64 (54.5–75)	66 (55–75)	0.116
Gender, *n*	F = 535 (41.25%) M = 762 (58.75%)	F = 322 (43.75%) M = 414 (56.25%)	F = 213(%37.97) M = 348 (62.03%)	0.036
Days of hospitalization, median (IQR)	7 (5-10)	6 (4-7)	11 (9-14)	< 0.001
Pneumonia, *n*	872 (67.23%)	436 (59.24%)	436 (77.72%)	0.000
COPD, *n*	625 (48.19%)	375 (50.95%)	250 (44.56%)	0.023
Bronchiectasis, *n*	107 (8.25%)	50 (6.79%)	57 (10.16%)	0.029
IAH, *n*	57 (4.39%)	33 (4.48%)	24 (4.28%)	0.858
Lung abscess, *n*	10 (0.77%)	4 (0.54%)	6 (1.07%)	0.283
HT, *n*	375 (28.91%)	216 (29.35%)	159 (28.34%)	0.692
DM, *n*	267 (20.59%)	161 (21.88%)	106 (18.89%)	0.188
CRF, *n*	63 (4.86%)	39 (5.30%)	24 (4.28%)	0.397
ABY, *n*	22 (1.70%)	10 (1.36%)	12 (2.14%)	0.281
KKY, *n*	223 (17.19%)	132 (17.93%)	91 (16.22%)	0.418
Comorbidity, *n*	889 (68.54%)	522 (70.92%)	367 (65.41%)	0.034
Type 1 SY, *n* Type 2 SY, *n*	590 (45.49%) 257 (19.81%)	341 (46.33%) 160 (21.74%)	249 (44.39%) 97 (17.29%)	0.027
WBC [× 10^3/mm^3] median, (IQR)	11.80 (8.92–15.7)	11.56 (8.85–15.15)	12.15 (9.03–16.52)	0.073
RBC	4.54 (4.09–5.03)	4.58 (4.18–5.05)	4.46 (3.91–4.98)	0.009
HGB [g/dl] median (IQR)	12.6 (11.2–14)	12.9 (11.5–14.2)	12.4 (10.8–13.9)	< 0.001
HCT median, (IQR)	38.7 (34.55–42.8)	39.4 (35.4–43.3)	37.9 (33.3–41.9)	< 0.001
PLT [× 10^3/µl] median, (IQR)	263 (204–344)	257 (199–328)	274 (211–366)	0.042
Neutrophil [× 10^3/m] median, (IQR)	8.82 (6.15–12.56)	8.52 (6.10–11.93)	9.47 (6.18–13.41)	0.061
Lymphocyte [× 10^3/m] median, (IQR)	1.41 (0.91–2.03)	1.45 (0.94–2.16)	1.35 (0.89–1.86)	0.085
NLO, median, (IQR)	6.28 (3.78–10.92)	5.73 (3.51–10.16)	6.94 (4.22–11.77)	< 0.001
CRP median, (IQR) [mg/dl]	79.2 (26.7–171.5)	61.5 (21.75–139.7)	109.4 (42.4–199.5)	< 0.001
PCT median, (IQR) [ng/ml]	0.23 (0.08–0.51)	0.2 (0.07–0.45)	0.28 (0.10–0.55)	0.055
Radiology, *n*	I = 427 (32.92%) II = 391 (30.15%) III = 259 (19.97%) IV = 220 (16.96%)	I = 304 (41.30%) II = 201 (27.31%) III = 120 (16.30%) IV = 111 (15.08%)	I = 123 (32.92%) II = 190 (33.87%) III = 139 (24.78%) IV = 109 (19.43%)	< 0.001
Reproduction, *n*	139 (10.72%)	39 (5.3%)	100 (17.83%)	< 0.001
Pleural fluid, *n*	176 (13.56%)	71 (9.64%)	105 (18.71%)	< 0.001
Parapneumonic fluid, *n*	I = 74 (42.05%) II = 48 (27.27%) III = 12 (6.82%) IV = 42(23.86%)	I = 34 (47.22%) II = 25 (34.72%) III = 3 (4.17%) IV = 10 (13.89%)	I = 40 (38.46%) II = 23 (22.12%) III = 9 (8.65%) IV = 32 (30.77%)	0.022
Pyothorax, *n*	55 (4.24%)	13 (1.77%)	42 (7.49%)	< 0.001
Hemoptysis%, *n*	98 (7.56)	69 (9.38%)	29 (5.17%)	0.005

COPD – chronic obstructive pulmonary disease, ILD – interstitial lung disease, HT – hypertension, DM – diabetes mellitus, CRF – chronic renal failure, ARF – acute renal failure, CHF – chronic heart failure, WBC – white blood cells, RBC – red blood cells, HGB – hemoglobin, HCT – hematocrit, PLT – platelets, NLR – Neutrophil lymphocyte ratio.

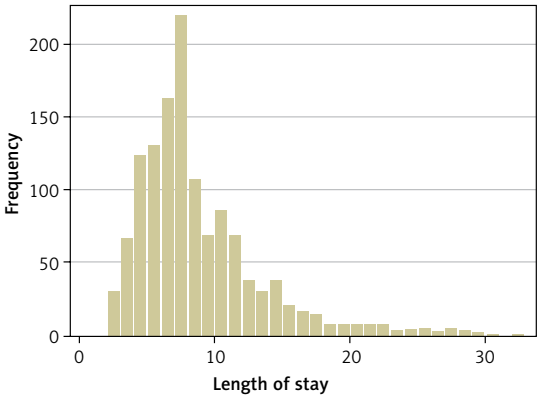

Figure 2. Frequency according to length of hospitalization

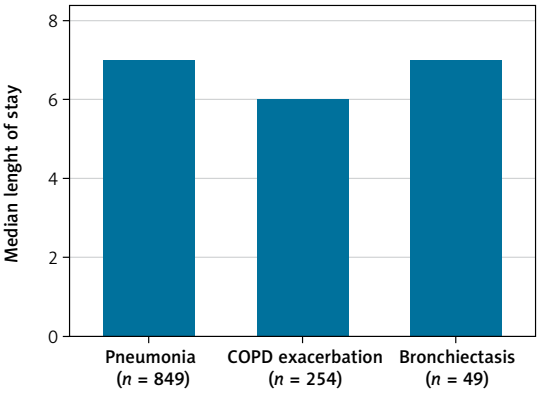

Figure 3. Median length of stay by subgroups

$10^3/mm^3$ (IQR: 0.91–2.03), NLR 6.28 (3.78–10.92), CRP 79.2 mg/l (IQR: 26.70–171.50 mg/l), PCT 0.23 ng/ml (IQR: 0.08–0.51 ng/ml).

Since the median value of clinical hospitalization was 7 days, > 7 days was considered as long-term hospitalization. Variables that may affect prolonged hospitalization were compared between patients hospitalized for 7 days or less and patients hospitalized for more than 7 days.

Separate hospitalization durations of the three most common groups LTRI of patients were evaluated. These are pneumonias, COPD infectious exacerbations and bronchiectasis exacerbations and are shown in Figure 3.

When we looked at the parameters, which were our basic research topic, the median value of NLO was 5.73 (IQR: 3.51–10.16) in patients hospitalized for ≤ 7 days and 6.94 (IQR: 4.22–11.77) in patients hospitalized for > 7 days, and the difference was statistically significant ($p < 0.001$). In the comparison for CRP, 61.5 mg/l (IQR: 21.75–139.7) was found in patients hospitalized for ≤ 7 days and 109.4 mg/l (IQR: 42.4–199.5) in patients hospitalized for longer than 7 days and the difference between them was statistically significant ($p < 0.001$). The median WBC value was 11.56 × $10^3/mm^3$ (IQR: 8.85–15.15) in the group hospitalized for ≤ 7 days and 12.15 × $10^3/mm^3$ (IQR: 9.03–16.52) in the group hospitalized for more than 7 days and no significant difference was found in their statistical analysis ($p = 0.073$). The median value of PCT was 0.2 ng/ml (IQR = 0.07–0.45) in the group hospitalized for ≤ 7 days and 0.28 ng/ml (IQR: 0.10–0.55) in the group hospitalized for more than 7 days and there was no significant difference in their statistical analysis ($p = 0.042$). Statistical results comparing laboratory tests, comorbidities, demographic findings and other conditions of the patients are given in Table I.

Microbiologic growth results of respiratory tract samples were analyzed in our patient group. In 139 patients, growth was detected in culture. The most frequently isolated agent was pseudomonas aeruginosa. There was a statistically significant difference between the group hospitalized longer than 7 days and the other group in terms of microbiologic agent growth ($p < 0.001$).

Patients were categorized according to whether they had respiratory failure or not and the type of respiratory failure, if any. The group without respiratory failure, the group with type 1 respiratory failure (PO_2 < 60 mm Hg), and the group with type 2 respiratory failure (PCO_2 > 55 mm Hg) were combined. When the difference between the short- and long-term hospitalized groups was evaluated, a significant difference was observed in favor of the short-term hospitalized group ($p = 0.027$).

The chest radiographs of the patients were examined and divided into four groups, including the group without infiltration on the chest radiograph, the group with infiltration on one side and in one zone on the chest radiograph, the group with infiltration in more than one zone in one lung on the chest radiograph, and the group with infiltration in both lung parenchyma. The numbers of these groups are given in Table I.

According to Table I, the variables of gender, days of hospitalization, presence of pneumonia, presence of COPD, presence of bronchiectasis, presence of at least one comorbidity, presence of respiratory failure, red blood cells (RBC), hemoglobin (HGB), hematocrit (HCT), platelets (PLT), CRP values, NLO, degree of radiological infiltration, growth status of respiratory tract samples, presence of pleural fluid, parapneumonic effusion, pyothorax and hemoptysis were statistically significant in long-term hospitalization (0.036, 0.000, 0.000, 0.023, 0.029, 0.034, 0.027, 0.009, 0.000, 0.000, 0.042, 0.000, 0.000, 0.000, 0.000, 0.000, 0.022, 0.000, 0.005, respectively).

Logistic regression analysis was performed to determine the factors affecting long-term hospitalization. Four models were preferred for this.

In Model 1, age, gender, leukocyte, NLO, CRP and procalcitonin were taken into account. In this model, gender was meaningful in predicting CRP long-term hospitalization. While male gender increased prolonged hospitalization 1.71-fold, CRP was found to be ineffective in/have no effect on predicting the length of stay (OR = 1) (Table II).

Table II. Model 1 in binary regression analysis

Lon-term hospitalization	OR	*P*-value	95% CI
Age	1.00	0.263	0.994–1.02
Gender	1.71	0.010	1.138–2.587
Leukocyte	0.99	0.895	0.92
CRP	1.00	0.000	1.001–1.006
NLO	0.99	0.850	0.974–1.021
PCT	1.01	0.788	0.895–1.157
Fixed	0.30	0.016	0.115–0.803

Table III. Model 2 in binary regression analysis

Long-term hospitalization	OR	*P*-value	95% CI
Age	0.186	0.015	0.036–0.033
Gender	0.545	0.012	0.120–0.970
Comorbidity	(–0.809)	0.002	(–1.320)–(–0.298)
Reproduction	1.002	0.003	0.345–1.659
Radiology	0.565	0.027	0.0638–1.067
WBC	(–0.001)	0.955	(–0.039)–(0.036)
CRP	0.003	0.002	0.001–0.005
NLO	(–0.003)	0.772	(–0.027)–(0.020)
PCT	(–0.002)	0.975	(–0.130)–(0.126)
Fixed/Constant	(–1.868)	0.000	(–2.920)–(–0.817)

Table IV. Model 3 in binary regression analysis

Long-term hospitalization	OR	*P*-value	95% CI
Age	0.010	0.112	(–0.002)–(0.023)
Gender	0.495	0.019	0.079–0.910
SY	(–0.388)	0.013	(–0.694)–(–0.083)
WBC	(–0.004)	0.789	(–0.041)–(0.031)
CRP	0.003	0.001	0.001–0.005
NLO	(–0.001)	0.887	(–0.024)–(0.021)
PCT	0.008	0.899	(–0.119)–(0.136)
Constant	(–0.976)	0.053	(–1.963)–(0.010)

Table V. Model 4 in binary regression analysis

Long-term hospitalization	OR	*P*-value	95% CI
CRP	0.003	< 0.001	0.001–0.005
NLO	0.001	0.910	(–0.018)–(0.020)
PCT	0.023	0.720	(–0.106)–(0.154)

Patients' age, gender, comorbidities, presence or absence of reproduction and radiologic infiltration grade, CRP, PCT and NLO were selected as the second model (Model 2).

In Model 2, the effect of age, gender, comorbidity, presence of reproduction, presence of radiological infiltration, WBC, CRP, NLO and PCT together on the length of stay was evaluated. For each age, the length of hospitalization increased 0.18-fold, while female gender was found to increase the length of hospitalization by 45.5%. In addition, according to this model, patients with at least one comorbidity showed an inverse relationship with longer length of stay, and reproduction and CRP found not to affect the length of stay, although they were significant (Table III).

Among the factors that may affect hospitalization, the evaluation based on age, gender, CRP, PCT, NLO along with respiratory failure was preferred as the third model (Model 3).

According to this model, similar to model 2, being female increased hospitalization by 50.5%, respiratory failure showed an inverse relationship with long-term hospitalization, and CRP, although significant, had a negligible effect on long-term hospitalization (OR = 0.003) (Table IV).

As the fourth and final model, we compared CRP, PCT and NLO values, the three parameters we compared at the beginning (Model 4). According to this model, although the relationship between CRP and prolonged hospitalization was statistically significant, it was found to be insufficient in predicting prolonged hospitalization, while NLO and procalcitonin were not significant in predicting prolonged hospitalization (Table V).

Correlation analysis

The correlation of the length of hospitalization with NLO, CRP and PCT was analyzed. Accordingly, although there was a statistically significant correlation between NLO and CRP and length of hospitalization, the correlation relationship was weak. There was no significant relationship with PCT.

In terms of correlation, the correlation of NLO with other known inflammation markers was also evaluated. In this respect, its correlation with CRP and PCT was examined. NLO had a significant statistical relationship with CRP and PCT, but the correlation was weak.

Discussion

In patients hospitalized in the chest diseases clinic for lower respiratory tract infections, neutrophil/lymphocyte ratio was found to be insignificant in predicting the length of hospitalization longer than 7 days in combination with other in-

flammation markers such as leukocytes, CRP and procalcitonin. However, when other parameters were examined in the prediction of prolonged hospitalization, it was found that the presence of microbiological growth and radiological infiltration in the samples taken from the respiratory tract were significant in the prediction of prolonged hospitalization when used in combination with CRP.

There was no significant difference in age distribution between the short-stay group and the long-stay group in the patients' demographic comparison. The three main groups of lower respiratory tract infections are pneumonias, COPD acute infectious exacerbations and bronchiectasis exacerbations. In the separate evaluation of these groups, the average length of hospitalization was 7 days for pneumonias, 6 days for COPD exacerbations and 7.5 days for bronchiectasis exacerbations. In the studies conducted, the length of hospitalization varies between centers. This difference varies according to the differences in the patient population as well as the level of development of the countries, the structure of the hospitals, economic status, cultural characteristics, in summary, local conditions. In a study by Cillóniz *et al.* looking at the mortality and hospitalization durations of approximately 1200 cases of pneumococcal pneumonia in Spain, the average hospitalization was 8 days in three of the four groups of 5 years, and 9 days in one [6]. In a study conducted by Cabre et al. in Spain, where they examined the reasons for long hospital stays in 1920 patients in 27 different centers, the average hospital stay in patients with community acquired pneumonia (CAP) was determined to be 10 days. In the study by Spoorenberg *et al*. in the Netherlands, in which microbiological agents, discharge status of patients, costs and length of stay were analyzed in 505 patients with CAP, the mean length of stay was 8.5 days [8]. In a study conducted by Altın *et al*. in Turkey in which cost analysis was performed in two different pulmonology centers, patients hospitalized due to pneumonia were hospitalized for an average of 10–11 days, and in the same study, the average length of stay of patients hospitalized with a diagnosis of COPD was found to be 8–10 days [9]. As seen in the study conducted in our center, the length of hospitalization was shortened by 3 days. This also draws attention as a finding that is in parallel with our study reasons. In the study by Dai *et al*. looking at the duration of hospitalization according to the type of infection of COPD episodes in China, a mean hospitalization period of 9.6 days was observed [10]. Wang *et al*. investigated the reasons for long-term hospitalization in patients hospitalized with COPD exacerbations in Norway and found that the median length of stay was 6 days in 599 patients [11]. For bronchiectasis exacerbations, in the study conducted by Polverino *et al.* in Spain, bronchiectasis but not pneumonia exacerbations and bronchiectasis with pneumonia were compared with 144 patients in terms of clinical outcomes. The duration of hospitalization was also examined in the results and the average duration of hospitalization in the group with bronchiectasis exacerbation but without pneumonia was found to be 9.5 days, while in the other group it was 8.5 days [12]. Uncontrolled migration like Istanbul, in a city where the influx of refugees has intensified in recent years, tertiary education and research hospitals face a high patient density due to the specific problems of other centers. This, in general, leads to an increase in the number of patients waiting for hospitalization in the emergency room and leads to earlier discharge of hospitalized patients.

It is thought that the use of these two parameters together may be meaningful in determining the infection since the neutrophil count increases in cases of infection and the lymphocyte count is relatively decreased. In addition, since it is an easily accessible parameter, the possibility of using it in undeveloped and developing countries has caused it to be the subject of many studies. While NLO has been used as a marker of inflammation in recent years, generally worse clinical and mortality-related results have been obtained. For example, de Jager et al. found that it was associated with the severity and mortality of community-acquired pneumonia cases in patients admitted to the emergency department [3]. Again, Yao *et al.* investigated the role of NLO in prognosis in hospitalizations in acute attacks of COPD and found that it was associated with mortality [13]. It was also found to be associated with 28-day mortality in patients hospitalized with sepsis in the intensive care unit [14]. When the literature in which NLO was evaluated in relation to long-term hospitalization were examined, significant relationships were found. In the study by Azab *et al.* investigating the relationship between adverse outcomes and NLO in patients with acute pancreatitis, a relationship was found between long-term hospitalization and high NLO rates [15]. Again, in the study by Gohil *et al*. investigating the relationship between NLO and serum albumin values before surgery and long-term hospitalization in patients with colorectal cancer, a significant relationship was found between long-term hospitalizations and high NLO rates [16].

NLO was positively correlated with CRP and PCT ($p < 0.001$, $r = 0.27$ and $p < 0.001$and $r = 0.19$, respectively). We also looked at the correlation between NLO and length of hospitalization and found a weak positive correlation. Considering that the length of hospitalization is also related

to the severity of the disease, we found that there was a significant correlation between long-term hospitalizations and NLO rate. However, in our regression analysis, we found that it was not effective in predicting short- and long-term hospitalizations when used with other parameters.

When the studies on CRP are examined, Van der Meer et al. found that CRP was useful in the definition of disease in LTRI and in differentiating between bacterial pneumonias and acute bronchial conditions, which are mostly viral in origin [17]. In several studies investigating the relationship between increased CRP levels and mortality in patients with community-acquired pneumonia, a significant relationship was found [18–20]. In the study by Farah *et al.* evaluating the duration of hospitalization and consecutive CRP measurements in patients with community-acquired pneumonia, it was seen that CRP levels measured on the second day were effective in predicting short- and long-term hospitalization according to the increase and decrease [21]. In our comparison of short- and long-term hospitalization in the LTRI group, we saw that the group with higher CRP levels at the first admission was associated with longer hospitalization. We also saw that this relationship was continued in the regression analysis.

The correlation between CRP and the length of hospitalization was also evaluated. In the evaluation made in this context, while there was a significant correlation between CRP and the length of hospitalization, the correlation was weak. However, it had a higher correlation than PCT and NLO, which were other parameters related to the length of hospitalization. When we look at other studies on this subject, the relationship between intercellular adhesion molecule-1 (ICAM-1) and the severity of patients with CAP was investigated in the study by Chang *et al.* In the study with 78 patients, there was no statistically significant relationship between the duration of hospitalization and CRP and the correlation was weak [22]. Again, in the thesis study conducted by Beyaz *et al*., no correlation was seen between CRP and the length of hospitalization and mortality in the relationship between NLO, CRP, PCT and length of hospitalization and mortality in patients with pneumonia [23].

PCT is generally a useful marker of inflammation in differentiating bacterial and viral infections [24, 25]. Bremmer *et al.* investigated PCT guidance in COPD attacks and showed that detection of bacterial infections and antibiotics initiated for this shortened the duration of hospitalization [26]. However, there are not many studies showing that PCT levels have an effect on predicting long-term hospitalizations. Pizzini *et al.* investigated the diagnostic and prognostic use of inflammatory markers in COPD, COPD exacerbations and pneumonia and found a significant correlation between CRP and length of hospitalization, while a low level of significance was observed for PCT [27]. In the study of Beyaz *et al.* in patients with pneumonia, a significant correlation was observed between PCT and length of hospitalization [23]. Although we found that it was useful in determining the infection in the LTRI group, we found that it was not effective in determining the length of hospitalization of the patients. In addition, there was no correlation in the correlation analysis. We think that the fact that all lower respiratory tract infections were present in our study may be the reason for this difference. For example, PCT levels may not increase in patients with empyema, but it is known that there is a group of patients with long-term hospitalization. In addition, the time of sample collection for PCT, which we consider among the limitations of our study, weakens the reliability of the result.

The impact of patients' comorbidities on the length of stay was examined, and additional diseases such as DM, HT, CHF, COPD and CRF were examined. Evaluation was made by comparing those who had at least one of these and those who did not have any comorbidities. Quintana *et al.* investigated the factors affecting the length of hospitalization in COPD attacks and showed that heart failure prolonged the length of hospitalization [28]. In the study by de la Iglesia *et al.* examining the factors affecting hospitalizations of more than 3 days in COPD attacks, no data were found to prolong the duration of hospitalization in patients with hypertension and diabetes [29]. In the study by Wang *et al.* investigating the reasons for long hospitalization in COPD acute attacks, it was found that prolonged hospitalization was associated with heart failure and diabetes, but not with hypertension and renal failure [11]. Looking at the studies conducted in patients with pneumonia, Cabre *et al.* investigated the reasons for prolonged hospitalization in cases with CAP in 27 centers and found that patients with COPD, CHF and DM did not prolong the duration of hospitalization [7]. In the study by Iqbal *et al.* investigating the relationship between hypercapnia and long-term hospitalization in cases with CAP, a significant relationship was found in patients with a diagnosis of COPD, whereas no relationship was found in patients with a diagnosis of hypertension and DM [30]. In our analysis, we found that hypercapnia alone or in combination did not have a statistically significant correlation in predicting prolonged hospitalization.

Our study had some limitations. First of all, it was a retrospective and single-center study. A heterogeneous group such as pneumonia, COPD infected attack, bronchiectasis exacerbation, which may be confused with each other, were included

in the study together. Disease diagnoses were obtained with ICD-10 diagnostic codes, but the diagnosis of pneumonia increased due to the necessity of entering a diagnosis of pneumonia in order to receive some antibiotics in hospital daily practice. However, this problem was tried to be overcome by examining all medical records. Again, scores such as PSI and CURB-65, with which we can compare the severity of the disease with the duration of hospitalization and other parameters, could not be calculated. The time of PCT collection, which we evaluated in the study, could not be standardized.

In conclusion, in patients hospitalized with a diagnosis of LTRI in the chest diseases clinic, CRP was found to be associated with long hospitalization, while NLO and PCT were found to be meaningless in predicting long hospitalization. There was a significant statistical significance for NLO as well as many other parameters in the stand-alone evaluation, but in the combined evaluation, i.e. regression analysis, it was seen that NLO had no effect on the prediction of long hospitalization in all four models used. However, isolation of the causative agent, the presence and severity of pleural effusion and radiologic infiltration were found to predict prolonged hospitalization.

Even though important data on the duration of hospitalization have been presented, there is a need for further studies on this issue since no important parameter that can be used for its prediction has been presented.

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Ethical approval

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Conflict of interest

The authors declare no conflict of interest.

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