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ABSTRACT

Objectives: To quantitatively compare diaphragmatic motion during tidal breathing in a standing position between chronic obstructive pulmonary disease (COPD) patients and normal subjects using dynamic chest radiography.

Materials and methods: Thirty-nine COPD patients (35 males; age, 71.3 ± 8.4 years) and 47 normal subjects (non-smoker healthy volunteers) (20 males; age, 54.8 ± 9.8 years) underwent sequential chest radiographs during tidal breathing using dynamic chest radiography with a flat panel detector system. We evaluated the excursions and peak motion speeds of the diaphragms. The results were analyzed using an unpaired *t*-test and a multiple linear regression model.

Results: The excursions of the diaphragms in COPD patients were significantly larger than those in normal subjects (right, 14.7 ± 5.5 mm vs. 10.2 ± 3.7 mm, respectively, P < 0.001; left, 17.2 ± 4.9 mm vs. 14.9 ± 4.2 mm, respectively, P = 0.022). Peak motion speeds in inspiratory phase were significantly faster in COPD patients compared to normal subjects (right, 16.3 ± 5.0 mm/s vs. 11.8 ± 4.2 mm/s, respectively, P < 0.001; left, 18.9 ± 4.9 mm/s vs. 16.7 ± 4.0 mm/s, respectively, P = 0.022). The multivariate analysis demonstrated that having COPD and higher body mass index were independently associated with increased excursions of the bilateral diaphragm (all P < 0.05), after adjusting for other clinical variables. *Conclusions:* Time-resolved quantitative evaluation of the diaphragm using dynamic chest radiography demonstrated that the diaphragmatic motion during tidal breathing in a standing position is larger and faster in COPD patients than in normal subjects.

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Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; CT, computed tomography; FEV, forced expiratory volume; FPD, flat panel detector; GOLD, global initiative for chronic obstructive pulmonary disease; MR, magnetic resonance; MRI, magnetic resonance imaging; SD, standard deviation; VC, vital capacity. * Corresponding authors at: Department of Radiology, Center for Pulmonary Functional Imaging, Brigham and Women's Hospital, Harvard Medical School, 75 Francis St.

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1. Introduction

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of morbidity and mortality worldwide [1]. The diagnosis of COPD is based on the results of pulmonary function tests; however, the analysis of respiratory kinetics is fundamental to systematic understanding of COPD [2]. Previous studies using X-ray fluoroscopy [3] and magnetic resonance (MR) fluoroscopy (dynamic MR imaging [MRI]) [2,4] have reported that diaphragmatic motion during forced breathing in COPD patients is smaller than that in normal subjects. However, to the best of our knowledge, diaphragmatic motion during tidal breathing in COPD patients has not been investigated, even though it is an essential part of their physiological respiratory conditions in their daily life. The abnormal gas exchange of oxygen and carbon dioxide in COPD [5] may be compensated by increased diaphragmatic motion; therefore, we hypothesized that diaphragmatic motion during tidal breathing in COPD patients may be larger than that in normal subjects.

Recently, dynamic chest radiography using a flat panel detector (FPD) with a large field of view was introduced for clinical use. This technique enables one to obtain sequential chest radiographs with high temporal resolution during respiration [6]. The radiation dose of dynamic chest radiography is lower than that of conventional X-ray fluoroscopy and computed tomography (CT), and its cost is lower than that of CT or MRI. Also, while CT and MRI are performed in a supine or prone position, dynamic chest radiography can be performed in a standing or sitting position, which reflects physiologically relevant daily activity.

The purpose of this study was to quantitatively compare diaphragmatic motion during tidal breathing in a standing position between COPD patients and normal subjects using dynamic chest radiography.

2. Materials and methods

2.1. Study population

This prospective study was approved by our institutional review board and all the participants provided written informed consent. From June 2009 to August 2011, consecutive 43 COPD patients who met the following inclusion criteria for the study were recruited: (1) clinical diagnosis of pure COPD based on clinical course, clinical symptoms, chest CT scans, and laboratory data, including airflow limitation assessed by pulmonary function tests with postbronchodilator inhalation, without acute respiratory infection or other respiratory diseases such as bronchiectasis or any type of interstitial lung disease; (2) current or ex-smokers; (3) over 20 years old; (4) scheduled for conventional chest radiography; (5) ability to follow instructions for tidal breathing. Patients with any of the following criteria were excluded: (1) pregnant or potentially pregnant or lactating (n=0); (2) incomplete dynamic chest radiography data sets (n=1); (3) diaphragmatic motion could not be analyzed by the software described below (n=3). Thus, a total of 39 COPD patients (35 men, 4 women; mean age, 71.3 ± 8.4 years; age range, 48-85 years) were finally included in the analysis. A normal (control) group of 49 consecutive volunteers who visited the health screening center of our hospital from May 2013 to February 2014 and met the following inclusion criteria was recruited for the study: (1) over 20 years old; (2) scheduled for conventional chest radiography; (3) normal pulmonary function test results (i.e., % vital capacity (%VC)>80% and forced expiratory volume (FEV)₁%>70%); (4) ability to follow tidal breathing instructions; (4) no smoking history; (5) no past medical history of respiratory diseases. Volunteers with any of the following criteria were excluded: (1) pregnant

or potentially pregnant or lactating (n = 0); (2) incomplete dynamic chest radiography data sets (n = 1); (3) diaphragmatic motion could not be analyzed by the software described below (n = 0); (4) suspected malnourishment (body weight < 30 kg) (n = 1). Thus, a total of 47 normal subjects (20 men, 27 women; age, 54.8 \pm 9.8 years; age range, 36–72 years) were finally included in the analysis as a control group. The heights and weights of the participants were measured, and the body mass index (BMI, weight in kilograms divided by height in meters squared) was calculated.

2.2. Imaging protocol of dynamic chest radiology ("dynamic X-ray phrenicography")

Posteroanterior dynamic chest radiography ("dynamic X-ray phrenicography") was performed using a prototype system (Konica Minolta, Inc., Tokyo, Japan) composed of an FPD (PaxScan 4030CB, Varian Medical Systems, Inc., UT, USA) and a pulsed X-ray generator (DHF-155HII with Cineradiography option, Hitachi Medical Corporation, Tokyo, Japan) [7]. All the subjects were scanned in the standing position and instructed to breathe normally in a relaxed way without deep inspiration/expiration (tidal breathing). The exposure conditions were as follows: tube voltage, 100 kV; tube current, 50 mA; duration of pulsed X-ray, 1.6-3.2 ms; source-toimage distance, 2 m; additional filter, 0.5 mm Al+0.1 mm Cu. The additional filter was used to filter out soft X-rays. The exposure time was approximately 10–15 s. The pixel size was $388 \times 388 \,\mu$ m, the matrix size was 1024×768 , and the overall image area was 40×30 cm. The gray-level range of the images was 16384 (14 bits), and the signal intensity was proportional to the incident exposure of the X-ray detector. The dynamic image data, captured at 7.5-30 frames/s, were synchronized with the pulsed X-ray. (Whereas conventional fluoroscopy utilizes a continuous X-ray beam, the dynamic chest radiography in this study utilizes pulsed X-rays, which prevent excessive radiation exposure to the subjects.) The entrance surface dose for dynamic chest radiography was approximately 0.3-1.0 mGy.

2.3. Image analysis

The diaphragmatic motions on sequential chest radiographs (dynamic image data) during tidal breathing were analyzed using prototype software (Konica Minolta, Inc., Tokyo Japan) installed in an independent workstation (Operating system: Windows 7 Pro SP1, Microsoft, Redmond WA; CPU: Intel[®] Core[™] i5-5200U, 2.20 GHz; memory 16 GB). The edges of the diaphragms on each dynamic chest radiograph were automatically determined by means of edge detection using a Prewitt Filter [8,9]. A boardcertified radiologist with 14 years of experience in interpreting chest radiography selected the highest point of each diaphragm as the point of interest on the radiograph of the resting end expiratory position (Figs. 1a and 2a). These points were automatically traced by the template-matching technique throughout the respiratory phase (Figs. 1b and 2b, supplementary videos 1 and 2), and the vertical excursions of the bilateral diaphragm were calculated (Figs. 1c and 2c): the null point was set at the end of the expiratory phase, i.e., the lowest point (0 mm) of the excursion on the graph is the highest point of each diaphragm at the resting end-expiratory position. Then, the peak motion speed of each diaphragm was calculated during inspiration and expiration by the differential method (Figs. 1c and 2c). In addition, the inspiratory phase time, expiratory phase time, and respiratory cycle time (inspiratory phase time plus expiratory phase time) were calculated based on the excursion information and the time information (Figs. 1c and 2c). The vertical length from lung apex to the highest point of each diaphragm at the resting end-inspiratory position was defined as the peak distance of apex-diaphragm (Fig. 1d). We



Peak Distance of Apex-Diaphragm Resting End-Inspiratory Position Deep-Inspiration Breath-Hold

Fig. 1. Representative sequential chest radiographs and the graphs of excursion and peak motion of the diaphragms obtained by dynamic chest radiography with flat panel detector system (dynamic X-ray phrenicography) in a normal subject, as well as conventional chest radiograph in the same subject.

(a) Radiograph of the resting end-expiratory position obtained by dynamic chest radiography. (b) Radiograph of the resting end-inspiratory position obtained by dynamic chest radiography. (c) Graph showing the vertical excursions and the peak motion speeds of the bilateral diaphragm. (d) Schema of the peak distance of the apex-diaphragm. (e) Conventional chest radiograph at deep-inspiration breath-hold. A board-certified radiologist placed a point of interest (red point) on the highest point of each diaphragm on the radiograph at the resting end-expiratory position (a). These points were automatically traced by the template-matching technique throughout the respiratory phase (double arrows in b) (Supplementary video 1); the red double arrow indicates the vertical excursion of the right diaphragm and the blue double arrow indicates that of the left (b). Based on locations of the points on sequential radiographs, the vertical excursions and the peak motion speeds of the bilateral diaphragms were calculated (c). The null point (0mm) of the excursion on the graph is set

determined the ratio of excursion to the peak distance of apexdiaphragm (%). We also calculated the ratio of the left excursion to the right excursion (ratio of left/right excursion) and expiratoryto-inspiratory time ratio. One respiratory cycle was defined as a cycle from a resting end-expiratory position to the next resting endexpiratory position. We analyzed the data from all of the sequential chest radiographs in this respiratory cycle. If several respiratory cycles were involved in the 10–15 s examination time, the averages of the measurements were calculated.

2.4. Statistical analysis

Descriptive statistics are expressed as mean \pm standard deviation (SD) for continuous variables and as frequency and percentages for nominal variables. The participants' demographic characteristics and parameters of diaphragmatic motion in dynamic chest radiology between the normal subjects and the COPD patients were compared using Student's *t* test for continuous variables and the chi-square test for nominal/categorical variables. The associations between the prevalence of COPD and the excursions of the diaphragms adjusted for participants' characteristics were evaluated with multiple linear regression models adjusting for other clinical variables. The significance level for all tests was 5% (two-sided). All data were analyzed using a commercially available software program (JMP; version 12, SAS, Cary, North Carolina, USA).

3. Results

3.1. Participants' demographic characteristics

Table 1 shows the demographic characteristics of the normal subjects and the COPD patients. While there were significant differences in age, gender, smoking history, and parameters in pulmonary function tests between the normal subjects and COPD patients, no significant differences in height, weight, or BMI were observed.

3.2. Parameters of dynamic chest radiography (dynamic X-ray phrenicography)

Table 2 provides a summary of the parameters compared between normal subjects and COPD patients with dynamic X-ray phrenicography. The excursions of the diaphragms were significantly larger in the COPD patients than those in the normal subjects (right, 14.7 ± 5.5 mm vs. 10.2 ± 3.7 mm, respectively, P < 0.001; left, 17.2 ± 4.9 mm vs. 14.9 ± 4.2 mm, respectively, P = 0.022). Fig. 2 and Supplementary video 2 show examples of diaphragmatic motion in COPD patients. The ratio of left/right excursion was significantly lower in COPD patients compared to normal subjects (1.31 ± 0.66 vs. 1.57 ± 0.46 , respectively, P = 0.036). The peak motion speeds of the diaphragms in the inspiratory phase were significantly faster in COPD patients compared to normal subjects (Table 2). The peak motion speed of the right diaphragm in the expiratory phase was

at the end of the expiratory phase and indicates the highest point of each diaphragm at the resting end-expiratory position (c). Then, the peak motion speeds of the bilateral diaphragm were calculated during inspiration and expiration by the differential method (c). In addition, the inspiratory phase time, expiratory phase time, and respiratory cycle time (inspiratory phase time plus expiratory phase time) were calculated based on the excursion information and the time information (c). The vertical length from lung apex to the highest point of each diaphragm at the resting endinspiratory position was defined as the peak distance of the apex-diaphragm (d). Note that the positions of the bilateral diaphragms on the conventional chest radiograph at deep-inspiratory position (b) obtained by dynamic chest radiography. Also note that we did not evaluate the conventional chest radiograph at deep-inspiratory breath-hold (e) in this study.





Fig. 2. Representative sequential chest radiographs and the graphs of excursion and peak motion of the diaphragms obtained by dynamic chest radiography with flat panel detector system (dynamic X-ray phrenicography) in a COPD patient, as well as conventional chest radiograph in the same patient.

(a) Radiograph at the resting end-expiratory position obtained by dynamic chest radiography. (b) Radiograph at the resting end-inspiratory position obtained by dynamic chest radiography. (c) Graph showing the vertical excursions and the peak motion speeds of the bilateral diaphragm. (d) Conventional chest radiograph at deep-inspiration breath-hold. A board-certified radiologist placed a point of interest (red point) on the highest point of each diaphragm on the radiograph of the resting end-expiratory position (a). These points were automatically traced by the template-matching technique throughout the respiratory phase (a, b) (Supplementary video 2). Based on locations of the points on sequential radiographs, the vertical excursions and the peak motion speeds of the bilateral diaphragm were calculated (c). Zero mm in the excursion indicates that the highest point is set at the end of the expiratory phase) (c). Then, the peak motion speeds of the bilateral diaphragm were calculated during inspiration and expiration by the differential method (c). Note that the positions of the bilateral diaphragms on the conventional chest radiograph

significantly faster in COPD patients compared to normal subjects, although there were no significant differences in the peak motion speed of the left diaphragm in the expiratory phase between the two groups (Table 2).

3.3. Multivariate analysis of associations between the prevalence of COPD and excursions of the diaphragms adjusted for participants' characteristics

Because a significant difference in age and gender between normal subjects and COPD patients was observed, the robustness of the results in the difference in excursion between the two groups was assessed with a multiple linear regression model. In this multiple linear regression model, age, gender, BMI, tidal volume, and %VC were included as factors, taking into account the correlation among variables (e.g., BMI, height and weight; COPD, smoking history, FEV₁, FEV₁%, and %FEV₁; VC and %VC) (Table 3). This multivariate analysis demonstrated that having COPD and higher BMI were independently associated with increased excursions of the bilateral diaphragm (all P < 0.05) after adjusting for other clinical variables, and other variables, including age, gender, tidal volume, or %VC, were not significantly associated with the excursion of the diaphragms (Table 3).

4. Discussion

Our study revealed that diaphragmatic motion during tidal breathing in a standing position in COPD patients was larger than that in normal subjects, contrary to the results of previous studies that evaluated diaphragmatic motion during forced breathing [2–4]. The findings in our study are important because greater diaphragmatic motion during tidal breathing in COPD patients could be related to respiratory fatigue in their daily living, which has an adverse effect on their quality of life [10]. The larger diaphragmatic excursion during tidal breathing in COPD patients found in this study may be due to compensation for the abnormal gas exchange of oxygen and carbon dioxide in COPD [5]. Our study also demonstrated that the peak motion speed of the bilateral diaphragm in the COPD patients was significantly faster than that of the normal subjects. To the best of our knowledge, this study is the first to evaluate the motion speed of diaphragms and shows that dynamic chest radiography with a flat panel detector system, dynamic X-ray phrenicography, can provide time-resolved data as well as information on the diaphragmatic position. The faster motion speed in the COPD patients compared with the normal subjects would be related to the larger excursion of the diaphragm in the COPD patients. Thus, our study demonstrated that dynamic X-ray phrenicography is a useful method for the quantitative evaluation of diaphragmatic motion with a radiation dose almost comparable to conventional posteroanterior and lateral chest radiography [11], and that it could detect the physiological differences between COPD patients and normal subjects.

The results of our study showed that the ratio of left/right excursion was significantly lower in COPD patients compared to normal subjects, and to the best of our knowledge, this phenomenon has not been reported before. The previous studies using fluoroscopy during forced breathing in a standing position have reported that the excursion of the left diaphragm is significantly larger than those of the right in normal subjects [3,12], which is in accord with our results. The ratio of left/right excursion may be a useful

at deep-inspiration breath-hold (d) are lower than those on the radiograph of the resting end-inspiratory position (b) obtained by dynamic chest radiography. Also note that we did not evaluate the conventional chest radiograph at deep-inspiration breath-hold (d) in this study.

Table 1

Demographic characteristics of the study population.

	Normal subjects (n = 47)	COPD patients (n = 39)	Comparison between normal subjects and COPD patients
Demographic variables	Mean \pm SD (range) or n (%)	Mean \pm SD (range) or n (%)	<i>P</i> value ^a
Age (years)	54.8 ± 9.8 (36-72)	$71.3 \pm 8.4 (48 - 85)$	<0.001*
Female/Male (%)	27 (57.4%)/20 (42.6%)	4 (10.3%)/35 (89.7%)	<0.001*
Height (cm)	$162.2 \pm 9.3 (146.1 - 183.7)$	$163.3 \pm 6.0 (149.0 - 176.0)$	0.544
Weight (kg)	$58.9 \pm 10.4 (37 - 78)$	$56.9 \pm 10.7 \ (42 - 94)$	0.398
BMI (kg/m ²)	$22.3 \pm 3.0 (15.1 - 31.1)$	$21.3 \pm 3.6 (16.3 - 34.5)$	0.189
Smoking history			<0.001*
Current or Former (%)	0 (0%)	39 (100%)	
Never (%)	47 (100%)	0 (0%)	
Pulmonary function test			
Tidal volume (L)	$0.75 \pm 0.35 \ (0.33 - 1.76)$	$0.98 \pm 0.36 (0.39 2.30)$	0.003*
VC (L)	$3.34 \pm 0.87 \ (2.11 - 5.70)$	$2.73 \pm 0.75 (1.49 4.34)$	<0.001*
%VC (%)	$110.4 \pm 14.5 (92.1 - 159.6)$	$87.8 \pm 23.3 (44.6 - 140.0)$	<0.001*
FEV_1 (L)	$2.71 \pm 0.73 (1.58 - 4.72)$	$1.26 \pm 0.50 (0.32 2.41)$	<0.001*
FEV ₁ % (%)	$82.4 \pm 6.2 \ (70.5 - 97.0)$	$47.5 \pm 10.6 (20.9 68.9)$	<0.001*
%FEV ₁ (%)	$107.1 \pm 14.8 \ (80.6 163.9)$	$49.0\pm20.7(11.8\text{-}97.9)$	<0.001*

SD indicates standard deviation; BMI, body mass index; VC, vital capacity; FEV, forced expiratory volume.

^a *P* values were calculated using Student's *t* test or chi-squared test.

* Indicates P<0.05.

physiological parameter to detect the differences between normal subjects and COPD patients.

We found that higher BMI as well as having COPD were independently associated with the increased excursions of the diaphragms after adjusting for other clinical variables. Although the exact mechanism of these relationships remains to be investigated, a previous study has shown that BMI is positively correlated with peak oxygen consumption [13], and the increased oxygen consumption in obese subjects may affect diaphragmatic movement.

Table 2

Comparison of parameters in dynamic chest radiography (dynamic X-ray phrenicography) between normal subjects and COPD patients.

Parameters		Normal subjects (n=47)	COPD patients (n=39)	Comparison between normal subjects and COPD patients
		Means ± SD (range)	Means \pm SD (range)	P value ^a
Excursion of the diaphragm (mm)	Right	10.2 ± 3.7	14.7 ± 5.5	<0.001*
		(3.6–23.7)	(3.0-27.8)	
	Left	14.9 ± 4.2	17.2 ± 4.9	0.022*
		(5.3-25.8)	(2.6-26.2)	
Ratio of left/right excursion		1.57 ± 0.46	1.31 ± 0.66	0.036*
		(0.88-3.11)	(0.43-4.51)	
Peak motion speed of the diaphragm (inspiratory	Right	11.8 ± 4.2	16.3 ± 5.0	<0.001*
phase) (mm/s)		(5.3-26.9)	(6.1-29.5)	
	Left	16.7 ± 4.0	18.9 ± 4.9	0.022*
		(7.8–27.3)	(4.6-30.8)	
Peak motion speed of the diaphragm (expiratory	Right	8.8 ± 3.2	12.0 ± 4.8	<0.001*
phase) (mm/s)		(3.6-21.8)	(1.7-21.1)	
	Left	13.5 ± 3.8	14.5 ± 5.2	0.331
		(5.1-22.6)	(2.2-32.5)	
Inspiratory phase time (s)	Right	1.64 ± 0.48	1.56 ± 0.48	0.441
		(1.02-2.97)	(0.94-2.87)	
	Left	1.63 ± 0.43	1.59 ± 0.45	0.641
		(1.02 - 2.77)	(0.98 - 2.93)	
Expiratory phase time (s)	Right	2.16 ± 0.57	2.42 ± 0.77	0.083
		(1.00-3.33)	(1.47 - 4.67)	
	Left	2.16 ± 0.60	2.38 ± 0.75	0.147
		(0.97-3.33)	(1.46-4.93)	
Respiratory cycle time (s)	Right	3.80 ± 0.95	3.96 ± 1.09	0.475
		(2.30-6.07)	(2.67 - 6.93)	
	Left	3.78 ± 0.94	3.94 ± 1.04	0.461
		(2.23-5.73)	(2.67-6.93)	
Expiratory-to-inspiratory time ratio	Right	1.36 ± 0.31	1.60 ± 0.51	0.007*
	U	(0.78-1.95)	(1.08 - 3.50)	
	Left	1.34 ± 0.27	1.53 ± 0.38	0.009*
		(0.78-1.85)	(1.05 - 2.80)	
Peak distance of apex-diaphragm (mm)	Right	216.3 ± 21.2	245.4 ± 29.1	< 0.001*
	U	(174.3-258.8)	(158.3-291.0)	
	Left	230.0 ± 20.0	259.9 ± 29.1	<0.001*
		(194.3-274.2)	(180.8-312.0)	
Percentage of excursion/apex-diaphragm-distance (%)	Right	4.8 ± 1.8	6.1±2.3	0.005*
	0	(1.6-10.6)	(1.1 - 11.3)	
	Left	6.5±1.9	6.7 ± 2.1	0.621
		(2.3-11.0)	(0.9–10.6)	
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^a *P* values were calculated using Student's *t* test.

* P<0.05.

Table	e 3
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Multivariate Analysis of Associations between Prevalence of COPD and Excursions of the Diaphragms Adjusted for Participants' Characteristics.

	For the excursion of right diaphragm			For the excursion of left diaphragm		
Variable	Coefficient ^a	SE	P value ^b	Coefficient ^a	SE	P value ^b
Intercept	0.35	5.07	0.945	-1.79	4.46	0.688
Normal vs. COPD (COPD)	2.72	0.79	0.001*	1.76	0.70	0.014*
Age	0.02	0.05	0.651	0.00	0.05	0.966
Gender (Female)	0.67	0.61	0.272	0.10	0.53	0.849
BMI	0.32	0.16	0.043*	0.70	0.14	< 0.001*
Tidal volume	1.00	1.56	0.521	0.12	1.37	0.931
%VC	0.03	0.03	0.303	0.02	0.02	0.329

The adjusted R²s were 0.28 for the excursion of the right diaphragm and 0.32 for the excursion of the left diaphragm.

^a Coefficient indicates increase in the dependent variable for one-unit increase in each independent variable.

^b *P* values were calculated using multiple linear regression analysis.

SE indicates standard error; BMI, body mass index.

indicates P < 0.05.</p>

Our study showed that the bilateral peak distances of the apexdiaphragm in COPD patients were significantly longer than those in the normal subjects, which is consistent with the results of previous reports using conventional radiography [14,15]. Additionally, we found that the percentage of excursion/apex-diaphragm-distance of the right was significantly larger in the COPD patients compared with the normal subjects. However, our results showed no significant differences in the percentage of excursion/apexdiaphragm-distance of the left between the two groups; the possible reason for the comparable percentage of excursion/apexdiaphragm-distance of the left between the two groups is that in COPD patients the larger excursion of the left diaphragm was canceled out by the longer peak distance of the left apex-diaphragm.

Although no significant differences in inspiratory phase time, expiratory phase time, or respiratory cycle time between normal subjects and COPD patients were observed in the present study, the expiratory-to-inspiratory time ratio in the COPD patients was significantly larger than that in the normal subjects and the expiratory phase time in COPD tended to be longer but without statistical significance. Our results are consistent with the previous reports describing that COPD patients have a prolonged expiratory phase time [16,17].

Our study has several limitations. First, our data is from a small number of participants recruited at a single institution, with 39 patients with COPD and 47 normal subjects. Additional studies with a larger cohort are needed to confirm our observations. The present study provided preliminary findings from the initial phase of the prospective study that can be validated in a larger cohort. Second, we evaluated only the motion of the highest point of the diaphragms for the sake of simplicity, and three-dimensional motion of the diaphragm could not be completely reflected in our results. This is because we believe that this simple method would be practical and more easily applicable in a clinical setting. Third, because of the small sample size, our COPD patients' data were not evaluated separately for each of the 4 severity categories defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD). A further study is in progress to evaluate the association between diaphragmatic motion and the severity of COPD by GOLD classification.

In conclusion, time-resolved quantitative evaluation of the diaphragm using dynamic chest radiography with flat panel detector system (dynamic X-ray phrenicography) demonstrated that diaphragmatic motion during tidal breathing in a standing position is larger and faster in COPD patients than in normal subjects.

Conflict of interest

HH received a research grant from Konica Minolta, Inc. The remaining authors (YY, MU, TA, TA, TA, MN, MJ, and SK) have no potential conflicts of interest related with this article.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ejrad.2016.12. 014.

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