Mass and Fat Infiltration of Intercostal Muscles Measured by CT Histogram Analysis and Their Correlations with COPD Severity

Mi Jung Park, MD, Jae Min Cho, MD, Kyung Nyeo Jeon, MD, Kyung Soo Bae, MD, Ho Cheol Kim, MD, Dae Seob Choi, MD, Jae Boem Na, MD, Ho Cheol Choi, MD, Hye Young Choi, MD, Ji Eun Kim, MD, Hwa Seon Shin, MD

Rationale and Objectives: Chronic obstructive pulmonary disease (COPD) is characterized by progressive respiratory function impairment and respiratory muscle dysfunction. We hypothesized that the mass and fat infiltration of respiratory muscles correlates with COPD severity and emphysema extent.

Materials and Methods: Ninety-eight male patients with COPD underwent chest computed tomography (CT) and spirometry. The mass and fat infiltrations of intercostal and latissimus muscles were quantified as the cross-sectional area (CSA) and attenuation of these muscles using CT histogram analysis. Intercostal index and latissimus index were defined as intercostal CSAs and latissimus CSAs divided by body mass index. The emphysema extent was measured as the ratio of the emphysematous lung volume to the total lung volume using a density-mask technique. Pearson correlation analyses were performed to evaluate the relationships between these parameters. Multiple regression analysis was performed using forced expiratory volume in 1 second (FEV_1) as the dependent parameter and the clinical and CT data as the independent parameters.

Results: FEV_1 was significantly correlated with intercostal index ($r = 0.57$), latissimus index ($r = 0.34$), intercostal attenuation ($r = 0.62$), and latissimus attenuation ($r = 0.38$). Emphysema extent was significantly correlated with intercostal index ($r = -0.36$) and intercostal attenuation ($r = -0.50$). Multiple regression analysis showed that FEV_1 was predicted by intercostal attenuation ($B = 0.40$), intercostal CSA ($B = 0.23$), emphysema extent ($B = -0.23$), and age ($B = -0.21$, $R^2 = 0.64$, $P < .001$).

Conclusions: A decrease in intercostal mass and an increase in intercostal fat are associated with worsening of COPD severity.

Key Words: Respiratory muscles; intercostal muscles; pulmonary emphysema; computed tomography; chronic obstructive pulmonary disease.

Chronic obstructive pulmonary disease (COPD) is a heterogeneous disease by progressive respiratory function impairment and skeletal muscle dysfunction (1). The emphysema extent measured by computed tomography (CT) has been correlated with COPD severity (forced expiratory volume in 1 second [FEV_1]) and airflow obstruction (FEV_1/ forced vital capacity [FVC]) in the previous studies (2–6). The loss of muscle mass and change of muscle composition are important factors for assessing the skeletal muscle dysfunction. It has been demonstrated that quadriceps muscle area was correlated with COPD severity (7), and the depletion of peripheral muscle mass was a better predictor of mortality than body mass index (BMI) in patients with COPD (7,8). Furthermore, the attenuation of the mid-thigh muscle in elderly persons was associated with muscle strength and mobility performance (9).

Among skeletal muscles, respiratory muscles are unique and crucial for alveolar ventilation (10). Respiratory muscle weakness may result in dyspnea and respiratory failure, which are associated with high risks of mortality in patients with COPD (1,11). Intercostal and latissimus dorsi muscles have major and minor roles for respiration, respectively. Few studies have investigated the structure and function of intercostal muscle (12–15) and latissimus muscle (16), but they did not fully address the mass and tissue composition of these muscles in patients with COPD. Therefore, we aimed

Acad Radiol 2014; 21:711–717

From the Department of Radiology, Gyeongsang National University Hospital, College of Medicine, 90, Chilam-Dong, Jinju City, Gyeongnam-Do, Republic of Korea (M.J.P., J.M.C., K.N.J., K.S.B., D.S.C., J.B.N., H.C.C., H.Y.C., J.E.K., H.S.S.) and Department of Pulmonology, Gyeongsang National University Hospital, College of Medicine, Jinju City, Gyeongnam-Do, Republic of Korea (H.C.K.). Received October 26, 2013; accepted February 4, 2014. **Address correspondence to:** J.M.C. e-mail: pichola@naver.com

http://dx.doi.org/10.1016/j.acra.2014.02.003

to quantify the mass and fat infiltration of intercostal and latissimus dorsi muscles and the emphysema extent using chest CT and to investigate their relationship with COPD severity and airflow obstruction.

MATERIALS AND METHODS

Subjects

From December 2010 to April 2012, 98 male subjects were retrospectively recruited from patients with COPD at a single institution. The inclusion criteria were age ≥50 years, clinical diagnosis of COPD, and FEV_1/FVC ratio of <0.7. Our study excluded the patients with infectious and interstitial lung diseases that could affect the attenuation and volume of the lung parenchyma. Additional exclusion criteria included fluid overload state (eg, pleural and pericardial effusion, ascites, or anasarca), history of chest surgery, chest wall deformity, and malignancy, which could affect the attenuation and mass of chest wall.

The age, BMI, and smoking history were recorded in all patients. Our retrospective study was approved by our institutional review board, and informed consent was waived.

Pulmonary Function Tests

Spirometry was performed using a Jaeger instrument (Würzburg, Germany) and included forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), and FEV_1/FVC ratio. FEV_1 was expressed as both an absolute value (FEV_1★) and a percentage of the predicted value (FEV_1 pred). FVC was expressed as an absolute value. All patients underwent obstructive spirometry with a postbronchodilator and were classified into four groups according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria (17): GOLD 1 ($FEV_1 \geq 80\%$), GOLD 2 ($50\% \leq FEV_1 < 80\%$), GOLD 3 ($FEV_1 < 50\%$), and GOLD 4 ($FEV_1 < 30\%$ or $FEV_1 < 50\%$ plus chronic respiratory failure). The time interval between spirometry and CT scan was <3 days.

Chest CT Protocol

CT examinations were performed using a 64-detector CT (Brilliance-64; Philips Medical Systems, The Netherlands). CT was performed with a detector configuration of 64×0.625 mm, a tube voltage of 120 kVp, a fixed tube current of 200 mAs, a pitch of 0.923, a gantry rotation time of 0.5 second, and a smooth reconstruction filter (Philips "B" filter). The scale of the attenuation coefficients ranged from −1024 to 3072 Hounsfield units (HU). The patient, in the arm-raised position, was asked to hold his breath at full inspiration. The whole lung parenchyma, from the lung apex to the diaphragm, was scanned in the craniocaudal direction. No patient received any intravenous contrast medium.

Respiratory Muscle Measurement

First, intercostal and latissimus dorsi muscles were selected as two representative respiratory muscles. Reconstructed images with a 3-mm slice thickness and 3-mm interval were analyzed using CT histogram software ("X section" analysis tool, Advantage Window 4.4; GE Healthcare, Milwaukee, WI, USA). Second, the region of interest (ROI) was placed as the outermost border of two muscles using freehand manual drawing. Third, the area of these muscles, which ranged from −29 to 100 HU, was calculated using CT histogram analysis. The different CT attenuation ranges were used to quantify the thigh muscle area (18–20), but there was no reference value for the quantification of respiratory muscle. We designated the CT attenuation range of respiratory muscle depending on the distribution of CT attenuation (pixel intensity) using CT histogram analysis. Last, the mass of respiratory muscles was calculated as cross-sectional area (CSA). The fat infiltration of respiratory muscles was calculated as the mean value of the voxel attenuation within ROI (Fig. 1).

Intercostal muscles were selected as the main respiratory muscle in this study. A representative coronal image was selected at the midline level, where the lateral arcs of the bilateral first ribs were visualized. All intercostal muscles can be contained in the coronal image of the midline, which is rarely affected by the angle of the rib. The CSAs of the bilateral third to eighth intercostal muscles were measured separately, and total 12 values were summed to measure intercostal muscle mass ("intercostal CSAs"). The first, second, and ninth to twelfth intercostal muscles were excluded because it was difficult to differentiate their boundaries with the adjacent chest wall and the diaphragm. BMI is a confounding factor for assessing the relationship between respiratory muscle mass and COPD severity. Therefore, the intercostal index was defined as intercostal CSAs divided by BMI. We measured the mean attenuation of the median fifth intercostal muscle among third to eighth intercostal muscles bilaterally and averaged both values ("intercostal attenuation").

Latissimus dorsi muscle was selected as the accessory respiratory muscle in this study. A representative axial image was selected at the level of eighth vertebra, because it was difficult to differentiate the boundaries with the adjacent teres major muscle at the upper thoracic vertebral level. The CSAs of the bilateral latissimus dorsi muscles were measured separately and summed both values ("latissimus CSAs"). The latissimus index was defined as latissimus CSAs divided by BMI. The mean attenuation of latissimus dorsi muscle was measured bilaterally and both values averaged ("latissimus attenuation").

To assess the interobserver variability of intercostal CSAs, intercostal attenuation, latissimus CSAs, and latissimus attenuation, these parameters were independently measured by two radiologists. The mean of the two values was used for the analysis.

Emphysema Extent

The segmentation of the emphysema volume was performed using the density-mask method with postprocessing software