Diaphragm dome height on chest radiography as a predictor of dynamic lung hyperinflation in COPD

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Shareable abstract (@ERSpublications)
Diaphragm dome height on chest radiography, a basic and inexpensive measure, is a good predictor of dynamic lung hyperinflation severity in COPD, independent of the low attenuation area on chest computed tomography and FEV_1 % pred https://bit.ly/44XJ8Qm

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Abstract

Background and objective Dynamic lung hyperinflation (DLH) can play a central role in exertional dyspnoea in patients with COPD. Chest radiography is the basic tool for assessing static lung hyperinflation in COPD. However, the predictive capacity of DLH using chest radiography 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 radiography.

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 (ΔIC=IC lowest − IC at rest). The right diaphragm dome height and lung height were measured on plain chest radiography.

Results Of the 48 patients included, 24 were classified as having higher DLH (ΔIC $\leqslant$−0.59 L from rest; −0.59 L, median of all) and 24 as having lower DLH. Dome height correlated with ΔIC (r=0.66, p<0.001). Multivariate analysis revealed that dome height was associated with higher DLH independent of % low attenuation area on chest computed tomography and forced expiratory volume in 1 s (FEV_1) % predicted. Furthermore, the area under the receiver operating characteristic curve of dome height to predict higher DLH was 0.86, with sensitivity and specificity of 83% and 75%, respectively, at a cut-off of 20.5 mm. Lung height was unrelated to ΔIC.

Conclusion Diaphragm dome height on chest radiography may adequately predict higher DLH in patients with COPD.

Introduction

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 was associated with decreased exercise capacity in patients with COPD and reduced diaphragm mobility, which was assessed by the maximum

level of diaphragmatic 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-min walk distance, dyspnoea [5] and increased mortality [6].

Given that a plain chest radiograph is readily available and inexpensive, it is a quick and basic diagnostic tool for evaluating patients' lungs. Chest radiography 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 radiography 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 radiograph 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 radiography. We hypothesised 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, who visited the Department of Respiratory Medicine and Allergology at Kindai University Hospital between January 2018 and November 2022, had clinically stable COPD. 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 radiography 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 CPET was conducted on a bicycle ergometer according to the Ramp 10 W protocol (load increase of 10 W per 1 min to 1 W per 6 s). We analysed the following: peak oxygen consumption (peak V'_{O_2}) and ventilation equivalents for carbon dioxide (minute ventilation/carbon dioxide production (V'_E/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 (ΔIC=IC lowest−IC 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 ΔIC: lower DLH group and higher DLH group.

Lung hyperinflation was evaluated by plain chest radiography as follows: 1) 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 2) 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, Tokyo, Japan). Moreover, emphysema was quantified by calculating the percentage of the low attenuation area, determined according to the cut-off value of −950 HU on whole-lung CT 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, placed it on the axis of diaphragmatic displacement on the stored image, measured the displacement (supplementary figure S1) during each of three deep breaths, and then measured the DE_{max}.

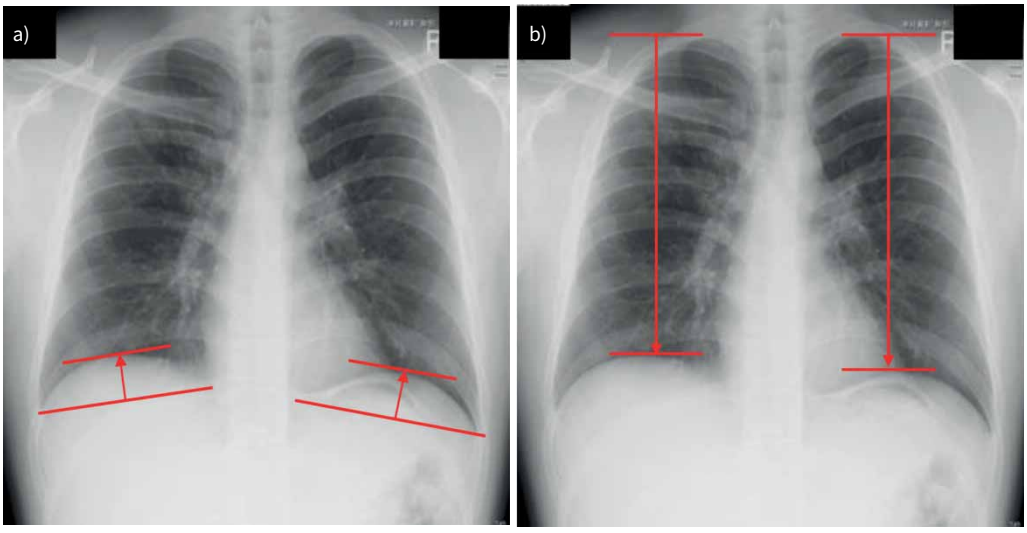

FIGURE 1 Illustrative example demonstrating the measurement of a) diaphragm dome height and b) lung height.

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 1 s (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 (P_{Imax}) 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 number 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 R software. The inclusion of 40 patients was required if the expected area under the curve 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±SD or median and interquartile range for parametric and nonparametric values. The higher DLH and lower DLH groups were compared using the t-test, Wilcoxon rank-sum test (% low attenuation area (LAA) and IC), or Chi-squared test (Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage), as appropriate.

The ROC curve method was used to determine the ability of dome height to predict the presence of higher DLH. The ability of variables to predict ΔIC was also evaluated using the multivariate logistic regression model, which included height, age and sex as covariates.

Given that ΔIC and dome height were normally distributed, the association between independent variables and ΔIC or dome height was analysed using the Pearson correlation coefficient. Univariate linear regression was included with ΔIC 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®, 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 two, pleural adhesions in two, post lung surgery in two and incomplete data in 12 patients. Incomplete data (n=12) included four cases with chest radiograph images that were taken >3 months after CPET, four cases without chest CT images and four cases without DLH measurements.

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

The ΔIC positively correlated with BMI, P_{Imax}, DE_{max}, right dome height (figure 3), and left dome height, FEV_1 % predicted and peak V'_{O_2} and negatively correlated with %LAA and V'_E/V'_{CO_2} (table 2). The correlation between ΔIC and right dome height was stronger than that between ΔIC and left dome height (table 2). Univariate linear regression was performed with ΔIC as the dependent variable and dome height as the independent variable, and the results were R^2=0.44, β=0.66, 95% CI 0.022–0.045 and p<0.001. The right dome height positively correlated with BMI, quadriceps muscle strength, P_{Imax}, DE_{max}, IC, FEV_1, FEV_1% predicted, FVC and peak V'_{O_2} and negatively correlated with V'_E/V'_{CO_2} (table 3). The association between ΔIC 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 higher DLH was 0.86, with a sensitivity of 83% and a specificity of 75% at a cut-off value of 20.5 mm (figure 4).

In the multivariate analysis, higher DLH (ΔIC from rest $\leqslant -0.59$ L) was the dependent variable, and dome height, %LAA and FEV_1 % predicted were the independent variables; variables %LAA and FEV_1 % predicted 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% CI 0.516–0.862, p=0.002; table 4).

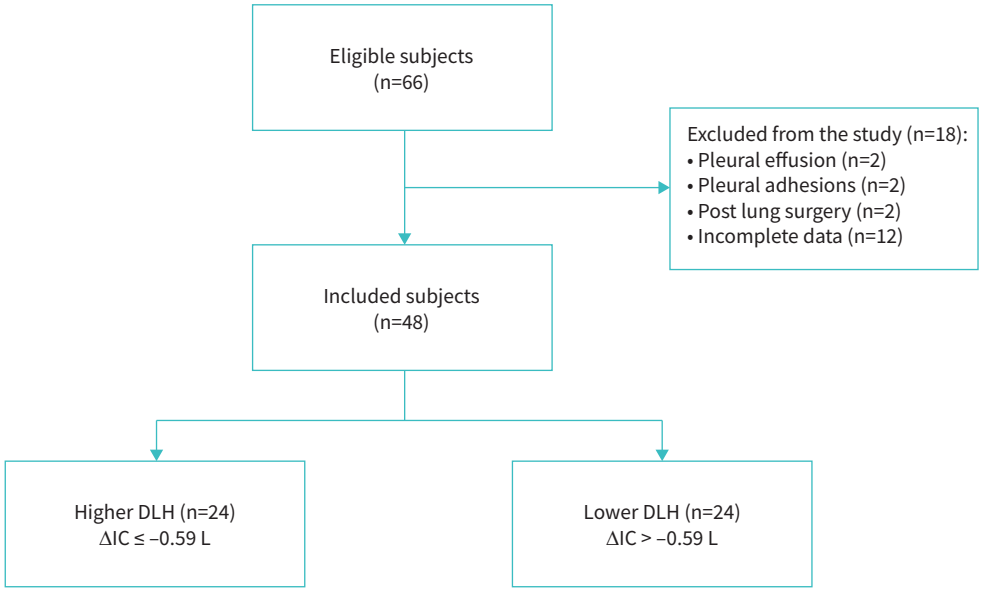

FIGURE 2 Flow diagram of study participants. DLH: dynamic lung hyperinflation; ΔIC: change of inspiratory capacity from rest during exercise.

TABLE 1 Baseline characteristics of study participants

	All	Higher DLH (ΔIC ⩽ −0.59 L)	Lower DLH (ΔIC > −0.59 L)	p-value[#]
Participants, n	48	24	24	
Male/female, n (%)	44/4 (91/9)	20/4 (80/20)	24/0 (100/0)	0.68
Age years	75±5	75±6	76±5	0.24
Body mass index kg·m^{-2}	21.4±3.3	20.3±3.1	22.4±3.2	<0.05
Body height cm	163.9±6.9	161.9±7.7	165.3±5.5	0.08
QMS kgf·kg^{-1}	0.52±0.13	0.52±0.14	0.57±0.16	0.36
P_{Imax} cmH$_2$O	54.4±21.8	41.8±15.0	67.0±24.1	<0.01
%P_{Imax}	80.3±33.4	66.0±26.0	94.7±33.8	<0.01
GOLD 1/2/3/4, n	6/19/18/5	1/8/10/5	5/11/8/0	<0.05[¶]
%LAA	20.4 (2.05–37.1)	33.9 (11.1–39.3)	8.9 (1.2–25.0)	<0.01[+]
DE$_{max}$ mm	46.7±8.6	40.5±5.6	53.0±6.2	<0.01
Plain chest radiograph				
Right dome height mm	21.2±5.9	17.6±5.2	24.7±4.1	<0.01
Left dome height mm	21.6±6.1	20.0±6.2	23.2±5.5	0.07
Right lung height mm	250.3±27.3	256.5±28.9	244.1±23.9	0.14
Left lung height mm	260.3±41.7	270.2±30.1	259.6±20.2	0.17
Spirometry				
IC L	1.99 (1.61–2.43)	1.89 (1.42–2.17)	2.39 (1.70–2.50)	<0.01[+]
FEV$_1$ L	1.39±0.55	1.14±0.51	1.60±0.50	<0.01
FEV$_1$ % predicted	55.6±22.0	47.0±20.4	64.3±20.1	<0.01
FVC L	2.98±0.72	2.83±0.70	3.13±0.68	0.23
FVC % predicted	89.2±18.4	87.7±17.2	90.8±19.4	0.58
Peak exercise measurements				
Peak V'_{O_2} mL·min^{-1}·kg^{-1}	11.6±3.5	9.0±2.3	14.2±2.3	<0.01
V'_E/V'_{CO_2}	48.6±7.3	52.1±7.1	45.2±5.6	<0.01
ΔIC from rest L	−0.57±0.30	−0.81±0.21	−0.33±0.15	<0.01

Data are presented as mean±SD or median (interquartile range) unless indicated otherwise. DLH: dynamic lung hyperinflation; ΔIC: change of inspiratory capacity from rest during exercise; QMS: quadriceps muscle strength; P_{Imax}: maximum inspiratory pressure; GOLD: Global Initiative for Chronic Obstructive Lung Disease; LAA: low attenuation area; DE$_{max}$: maximum diaphragmatic excursion; IC: inspiratory capacity; FEV$_1$: forced expiratory volume in 1 s; FVC: forced vital capacity; V'_{O_2}: oxygen uptake; V'_E/V'_{CO_2}: minute ventilation/carbon dioxide production. [#]: t-test, unless otherwise stated; [¶]: Chi-squared test; [+]: Wilcoxon rank-sum test.

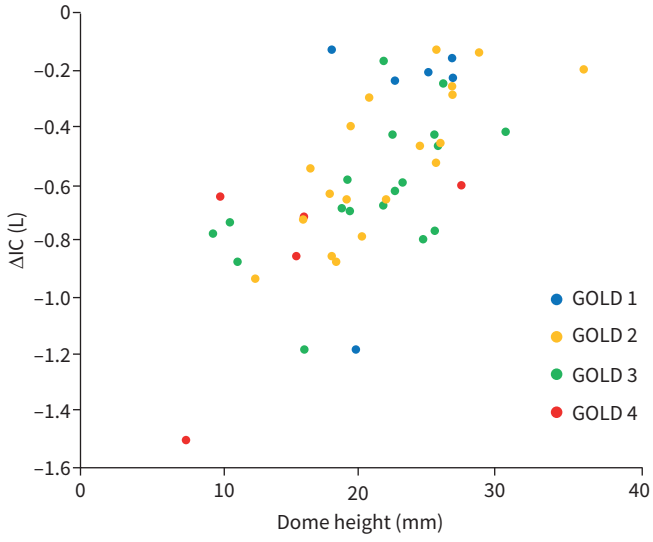

FIGURE 3 Correlation between change of inspiratory capacity from rest during exercise (ΔIC) and dome height of the right diaphragm: r=0.66, p<0.001 in all patients (n=48); r=0.86, p=0.062 in Global Initiative for Chronic Obstructive Lung Disease (GOLD) 1 (n=5); r=0.64, p=0.003 in GOLD 2 (n=19); r=0.53, p=0.019 in GOLD 3 (n=19); r=0.62, p=0.27 in GOLD 4 (n=5).

TABLE 2 Correlation coefficients for ΔIC (total patients n=48)

Independent variable	Pearson correlation coefficient (r)	p-value
Age years	0.12	0.43
Body mass index kg·m^{-2}	0.31	<0.05
Quadriceps muscle strength kgf·kg^{-1}	0.23	0.13
P_{Imax} cmH_2O	0.58	<0.001
%P_{Imax}	0.24	0.95
%LAA	−0.34	<0.05
DE_{max} 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_1 % predicted	0.43	<0.01
Peak V'_{O_2} mL·min^{-1}·kg^{-1}	0.81	<0.001
V'_E/V'_{CO_2}	−0.44	<0.01

ΔIC: change of inspiratory capacity from rest during exercise; P_{Imax}: maximum inspiratory pressure; LAA: low attenuation area; DE_{max}: maximum diaphragmatic excursion; FEV_1: forced expiratory volume in 1 s; V'_{O_2}: oxygen uptake; V'_E/V'_{CO_2}: minute ventilation/carbon dioxide production.

Finally, we performed multivariate ROC curve analysis with higher DLH (ΔIC $\leqslant -0.59$ L 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 appeared to be the best for model 3, *i.e.* a model without any adjustment including height (supplementary 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 radiography was useful for predicting ΔIC reflecting DLH in patients with COPD.

In this study, reduced dome height by plain chest radiography was a better predictor of higher DLH than %LAA or %FEV_1 in the multivariate analysis. In addition, dome height had higher sensitivity (83%) and specificity (75%) at a cut-off value of 20.5 mm for predicting higher DLH. Although mechanisms

TABLE 3 Correlation coefficients for dome height (total patients n=48)

	Pearson correlation coefficient (r)	p-value
Age years	0.10	0.43
Body mass index kg·m^{-2}	0.32	<0.01
Quadriceps muscle strength kgf·kg^{-1}	0.32	<0.05
P_{Imax} cmH_2O	0.53	<0.01
%P_{Imax}	0.49	<0.01
%LAA	−0.19	0.18
DE_{max} mm	0.65	<0.001
IC L	0.32	<0.05
ΔIC L	0.66	<0.001
FEV_1 L	0.44	<0.01
FEV_1 % predicted	0.34	<0.05
FVC L	0.40	<0.01
FVC % predicted	0.18	0.22
Peak V'_{O_2} mL·min^{-1}·kg^{-1}	0.63	<0.01
V'_E/V'_{CO_2}	−0.32	<0.05

P_{Imax}: maximum inspiratory pressure; LAA: low attenuation area; DE_{max}: maximum diaphragmatic excursion; IC: inspiratory capacity; ΔIC: change of inspiratory capacity from rest during exercise; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; V'_{O_2}: oxygen uptake; V'_E/V'_{CO_2}: minute ventilation/carbon dioxide production.

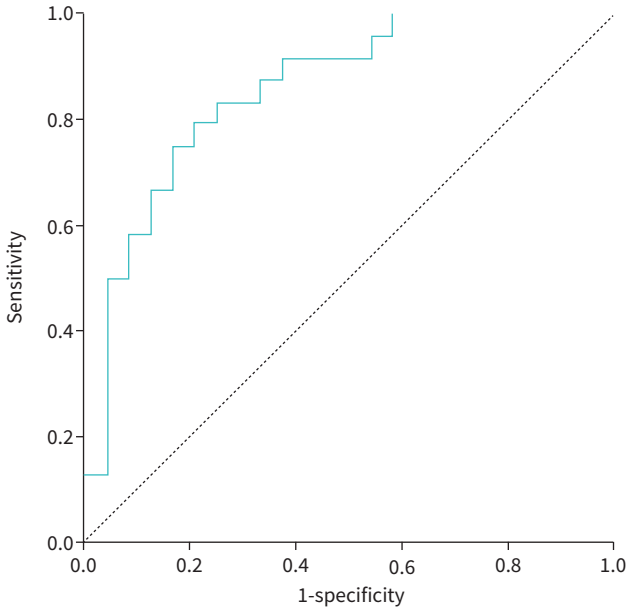

FIGURE 4 Receiver operating characteristic (ROC) curve of the dome height of the right diaphragm measured by plain chest radiography. The area under the ROC curve of dome height to predict higher dynamic lung hyperinflation was 0.86, with a sensitivity of 83% and a specificity of 75% at a cut-off value of 20.5 mm of dome height.

underlying the association between reduced dome height and higher 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 higher 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 radiography.

TABLE 4 Multivariate analysis for higher DLH (ΔIC from rest ⩽ −0.59 L)

Index	OR (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
FEV_1 % predicted	0.97 (0.929–1.012)	0.161

DLH: dynamic lung hyperinflation; ΔIC: change of inspiratory capacity from rest during exercise; LAA: low attenuation area; FEV_1: forced expiratory volume in 1 s.

Emphysema, as evaluated by CT, is associated with shorter 6-min walk distances, lower peak 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 radiography has low sensitivity for detecting emphysema [35]. CT 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 radiography [7]. In this study, %LAA correlated with DLH but was only marginally a predictor. One reason why dome height was a better predictor than %LAA might be that CT is taken in the supine position, whereas the radiograph is taken in the same standing position as during exercise. Therefore, plain chest radiography 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 radiography 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 standardised, thereby likely hampering the routine use of DE_{max}. Therefore, diaphragm evaluation by plain chest radiography 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 radiograph was obtained at the TLC level. However, in erect chest radiographs, individuals with normal respiratory function routinely inhale to ∼95% of TLC without vigorously coaxing [38]; 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 radiograph measurements of the diaphragm dome height could adequately predict DLH in patients with COPD. A plain chest radiograph is a rapid and basic diagnostic tool for evaluating patients' lungs. Measurement of a plain chest radiograph 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.

Provenance: Submitted article, peer reviewed.

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).

Conflict of interest: None declared.

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