



# Difference in diaphragmatic motion during tidal breathing in a standing position between COPD patients and normal subjects: Time-resolved quantitative evaluation using dynamic chest radiography with flat panel detector system (“dynamic X-ray phrenicography”)

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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,  $71.3 \pm 8.4$  years) and 47 normal subjects (non-smoker healthy volunteers) (20 males; age,  $54.8 \pm 9.8$  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,  $14.7 \pm 5.5$  mm vs.  $10.2 \pm 3.7$  mm, respectively,  $P < 0.001$ ; left,  $17.2 \pm 4.9$  mm vs.  $14.9 \pm 4.2$  mm, respectively,  $P = 0.022$ ). Peak motion speeds in inspiratory phase were significantly faster in COPD patients compared to normal subjects (right,  $16.3 \pm 5.0$  mm/s vs.  $11.8 \pm 4.2$  mm/s, respectively,  $P < 0.001$ ; left,  $18.9 \pm 4.9$  mm/s vs.  $16.7 \pm 4.0$  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.

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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 post-bronchodilator 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,  $71.3 \pm 8.4$  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)<sub>1</sub> >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-to-image 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  $388 \times 388 \mu\text{m}$ , the matrix size was  $1024 \times 768$ , and the overall image area was  $40 \times 30$  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, 2.20GHz; 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 board-certified 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

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