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Prognostic marker for severe acute exacerbation of chronic obstructive pulmonary disease: analysis of diffusing capacity of the lung for carbon monoxide (D_{LCO}) and forced expiratory volume in one second (FEV_1)

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Abstract

Background: It is important to assess the prognosis of patients with chronic obstructive pulmonary disease (COPD) and acute exacerbation of COPD (AECOPD). Recently, it was suggested that diffusing capacity of the lung for carbon monoxide (D_{LCO}) should be added to multidimensional tools for assessing COPD. This study aimed to compare the D_{LCO} and forced expiratory volume in one second (FEV_1) to identify better prognostic factors for admitted patients with AECOPD.

Methods: We retrospectively analyzed 342 patients with AECOPD receiving inpatient treatment. We classified 342 severe AECOPD patients by severity of D_{LCO} and FEV_1 (\leq vs. $>$ 50% predicted). We tested the association of FEV_1 and D_{LCO} with the following outcomes: in-hospital mortality, need for mechanical ventilation, need for intensive care unit (ICU) care. We analyzed the prognostic factors by multivariate analysis using logistic regression. In addition, we conducted a correlation analysis and receiver operating characteristic (ROC) curve analysis.

Results: In multivariate analyses, D_{LCO} was associated with mortality (odds ratio = 4.408; 95% CI 1.070–18.167; $P=0.040$) and need for mechanical ventilation (odds ratio = 2.855; 95% CI 1.216–6.704; $P=0.016$) and ICU care (odds ratios = 2.685; 95% CI 1.290–5.590; $P=0.008$). However, there was no statistically significant difference in mortality rate when using FEV_1 classification ($P=0.075$). In multivariate linear regression analyses, D_{LCO} ($B = -0.542 \pm 0.121$,

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$P < 0.001$) and FEV_1 ($B = -0.106 \pm 0.106$, $P = 0.006$) were negatively associated with length of hospital stay. In addition, D_{LCO} showed better predictive ability than FEV_1 in ROC curve analysis. The area under the curve (AUC) of D_{LCO} was greater than 0.68 for all prognostic factors, and in contrast, the AUC of FEV_1 was less than 0.68.

Conclusion: D_{LCO} was likely to be as good as or better prognostic marker than FEV_1 in severe AECOPD.

Keywords: COPD, D_{LCO} , FEV_1

Background

Chronic obstructive pulmonary disease (COPD) is a chronic airway disease defined by persistent respiratory symptoms and irreversible airflow limitation [1–3]. Patients with COPD present with various symptoms, such as cough, sputum, and dyspnea, and these symptoms are closely related to the quality of life and prognosis [4, 5]. The global initiatives for chronic obstructive lung disease (GOLD) reports emphasize treatment based on patient history and symptoms, such as exacerbation history, the modified medical research council dyspnea scale (mMRC), and COPD assessment test (CAT) [6]. Forced expiratory volume in one second (FEV_1) is still used to grade the severity of airflow obstruction, but the 'refined ABCD assessment tool' excludes FEV_1 from the criteria for evaluating the 'ABCD' group. This is because the FEV_1 value is weakly correlated with the patient's symptoms and health status [7, 8]. However, pulmonary function tests (PFT) are still important tests for diagnosing and treating COPD in the clinical field. Therefore, we want other PFT factors related to the patient's symptoms and health status rather than FEV_1 . Several studies have shown that the diffusing capacity of the lung for carbon monoxide (D_{LCO}) among the various values of PFT is closely related to patient symptoms, prognosis, and oxygen demand in COPD [9, 10]. In addition, there was a recent opinion that D_{LCO} should be added to multidimensional tools assessing COPD [11]. This study aimed to compare FEV_1 and D_{LCO} through the prognosis of severe acute exacerbations of COPD (AECOPD).

Method

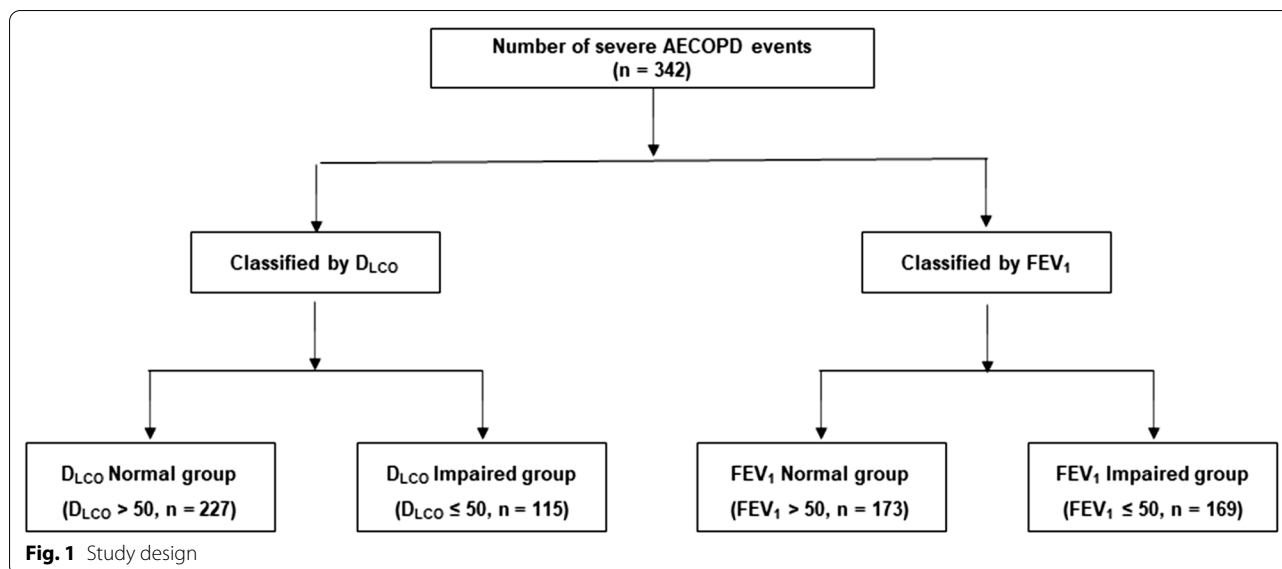
Study population

We retrospectively analyzed the medical records of 342 patients admitted to Korea University Guro Hospital from January 2011 to May 2017. We searched our electronic medical records database with the keywords "COPD" and "Acute exacerbation." This study was approved by the Institutional Review Board of Korea University Guro Hospital (KUGH16131-002). The requirement for informed consent from the patients

was waived due to the retrospective nature of this study by the institutional review committee.

All patients included only patients who were followed up for more than 1 year in our hospital under the diagnosis of COPD. COPD and airflow limitation were diagnosed by synthesizing patient-reported respiratory symptoms, PFT (the ratio of FEV_1 to forced vital capacity (FVC) was less than 70% in post-bronchodilator spirometry), chest image, and patient's history (smokers with at least ten pack-years of tobacco exposure, etc.) by an experienced pulmonologist [6]. AECOPD was defined as worsening of the patient's respiratory symptoms beyond normal day-to-day variation. Severe AECOPD was defined as 'if the patient needs hospitalization due to AECOPD.' The spirometry data used in the analysis was previously performed in the outpatient clinic during the stable period. Spirometry value that was measured within 1 year from the hospitalization day were used. Patients were excluded with the following criteria: (1) the cause of admission was not AECOPD; for example, acute heart failure, acute pulmonary edema, acute pulmonary embolism, pneumothorax, and arrhythmia (These diseases were excluded through cardiac enzyme, electrocardiogram, echocardiogram and chest image.), (2) the patient had undergoing active cancer treatment, (3) the patient received a major operation within 3 months, (4) the patient had an acute coronary syndrome, brain hemorrhage, or brain infarction within 3 months, (5) the patient had previously been diagnosed with asthma, and (6) the patient had no D_{LCO} results. All patients were 40 years old or older. We retrospectively analyzed the charts by two experienced pulmonologists to exclude various exclusion factors. "events" is synonymous with "patients" in this study.

We classified 342 severe AECOPD patients by severity of D_{LCO} and FEV_1 (\leq vs. $>$ 50% predicted). When the D_{LCO} value is more than 50 (% of predicted value), it is defined as the ' D_{LCO} normal group' and when it is 50 (% of predicted value) or less, it is defined as the ' D_{LCO} impaired group' [11]. Likewise, when the FEV_1 value is more than 50 (% of predicted value), it is defined as the ' FEV_1 normal group' and when it is 50 (% of predicted value) or less, it is defined as the ' FEV_1 impaired group' (Fig. 1).



Data collection

We tested the association of FEV_1 and D_{LCO} with the following outcomes: in-hospital mortality, need for mechanical ventilation, need for intensive care unit (ICU) care. When the patient was hospitalized more than once, only the first hospitalized events were included, and the others were excluded. The following medical data were analyzed: age, sex, smoking history, comorbidities, baseline spirometry, inhaler and oral medication before admission, length of hospital stay, hospital mortality, experience of mechanical ventilation, and experience of ICU care in hospital.

Statistical analysis

Data were analyzed using SPSS 20 software (SPSS for Windows, SPSS Inc., Chicago, IL, USA). Data are presented as average \pm standard deviation or number (percentage). We performed a statistical analysis in two directions. First, two groups were classified using D_{LCO} and FEV_1 and analyzed statistically. Continuous variables were compared using the independent t-test, and categorical variables were compared using the chi-squared test. We analyzed the prognostic factors (except length of hospital stay) by multivariate analysis through logistic regression. Multivariate analysis was conducted for variables with a P value of less than 0.05 in the univariate analysis, except for baseline spirometry (D_{LCO} and FEV_1). In the case of D_{LCO} , multivariate analysis included sex, previous TB history, cerebrovascular accident, inhaler use before admission, oral β_2 adrenoreceptor agonist, roflumilast, and mucolytic agent. In the case of FEV_1 , multivariate analysis included age, sex, previous TB history, inhaler use before admission, roflumilast, and mucolytic

agent. Multivariate analysis was conducted using a backward elimination procedure and was assessed by the Hosmer–Lemeshow test.

Second, the linear correlation between spirometry factors (D_{LCO} and FEV_1) and length of hospital stay were analyzed. In univariate analysis, the correlation coefficients between spirometry factors and length of hospital stay were analyzed using the Pearson correlation analysis. In addition, we performed a multivariate linear regression analysis that included variables with a P value of less than 0.05 in the univariate analysis, except baseline spirometry. In addition, multivariate linear regression analysis was conducted using a backward elimination procedure. In the multivariate analysis, B was the regression coefficient, and a negative sign of the regression coefficient meant that the variables were negatively associated.

Third, we used receiver operating characteristic (ROC) curve analysis to predict the sensitivity and specificity of D_{LCO} , FEV_1 and $D_{LCO} + FEV_1$ as prognostic markers in severe AECOPD. When analyzing the ROC curve, D_{LCO} , FEV_1 and $D_{LCO} + FEV_1$ were analyzed as continuous variables. A P value of less than 0.05 was considered statistically significant.

Results

Characteristics of studied subjects

Among the 342 events, the D_{LCO} normal group comprised 227 events (the D_{LCO} value was more than 50% of the predicted value), and 115 in the D_{LCO} impaired group. In the FEV_1 normal group (the FEV_1 value was more than 50% of the predicted value), there was 173 events, and the FEV_1 impaired group

had 169 events. The average age was 71.5 ± 9.2 years. A total of 238 (69.6%) events were male and 104 (30.4%) were female. Sixty-three (18.4%) events were

current smokers and the average pack/year history was 41.3 ± 17.1 years. A total of 225 (65.38) events were using inhalers, and 165 (48.2%) were taking

Table 1 Baseline characteristics of patients with AECOPD

	D_{LCO} normal group (D_{LCO} > 50, n = 227)	D_{LCO} Impaired group (D_{LCO} ≤ 50, n = 115)	P value	FEV₁ normal group (FEV₁ > 50, n = 173)	FEV₁ impaired group (FEV₁ ≤ 50, n = 169)	P value	Total (n = 342)
Age (years) [†]	71.1 ± 9.5	72.4 ± 8.6	0.223	72.7 ± 9.8	70.4 ± 8.5	0.023	71.5 ± 9.2
<i>Sex, no. of exacerbations</i>							
Male [‡]	144 (63.4%)	94 (81.7%)	0.001	105 (60.7%)	133 (78.7%)	< 0.001	238 (69.6%)
Female [‡]	83 (36.6%)	21 (18.3%)		68 (39.3%)	36 (21.3%)		104 (30.4%)
<i>Smoking history, no. of exacerbations</i>							
Current smoker [‡]	42 (18.5%)	21 (18.3%)	0.957	32 (18.5%)	31 (18.3%)	0.971	63 (18.4%)
Ex-smoker [‡]	185 (81.5%)	94 (81.7%)		141 (81.5)	138 (81.7%)		279 (81.6%)
Pack-year history [†]	41.1 ± 16.8	41.8 ± 17.9	0.446	40.9 ± 16.5	41.7 ± 17.8	0.987	
<i>Comorbidities, no. of exacerbations</i>							
Hypertension [‡]	111 (48.9%)	53 (46.1%)	0.623	85 (49.1%)	79 (46.7%)	0.659	164 (48.0%)
Diabetes [‡]	54 (23.8%)	25 (21.7%)	0.671	43 (24.9%)	36 (21.3%)	0.436	49 (23.1%)
Previous TB history [‡]	58 (25.6%)	43 (37.4%)	0.023	35 (20.2%)	66 (39.1%)	< 0.001	101 (29.5%)
Coronary artery disease [‡]	37 (16.3%)	17 (14.8%)	0.716	32 (18.5%)	22 (13.0%)	0.165	54 (15.8%)
Cerebrovascular accident [‡]	6 (2.6%)	9 (7.8%)	0.027	5 (2.9%)	10 (5.9%)	0.172	15 (4.4%)
<i>Inhaler use before admission</i>							
LABAs [‡]	2 (0.9%)	1 (0.9%)	0.015	2 (1.2%)	1 (0.6%)	< 0.001	3 (0.9%)
LAMAs [‡]	24 (10.6%)	14 (12.2%)		27 (15.6%)	11 (6.5%)		38 (11.1%)
LABAs + LAMAs [‡]	36 (15.9%)	16 (13.9%)		24 (13.9%)	28 (16.6%)		52 (15.2%)
ICS/LABAs [‡]	25 (11.0%)	7 (6.1%)		21 (12.1%)	11 (6.5%)		32 (9.4%)
Triple therapy [‡]	53 (23.3%)	47 (40.9%)		32 (18.5%)	68 (40.2%)		100 (29.2%)
None [‡]	87 (38.3%)	30 (26.1%)		67 (38.7%)	50 (29.6%)		117 (34.2%)
<i>Oral medication before admission</i>							
Oral β2 adrenoreceptor agonist [‡]	8 (3.5%)	19 (16.5%)	< 0.001	9 (5.2%)	18 (10.7%)	0.062	27 (7.9%)
Roflumilast [‡]	7 (3.1%)	10 (8.7%)	0.024	1 (0.6%)	16 (9.5%)	< 0.001	17 (5.0%)
Mucolytic agent [‡]	92 (40.5%)	65 (56.5%)	0.005	68 (43.3%)	89 (52.7%)	0.013	157 (45.9%)
Oral steroids [‡]	6 (2.6%)	2 (1.7%)	0.722	2 (1.2%)	6 (3.6%)	0.170	8 (2.3%)
Oral antibiotics [‡]	7 (3.1%)	4 (3.5%)	1.000	3 (1.7%)	8 (4.7%)	0.116	11 (3.2%)
<i>Baseline spirometry</i>							
FEV ₁ (liters) [†]	1.5 ± 0.5	1.1 ± 0.4	< 0.001	1.6 ± 0.5	1.0 ± 0.3	< 0.001	1.3 ± 0.5
FEV ₁ (% of predicted value) [†]	59.9 ± 18.1	42.1 ± 16.0	< 0.001	69.5 ± 13.6	38.0 ± 8.1	< 0.001	54.0 ± 19.3
D _{LCO} (liters) [†]	12.5 ± 5.0	6.6 ± 2.2	< 0.001	11.9 ± 5.3	8.9 ± 4.1	< 0.001	10.6 ± 5.1
D _{LCO} (% of predicted value) [†]	73.5 ± 16.4	38.7 ± 8.8	< 0.001	71.4 ± 20.4	52.0 ± 18.7	< 0.001	61.8 ± 21.8

AECOPD acute exacerbations of chronic obstructive pulmonary disease, LABAs long acting B agonist bronchodilator, LAMAs long acting antimuscarinic agent bronchodilator, ICS inhaled corticosteroids, FEV₁ forced expiratory volume in one second, D_{LCO} diffusing capacity of the lung for carbon monoxide

[†] Numbers are presented as mean ± standard deviation

[‡] Numbers are presented as n (%)

respiratory-related oral medications. Averaged FEV₁ was 1.3 ± 0.5 L (54.0 ± 19.3%) and D_{LCO} was 10.6 ± 4.8 L (59.3 ± 21.4%). (Table 1) In both groups, the average length of hospital stay was 10.0 ± 5.1 days. The mortality rate was 11 (3.2%), the experience of ventilator care was 29 (8.5%), and the experience of ICU care was 39 (11.4%).

Prognostic factor analysis classified using D_{LCO} and FEV₁
 When classified through D_{LCO}, the D_{LCO} impaired group showed a poor prognosis in all four factors by univariate analysis (Fig. 2). When classified through FEV₁, the FEV₁ impaired group showed a poor prognosis in three factors by univariate analysis (Fig. 3). However, there was no statistically significant mortality rate when classified as FEV₁ (P value = 0.116) (Fig. 3B).

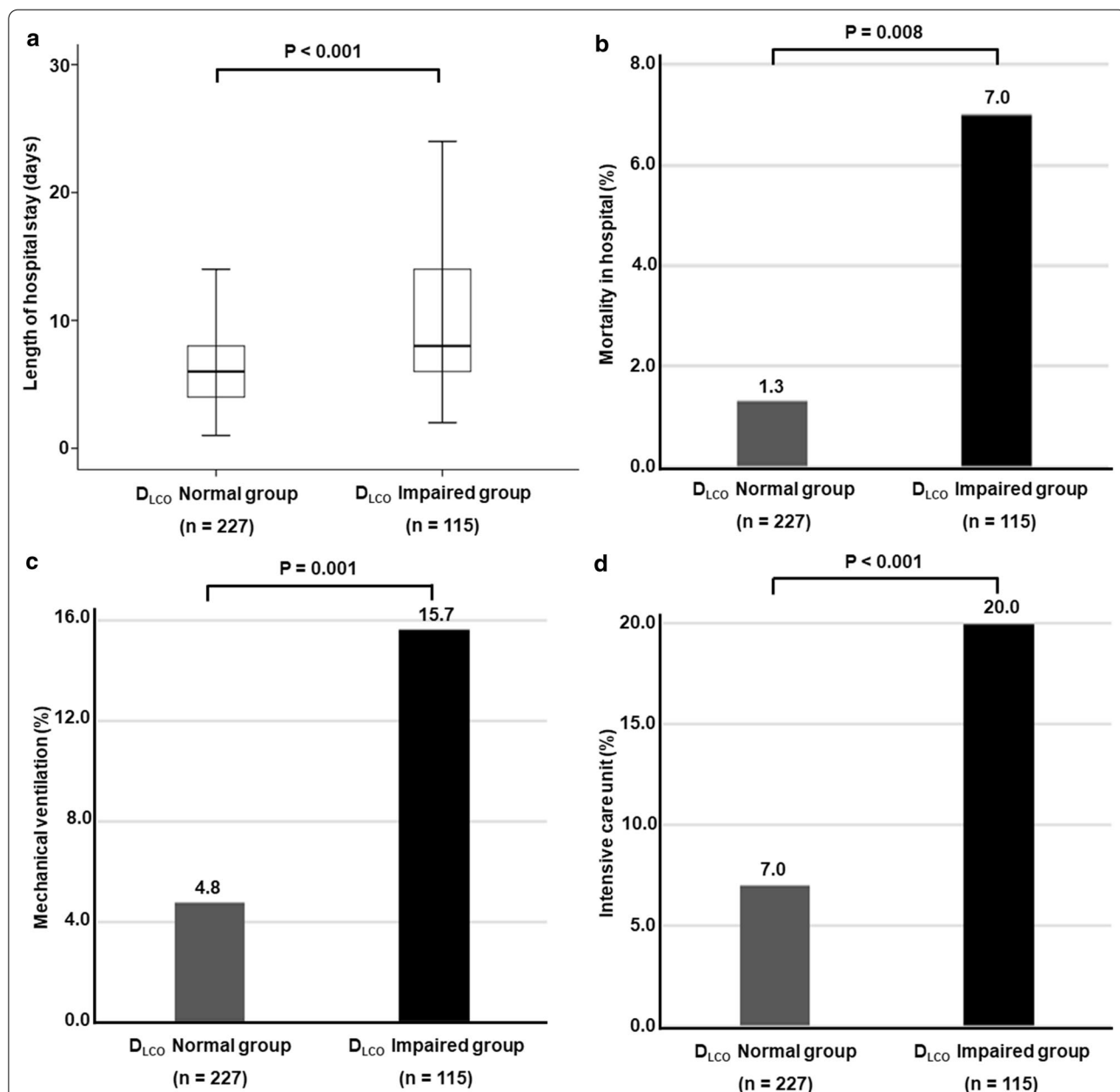
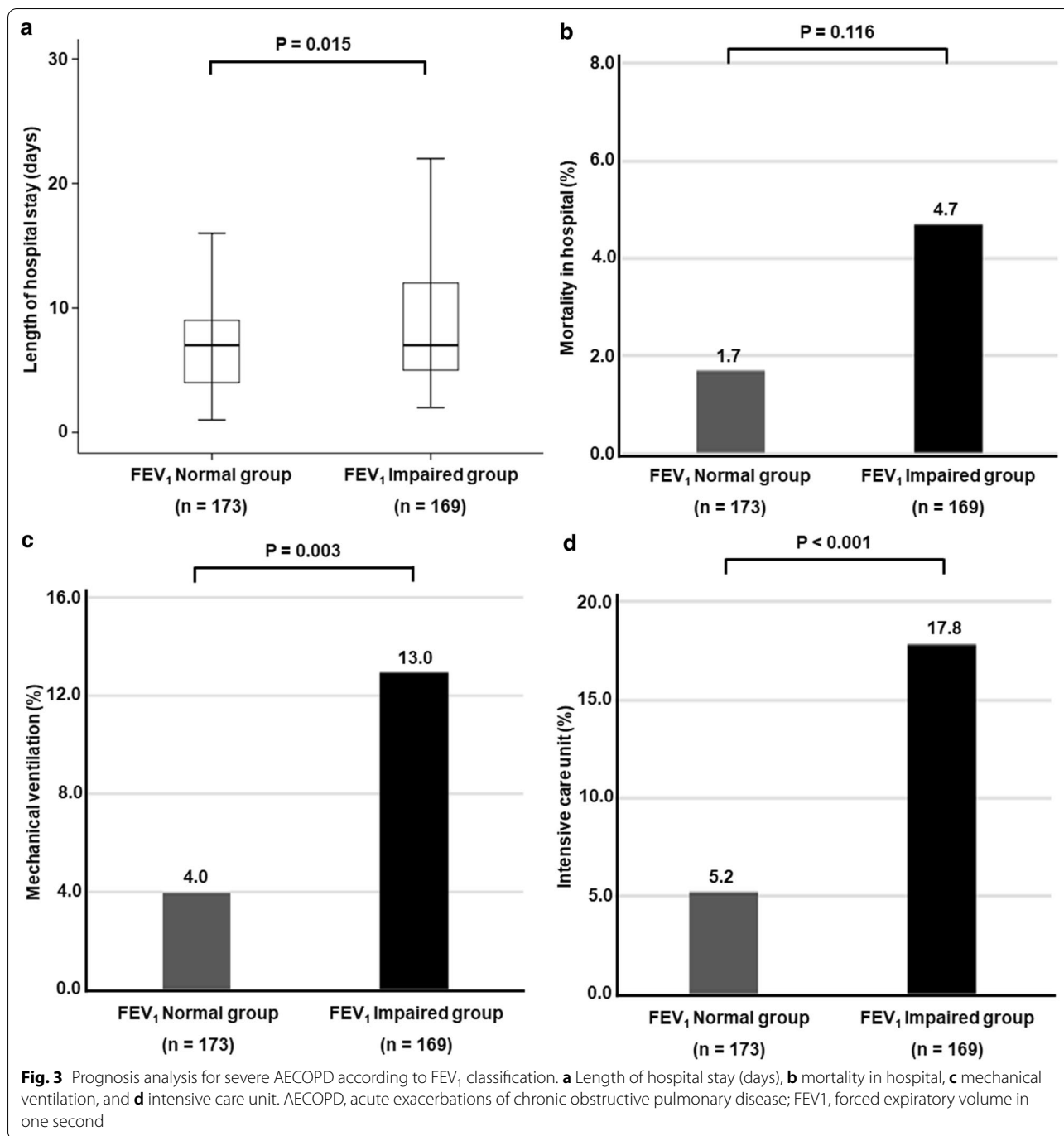


Fig. 2 Prognosis analysis for severe AECOPD according to D_{LCO} classification. **a** Length of hospital stay (days), **b** mortality in hospital, **c** mechanical ventilation, and **d** intensive care unit. AECOPD, acute exacerbations of chronic obstructive pulmonary disease; D_{LCO}, diffusing capacity of the lung for carbon monoxide



In multivariate analyses, D_{LCO} was associated with mortality (odds ratio=4.408; 95% CI 1.070–18.167; $P=0.040$) and need for mechanical ventilation (odds ratio=2.855; 95% CI 1.216–6.704; $P=0.016$) and ICU care (odds ratios=2.685; 95% CI 1.290–5.590; $P=0.008$). In severe AECOPD, D_{LCO} has been shown to predict mortality rate, ventilator, and ICU possibilities. When classified as FEV₁, the experience of mechanical

ventilation and ICU showed statistical significance. However, there was no significant difference in mortality rate ($P=0.075$) (Table 2).

Correlation analysis between spirometer factors and length of hospital stay

The length of hospital stay of the D_{LCO} normal group was 7.3 ± 5.0 days and the D_{LCO} impaired group was

Table 2 Prognosis analysis for severe AECOPD

Parameter	Univariate analysis			Multivariate analysis		
	D _{LCO} normal group (D _{LCO} > 50, n = 227)	D _{LCO} impaired group (D _{LCO} ≤ 50, n = 115)	P value	Odds ratio	95% CI	P value
Mortality in hospital [†]	3 (1.3%)	8 (7.0%)	0.008	4.408	1.070–18.167	0.040
Mechanical ventilation [†]	11 (4.8%)	19 (15.7%)	0.001	2.855	1.216–6.704	0.016
Intensive care unit [†]	16 (7.0%)	23 (20.0%)	<0.001	2.685	1.290–5.590	0.008
	FEV ₁ normal group (FEV ₁ > 50, n = 173)	FEV ₁ impaired group (FEV ₁ ≤ 50, n = 169)				
Mortality in hospital [†]	3 (1.7%)	8 (4.7%)	0.116	4.633	0.858–25.036	0.075
Mechanical ventilation [†]	7 (4.0%)	22 (13.0%)	0.003	3.518	1.335–9.270	0.011
Intensive care unit [†]	9 (5.2%)	30 (17.8%)	<0.001	4.527	1.886–10.869	0.001

Multivariate analysis was conducted for variables with a *P* value of less than 0.05 in the univariate analysis, except for baseline spirometry

AECOPD acute exacerbations of chronic obstructive pulmonary disease, FEV₁ forced expiratory volume in one second, D_{LCO} diffusing capacity of the lung for carbon monoxide

[†] Numbers are presented as mean ± standard deviation

* Numbers are presented as n (%)

Table 3 Correlation analysis of length of hospital stay

Parameter	Univariate (Pearson correlation analysis)		Multivariate (multivariate linear regression analysis)		
	Correlation coefficient	P value	B	Standard deviation	P value
D _{LCO}	-0.272	<0.001	-0.542	0.121	<0.001
FEV ₁	-0.176	0.001	-0.293	0.106	0.006

Multivariate analysis was conducted for variables with a *P* value of less than 0.05 in the univariate analysis, except for baseline spirometry. *B* is the regression coefficient, and the negative sign of the regression coefficient means that the variables are negatively associated

FEV₁ forced expiratory volume in one second, D_{LCO} diffusing capacity of the lung for carbon monoxide

12.4 ± 13.2 days. The length of hospital stay of the FEV₁ normal group was 7.7 ± 5.4 days and the FEV₁ impaired group was 10.4 ± 11.4 days. In the Pearson

correlation analysis, both D_{LCO} and FEV₁ showed a negative correlation. In multivariate linear regression analyses, D_{LCO} ($B = -0.542 \pm 0.121$, $P < 0.001$) and FEV₁ ($B = -0.106 \pm 0.106$, $P = 0.006$) were negatively associated with length of hospital stay. Additionally, the regression coefficient was more pronounced in the D_{LCO} analysis (Table 3).

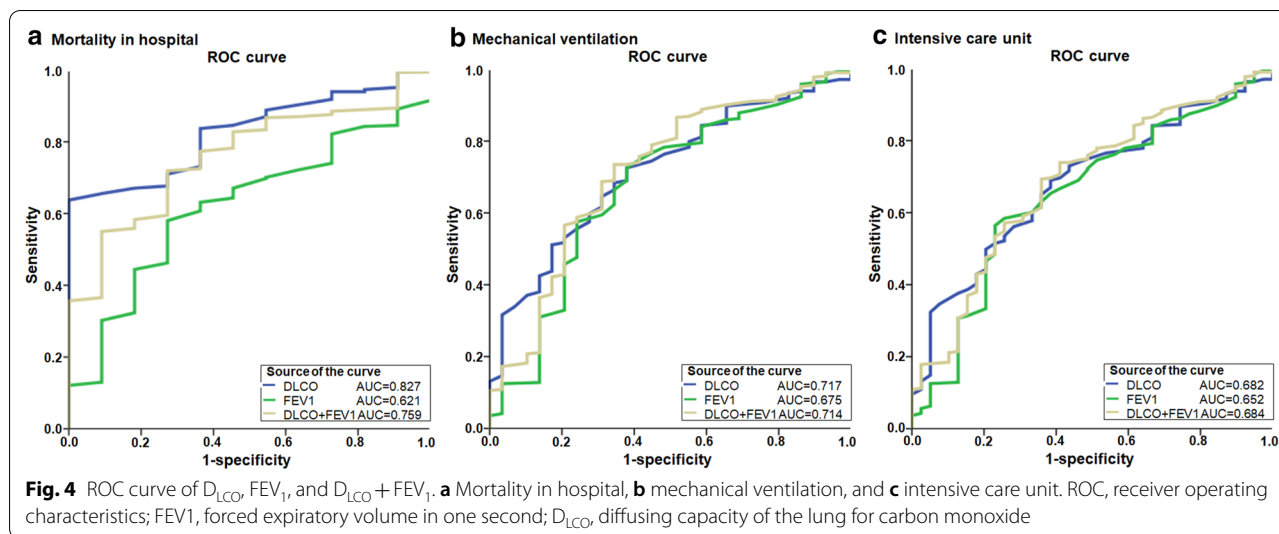
ROC curve analysis of D_{LCO} and FEV₁

When analyzing the sensitivity and specificity using the ROC curve, D_{LCO} showed better predictive ability than FEV₁ (Table 4). When analyzing three prognostic factors (mortality in hospital, mechanical ventilation, and ICU care) through ROC curve analysis, area under the curve (AUC) was greater than 0.68 in all cases of D_{LCO} (Fig. 4). In contrast, the AUCs of FEV₁ were below 0.68 in all three prognostic factors. In addition, the sensitivity and specificity of D_{LCO} were more than 64.1%, which was

Table 4 ROC curve analysis of D_{LCO}, FEV₁, and D_{LCO} + FEV₁

Parameter	Prognostic factor	Optimal cut-off	Sensitivity	Specificity	AUC	95% confidence interval	P value
Mortality in hospital	D _{LCO}	48.5	71.0	72.7	0.827	0.749–0.905	<0.001
	FEV ₁	45.5	63.1	63.6	0.621	0.481–0.760	0.173
	D _{LCO} + FEV ₁	47.25	72.7	71.9	0.759	0.649–0.870	0.003
Mechanical ventilation	D _{LCO}	51.5	68.4	65.5	0.717	0.629–0.804	<0.001
	FEV ₁	44.5	66.5	65.5	0.675	0.566–0.784	0.002
	D _{LCO} + FEV ₁	50.25	69.0	68.7	0.714	0.612–0.816	<0.001
Intensive care unit	D _{LCO}	53.5	65.0	64.1	0.682	0.602–0.762	<0.001
	FEV ₁	46.5	63.0	64.1	0.652	0.560–0.743	0.002
	D _{LCO} + FEV ₁	50.25	64.1	69.3	0.684	0.597–0.771	<0.001

ROC receiver operating characteristics, AUC area under the curve, FEV₁ forced expiratory volume in one second, D_{LCO} diffusing capacity of the lung for carbon monoxide



generally higher than FEV_1 . $D_{LCO} + FEV_1$ showed similar values to D_{LCO} .

Discussion

This is the study to compare FEV_1 and D_{LCO} as prognostic markers in severe patients with AECOPD in Korea. In our study, the factors of prognosis were defined as the length of hospital stay, mortality rate in the hospital, experience of ventilation, and experience of ICU care. Classification by D_{LCO} showed significant differences in all prognostic factors. However, classification by FEV_1 did not show a statistically significant mortality rate. The number of deaths was small, so caution is needed in the interpretation about death (the 95% confidence interval of the odds ratio was large and the P value was marginal). In the correlation analysis, both D_{LCO} and FEV_1 showed a negative correlation with the length of hospital stay. The correlation coefficient was more pronounced in the D_{LCO} classification. In addition, when analyzing the ROC curve, D_{LCO} showed better predictive ability than FEV_1 . Of course, some odds ratio values were better when classified as FEV_1 in our study. However, D_{LCO} was better in various analysis methods (correlation analysis, ROC curve analysis), which was likely to be as good as or better than FEV_1 .

The PFT has various parameters. In general, we used FEV_1 to grade COPD and select the inhaler. In addition to FEV_1 , D_{LCO} is an important prognostic factor. In a study of smokers who did not show an obstruction pattern in PFT, a low D_{LCO} group showed quickly decreased pulmonary function and COPD progression [12]. Studies have shown that D_{LCO} is a more accurate prognostic factor than FEV_1 when assessing postoperative risk [13, 14]. In addition, D_{LCO} is known to accurately represent the

actual emphysema level and performance status [15, 16]. These results suggest that D_{LCO} can be a good predictor of early pulmonary dysfunction and prognosis.

If we know the prognosis of the patient early, we can focus on high-risk patients and improve the prognosis. The prognostic factors that can be used in the clinic are laboratory findings, scoring systems such as CAT or mMRC, and baseline spirometry [17, 18]. In some studies, high-C-reactive protein, eosinopenia, and thrombocytopenia are associated with poor outcomes in AECOPD [19–21]. Although various scoring systems—such as St. George’s Respiratory Questionnaire, mMRC, and CAT, are useful—patients with severe symptoms may not be graded or might have similar scores, making them difficult to use. Instead, we focused on baseline spirometry and confirmed that D_{LCO} is more accurate in evaluating the prognosis of hospitalized patients than FEV_1 . If a grading system that considers both D_{LCO} and FEV_1 is developed, the prognosis can be predicted more accurately.

Our study was limited because it was a retrospective single-center study. We were unable to analyze including important prognostic factors such as frequent exacerbations, obstructive sleep apnea, and body mass index. As this study is a retrospective study, data on these factors were not available or inaccurate. To compensate for this, we carefully analyzed the charts by two experienced pulmonologists. Also, we included as many factors as possible in baseline characteristics and multivariate analysis. In addition, the treatment received during the hospitalization period and the prognosis after discharge were not evaluated. Large prospective clinical studies that include information on treatment during hospitalization and post discharge may be required.

Conclusion

D_{LCO} was likely to be as good as or better as a prognostic marker than FEV_1 in severe AECOPD. Accurate classification using D_{LCO} may help to treat severe ACEOPD patients.

Abbreviations

COPD: Chronic obstructive pulmonary disease; AECOPD: Acute exacerbation of chronic obstructive pulmonary disease; D_{LCO} : Diffusing capacity of the lung for carbon monoxide; FEV_1 : Forced expiratory volume in one second.

Acknowledgements

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Author's contributions

JC performed data collection, interpretation and was major contributor in writing the manuscript. JKS, JYO, and YSL performed data collection and interpretation. GYH, SYL, and JJS performed data analysis and interpretation. CKR and KHM designed and supervised study. All authors have read and approved the final manuscript.

Funding

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Availability of data and materials

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the 'Declaration of Helsinki' as a statement of ethical principles for medical research involving human subjects, including the study of identifiable human substances and data. This study was approved by the Institutional Review Board of Korea University Guro Hospital (KUGH16131-002) for all research-related matters prior to the start of the study and was conducted in compliance with the relevant research regulations throughout the study. This study is a study through retrospective data analysis, and since there is no reason to estimate the subject's refusal to consent and the risk to the subject is low even without consent, it was approved as a 'signature consent waiver study' by the institutional review committee. In the course of the research, all personally identifiable data were anonymized to further minimize the impact on the research subject.

Consent to publication

Not applicable.

Competing interests

There is no competing interest. All authors declare they have no competing interest.

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