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Original Article

Factors Associated with Increasing Costs in Severe Chronic Obstructive Pulmonary Disease Exacerbation: Turkish Thoracic Society Chronic Obstructive Pulmonary Disease Assembly

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Abstract

OBJECTIVE: Chronic obstructive pulmonary disease (COPD) that is the third leading cause of death in the world is one of the main economic burden. The cost is primarily due to COPD exacerbations and hospitalizations. We aimed to determine the factors associated with increasing costs in severe COPD exacerbation.

MATERIAL AND METHODS: It was a multicenter and prospective observational recording study. 294 patients who severe COPD exacerbation were included in the study. An amount of more than 429.58 euros was accepted as increasing costs (IC). Factors associated with IC were determined by regression analysis.

RESULTS: Mean age was 69.90 ± 9.79/years (minimum: 40 maximum: 95), mean costs were 594.9 ± 70.9 euros. About 83.7% of the patients were male, 24.1% (71) were active smokers, and 81% (238) had at least 1 comorbidity. Factors associated with IC in the regression analysis were delay of discharge (due to prolonged consultation), antibiotic use longer than 7 days, need to enteral/parenteral feeding, application of pulmonary rehabilitation (physiotherapy) at hospitalization, and refusal to be discharged.

CONCLUSION: The increasing costs in severe COPD exacerbation depends not only treatment but also the patient's social status and hospital-related factors. We think that the cost of severe COPD exacerbation can be reduced by interventions on interchangeable factors such as patient's social status and hospital-related factors.

KEYWORDS: COPD, severe exacerbation, costs, discharge, antibiotic, nutrition, pulmonary rehabilitation

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a multicausal global health crisis. According to World Health Organization (WHO), chronic obstructive pulmonary disease COPD is one of the most common noncommunicable diseases.[1] The prevalence of chronic pulmonary disease, which also includes COPD, increased by 40% from 1990 to 2017, and currently COPD is the third major cause of mortality.[1,2] The main cause of mortality is exacerbations. Every exacerbation is related to decrease in pulmonary function, deterioration in quality of life, and economic burden (increased cost).[3] Acute exacerbation of COPD (AECOPD) is defined as an acute event that worsens symptoms and is expressed as clinical instability.[3] Acute exacerbation of COPD can range in severity from the form that can be treated as an outpatient to the form that requires intensive care, and it is mainly triggered by airway infections or environmental exposure (dust and gases).[3] Although a definition of exacerbation has been made, it does not contain clear criteria. For this reason, the perception of the severity of exacerbation by both patients and healthcare providers varies. But the process of treatment in the hospital depends not only on the

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characteristics of the disease but also on the characteristics of the hospital and social environment. Therefore, all these components affect the cost associated with treatment. Acute exacerbation of COPDs account for a prominent amount of the direct costs associated with COPD.[4] In the United States, the direct cost of COPD is estimated at $29.5 billion, and the indirect cost is estimated at $20.4 billion.[5]

The cost varies from country to country. For example, in 2011, the cost per exacerbation was $269 in the United States, while in 2006 it was $649 in Canada.[6,7] The mean cost for hospitalized AECOPD was $3164 in Italy (2013), while it was $18.120 in the United States (2011).[6,8] The variability of costs among countries is remarkable, even if the currency and cost year are different.

In this study, we aimed to determine the factors associated with increased costs in severe COPD exacerbations.

MATERIAL AND METHODS

This was a multicenter prospective observational recording study that was approved by the Gazi University Faculty of Medicine Ethics Committee (Approval No: 687/2018, Date: 2018) with respect to the ethical standards specified in the 1964 Declaration of Helsinki. Informed consent was obtained from all patients.

Patient Selection

Between October 1, 2018, and September 30, 2019, all severe COPD exacerbation patients who were hospitalized in an emergency or outpatient clinic were enrolled. A total of 294 patients from 9 centers (7 university hospitals and 2 training and research hospitals) were included in the study.

Inclusion criteria were the patients who were aged >40 years, had COPD diagnosis (according to GOLD 2017)[9] of at least 1 year, had severe exacerbation,[9] and hospitalized from an emergency department or outpatient clinic. Exclusion criteria were patients who were aged <40 years, had no pulmonary function test in the last year, were hospitalized from the emergency department to the intensive care unit, and were transferred from the intensive care unit to the ward, with stable COPD, and hospitalized for another reason such as pneumonia, heart failure, and lung cancer.

In the study, GOLD 2017 was accepted as a reference for COPD diagnosis, staging, COPD exacerbation definition, exacerbation treatment, criteria for transfer to intensive care unit, and discharge criteria.[9]

Main Points

- When considering factors affecting cost, it is not enough to use only laboratory and clinical parameters.
- In particular, the total cost of patients with severe COPD exacerbation in the hospital was related to the treatment costs, as well as social situation of the patient and the facilities of the hospital.
- Therefore, this study revealed the necessity of multifactorial evaluation when it comes to total cost calculation.

The parameters in the recording form are shown in Figure 1. Hemogram, biochemistry, including liver and kidney functions, C-reactive protein, arterial blood gas, chest x-ray, and electrocardiogram were examined in all patients on the day of hospital admission and, if necessary, during follow-up. Patient declaration and used drugs were taken into account in comorbidity screening. The STOP-BANG questionnaire was applied to all patients for the risk assessment of obstructive sleep apnea. Vitamin D, cardiac enzymes, *N*-terminal pro-brain natriuretic peptide (NT-proBNP), echocardiography (ECO), and hemoglobin A1c (HbA1c) were examined in accordance with the conditions of each center and if necessary. If the clinician found it necessary, D-dimer, thorax computed tomography (CT), thorax CT angiography, bronchoscopy, and consultation (with other clinics) were performed. The follow-up of the patients ended in 4 ways: discharge, transfer to intensive care, transfer to another department, or exitus. The length of hospital stay was accepted as the total time in both the emergency room and the ward.

Total hospitalization costs were obtained from the data processing units of the centers participating in the study. Costs were recorded in Turkish lira, written down on the euro equivalent of that date. Because the cost ratios do not show a normal distribution, the median value corresponding to the 50% percentile is the limit. Values above 50% were accepted as increased cost. The cost calculation was made over the total cost. In order to determine the factors affecting the cost, the patients were examined under 2 groups. These are normal cost and increased cost groups.

Statistical Analysis

The statistical analyses were performed using the Statistical Package for the Social Sciences Statistics software, version 23.0 (IBM Corp.; Armonk, NY, USA). In the statistical analysis, categorical variables are given as numbers and percentages, and continuous variables are presented as mean ± standard deviation (SD) and as median (minimum–maximum value) for descriptive analyses. In the data that does not fits the normal distribution, the Mann–Whitney *U*-test was used for comparative analysis between the 2 independent groups, and the independent sample *t*-test was used for the data that fit the normal distribution. Comparison analyses for categorical variables between separate groups were done by the chi-square test. Logistic regression analysis was used to determine the factors affecting the increased cost. Variables with $P < .05$ in the univariate analysis were entered into multivariate logistic regression analysis.

RESULTS

This study included 294 COPD patients with the mean age of 69.90±9.79 (minimum: 40, maximum: 95) from 9 hospitals. About 246 (83.7%) of the patients were male, and 48 (16.3%) were female. 86 (30.4%) had low, 177 (62.5%) had medium, and 20 (7.1%) had high socioeconomic status. Among them, 21 (7.1%) never smoked, 190 (64.6%) were ex-smokers, 12 (4.1%) were passive smokers, and 71 (24.1%) were active smokers. 193 (65.6%) had biomass exposure. 56 (19%) patients had at least 1 comorbid disease. 171 (58.1%) patients had LTOT, and 227 (77.2%) patients were using bi-level positive airway pressure (BPAP) at home. Looking at STOP-BANG

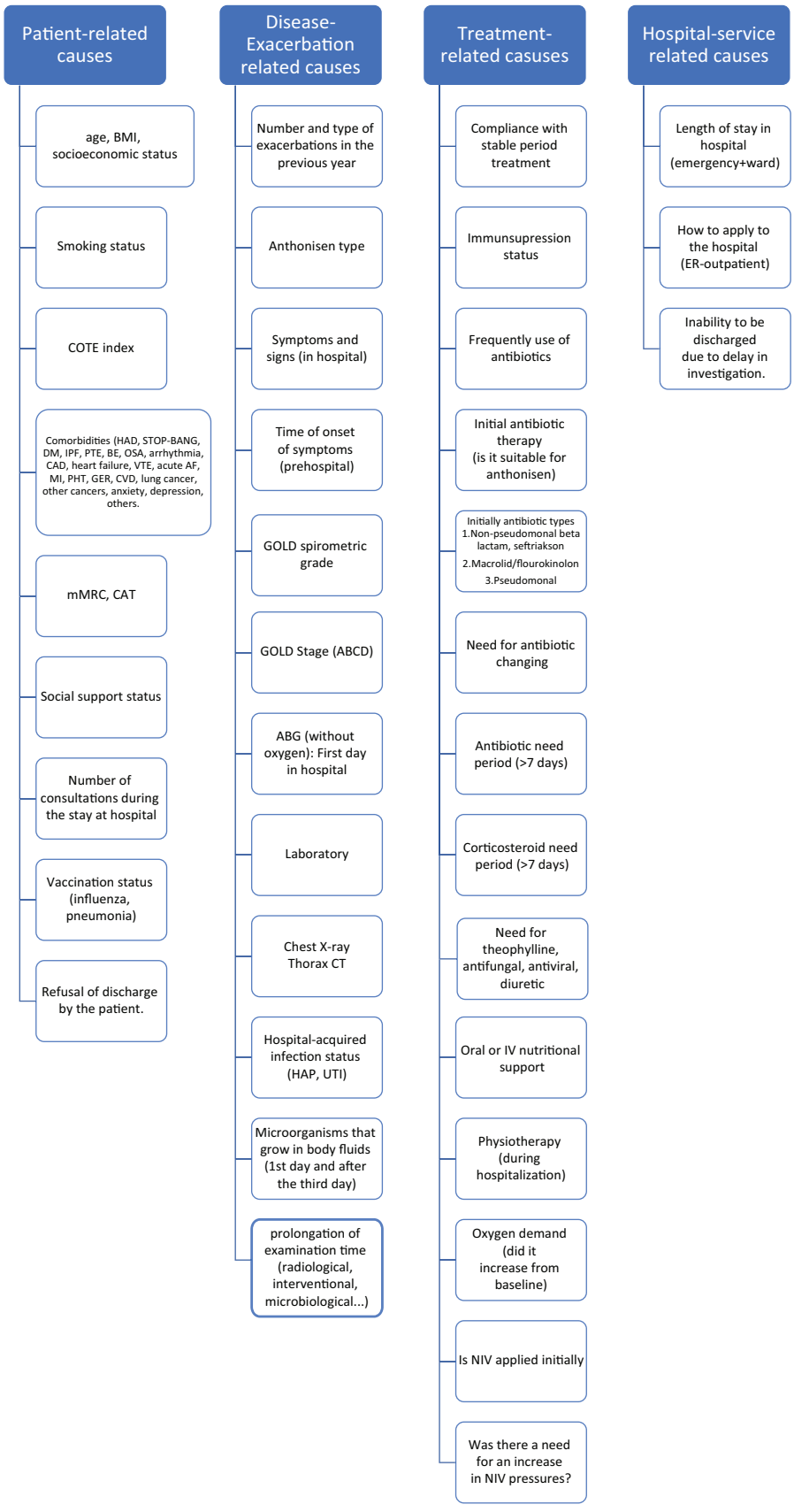

Figure 1. The parameters in the recording form. ABG, arterial blood gases; AF, atrial fibrillation; BE, bronchiectasis; BMI, body mass index; CAD, coronary artery disease; CAT, COPD Assessment Test; CT, computed tomography; CVD, cerebrovascular disease; DM, diabetes mellitus; ER, emergency room; GER, gastroesophageal reflux; HAD, Hospital Anxiety and Depression Scale; HAP, hospital-acquired pneumonia; IPF, idiopathic pulmonary fibrosis; IV, Intravenous; MI, myocardial infarction; mMRC; modified Medical Research Council; NIV, noninvasive ventilation, OSA, obstructive sleep apnea; PHT, pulmonary hypertension; PTE, pulmonary thromboembolism; UTI, urinary tract infection; VTE, venous thromboembolism.

Table 1. Relationship Between Main Demographic Characteristics of Patients and Increased Cost

Parameters	Total Patient*	Normal Cost Patient	Increased Cost Patient**	*P*
Age (years), n = 294 n(%)				
Mean ± SD	69.90 ± 9.79	n = 147	n = 147	.052[1]
Median (minimum–maximum)	69.00 (40-95)	68.18 ± 10.01	70.40 ± 9.47	
Age range, n = 294 n (%)				
<65 years old	88 (29.9)	52 (59.1)	36 (40.9)	**.042**[2]
>64 years old	206 (70.1)	95 (46.1)	111 (53.9)	
Sex, n = 294, n (%)				
Male	246 (83.7)	127(51.6)	119(48.4)	0.207[2]
Female	48 (16.3)	20(41.7)	28(58.3)	
BMI, n = 286, n (%)				
BMI <25	156 (54.5)	78 (50)	78 (50)	0.814[2]
BMI 25-30	75 (26.2)	38 (50.7)	37 (49.3)	
BMI >30	55 (19.2)	25 (45.5)	30 (54.5)	
SES n = 283				
Low	86 (30.4)	41 (47.7)	45 (52.3)	.370[2]
Medium	177 (62.5)	88 (49.7)	89 (50.3)	
High	20 (7.1)	13 (65)	7 (35)	
Cigarette n = 294 n (%)				
Never smoked	21 (7.1)	6 (28.6)	15 (71.4)	**<.001**[2]
Ex-smoker	190 (64.6)	83 (43.7)	107 (56.3)	
Passive smoker	12 (4.1)	5 (41.7)	7 (58.3)	
Active smoker	71 (24.1)	53 (74.6)	18 (25.4)	
Cigarette n = 294, n (%)				
Nonactive smoker	223 (75.9)	94 (42.2)	129 (57.8)	**<.001**[2]
Active smoker	71 (24.1)	53 (74.6)	18 (25.4)	
Biomass n = 294, n (%)				
None	193 (65.6)	104 (53.9)	89 (46.1)	.065[2]
Yes	101 (34.4)	43 (42.6)	58 (57.4)	
Comorbidity n = 294 n (%)				
None	56 (19)	34 (60.7)	22 (39.3)	.075[2]
Yes	238 (81)	113 (47.5)	125 (52.5)	
Influenza vaccine n = 294, n (%)				
None	230 (78.2)	126 (54.8)	104(45.2)	**.002**[2]
Yes	64 (21.8)	21 (32.8)	43(67.2)	
Pneumonia vaccine n = 294, n (%)				
None	228 (77.6)	121 (53.1)	107(46.9)	**.050**[2]
Yes	66 (22.4)	26 (39.4)	40 (60.4)	
LTOT n = 294, n (%)				
None	171 (58.1)	110 (64.3)	61(35.7)	**<.001**[2]
Yes	173 (41.9)	37 (30.1)	86 (69.9)	
BPAP n = 294, n (%)				
None	227 (77.2)	130 (57.3)	97 (42.7)	**<.001**[2]
Yes	67 (22.8)	17 (25.4)	50 (74.6)	
Stop-BANG n = 268, n (%)				
Low	40 (14.9)	21 (52.5)	19 (47.5)	**.015**[2]
Medium	134 (50)	74 (55.2)	60 (44.8)	
High	94 (35.1)	34 (36.2)	60 (63.8)	
Refusal to discharge n = 294, n (%)				
Yes	19 (6.4)	5 (26.3)	14 (73.7)	**.033**[2]
None	275 (93.6)	142 (51.6)	133 (48.4)	
Caregiver n = 294, n (%)				
None	95 (32.4)	58 (61.1)	37 (38.9)	**.009**[2]
Yes	199 (67.6)	89 (44.7)	110 (55.3)	

BMI, body mass index; BPAP, bi-level positive airway pressure; SES, socioeconomic status.
*Column percentage.**Line percentage.[1]Student's *t*-test.[2]Chi-square test.

scores, 40 (14.9%) patients had low scores, 134 (50%) had medium scores, and 94 (35.1%) patients had high scores. 64 (21.8%) patients had received the influenza vaccine within the last year. 66 (22.4%) patients had pneumococcal vaccination. 95 (32.4%) patients did not have a caregiver at home. Demographic characteristics are shown in Table 1.

The average cost per patient is 594.9 ± 70.9 euros (minimum: 22.4 euros, maximum: 7224.45 euros). Costs above 429.58 euros are classified as increased cost, and those below are classified as normal costs. Because the cost ratios do not show a normal distribution, the median value corresponding to 50% is the limit (Table 2).

Factors that increase the cost of hospitalization due to COPD exacerbation are examined under 4 main headings. These are patient-related factors, exacerbation-related factors, treatment-related factors, and hospital-related factors.

Patient-Related Factors

Patients of 65 years and over (P = .042), active smoking (P < .001), extrapulmonary malignancy (P = .02), LTOT at home (P < .001), BPAP at home (P < .001), not getting influenza vaccine (P = .002), not getting pneumococcal vaccine (P = .05), high risk in STOP-BANG (P = .015), refusing to be discharged (although the patient can be discharged) (P = .003), and lack of caregiver (P = .009) were the risk factors that related to increased cost.

Sex (P = .207), body mass index (BMI) (P = .814), biomass (P = .065), pulmonary embolism (PE) (P = .821), TB history (P = .515), bronchiectasia (P = .670), lung cancer (P = .077), and anemia (P = .409) vs. ejection fraction (EF) on the echocardiography lower than 40% (P = .774) were not related to increasing cost. Table 3 shows the logistic regression model of increased costs associated with patient-related factors. According to this, passive smoking was related to increased cost.

Exacerbation-Related Factors

History of 2 or more exacerbations in the last 1 year (P = .007), 1 or more severe exacerbations in the last 1 year (P < .001), GOLD-D (P < .001), FEV1 < 30% (P < .001), high procalcitonin (P < .001), low albumin/protein ratio (P = .04), pneumonia on chest x-ray (P < .001), pleural effusion on chest x-ray (P < .001), mass on chest x-ray (P = .019), pneumonia on thorax CT scan (P = .01), emphysema on thorax CT scan (P = .041), mass on thorax CT scan (P = .002), and hospital-acquired pneumonia (P = .006) were the risk factors that related to increased cost. Table 3 shows the logistic regression model of increased cost for associated exacerbation-related factors. Gold stage, procalcitonin, mass on chest x-ray, mass on thorax CT scan, and albumin/protein ratio variables were not included in the logistic regression model because they disturbed the model fit while creating the model.

Treatment-Related Factors

Frequently using antibiotic (P = .001), need to change antibiotics during hospitalization (P < .001), treatment antibiotics for more than 7 days (P < .001), use of corticosteroids for more than 7 days (P < .001), treatment combination of SABA/SAMA for more than 3 days (P < .001), need to antiviral treatment (P = .006), need to diuretic treatment (P < .001), increasing in oxygen demand during hospitalization (P < .001), need to NIMV during hospitalization (P < .001), need to increase NIV pressure during hospitalization (P < .001), need to Enteral/Parenteral feeding (P < .001) vs. applied of physiotherapy during hospitalization (P < .001) were the risk factors for increased cost. Table 3 shows the logistic regression model of increased costs associated with treatment-related factors.

Hospital-Related Factors

Hospitalization longer than 14 days (P < .001), hospitalization from the emergency department (P = .048), and delay in discharge (prolonged consultation) (P < .001) were associated with increased cost. Table 3 shows the logistic regression model of increased costs associated hospital-related factors.

The results of logistic regression analysis of all factors that have an effect on the increased cost are shown in Table 4. When the factors that were found to be significant here were modeled for the second time, it was found that the most effective factors on the increased cost were delay in discharge (due to prolonged consultation) [P = .001, OR (95% CI): 6.24 (2.09-18.59)], antibiotic use longer than 7 days [P < .001, OR (95% CI): 5.38 (2.99-9.68)], need for enteral/parenteral feeding [P = .001, OR (95% CI): 4.49 (1.88-10.72)], application of physiotherapy at hospitalization [P < .001, OR (95% CI): 2.94 (1.62-5.34)] and refusal to be discharged [P = .013, OR (95% CI): 4.57 (1.39-15.11)].

DISCUSSION

This study has shown that there are many factors related to increased cost for hospitalized patients with severe COPD exacerbation. The factors most associated with increased cost were delay of discharge (due to prolonged consultation), antibiotic use longer than 7 days, need for enteral/parenteral feeding, application of pulmonary rehabilitation (physiotherapy) at hospitalization, and refusal to be discharged.

In studies to date, the cost of AECOPD has been calculated, but the factors that increased cost have not been investigated in detail.

Table 2. Distribution Between Groups According to Cost

Cost Group	n	Mean	SS	Median	Minimum	Maximum
Normal cost	147	220.15 euros	106.74 euros	197.33 euros	22.4 euros	427.82 euros
Increased cost	147	969.58 euros	893.14 euros	668.67 euros	431.34 euros	7224.45 euros
Total	294	594.87 euros	737.60 euros	429.58 euros	22.4 euros	7224.45 euros

Table 3. Logistic Regression Model of Increased Cost Associated Patient-Related Factors, Exacerbation-Related Factors, Treatment-Related Factors, and Hospital-Related Factors

			OR (95% CI)	
Patient-Related Factors	***P***	**OR**	**Lower**	**Upper**
65 years and over (ref: <65 years)	.444	0.74	0.34	1.60
Caregiver (ref: none)	.363	1.44	0.66	3.14
Influenza vaccine (ref: none)	.898	1.07	0.39	2.95
Pneumococcal vaccine (ref: none)	.317	1.73	0.59	5.02
Extrapulmonary cancer (ref: none)	.951	1.04	0.29	3.78
Refusal to be discharged (ref: accept)	**.051**	4.61	0.99	21.42
Active smoker (ref)	.164	1		
Passive smoker	.038	5.24	1.10	25.03
Ex-smoker	.200	1.81	0.73	4.48
Never smoked	.227	3.07	0.50	18.98
LTOT (ref: none)	.090	2.09	0.89	4.89
BPAP (ref: none)	.277	1.85	0.61	5.59
Stop-BANG low	.091	1		
Stop-BANG middle	.296	0.57	0.19	1.65
Stop-BANG high	.653	1.30	0.42	4.08
EF (%)	.528	0.99	0.95	1.03
Exacerbation-Related Factors				
Average number of exacerbations in the last 1 year	.155	1.12	0.96	1.30
Average number of severe exacerbations in the last 1 year	.564	1.12	0.77	1.64
Pleural effusion on chest x-ray (ref: none)	.054	4.40	0.98	19.84
Pneumonia on chest x-ray (ref: none)	.638	0.76	0.23	2.44
Pneumonia (CT) (ref: none)	.217	2.13	0.64	7.04
Emphysema (CT) (ref: none)	.544	0.73	0.26	2.04
Hospital-acquired pneumonia (ref: none)	.217	2.14	0.64	7.14
GOLD spirometry grade 1	.078	1		
GOLD spirometry grade 2	.113	0.12	0.01	1.64
GOLD spirometry grade 3	.773	0.69	0.06	8.40
GOLD spirometry grade 4	.515	0.44	0.04	5.15
Treatment-Related Factors				
Frequently use of antibiotics (ref: none)	.220	1.48	0.79	2.74
Treatment antibiotics for more than 7 days (ref: none)	**<.001**	3.88	1.95	7.75
Treatment oral/IV corticosteroids for more than 7 days (ref: none)	.803	1.11	0.50	2.45
Treatment combination of SABA/SAMA for more than 3 days (ref: none)	.372	1.35	0.70	2.59
Antiviral treatment (ref: none)	.261	1.99	0.60	6.56
Diuretic treatment (ref: none)	.827	0.92	0.44	1.93
Increase in oxygen demand during hospitalization (ref: none)	.309	1.45	0.71	2.94
Need to NIV during hospitalization (ref: none)	.026	2.41	1.11	5.24
Need to increase NIV pressure during hospitalization (ref: none)	.209	2.24	0.64	7.88
Need to enteral/parenteral feeding (ref: none)	**.007**	3.87	1.45	10.31
Application of physiotherapy during hospitalization (ref: none)	**.003**	2.54	1.38	4.65
Hospital Related Factors				
Hospitalization from the emergency (ref: outpatient)	.054	1.70	0.99	2.91
Delay in discharge (due to consultation) (ref: none)	**<.001**	5.31	2.11	13.36

BPAP, bi-level positive airway pressure; CT, computed tomography; EF, ejection fraction; IV, intravenous; LTOT, long-term oxygen treatment; NIV, noninvasive ventilation; SABA, short-acting beta-agonists; SAMA, short-acting muscarinic antagonists; STOP-BANG, Score for Obstructive Sleep Apnea.

Table 4. Logistic Regression Analyses of the Most Effective Factors on the Increased Cost

	LR Model 1			LR Model 2			LR Model 3	
	OR (95% CI)	***P***		**OR (95% CI)**	***P***		**OR (95% CI)**	***P***
≥65 years	0.74 (0.34-0.60)	.444	Average Number of Exacerbations in the Last 1 Year	1.12 (0.96-1,.0)	.155	Frequently Using of Antibiotics (ref:none)	1.48 (0.9-2.74)	.22
Caregiver	1.44 (0.66-3.14)	.363	Average Number of Severe Exacerbations in the Last 1 Year	1.12 (0.77-1.64)	.564	Using oral/IV corticosteroids for more than 7 days (ref: none)	**3.88 (1.95-7.75)**	**<.001**
Influenza vaccination	1.07 (0.9-2.5)	.898	Pleural effusion (chest x-ray)	4.40 (0.98-19.84)	.054	Using oral/IV corticosteroids for more than 7 days (ref: none)	1.11 (0.50-2.45)	.803
Pneumococcal vaccination	1.73 (0.9-5.02)	.317	Pneumonia (chest x-ray)	0.76 (0.23-2.44)	.638	Using combination of SABA/ SAMA for more than 3 days (ref: none)	1.35 (0.70-2.59)	.372
Extrapulmonary malignancy	1.04 (0,.9-3.78)	.951	Pneumonia (CT)	2.13 (0.64-7,04)	.217	Antiviral treatment (ref: none)	1.99 (0.60-6.56)	.261
Refusal to be discharged	4,.1 (0.99-21.42)	.051	Emphysema (CT)	0,73 (0,26-2.04)	.544	Diuretic treatment (ref: none)	0.92 (0.44-1.93)	.827
Active smoker	1	.164	Hospital-acquired pneumonia	2.14 (0.64-7.14)	.217	increase in oxygen demand (ref: none)	1.45 (0.71-2.94)	.309
Passive smoker	5.24 (1,.0-25.03)	.038	GOLD spirometry grade 1		.078	Need to NIV (ref: none)	2.41 (1.11-5.24)	.026
Ex-smoker	1.81 (0.73-4.48)	.200	GOLD spirometry grade 2	0.12 (0.01-1.64)	.113	Need to increase NIV pressure (ref: none)	2,.4 (0.64-7.88)	.209
Never smoked	3.07 (0.50-18.98)	.227	GOLD S spirometry grade 3	0.69 (0.06-8.40)	.773	Need to enteral/Parenteral feeding (ref: none)	**3.87 (1.45-10.31)**	**.007**
LTOT	2.09 (0.89-4.89)	.090	GOLD spirometry grade 4	0.44 (0.04-5.15)	.515	Physiotherapy (ref: none)	**2.54 (1.38-4.65)**	**.003**
BPAP	1.85 (0.61-5.59)	.277				Hospitalization from the emergency (ref: outpatient)	1.70 (0.99-2.1)	.054
Stop-BANG low	1	.091				Delay in Discharge (due to consultation) (ref: none)	**5.31 (2.11-13.36)**	**<.001**
Stop-BANG middle	0.57 (0.19-1.65)	.296						
Stop-BANG high	1.30 (0.42-4.08)	.653						
EF (%)	0.99 (0.95-1.03)	.528						

BPAP, bi-level positive airway pressure; CT, computed tomography; EF, ejection fraction; LTOT, long-term oxygen therapy; NIV, noninvasive ventilation; STOP-BANG, Score for Obstructive Sleep Apnea.

Goossens et al showed that early discharge was cost effective than in hospital treatment for 7 days.[10] But degree of clinical improvement was greater in patients treated in hospital for 7 days. In conclusion of this study, the authors said that there is no clear evidence was found to decide that both of treatment was less costly or more effective.[10] Prolonged hospitalization is associated not only the existence of comorbidities[11] but also complicated discharge planning that requires additional home care or caregiver organizations.[12] The presence of comorbidity is important not only in terms of treatment management but also in terms of accessing other branches that will evaluate the comorbid condition. Just like in our country, in places where the number of patients is high, consultation services may be disrupted. In addition, factors such as the patient's problem of transportation to the hospital after discharge, unsuitable health condition to go out of the home, or difficulty reaching the doctor sometimes necessitate an elective consultation in the hospital.

However, if the consultation is delayed, possible investigations are delayed, and every hour spent in the hospital adds to the cost. In our study, delayed discharge due to prolonged/incomplete consultation was most associated with increased cost.

Antibiotics are generally used in the management for COPD during hospitalization, as infection is one of the main etiologic factors for AECOPD.[13] Li et al[14] reported that antibiotic use (0.086; 95% CI 0.131-0.178) were significantly (P = .001) associated with total hospitalization costs. In a study from Turkey, it was found that hospital antibiotic treatment ($111.6 ± 77.3; 86.6 ± 60.0) is one of the main reasons (P < .001) for increasing the cost.[15] Even under normal conditions, antibiotic treatment increases the cost. Therefore, if the duration of antibiotic use increases due to antibiotic resistance and/or hospital-acquired infections, the cost increases even more.

Nutrition is one of the important factors in COPD exacerbation management and has become popular in recent years. In the study of Zhang et al,[16] standard enteral nutrition significantly improved nutritional status and immunological functioning, reduced inflammatory markers, and improved cardiopulmonary function of AECOPD patients with respiratory failure. Wang et al[17] showed that enteral and/or parenteral nutrition support can successfully improve the pulmonary function of COPD patients who have respiratory failure and can reduce acute inflammation and oxidative stress. No data were available on the cost of enteral or parenteral nutrition administered to hospitalized patients with COPD exacerbations. In our study, enteral and parenteral nutrition were found to be associated with increased cost.

Pulmonary rehabilitation is stated to be a safe intervention during a COPD exacerbation.[18] Exercise, breathing techniques, education, and psychosocial support are essential components of rehabilitation.[18] Many studies have shown that rehabilitation interventions applied during hospitalization prevent a decrease in lower extremity muscle function, balance, and exercise performance and facilitate recovery afterward.[19-23] No data were available on the cost of pulmonary rehabilitation initiated during hospitalization. In our study, pulmonary rehabilitation practices initiated during hospitalization were associated with increased cost.

Early discharge is the main goal for all diseases requiring hospitalization because the longer the hospital stay, the higher the risk and cost of hospital-acquired infections. However, one of the factors affecting the discharge decision is the social status of the patient. Considering the relationship of COPD with poverty and poor socioeconomic status, we have to acknowledge the existence of a group of patients in underdeveloped and developing countries who have concerns about home care, nutrition, and heating. Patients with these and similar concerns refuse to be discharged, even though they are in the discharge state. However, considering that each day spent in the hospital increases the cost of hospitalization, we can conclude that refusing to be discharged also increases the cost. In our study, refusal to discharge was identified as one of the factors associated with increased cost.

The strengths of our work can be listed as follows: (1) It is a multicenter (representing a large part of the country) and prospective study. (2) The factors affecting the cost were not only limited to clinical and laboratory parameters but also the patient and hospital aspects of the event. The weaknesses of our study are as follows: (1) Since the access conditions for some laboratory tests are not standard in every hospital, there is a small amount of missing data. (2) Although the number of patients included in the study was large, the data here cannot be generalized to all COPD patients because the centers where the study was conducted are tertiary care hospitals. (3) The sociodemographic and administrative differences of each country, even the different regions within each country, may affect the results.

In this study, which is thought to represent a large part of the country, it was concluded that not only the laboratory or clinical parameters but also the social characteristics of the patients, the facilities of the hospital, and the working system affect the cost. Therefore, this study revealed the necessity of multifactorial evaluation when it comes to total cost calculation. Considering the occupancy of hospitals in densely populated areas, the delay of procedures such as consultation and radiological imaging due to in-hospital workload is a known but not documented fact. In order to find solutions to these issues, we think that pilot studies should be conducted for each region of the countries, and they should determine their own internal dynamics.

Ethics Committee Approval: This study was approved by Ethics Committee of Gazi University (Approval No: 687/2018, Date: 2018).

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

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