



## Early View

Original research article

# Diaphragm dome height in chest X-ray as a predictor of dynamic lung hyperinflation in COPD

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## **Unmarked manuscript**

### **TITLE:**

Diaphragm dome height in chest X-ray as a predictor of dynamic lung hyperinflation in COPD

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### **Summary of take-home message**

Diaphragm dome height on chest X-ray, a basic and inexpensive measure, is a good predictor of high dynamic hyperinflation in COPD, independent of the low attenuation area on chest computed tomography and %FEV<sub>1</sub>.

## **Abstract**

*Background and objective:* Dynamic lung hyperinflation (DLH) can play a central role in exertional dyspnoea in patients with chronic obstructive pulmonary disease (COPD). Chest X-ray is the basic tool for assessing static lung hyperinflation in COPD. However, the predictive capacity of DLH using chest X-ray remains unknown. This study was conducted to determine whether DLH can be predicted by measuring the height of the right diaphragm (dome height) on chest X-ray.

*Methods:* This single-centre, retrospective cohort study included patients with stable COPD with pulmonary function test, cardiopulmonary exercise test, constant load test, and pulmonary images. They were divided into two groups according to the median of changes of inspiratory capacity ( $\Delta IC = IC_{\text{lowest}} - IC_{\text{at rest}}$ ). The right diaphragm dome height and lung height were measured on plain chest X-ray.

*Results:* Of the 48 patients included, 24 were classified as having high DLH ( $\Delta IC \leq -0.59$  L from rest;  $-0.59$  L, median of all) and 24 as having low DLH. Dome height correlated with  $\Delta IC$  ( $r = 0.66, p < 0.001$ ). Multivariate analysis revealed that dome height was associated with high DLH independent of %low attenuation area on chest computed tomography and %FEV<sub>1</sub>. Furthermore, the area under the receiver operating characteristic curve of dome height to predict high DLH was 0.86, with sensitivity and specificity of 83% and 75%, respectively, at a cutoff of 20.5 mm. Lung height was unrelated to  $\Delta IC$ .

*Conclusion:* Diaphragm dome height on chest X-ray may adequately predict high DLH in patients with COPD.

## **Short title:**

Diaphragm dome height on X-ray and DLH

**Keywords:** dynamic lung hyperinflation, COPD, plain chest X-ray, diaphragm

**Conference presentation:** none in the International Conference

## Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive disorder characterised by minimally reversible airflow limitation.[1] Its primary feature is the inability to cope with activities of daily living due to exertional dyspnoea. Although the pathophysiological mechanisms involved in dyspnoea development and poor exercise tolerance in patients with COPD are complex, dynamic lung hyperinflation (DLH) can play a central role[2] by increasing ventilatory workload and decreasing the pressure-generating capacity of the inspiratory muscles despite the compensatory mechanisms.[3] Therefore, DLH evaluation is important in COPD management.

In patients with COPD, the diaphragm, which is the main muscle employed for respiration, significantly changes in terms of mass, thickness, and area, and its mobility is associated with DLH. We previously reported that increased dyspnoea caused by DLH on exercise is associated with decreased exercise capacity in patients with COPD and reduced diaphragm mobility, which was assessed by the maximum level of diaphragm excursion ( $DE_{max}$ ) using ultrasonography.[4] Other research groups also reported that ultrasonographic assessment of diaphragmatic mobility in COPD is useful in understanding its association with 6-minute walk distance, dyspnoea,[5] and increased mortality.[6]

Given that a plain chest X-ray is readily available and inexpensive, it is a quick and basic diagnostic tool for evaluating patients' lungs. Chest X-ray is essential in COPD management; thus, most of the patients with COPD undergo this diagnostic examination. The applied radiation dose is relatively low, with an average effective dose of 0.05 mSv for a single posterior–anterior image.[7, 8] Chest X-ray also provides information on physiological changes in COPD. On a frontal chest radiograph, the normal dome of each hemidiaphragm should rise at least 15 mm above a line connecting the costophrenic angle laterally and cardiophrenic angle medially.[8, 9] Meanwhile, in lung hyperinflation, the diaphragm is flattened, generally because of emphysema, which is one of the most sensitive signs on chest radiographs.[10, 11] However, the relationship between plain chest X-ray measurements of the diaphragm and DLH remains unreported.

Thus, this study aimed to determine the predictive capacity of DLH according to dome height on chest X-ray. We hypothesized that measuring the dome height is useful in assessing DLH in patients with COPD, reflecting diaphragmatic mobility.

## Methods

### Study design and subjects

This was a single-centre, retrospective cohort study. The participants had clinically stable COPD, who visited the Department of Respiratory Medicine and Allergology at Kindai University Hospital between January 2018 and November 2022. We included patients who received the cardiopulmonary exercise test (CPET) and the following examinations and measurements within 3 months before and after CPET: (1) ultrasonographic measurement of maximum diaphragmatic excursion, (2) spirometry, (3) DLH finding by constant load test, (4) chest X-ray, and (5) computed tomography (CT). The exclusion criteria were unclear diaphragm angle on radiographic images caused by pleural effusion or adhesions, diaphragmatic eventration, phrenic nerve palsy, and post lung surgery. This study included our previously reported 46 participants and an additional 20 participants. All participants were those whose attending physicians considered outpatient rehabilitation necessary in actual clinical practice and who had no problems with time constraint or accessibility.[4] [12]

### Measurements

Symptom-limited cardiopulmonary exercise test (CPET) was conducted on a bicycle ergometer according to the Ramp 10 W protocol (load increase of 10 watts per 1 minute – 1 watt per 6 seconds). We analysed the following: peak oxygen consumption (peak  $\dot{V}O_2$ ) and ventilation equivalents for carbon dioxide ( $\dot{V}E/\dot{V}CO_2$ ). Inspiratory capacity (IC) manoeuvres were performed at rest, and during constant load exercise (peak 70%). Throughout exercise testing, IC was measured every 1 min and at the end of the exercise.

We measured the change in IC ( $\Delta IC = IC_{\text{lowest}} - IC_{\text{at rest}}$ ) during exercise as a surrogate marker of DLH.[13, 14] Using the data obtained from the exercise test, we divided the patients into two groups according to the median  $\Delta IC$ : low DLH group and high DLH group.

Lung hyperinflation was evaluated by plain chest X-ray as follows: (a) the dome height of the right and left diaphragm was assessed by drawing a line from costophrenic angles to cardiophrenic angles and measuring the longest line perpendicular to the diaphragm silhouette (Figure 1a); and (b) lung height was measured as the distance from the top of the right and left diaphragm dome to the tubercle of the first rib (lung height) (Figure 1b).[9, 15] Drawing lines and measuring the distance were performed using Synapse (Fujifilm Medical). Moreover, emphysema was quantified by calculating the percentage of the low attenuation area, determined according to the cutoff value of  $-950$  HU on whole-lung computed

tomographic images (Aquilion 64 scanner; Toshiba, Tokyo, Japan) using Synapse Vincent (Fujifilm Medical), as described previously.[16, 17]

We also measured  $DE_{max}$  through ultrasonography (Xario 200; Canon Medical Systems, Tokyo, Japan). Excursions of the right hemidiaphragm were measured using a 3.5-MHz convex probe according to previously described techniques.[4] The liver was used as an acoustic window. We rotated the M-mode cursor was rotated placed it on the axis of diaphragmatic displacement on the stored image, measured the displacement (Figure S1) during each of three deep breaths, and then measured the  $DE_{max}$ .

Patients underwent spirometry (CHESTAC-800; Chest, Tokyo, Japan) according to the 2014 American Thoracic Society recommendations [18] for measuring forced vital capacity (FVC), forced expiratory volume in one second ( $FEV_1$ ), and IC.  $FEV_1\%$  predicted and  $FVC\%$  predicted were calculated using the Global Lung Function Initiative (GLI) method that was recommended by the 2022 European Respiratory Society/American Thoracic Society technical standard [19] and had been used in the Japanese Respiratory Society to calculate reference values for spirometry. [20]

To assess respiratory muscle strength, we measured the maximum inspiratory pressure ( $PI_{max}$ ) generated against an occluded airway at residual volume[21] (IOP-01; Kobata Instrument Manufacturing Ltd., Osaka, Japan).

The ethics committee of Kindai University School of Medicine approved this study (approval No.: R04-192). Informed consent was obtained from each patient by using an opt-out approach in agreement with the institutional review board.

### **Sample size**

The sample size was estimated using the R software. The inclusion of 40 patients was required if the expected area under the curve (AUC) of the receiver operating characteristic (ROC) was 0.80, the power was 90%, and the significance level was 0.01.

### **Statistical analysis**

Continuous data are expressed as mean  $\pm$  standard deviation or median and interquartile range (IQR) for parametric and nonparametric values. The high DLH and low DLH groups were compared using the *t*-test, Wilcoxon rank-sum test ( $\%LAA$  and IC), or  $\chi^2$  test (GOLD stage), as appropriate.

The ROC curve method was used to determine the ability of dome height to predict the presence of high DLH. The ability of variables to predict  $\Delta IC$  was also evaluated using the

multivariate logistic regression model, which included height, age, and sex as covariates.

Given that  $\Delta IC$  and dome height were normally distributed, the association between independent variables and  $\Delta IC$  or dome height was analysed using the Pearson correlation coefficient. Univariate linear regression was included with  $\Delta IC$  as the dependent variable and right dome height as the independent variable. Statistical data were analysed using the IBM SPSS statistics software, version 22 (IBM SPSS, Armonk, NY, USA), and JMP software, version 14 (JMP<sup>®</sup>, SAS Institute Inc., Cary, NC, USA). A  $p$  value  $< 0.05$  was considered statistically significant.

## Results

Out of 66 enrolled patients with COPD, 48 were eligible for the analysis (Figure 2). We excluded 18 patients because of pleural effusion in 2, pleural adhesions in 2, post lung surgery in 2, and incomplete data in 12 patients. Incomplete data ( $n = 12$ ) included four cases with chest X-ray images that were taken more than 3 months after CPET, four cases without chest CT images, and four cases without DLH measurements.

Table 1 presents the participants' baseline characteristics. The  $\Delta IC$  values were varied from  $-0.12$  L to  $-1.50$  L, and the median was  $-0.59$  L. Furthermore, 24 patients were classified as the high DLH group ( $\Delta IC$  from rest  $\leq -0.59$  L), and 24 as the low DLH group ( $\Delta IC$  from rest  $> -0.59$  L). Body mass index (BMI),  $PI_{max}$ , GOLD stage,  $DE_{max}$ , diaphragm dome height,  $FEV_1$ ,  $FEV_1\%$  predicted, and peak  $\dot{V}O_2$  were significantly lower, whereas %LAA and  $\dot{V}E/\dot{V}CO_2$  were higher in the high DLH group than in the low DLH group (Table 1). Lung height showed no difference between groups.

The  $\Delta IC$  positively correlated with BMI,  $PI_{max}$ ,  $DE_{max}$ , right dome height (Figure 3), and left dome height,  $FEV_1\%$  predicted, and peak  $\dot{V}O_2$  and negatively correlated with %LAA and  $\dot{V}E/\dot{V}CO_2$  (Table 2). The correlation between  $\Delta IC$  and right dome height was stronger than that between  $\Delta IC$  and left dome height (Table 2). Univariate linear regression was performed with delta IC as the dependent variable and dome height as the independent variable, and the results were  $R^2 = 0.44$ ,  $\beta = 0.66$ , 95% CI = 0.022–0.045, and  $p < 0.001$ . The right dome height positively correlated with BMI, QMS,  $PI_{max}$ ,  $DE_{max}$ , IC,  $FEV_1$ ,  $FEV_1\%$  predicted, FVC, and peak  $\dot{V}O_2$  and negatively correlated with  $\dot{V}E/\dot{V}CO_2$  (Table 3). The association between  $\Delta IC$  and right dome height remained significant, even when analysed by COPD subtype (GOLD 2,  $n = 19$ ,  $r = 0.64$ ,  $p = 0.003$ , GOLD 3,  $n = 19$ ,  $r = 0.53$ ,  $p = 0.019$ ). Regarding GOLD 1 and 4, they also showed moderate-to-strong correlation, but they did not meet the 5% significance level due to the small sample size, i.e., each with five cases (GOLD

1,  $r = 0.86$ ,  $p = 0.062$  ; GOLD 4,  $r = 0.62$ ,  $p = 0.27$ ).

The area under the ROC curve of dome height for predicting high DLH was 0.86, with a sensitivity of 83% and a specificity of 75% at a cutoff value of 20.5 mm (Figure 4).

In the multivariate analysis, high DLH ( $\Delta IC$  from rest  $\leq -0.59L$ ) was the dependent variable, and dome height, %LAA, and FEV<sub>1</sub>% predicted were the independent variables; variables %LAA and %FEV<sub>1</sub> were considered clinically important. The right dome height and %LAA were found to be the significant independent explanatory variables, with right dome height being the most significant independent explanatory variable (odds ratio, 0.67; 95% confidence interval, 0.516–0.862,  $p = 0.002$ , Table 4).

Finally, we performed multivariate ROC curve analysis with high DLH ( $\Delta IC \leq -0.59L$  from rest) as the dependent variable. Compared with models that included height as a covariate, the conformity as expressed as lower Akaike Information Criterion corrected for small samples (AICc) appeared to be the best for Model 3, i.e., a model without any adjustment including height (Table S1).

## Discussion

Airflow limitation and DLH can be major contributors to dyspnoea in patients with COPD, and DLH is tightly linked to dyspnoea and exercise tolerance.[2] To our best knowledge, this is the first study to demonstrate that dome height on plain chest X-ray was useful for predicting  $\Delta IC$  reflecting DLH in patients with COPD.

In this study, reduced dome height by plain chest X-ray was a better predictor of high DLH than %LAA or %FEV<sub>1</sub> in the multivariate analysis. In addition, dome height had high sensitivity (83%) and specificity (75%) at a cutoff value of 20.5 mm for predicting high DLH. Although mechanisms underlying the association between reduced dome height and high DLH during exercise remain unclear, they may be explained by the association between the degree of hyperinflation at rest and the degree of DLH during exercise.[22] DLH consists of static and dynamic components. The static component results from pulmonary parenchyma destruction and elastic recoil loss by the lung. Even in the static phase, patients with COPD have an elevated resting end-expiratory lung volume (EELV; total lung capacity [TLC]-IC) caused by airway resistance increase resulting from airway inflammation and airway wall thickening, and/or by lung elastic recoil reduction resulting from alveolar destruction and emphysema. The dynamic component occurs when patients with COPD breathe in before achieving a complete exhalation, and EELV further increases in association with respiratory rate elevations because it occurs during exercise.[23] Critical inspiratory constraint (CIC)



resulted in a plateau in tidal volume and an associated increase in dyspnoea as a function of ventilation volume, and CIC was useful in explaining the presence and severity of exertional dyspnoea.[24-27] Although we did not have the data of IC/TLC that reflects static hyperinflation, reduced dome height may reflect the degree of hyperinflation at rest. Therefore, patients with reduced dome height, that is, diaphragm flattening, possibly had higher resting EELV at rest, resulting in even higher dynamic EELV during exercise and more high DLH.

Previous studies also investigated other possible biomarkers for DLH, including exertional oxygen desaturation during 6-min-walk testing, [28] or even 8-isoprostane levels in exhaled breath condensate.[29] However, the former is time-consuming and not always implemented in the outpatient clinic. The latter needs specific equipment and cost compared with routine chest X-ray.

Emphysema, as evaluated by CT, is associated with shorter 6-min-walk distances, lower peak  $\dot{V}O_2$ , and lower exercise ventilation efficiency in patients with COPD.[30-33] CT is a validated imaging technique used to visually and quantitatively assess the presence, extent, and pattern of emphysema,[34] whereas plain chest X-ray has low sensitivity for detecting emphysema.[35] Computed tomography emphysema and airway metrics [33] and homogeneous and heterogeneous emphysema on CT [36] have been reported as markers of DLH. However, currently chest CT is not considered a standard of care in the diagnosis and management of mild-to-moderate COPD.[37] Furthermore, the use of CT is limited because of the high radiation exposure compared with plain chest X-ray.[7] In this study, %LAA correlated with DLH but was only marginally as a predictor. One reason why dome height was a better predictor than %LAA might be that CT is taken in the supine position, whereas X-ray is taken in the same standing position as during exercise. Therefore, plain chest X-ray evaluation of diaphragm height may be superior in DLH prediction when considering cost-effectiveness and radiation exposure, and the prediction accuracy is higher than that by other methods.

Dome height by plain chest X-ray also correlated with  $DE_{max}$  measured by ultrasonography that was strongly associated with DLH and dyspnoea during exercise, as we reported previously.[4] However,  $DE_{max}$  assessment has a limitation. The procedures pertaining to patient positioning, breathing patterns, and the selected hemidiaphragm are currently not standardized, thereby likely hampering the routine use of  $DE_{max}$ . Therefore, diaphragm evaluation by plain chest X-ray may be useful for facilities that cannot perform ultrasonography and achieve equivalent results in DLH prediction.

This study has some limitations. It is a single-centre study involving a relatively small sample size, and the patients' baseline condition was relatively preserved. However, DLH assessment is also warranted in patients with relatively preserved pulmonary function, given that proactive intervention may prevent deterioration of activities of daily living. In addition, owing to the retrospective nature of this study, we could not confirm if the chest X-ray was obtained at the TLC level. However, in erect chest radiographs, individuals with normal respiratory function routinely inhale to approximately 95% of TLC without vigorously coaxing;<sup>[38]</sup> therefore, our study findings may be largely reliable. Finally, due to the small sample size of mild (GOLD 1) and most severe (GOLD 4) cases, it is not clear whether this "biomarker" is clinically relevant in all severities of COPD. Further studies are required to increase the number of cases so that subtyping can also be included. In conclusion, plain chest X-ray measurements of the diaphragm dome height could adequately predict DLH in patients with COPD. A plain chest X-ray is a rapid and basic diagnostic tool for evaluating patients' lungs. Measurement of plain chest X-ray is easy to perform, safe, and well tolerated in patients with chronic lung disease. This ease of use makes the assessment of dome height in this study a more feasible and attractive option in routine clinical practice. Therefore, assessing the diaphragm dome height may aid in making medical decisions associated with therapeutic strategies.

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**Conflict of Interest:** None declared

**Data Availability Statement:** The data supporting the findings of this study are available on reasonable request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

**Human/Animal Ethics Approval Declaration:** This study was approved by the Ethics Committee of Kindai University School of Medicine (R04-192).

**Abbreviations:** AUC: area under the curve, COPD: chronic obstructive pulmonary disease, CPET: cardiopulmonary exercise test,  $DE_{max}$ : maximum level of diaphragm excursion, DLH: dynamic lung hyperinflation, EELV: end-expiratory lung volume,  $FEV_1$ : forced expiratory

volume in 1 s, FVC: forced vital capacity, IC: inspiratory capacity, %LAA: low attenuation area,  $PI_{\max}$ : maximum inspiratory pressure, ROC: receiver operating characteristic, TLC: Total Lung Capacity,  $\dot{V}O_2$ : oxygen uptake,  $\dot{V}E / \dot{V}CO_2$ : minute ventilation/carbon dioxide

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Table 1. Baseline characteristics of study participants

	ALL n=48	High DLH ( $\Delta$ IC $\leq$ -0.59 L) n=24	Low DLH ( $\Delta$ IC $>$ -0.59 L) n=24	p value*
Male/female, %	44 / 4 (91 / 9)	20 / 4 (80 / 20)	24 / 0 (100 / 0)	0.68
Age, yr	75 $\pm$ 5	75 $\pm$ 6	76 $\pm$ 5	0.24
Body mass index, kg/m <sup>2</sup>	21.4 $\pm$ 3.3	20.3 $\pm$ 3.1	22.4 $\pm$ 3.2	< 0.05
Body height, cm	163.9 $\pm$ 6.9	161.9 $\pm$ 7.7	165.3 $\pm$ 5.5	0.08
QMS, Kgf/Kg	0.52 $\pm$ 0.13	0.52 $\pm$ 0.14	0.57 $\pm$ 0.16	0.36
PI <sub>max</sub> , cm H <sub>2</sub> O	54.4 $\pm$ 21.8	41.8 $\pm$ 15.0	67.0 $\pm$ 24.1	< 0.01
%PI <sub>max</sub> , %	80.3 $\pm$ 33.4	66.0 $\pm$ 26.0	94.7 $\pm$ 33.8	< 0.01
GOLD (1/2/3/4)	6 / 19 / 18 / 5	1 / 8 / 10 / 5	5 / 11 / 8 / 0	< 0.05 <sup>‡</sup>
%LAA	20.4 (2.05–37.1)	33.9 (11.1–39.3)	8.9 (1.2–25.0)	< 0.01 <sup>†</sup>
DE <sub>max</sub> , mm	46.7 $\pm$ 8.6	40.5 $\pm$ 5.6	53.0 $\pm$ 6.2	< 0.01
<b>Plain chest X-ray</b>				
Right dome height, mm	21.2 $\pm$ 5.9	17.6 $\pm$ 5.2	24.7 $\pm$ 4.1	< 0.01
Left dome height, mm	21.6 $\pm$ 6.1	20.0 $\pm$ 6.2	23.2 $\pm$ 5.5	0.07
Right lung height, mm	250.3 $\pm$ 27.3	256.5 $\pm$ 28.9	244.1 $\pm$ 23.9	0.14
Left lung height, mm	260.3 $\pm$ 41.7	270.2 $\pm$ 30.1	259.6 $\pm$ 20.2	0.17
<b>Spirometry</b>				
IC, L	1.99 (1.61–2.43)	1.89 (1.42–2.17)	2.39 (1.70–2.50)	< 0.01 <sup>†</sup>
FEV <sub>1</sub> , L	1.39 $\pm$ 0.55	1.14 $\pm$ 0.51	1.60 $\pm$ 0.50	< 0.01
%predicted FEV <sub>1</sub> , %	55.6 $\pm$ 22.0	47.0 $\pm$ 20.4	64.3 $\pm$ 20.1	< 0.01
FVC, L	2.98 $\pm$ 0.72	2.83 $\pm$ 0.70	3.13 $\pm$ 0.68	0.23
%predicted FVC, %	89.2 $\pm$ 18.4	87.7 $\pm$ 17.2	90.8 $\pm$ 19.4	0.58
<b>Peak exercise measurements</b>				
peak $\dot{V}O_2$ , ml/min/kg	11.6 $\pm$ 3.5	9.0 $\pm$ 2.3	14.2 $\pm$ 2.3	< 0.01
$\dot{V}E/\dot{V}CO_2$ , ml/ml	48.6 $\pm$ 7.3	52.1 $\pm$ 7.1	45.2 $\pm$ 5.6	< 0.01
$\Delta$ IC from rest, L	-0.57 $\pm$ 0.30	-0.81 $\pm$ 0.21	-0.33 $\pm$ 0.15	< 0.01

Values are presented as mean  $\pm$  standard deviation or median (interquartile). DE<sub>max</sub> = maximum diaphragmatic excursion; DLH = dynamic lung hyperinflation; FEV<sub>1</sub> = forced expiratory volume in 1 s; FVC = forced vital capacity; GOLD = Global Initiative for Chronic



Obstructive Lung Disease; IC = inspiratory capacity;  $\Delta$ IC = change of IC from rest during exercise; LAA = low attenuation area;  $PI_{\max}$  = maximum inspiratory pressure; QMS = quadriceps muscle strength;  $\dot{V}E/\dot{V}CO_2$  = minute ventilation/carbon dioxide;  $\dot{V}O_2$  = oxygen uptake. \* = *t*-test, unless otherwise stated. † = Wilcoxon rank-sum test, ‡ =  $\chi^2$

Table 2. Correlation coefficients for  $\Delta$ IC

Independent variable	Total patients (n = 48)	
	Pearson correlation coefficient (r)	p value
Age, yr	0.12	0.43
Body mass index, kg/m <sup>2</sup>	0.31	< 0.05
Quadriceps muscle strength, Kgf/Kg	0.23	0.13
PI <sub>max</sub> , cm H <sub>2</sub> O	0.58	< 0.001
%PI <sub>max</sub> , %	0.24	0.95
%LAA, %	-0.34	< 0.05
DE <sub>max</sub> , mm	0.75	< 0.001
Right dome height, mm	0.66	< 0.001
Left dome height, mm	0.38	< 0.01
Right lung height, mm	0.21	0.16
Left lung height, mm	0.16	0.28
FEV <sub>1</sub> %predicted	0.43	< 0.01
peak $\dot{V}O_2$ , ml/min/kg	0.81	< 0.001
$\dot{V}E/\dot{V}CO_2$ , ml/ml	-0.44	< 0.01

DE<sub>max</sub> = maximum diaphragmatic excursion; FEV<sub>1</sub> = forced expiratory volume in 1 s;  $\Delta$ IC = change of inspiratory capacity from rest during exercise; LAA = low attenuation area; PI<sub>max</sub>: maximum inspiratory pressure;  $\dot{V}E/\dot{V}CO_2$  = minute ventilation/carbon dioxide;  $\dot{V}O_2$  = oxygen uptake.

Table 3. Correlation coefficients for dome height

Independent variable	Total patients (n = 48)	
	Pearson correlation coefficient (r)	p value
Age, yr	0.10	0.43
Body mass index, kg/m <sup>2</sup>	0.32	< 0.01
Quadriceps muscle strength, Kgf/Kg	0.32	< 0.05
PI <sub>max</sub> , cm H <sub>2</sub> O	0.53	< 0.01
%PI <sub>max</sub> , %	0.49	< 0.01
%LAA, %	-0.19	0.18
DE <sub>max</sub> , mm	0.65	< 0.001
IC, L	0.32	< 0.05
ΔIC, L	0.66	< 0.001
FEV <sub>1</sub> , L	0.44	< 0.01
%predicted FEV <sub>1</sub> , %	0.34	< 0.05
FVC, L	0.40	< 0.01
%predicted FVC, %	0.18	0.22
peak $\dot{V}O_2$ , ml/min/kg	0.63	< 0.01
$\dot{V}E/\dot{V}CO_2$ , ml/ml	-0.32	< 0.05

DE<sub>max</sub> = maximum diaphragmatic excursion; FEV<sub>1</sub> = forced expiratory volume in 1 s; ΔIC = change of inspiratory capacity from rest during exercise; LAA = low attenuation area; PI<sub>max</sub>: maximum inspiratory pressure;  $\dot{V}E/\dot{V}CO_2$  = minute ventilation/carbon dioxide;  $\dot{V}O_2$  = oxygen uptake.

Table 4. Multivariate analysis for high DLH ( $\Delta$ IC from rest  $\leq$  -0.59 L)

Index	Odd ratios	95%CI	p value
Right dome height, mm	0.67	0.516–0.862	0.002
%LAA, %	0.59	1.002–1.123	0.044
%predicted FEV <sub>1</sub> , %	0.97	0.929–1.012	0.161

DLH = dynamic lung hyperinflation; FEV<sub>1</sub> = forced expiratory volume in 1 s;  $\Delta$ IC = change of inspiratory capacity from rest during exercise; LAA: low attenuation area;.

## Figure legends

Figure 1.

Illustrative example demonstrating the measurement of diaphragm dome height (a) and lung height (b).

Figure 2.

Flow diagram of study participants.

Figure 3.

Correlation between  $\Delta$ IC and dome height of the right diaphragm:  $r = 0.66$ ,  $p < 0.001$  in all patients ( $n = 48$ );  $r = 0.86$ ,  $p = 0.062$  in GOLD 1 ( $n = 5$ );  $r = 0.64$ ,  $p = 0.003$  in GOLD 2 ( $n = 19$ );  $r = 0.53$ ,  $p = 0.019$  in GOLD 3 ( $n = 19$ );  $r = 0.62$ ,  $p = 0.27$  in GOLD 4 ( $n = 5$ ).

Figure 4.

Receiver operating characteristic (ROC) curve of the dome height of the right diaphragm measured by plain chest X-ray: The area under the ROC curve of dome height to predict high DLH was 0.86, with a sensitivity of 83% and a specificity of 75% at a cutoff value of 20.5 mm of dome height.

Figure 1 (a)

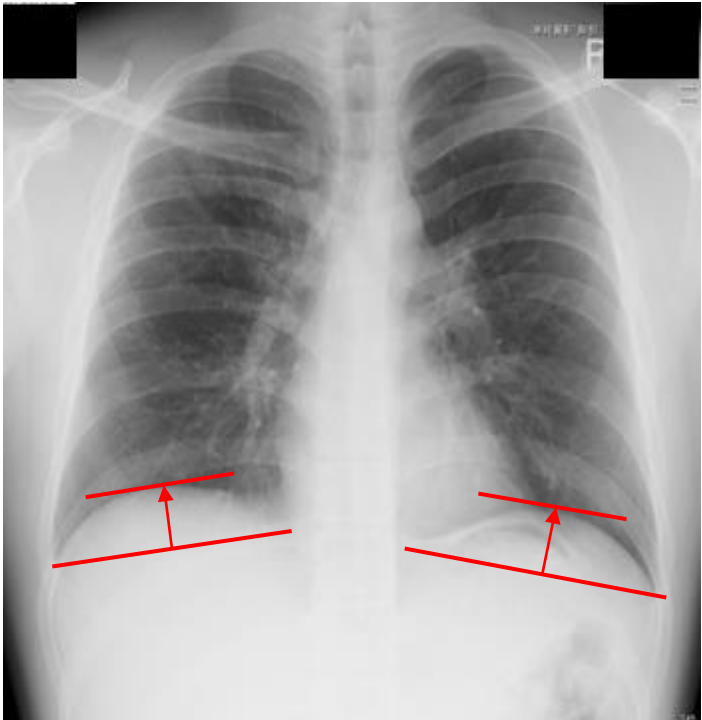


Figure 1 (b)

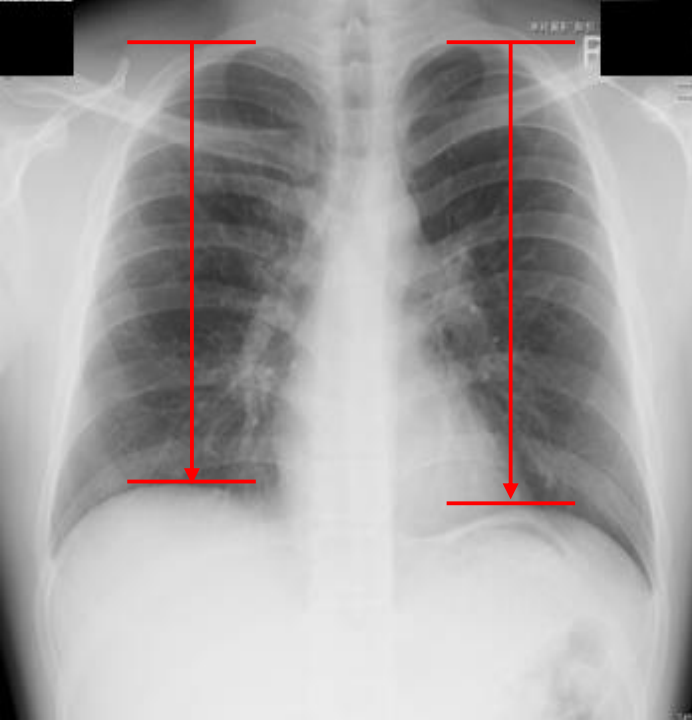


Figure 2

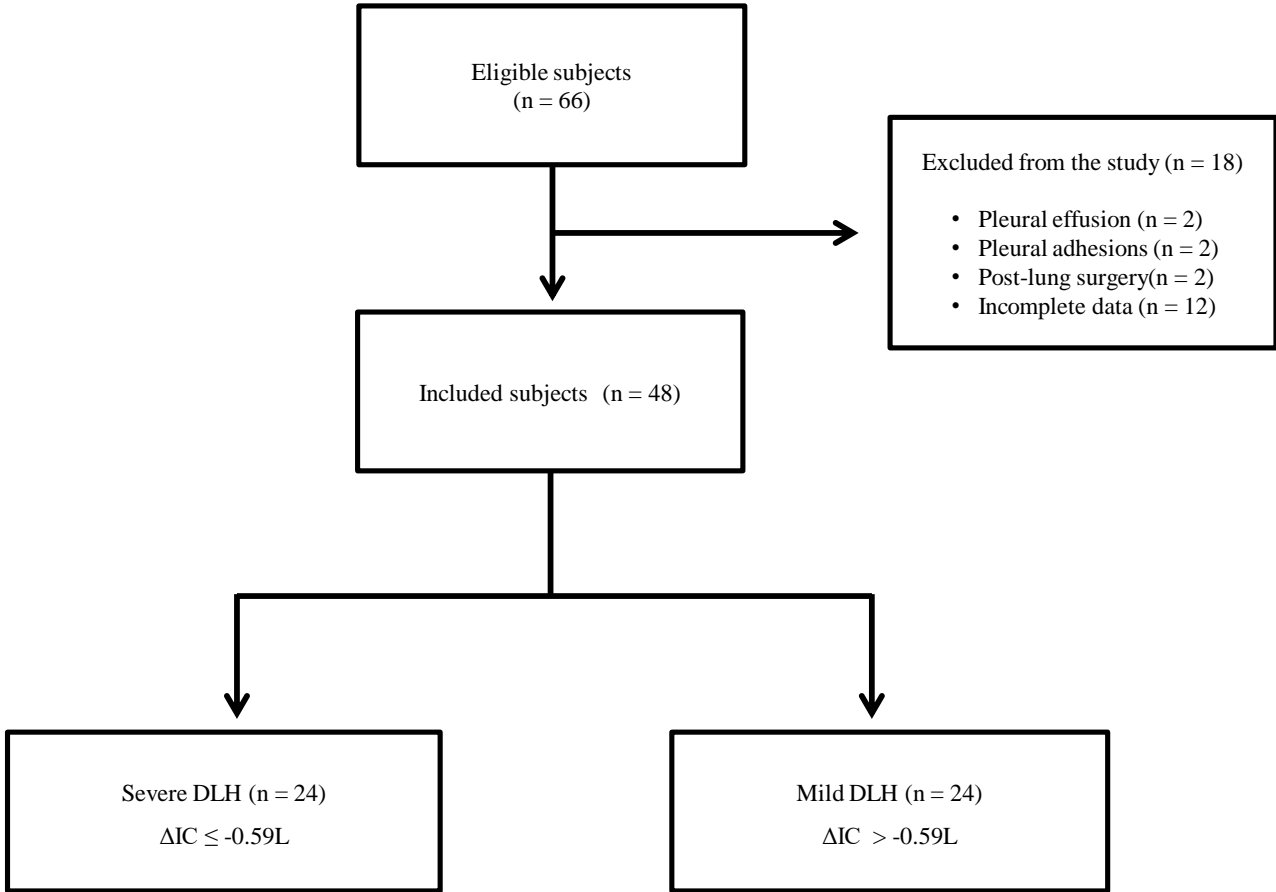




Figure 3

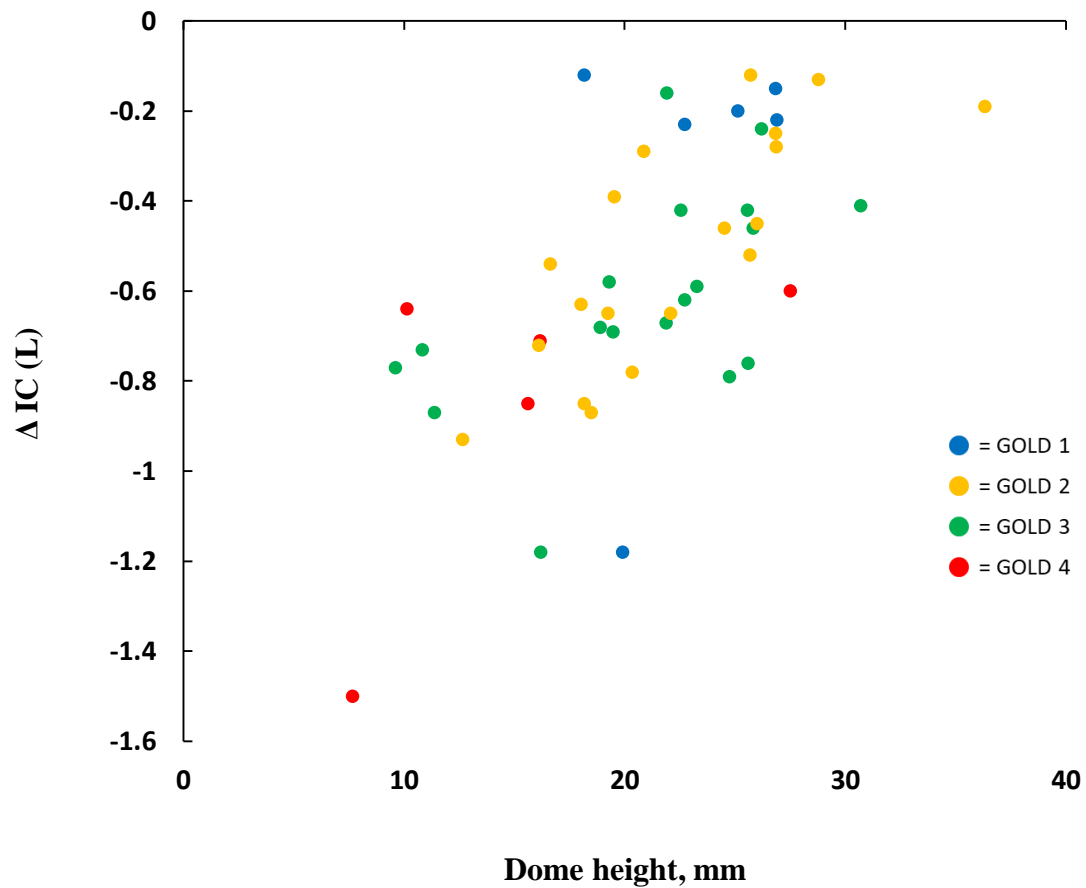
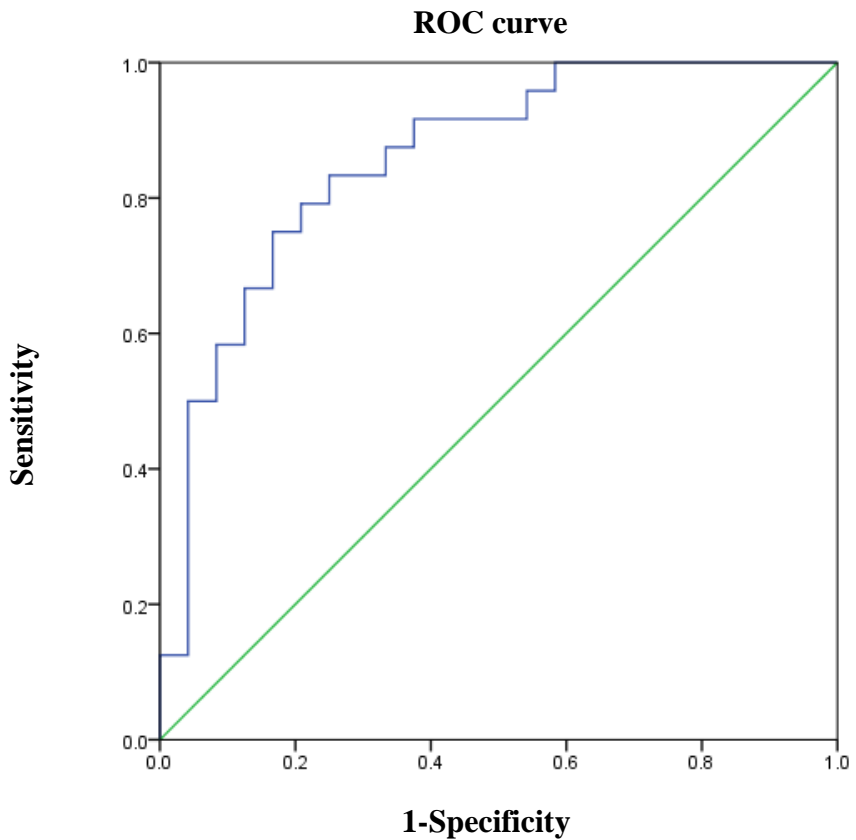


Figure 4



## **SUPPLEMENTARY INFORMATION**

### **Diaphragm dome height in chest X-ray as a predictor of dynamic lung hyperinflation in COPD**

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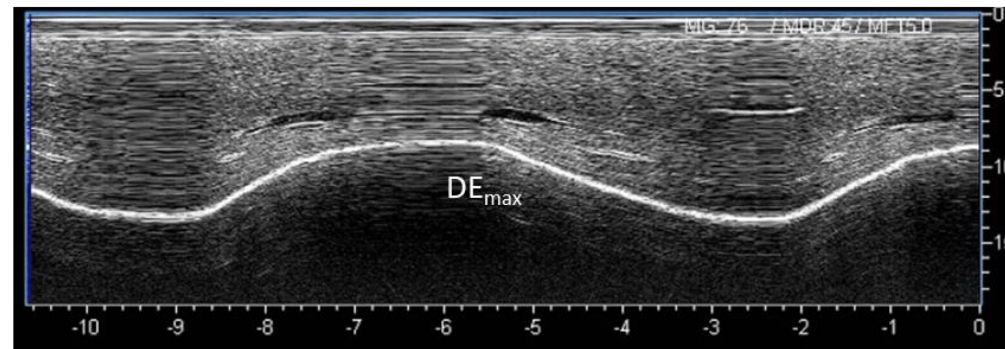
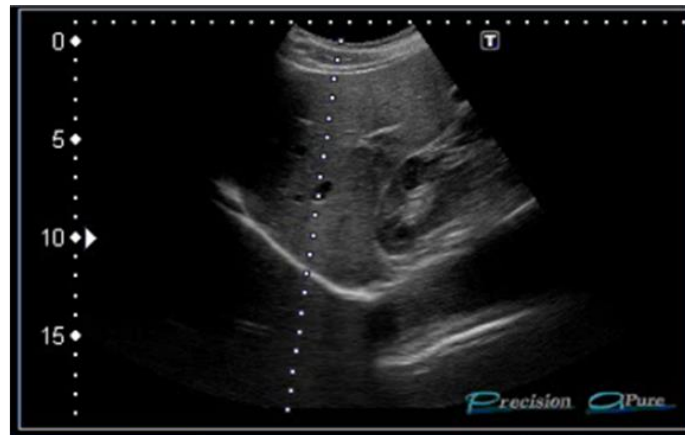
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Figure S1: Representative image of the right diaphragm.

Table S1: Multivariate ROC curve analysis with three models.

Figure S1: Representative image of the right diaphragm.



TableS1. Multivariate ROC curve analysis with three models.

Model 1	AICc	AUC	p value	Model 2	AICc	AUC	p value	Model 3	AICc	AUC	p value
Right dome height	48.8	0.858	<0.001	Right dome height	50.9	0.859	<0.001	Right dome height	54.5	0.859	<0.001
Height			0.914	Height			0.756				
Age			0.567								
Sex			0.999								

AICc = Akaike Information Criterion corrected, AUC = Area under the curve