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Original Article

Peripheral Blood Eosinophilia and Neutrophil Lymphocyte Ratio in the Choice of Antibiotic and/or Steroid in Patients Hospitalized with Acute Exacerbations of Chronic Obstructive Pulmonary Disease

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Abstract

OBJECTIVE: The choice of steroids and antibiotics is optional for the management of acute exacerbation of chronic obstructive pulmonary diseases according to international guidelines. The study hypothesized that the steroid and antibiotic choice can be decided by using the neutrophil–lymphocyte ratio and peripheral blood eosinophilia in patients with acute exacerbation of chronic obstructive pulmonary diseases. This would reduce the rate of re-hospitalization in 28 days.

MATERIAL AND METHODS: Patients were hospitalized due to acute exacerbation of chronic obstructive pulmonary diseases from February 1, 2018, to January 31, 2019. Patients were divided into 2 groups: Sureyyapasa protocol group and conventional group. In the Sureyyapasa protocol group, patients were divided into 4 subgroups according to peripheral blood eosinophilia and neutrophil–lymphocyte ratio values. Treatment success was defined as 5-7 days acute exacerbation of chronic obstructive pulmonary diseases treatment was enough to discharge and no re-hospitalization within 28 days. Treatment failure was defined that the hospital stay was longer than 7 days or transport to intensive care and death or readmission to the hospital due to acute exacerbation of chronic obstructive pulmonary diseases within 28 days after discharge.

RESULTS: The Sureyyapasa protocol group (n = 96) and the conventional group (n = 95) were randomly selected. The conventional group and Sureyyapasa protocol group had similar hospital stay ($P = .22$), and antibiotic and steroid uses were significantly higher in the conventional group than the Sureyyapasa protocol group (antibiotic use 100% vs. 83%, $P < .001$ and steroid use 84% vs. 29%, $P < .001$, respectively). Treatment failure in the conventional Group (n = 23, 24%) is higher than the Sureyyapasa protocol group (n = 17, 18%).

CONCLUSIONS: Initiating treatment by evaluating eosinophilia and neutrophil–lymphocyte ratio in patients with acute exacerbation of chronic obstructive pulmonary diseases in the ward reduces unnecessary antibiotic and steroid use and cost rates in hospitalizations.

KEYWORDS: Respiratory infections, COPD, interstitial lung disease, tuberculosis, respiratory intensive care

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INTRODUCTION

Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) increases morbidity and mortality of patients especially if needed hospitalization.[1,2] The most common treatments for AECOPD are antibiotics and corticosteroids.[1] Two-thirds of AECOPD is caused by lower respiratory infections, and two-thirds of these infections are caused by bacterial infections.[3] Due to Antonisen criteria, a high leukocyte count, C-reactive protein (CRP), and other anti-inflammatory biomarkers are partially useful for antibiotic selection.[4-6] However, CRP elevation is not limited to bacterial infections; viral and non-infectious causes also contribute to its elevation. Clinicians need objective criteria in addition to the subjective Antonisen Criteria and CRP elevation to avoid prescribing unnecessary antibiotics.[6-9] According to promising studies; inflammatory biomarkers such as neutrophil–lymphocyte ratio (NLR) and peripheral blood eosinophilia (PBE) may be useful in AECOPD management.[10-14] Studies have shown that steroid use is beneficial in patients with a PBE ratio above 2%.[14-18]

Also the Global initiative obstructive lung diseases (GOLD) 2019 guidelines emphasized the need for inhaled steroids in the treatment of eosinophilic COPD (PBE count >300) and oral systemic steroids in non-life-threatening AECOPD (GOLD).[19-23] Also PBE, NLR, platelet–lymphocyte ratio, mean platelet volume (MPV), and platelet–MPV ratio have been identified in the management of AECOPD patients.[20-25] The physicians have advised to "consider" the use of corticosteroids, antibiotics, or combination therapy in the treatment of AECOPD; however, the objective criteria in the guidelines have not been adequately explained. In the current study, it is hypothesized that the treatment protocol, which met the criteria of PBE ratio equal or greater than 2% for systemic steroid therapy, and NLR equal or greater than 4 is for antibiotic therapy, would reduce hospital stay and re-hospitalization in the first 28 days in AECOPD patients.

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This study's primary objective is to establish a standard treatment using the PBE ratio and NLR in hospitalized patients with AECOPD to shorten their length of stay. The secondary objective of this study is to reduce unnecessary antibiotic and steroid usage. The significance of this study is its contribution of objective data in terms of adding systemic steroids and antibiotics to the treatment of hospitalized AECOPD patients.

MATERIAL AND METHODS

This prospective cohort study was conducted between February 1, 2018, and January 31, 2019, at the University of Health Sciences Süreyyapaşa Training and Research Hospital for Chest Diseases.

The research was authorized by the University of Health Sciences Süreyyapaşa Chest Diseases and Thorasic Surgery Training and Research Hospital Ethics Committee (Approval No: 116, Date: 2017). The research conformed to the Declaration of Helsinki.

Patients

Eighty percent power and 95% CI were used to analyze sample size, and each group contained at least 80 patients. Patients were included who were admitted to the hospital with AECOPD. Figures 1 and 2 provide a summary of the treatment strategies for the Sureyyapasa protocol group (SPG). Conventional AECOPD treatment was given as per the 2017 GOLD guideline. Inhalation of short-acting beta 2 agonist as salbutamol and/or anticholinergic ipratropium bromide comprised the majority of bronchodilator treatment. Antibiotic therapy was 4 × 1 g amoxicillin clavulonic acid, and steroid therapy was 1-0.5 mg/kg of methylprednisolone per day, orally administered over a period of 5-7 days. Supplemental oxygen was administered if the pulse oxygen saturation was less than 88%; low molecular weight heparin (LMWH) is also administered to every patient unless there is a contraindication (e.g., platelet count of less than 50 000/mL or a history of hypersensitivity to LMWH).

Definitions

Blood neutrophil to lymphocyte count ratio (NLR) was calculated, and groups were defined based on NLR values; steroids and antibiotics were administered based on PBE ratio and NLR values (Figure 2). Patients in the SPG were divided into 4 subgroups based on their PBE and NLR values. The SPG-1 (symptomatic group): NLR <4 and PBE <2%; SPG-2 (steroid group): NLR <4 and PBE ≥2%; SPG-3 (antibiotic group): NLR ≥4 and PBE <2%; and SPG-4 (combined group): NLR ≥4 and PBE ≥2% (Figures 1 and 2). The selection of steroids and antibiotics for the conventional therapy group (CG) was determined by physicians regardless of PBE and/or NLR values. The treatment was considered successful if the patient was discharged 5-7 days after AECOPD treatment and did not require readmission within 28 days. Treatment failure was defined as a hospital stay longer than 7 days, transport to intensive care unit (ICU), death in or out of hospital, or readmission due to AECOPD within 28 days after discharging (Figure 1). The criteria for patient discharge and

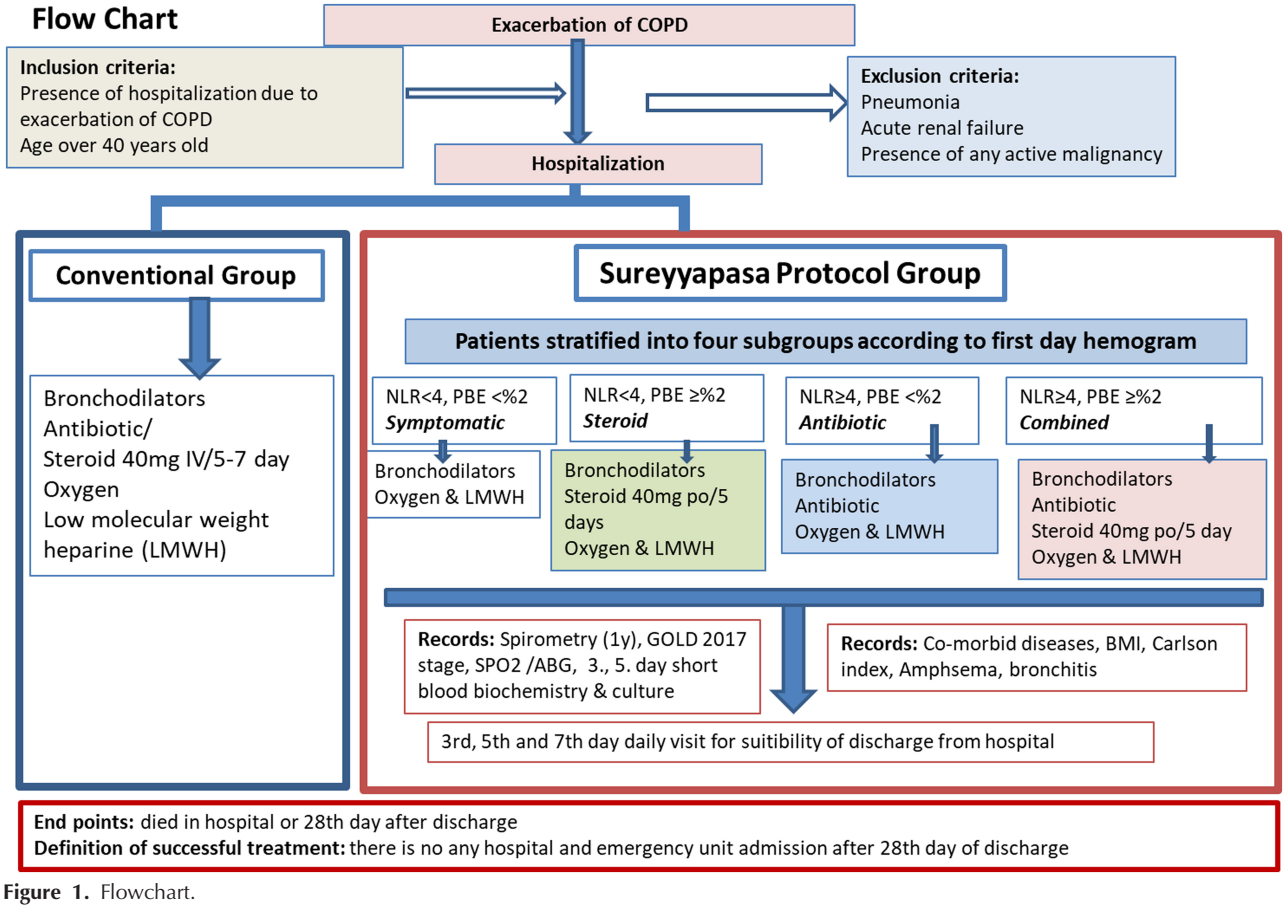

Figure 1. Flowchart.

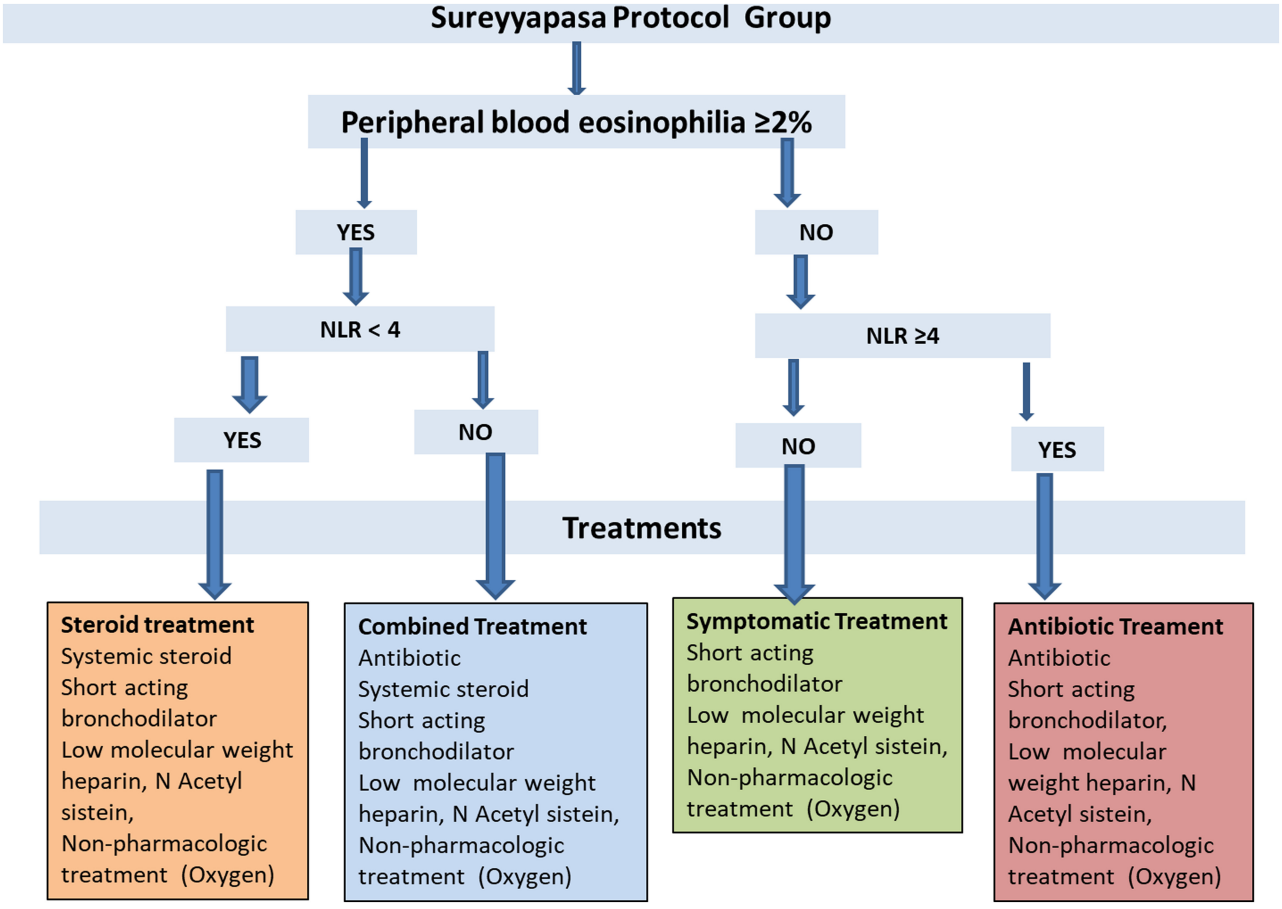

Figure 2. Subgroup classification of the Sureyyapasa protocol group according to peripheral blood eosinophilia and neutrophil–lymphocyte ratios.

recommendations for follow-up were determined in accordance with the 2017 GOLD guidelines.[26] The duration of follow-up after hospital discharge was 28 days.

Recording Data

The patient's file contains the patient's demographic information, co-morbidities, pulmonary function tests (within the past 2 years), hemogram, biochemistry, and arterial blood gas values on the day of hospital admission and discharge. On the first, third, fifth, seventh, and the final day of hospitalization, blood eosinophil, neutrophil, and lymphocyte counts and percentages were recorded.

Statistical Analysis

Statistical analyses were done by Statistical Package for Windows (IBM Corp.; Armonk, NY, USA). The dichotomous variables were analyzed by the Pearson chi-square test. Fisher's exact test was used if number was less than 5. Continuous variables such as age, pulmonary function test results, arterial gas values, and length of hospital stay in days are shown as mean with SD if normally distributed, and the Student's *t*-test was used for 2 group comparisons. Two groups that are not normally distributed were compared by the Mann–Whitney *U*-test. The *P*-value of .05 was considered statistically significant.

RESULTS

Two hundred patients were included in the study who met the inclusion criteria. The exclusion of 9 patients was due to complications that arose after hospitalization. Using random randomization methods, 96 patients with AECOPD were assigned to the SPG and 95 patients with AECOPD were assigned to the CG. There was no statistical difference between these groups in terms of age, gender, body mass index, smoking status, use of respiratory devices, and comorbidities (Table 1). Also, the groups had similar results in spirometric measurements and arterial blood gas values (Table 2). Both groups had moderate to severe volume loss on pulmonary function tests.

Table 3 summarizes the number and ratio of blood eosinophil levels with AECOPD on the day of hospitalization (basal eosinophil) and on the third, fifth, and seventh days and over the seventh day of hospitalization. There were 3 categories of eosinophil level: 2% as ratio and 100 and 300 cells/mL as count.[5] The SPG exhibited a statistically significant increase in blood eosinophil ratio and cell count on the third and fifth day of the hospitalization (Table 3). Table 3 indicates the comparison of NLR and PBE values for each study group. On the first day of hospitalization, the SPG had significantly higher NLR values than the CG (P = .047); on the third day both groups had similar NLR values (P = .11); on the fifth and seventh day of hospitalization, the CG had a significantly higher NLR value than the SPG (P = .001 and P = .005) (Table 3). On the fifth day of hospitalization, platelet lymphocyte ratio (PLR) values in the CG were significantly higher than in the SPG (P = .001). Platelet/MPV ratios were similar in 2 groups on all hospitalization days.

Table 1. Demographic Features of Conventional Therapy and Sureyyapasa Protocol Groups

	Conventional Therapy Group (n = 95)	Sureyyapasa Protocol Group (n = 96)	*P*
Male, n (%)	68 (72)	76 (79)	.22
Age, years, mean (SD)	69 (10)	69 (9)	.90
BMI—kg/m^2 median (25%-75%)	25 (22-29)	25 (22-29)	.65
Biomass exposure n (%)	29 (31)	33 (35)	.57
Smoking history			
Former smoker, n (%)	47 (61)	58 (71)	.16
Current smoker, n (%)	78 (82)	82 (85)	.54
Packet-year, median			
25%-75%	50 (35-60)	50 (30-60)	
LTOT, n (%)	41 (43)	42(44)	.93
NIMV at home, n (%)	20 (21)	21 (22)	.89
mMRC, mean (SD)	3 (1)	3 (1)	.57
Comorbidities, n (%)			
Hypertension	58 (61)	56 (58)	.70
Diabetes mellitus	24 (25)	30 (31)	.36
CHF	19 (20)	25 (26)	.32
CAD	41 (43)	43 (45)	.82
CRF	12 (13)	10 (10)	.63
Liver disease	3 (3)	0 (0)	.07
Hyperlipidemia	7 (7)	6 (6)	.76
Hypo/ Hyperthyroidism	5 (5)	3 (3)	.46
Psychiatric disorders	16 (17)	13 (14)	.53
Cerebrovascular diseases	5 (5)	5 (5)	.97
Tuberculosis history	11 (12)	18 (19)	.17
Osteoporosis	12 (13)	8 (8)	.33
Lung surgery	8 (8)	5 (5)	.38

BMI, body mass index; CAD, coronary artery disease; CHF, congestive heart failure; CRF, chronic renal failure; LTOT, long-term oxygen therapy; mMRC, modified medical research council; NIMV, noninvasive mechanical ventilation.

Table 2. Spirometric Measurements and Arterial Blood Gas Values of Conventional Therapy and Sureyyapasa Protocol Groups

Spirometric measurements	Conventional Therapy Group (n = 95)	Sureyyapasa Protocol Group (n = 96)	*P*
FEV1, %, median (25%-75%)	33 (26-47)	33 (25-46)	.63
FEV1, mL, median (25%-75%)	830 (620-1130)	860 (620-1110)	.78
FVC, %, median (25%-75%)	45 (36-62)	45 (36-56)	.74
FVC, mL, median (25%-75%)	1405 (1040-1850)	1510 (1200-1780)	.46
FEV1/FVC, mean (SD)	60 (10)	60 (10)	.78
MEF 25%-75%, median (25%-75%)	20 (13-29)	18 (13-28)	.50
OH SPO_2, mean (SD)	84 (9)	85 (9)	.78
ABG			
PH, mean (SD)	7.40 (0.04)	7.41 (0.04)	.09
PO_2, median (25%-75%)	60 (51-89)	59 (52-76)	.70
PCO_2, mean (SD)	49 (10)	46 (10)	.09
HCO_3, mean (SD)	29.4 (5)	28.4 (5)	.28
BE, median (25%-75%)	4.8 (2.2-7.9)	3.8 (1.3-6.9)	.21
SO_2, mean (SD)	90 (7)	91 (6)	.79
FiO_2, median (25%-75%)	21 (20-40)	21 (20-40)	.41

ABG, arterial blood gases; BE, base excess; FEV1, forced expiratory volume at first second; FiO_2, fractioned oxygen in respiratory air; FVC, forced vital capacity; HCO_3, serum bicarbonate; MEF, mid-expiratory flow; OH SPO_2, room air partial oxygen saturation; PCO_2, partial carbon dioxide pressure; PO_2, partial oxygen pressure; SO_2, oxygen saturation.

The sputum culture obtained cases and their results, antibiotic-free cases, corticosteroid usage rate and length of hospital stay for study groups are summarized in Table 4. One of the 51 patients in the CG with a positive sputum culture for *Pseudomonas aeruginosa*, while the others had positivity for gram-positive bacteria. The SPG group had 60 sputum culture positivity of which 2 cases were positive for *Pseudomonas aeruginosa*, 2 cases were positive for *Klebsiella pneumonia*, and the remaining cases were positive for gram-positive bacteria. There were no significant differences between the groups. According to NLR values, all patients in the CG used antibiotics, whereas 17% of patients in the SPG did not use antibiotics. According to serum eosinophil level, 29% of the SPG and 84% of the CG utilized corticosteroids (*P* = .001). Both groups had similar hospitalization lengths (Table 4). According to NLR criteria, the majority of patients with AECOPD required to be prescribed antibiotics (83%). The majority of patients with AECOPD were discharged from the hospital after 5 days. In the first 28 days after discharge, 38 patients [CG: n = 23 (24.2%); SPG: n = 17 (17.7%)] were admitted to the emergency unit or re-hospitalized. In SPG, the rate of AECOPD patients readmitted within 28 days of discharge was significantly lower than the CG (*P* = .008) (Tables 4 and 5). The readmission rate of the patients who were discharged on the sixth day of the hospitalization was significantly higher in the CG.

DISCUSSION

In this study, considering that prescribing steroids when PBE ratio ≥2% and prescribing antibiotics when NLR ≥4

Table 3. Comparison of NLR and the Mean PBE Levels of the Groups by the Treatment

	Conventional Therapy Group (n = 95)	Sureyyapasa Protocol Group (n = 96)	*P*
Baseline			
Cases of eosinophil ≥2%, n (%)*	24 (25)	30 (31)	.36
Cases of eosinophil ≥100 cc/mL, n (%)†	41 (43)	42 (43)	.93
Cases of eosinophil ≥300 cc/mL, n (%)‡	17 (18)	22 (23)	.39
NLR	4.80 (3-10)	6 (4-11)	.047
Third day			
*Cases of eosinophil ≥2%, n (%)	6 (6)	23 (24)	.001
Eosinophil ≥100 cc/mL, n (%)	14 (15)	36 (38)	<.001
Cases of eosinophil ≥300 cc/mL, n (%)‡	3 (3)	10 (10)	.046
NLR	6.60 (3-11)	4.70 (3-8)	.11
Fifth day eosinophil			
Cases of eosinophil ≥2%, n (%)*	7 (9)	37 (45)	<.001
Cases of eosinophil ≥100 cc/mL, n (%)†	15 (20)	48 (58)	<.001
Cases of eosinophil ≥300 cc/mL, n (%)‡	3 (4)	13 (16)	.015
NLR	6.60 (3-11)	4 (3-6)	<.001
Seventh day			
Cases of eosinophil ≥2%, n (%)*	9 (23)	22 (47)	.018
Cases of eosinophil ≥100 cc/mL, n (%)†	13 (33)	31 (66)	.002
Cases of eosinophil ≥300 cc/mL, n (%)‡	3 (8)	6 (13)	.42
NLR	5.40 (4-14)	3.50 (2-6)	.005
Over 7 days			
Cases of eosinophil ≥ 2%, n (%)*	3 (19)	7 (33)	.32
Cases of eosinophil ≥100 cc/mL, n (%)†	8 (50)	10 (48)	.89
Cases of eosinophil ≥300 cc/mL, n (%)‡	1 (6)	2 (10)	.72
NLR	8.18 (4-19)	5.25 (3-7)	.17

*Ref. 13, 17, and 18.
†Ref. 5.
‡Ref. 5.
NLR, neutrophil–lymphocyte ratio; PBE, peripheral blood eosinophilia.

Table 4. The Sputum Culture Positivity Rates, Antibiotic and Steroid Treatment Ratios, and the Length of Hospitalization Days in the Patients with AECOPD and Hospital Admission after Discharge from Hospital in the First 28 Days

	Conventional Therapy Group	Sureyyapasa Protocol Group	*P*
Sputum culture positivity, n (%)	51 (85)	60 (94)	.069
Antibiotic free, n (%)	0 (0)	13 (17)	<.001*
Corticosteroid usage, n (%)	80 (84)	28 (29)	<.001
Length of hospital stay day, median (25%-75%)	6 (5-8)	7 (5-8)	.22
Length of hospitalization days			
Fifth day and below	37 (39)	33 (34)	.51
Above fifth day	58 (61)	63 (66)	
Length of hospitalization days			
Seventh day and below	71 (75)	64 (67)	.52
Above the seventh day	24 (25)	32 (33)	
First month of admission to hospital, n (%)			
Due to COPD	21 (91)	9 (52)	.008*
Other reasons	2 (9)	8 (48)	
Sixth day discharge and first-month admission	21 (22.1)	9 (9.4)	.016

*Fisher's exact test, if n < 5.
AECOPD, acute exacerbation of chronic obstructive pulmonary disease; COPD, chronic obstructive pulmonary disease.

in patients hospitalized with acute COPD exacerbation, it was shown that it shortened the length of hospitalization and reduced readmission rate in the first 28 days due to chronic obstructive pulmonary (COPD)-related symptoms.

All Anthonisen-eligible CG patients received antibiotics. The SPG reduced unnecessary antibiotic use by 17%. In the CG, 84% of AECOPD patients used steroids based on clinical status and pulmonary oscultation; 29% of AECOPD patients in the SPG group have prescribed steroids whose blood eosinophil ratio was ≥2%.

Bacterial, viral, eosinophilic, and pauciinflammatory AECOPD groups had similar FEV_1 and FEV_1/FVC values.[13] Anthonisen et al[4] studied antibiotic initiation in AECOPD. In GOLD 2017 guidelines, the decision for antibiotic initiation for AECOPD was based on clinical history and "physician opinion" guided by Anthonisen criteria.[26] GOLD 2019 defined eosinophilic COPD endotype and its treatment which led to new treatment approaches in this field.[5] In the current study, COPD endotype distribution was similar between groups (Table 3). If the blood eosinophil ratio is ≥2%, the cell count per liter is between 2 and 1/5. If eosinophil counts were ≥300 cells/L, mortality was found to be 1%-5% (Table 3). As a biomarker for AECOPD risk and treatment response, peripheral blood eosinophil level is being monitored. Recent studies[15–17] show that systemic steroid treatment improves COPD exacerbation symptoms faster. Corticosteroid treatment was more effective when there was peripheral blood

Table 5. First Twenty-Eighth Day Hospital Admission

	Conventional Therapy Group Failure (Readmission to Hospital), n = 23		Sureyyapasa Protocol Group Failure (Readmission to Hospital), n = 17	
	n	%	n	%
Male	17	73.9	13	76.5
Hypertension	17	73.9	11	64.7
Diabetes Mellitus	6	26.1	6	35.3
Hearth failure	8	34.8	5	29.4
Coronary artery disease	10	43.5	8	47.1
Long-term Oxygen user	16	69.6	10	58.8
Home NIV user	10	43.5	6	35.3
Steroid use in AECOPD	19	82.6	6	35.3
Antibiotic use in AECOPD	23	100.0	14	82.4
Sputum pathogen	12	100.0	9	90.0
Sixth day discharge and rehospitalization in the first 28th day	21	91.3	9	52.9
Bradycardia	0	0.0	1	5.9
Home NIV device problem	1	4.3	0	0.0
Ileus	0	0.0	1	5.9
Pneumonia	0	0.0	5	29.4
Discharge EOS 2%	0	0.0	1	33.3
Discharge EOS100	1	33.3	2	66.7
Discharge EOS300	0	0.0	0	0.0

AECOPD, acute exacerbation of chronic obstructive pulmonary disease; EOS, eosinophilia; NIV, noninvasive mechanical ventilation.

eosinophilia (2%). In 4 studies on eosinophilic AECOPD, corticosteroid treatment had a better treatment response, and also intensive care and ward hospitalization rates were lower, noninvasive mechanical ventilation response was better.[15,24,27] In the current study, ICU-admitted AECOPD patients were excluded. Bafadhel et al[28] evaluated peripheral blood eosinophilia in AECOPD. Treatment failures were hospitalization due to AECOPD within 90 days, re-treatment, and death. In that study, patients were categorized by prednisolone treatment and peripheral blood eosinophil ratio (<2% or ≥2%). Non-prednisolone group failed in 66% of patients with a blood eosinophil ratio of ≥2%, while prednisolone group failed in 11% of patients. In that study, patients with a blood eosinophil ratio less than 2% did not differ significantly in treatment failure.[28] In 2018, Aksoy et al[27] reported that 86% of eosinophilic AECOPD patients were followed up through outpatient clinics, 10% of patients were hospitalized in inpatient clinics, and 4% were treated at ICU. The eosinophilic endotype, defined as peripheral blood eosinophil ≥2%, was found in 20% of ward patients, 9.6% of ICU patients, and 5% of outpatients with chronic respiratory failure and home noninvasive mechanical ventilation. A study in 2019 by Müllerová et al[29] recommended multiple inhalers (including inhaler corticosteroid) for exacerbation patients with 150 eosinophil cells/mL and at least 2 severe COPD exacerbations or 1 hospitalization due to COPD exacerbation. In the current study, 28 out of 96 (29%) in the SPG patients received steroids because they had ≥2% peripheral blood eosinophil ratio, whereas 24 out of 95 (26%) in the CG patients had ≥2% peripheral blood eosinophils and 80 patients (84%) were treated with steroids. Also in the 28 patients who were readmitted due to AECOPD, only 8 patients (28.5%) were in the SPG group. The "neutrophilic endotype" increases as COPD exacerbations increase in number and severity.[16,24,27] In Iran, in 2017, patients with NLR ≥4 had a higher mortality rate (9.5% vs. 24.0%, $P = .001$). In the same study, PLR and lymphocyte-to-monocyte ratios were investigated, but no significant difference was found; however, a high NLR was the first positive indicator of in-hospital mortality in AECOPD patients.[30] Recent clinical studies link a high NLR and leukocyte count to cardiovascular disease severity, mortality, and prognosis.[31] Patients with stable COPD and AECOPD had significantly higher NLR values than healthy subjects. In that study, stable COPD patients had NLR values similar to AECOPD patients, and researchers could not find a correlation between NLR values and disease severity. This study revealed a significant correlation between CRP and NLR.[9] In Korea, the study including 148 AECOPD patients, stable COPD, and healthy controls had significantly different NLRs ($P = .001$).[32] In a study of 100 cases of AECOPD, 80 healthy subjects were examined for NLR during the diagnosis, and also NLR was assessed in the stable period for COPD, 3 months after diagnosis. The NLR, CRP, leukocytes, and erythrocyte sedimentation rate correlate during COPD exacerbation.[33] In the same study, AECOPD patients had higher NLR than stable COPD patients and healthy subjects.[33] In the current literature, numerous studies indicated correlation between NLR and CRP. C-reactive protein evaluation is more expensive than hemogram. Cost and feasibility motivate physicians' use of NLR over CRP in AECOPD. Neutrophil–lymphocyte ratio is an easy-to-access, inexpensive biomarker of AECOPD that can help hospitalization decisions.[9,31-33] In our study, AECOPD treatment was based on NLR and blood eosinophil ratio and the SPG's NLR values decreased as expected after treatment. Platelet/MPV and PLR ratios did not differ between groups, except the fifth day PLR. Tanrıverdi et al[34] researched the significance of NLR in AECOPD due to infectious causes and found that NLR was elevated in bacterial infections, with a cutoff value of 11.5, achieving 61% sensitivity and 58% specificity. Procalcitonin is more specific for bacterial infections, but its high cost makes routine use difficult.[34] Neutrophil–lymphocyte ratio can be used more broadly than CRP because CRP is elevated also in noninfectious and viral diseases and requires laboratory equipment and more time.

Our study involves a single center. However, the study center is a specific training and research hospital for chest diseases. Additionally, the SPG for AECOPD with distinct endotypes cannot be applied universally. In the meantime, our research findings can be applied to a larger sample of AECOPD patients with various endotypes.

CONCLUSION

The rate of readmission of COPD patients within 28 days of discharge is reduced if AECOPD is treated with steroids when the blood eosinophil ratio is ≥2% and antibiotics when NLR is ≥4. The SPG reduces the need for steroids and antibiotics. The SPG patients had 90% less re-exacerbation at 28 days. Sureyyapasa protocol group reduced AECOPD steroid use. Neutrophil–lymphocyte ratio was used for antibiotic prescribing and peripheral blood eosinophil ratio was used for steroid selection. This study did not support standardizing treatment using the PBE and NLR to shorten hospital stays for AECOPD patients; however, the study showed that reduced use of antibiotic and steroid in AECOPD patients. This study adds objective data to steroid and antibiotic initiation guidelines for hospitalized AECOPD.

Ethics Committee Approval: This study was approved by Ethics committee of the University of Health Sciences Süreyyapaşa Chest Diseases and Thorasic Surgery Training and Research Hospital (Approval No: 116, Date: 2017).

Informed Consent: Verbal and written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review
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Author Contributions: Concept – N.K.K., Z.K.; Design – N.K.K., Z.K.; Supervision – N.K.K.; Materials – N.K.K., A.G.; Data Collection and/or Processing – N.K.K., K.A.; Analysis and/or Interpretation – N.K.K., B.G.; Literature Search – N.K.K., H.T.; Writing – N.K.K., Z.K.; Critical Review – N.K.K., Z.K.

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