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Association of pectoralis muscle area on computed tomography with airflow limitation severity and respiratory outcomes in COPD: A population-based prospective cohort study

K. Zhou[a,1], F. Wu[a,b,1], N. Zhao[a], Y. Zheng[a], Z. Deng[a], H. Yang[a], X. Wen[a], S. Xiao[a], C. Yang[c], S. Chen[d], Y. Zhou[a,b,*], P. Ran[a,b,*], on behalf of the ECOPD study investigators

[a] *State Key Laboratory of Respiratory Disease, National Clinical Research Center for Respiratory Disease, National Center for Respiratory Medicine, Guangzhou Institute of Respiratory Health, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China*
[b] *Guangzhou Laboratory, Bio-island, Guangzhou, China*
[c] *Department of Pulmonary and Critical Care Medicine, Wengyuan County People's Hospital, Shaoguan, China*
[d] *Medical Imaging Center, Wengyuan County People's Hospital, Shaoguan, China*

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Abstract
Background: Previous studies have shown that patients with chronic obstructive pulmonary disease (COPD) of severe or very severe airflow limitation have a reduced pectoralis muscle area (PMA), which is associated with mortality. However, whether patients with COPD of mild or moderate airflow limitation also have a reduced PMA remains unclear. Additionally, limited evidence is available regarding the associations between PMA and respiratory symptoms, lung function, computed tomography (CT) imaging, lung function decline, and exacerbations. Therefore, we conducted this study to evaluate the presence of PMA reduction in COPD and to clarify its associations with the referred variables.
Methods: This study was based on the subjects enrolled from July 2019 to December 2020 in the Early Chronic Obstructive Pulmonary Disease (ECOPD) study. Data including questionnaire, lung function, and CT imaging were collected. The PMA was quantified on full-inspiratory CT at the aortic arch level using predefined -50 and 90 Hounsfield unit attenuation ranges. Multivariate linear regression analyses were performed to assess the association between the PMA and airflow limitation severity, respiratory symptoms, lung function, emphysema, air trapping, and the

* Corresponding authors at: State Key Laboratory of Respiratory Disease, National Clinical Research Center for Respiratory Disease, National Center for Respiratory Medicine, Guangzhou Institute of Respiratory Health, The First Affiliated Hospital of Guangzhou Medical University, 151 Yanjiang Xi Road, Guangzhou 510120, China.
E-mail addresses: zhouyumin410@126.com (Y. Zhou), pxran@gzhmu.edu.cn (P. Ran).
[1] These authors contributed equally to this work.

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annual decline in lung function. Cox proportional hazards analysis and Poisson regression analysis were used to evaluate the PMA and exacerbations after adjustment.
Results: We included 1352 subjects at baseline (667 with normal spirometry, 685 with spirometry-defined COPD). The PMA was monotonically lower with progressive airflow limitation severity of COPD after adjusting for confounders (vs. normal spirometry; Global Initiative for Chronic Obstructive Lung Disease [GOLD] 1: β=-1.27, P=0.028; GOLD 2: β=-2.29, P<0.001; GOLD 3: β=-4.88, P<0.001; GOLD 4: β=-6.47, P=0.014). The PMA was negatively associated with the modified British Medical Research Council dyspnea scale (β=-0.005, P=0.026), COPD Assessment Test score (β=-0.06, P=0.001), emphysema (β=-0.07, P<0.001), and air trapping (β=-0.24, P<0.001) after adjustment. The PMA was positively associated with lung function (all P<0.05). Similar associations were discovered for the pectoralis major muscle area and pectoralis minor muscle area. After the 1-year follow-up, the PMA was associated with the annual decline in the post-bronchodilator forced expiratory volume in 1 s percent of predicted value (β=0.022, P=0.002) but not with the annual rate of exacerbations or the time to first exacerbation.
Conclusion: Patients with mild or moderate airflow limitation exhibit a reduced PMA. The PMA is associated with airflow limitation severity, respiratory symptoms, lung function, emphysema, and air trapping, suggesting that PMA measurement can assist with COPD assessment.

Introduction

Chronic obstructive pulmonary disease (COPD) is one of the most common chronic respiratory diseases. It is characterized by persistent airflow limitation and is associated with extrapulmonary comorbidities such as heart disease, osteoporosis, diabetes, and muscle wasting.[1] With an increased understanding of extrapulmonary comorbidities, we are now aware that muscle wasting is associated with quality of life and mortality.[2–4] The body mass index (BMI) is commonly used to clinically assess muscle wasting in patients with COPD; however, it reflects wasting of tissues including muscle, bone, and fat, which is not simultaneously accompanied by a corresponding loss in muscle wasting.[5–8] Additionally, the BMI does not accurately reflect muscle wasting in patients with COPD.[8] One study showed that the pectoralis muscle area (PMA) quantified by computed tomography (CT) at full-inspiration at the level of the aortic arch was more effective than the BMI in the assessment of muscle wasting.[9] The PMA on CT plays an important role in the assessment of muscle and muscle wasting in patients with COPD.[9,10]

A small-sample study showed that the PMA was significantly smaller in patients with Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage 3 (severe) or 4 (very severe) COPD, but not GOLD stage 2 (moderate) COPD, than in subjects with normal spirometry.[10] Whether the PMA is smaller in patients with GOLD stage 1 (mild) or 2 COPD than in subjects with normal spirometry remains unclear. To our knowledge, there are no studies on the associations between the PMA and respiratory symptoms, lung function, and CT imaging. Although the PMA is specifically associated with all-cause mortality in patients with COPD, whether it is associated with the annual decline in lung function and exacerbations in these patients remains unclear.

In view of this evidence gap, we conducted the present study aimed to evaluate the presence of PMA reduction in COPD and to clarify its association with airflow limitation severity, respiratory symptoms, lung function, CT imaging, lung function decline, and exacerbations.

Methods

Study design and subjects

The Early Chronic Obstructive Pulmonary Disease (ECOPD) study (ChiCTR1900024643) is a multicenter cohort study that initially enrolled about 2000 subjects.[11] The subjects in the current analysis were the first 1352 subjects who returned for a second visit approximately 1 year after their initial visit (up to December 2021). The key inclusion criteria were aged of 40 to 80 years, completion of the questionnaire interview, and complete quality-control spirometry and CT. The key exclusion criteria were acute exacerbation occurring within 4 weeks before study participation; chest, abdominal, or eye surgery within 3 months prior to screening; heart damage within 3 months before screening; and active pulmonary tuberculosis or malignant tumors. Finally, this study included 1352 subjects for baseline analysis (685 with spirometry-defined COPD and 667 with normal spirometry). Subjects included in the baseline analysis were followed up for 1 year until December 2021.

Written informed consent was obtained from all subjects prior to screening. The ECOPD study was approved by the Ethics Committee of The First Affiliated Hospital of Guangzhou Medical University (No.2018-53). This present study was in line with the principles of the Declaration of Helsinki.

High-resolution computed tomography

High-resolution CT was performed following the previously published protocol,[11] using a multidetector-row CT scanner (Siemens Definition AS Plus 128-slicer CT system; Siemens Healthineers, Erlangen, Germany and uCT 760 128-slicers CT system; United Imaging, Shanghai, China). The Parameters and acquisition details of CT images have been published previously.[11] The CT images were quantitatively assessed using the Chest Imaging Platform (www.chestimagingplatform.org) on the 3D Slicer 4.11 software (www.slicer.org).[12] The PMA was quantified in inspiratory CT at the level of the

aortic arch by the software using predefined −50 and 90 Hounsfield unit (HU) attenuation ranges.[10] The left and right pectoralis major muscles and pectoralis minor muscles were identified, and their areas (cm^2) were measured. The PMA was presented as the aggregate area of the left and right pectoralis major and minor muscles assessed in the axial plane. Emphysema was defined by the percentage of low-attenuation areas below −950 HU in full-inspiratory CT (inspiratory LAA_{-950}). Air trapping was defined by the percentage of low-attenuation areas below −856 HU in expiratory CT (expiratory LAA_{-856}).[13]

Questionnaire

A questionnaire interview was performed by well-trained staff. The standard respiratory epidemiological questionnaire in this study was modified from a COPD epidemiological study in China.[14] The smoking status was classified as never smoker, ex-smoker, and current smoker. Never smoker was defined as having smoked <100 cigarettes over a lifetime. Ex-smoker was defined as having smoked >100 cigarettes but having not smoked within the last 6 months at baseline. Current smoker was defined as smoking at baseline. The smoking index was defined as smoking years multiplied by the daily number of packs of cigarettes. Biomass exposure was defined as cooking or heating using biomass such as crop residues and wood for >1 year.[15] Occupational history of dust/gasses/fumes was defined as engagement in occupational exposure to dust/gasses/fumes for >1 year over a lifetime. Family history of respiratory diseases was defined as having parents, siblings, and/or children diagnosed with respiratory diseases by doctors (chronic bronchitis, emphysema, asthma, COPD, cor pulmonale, bronchiectasis, lung tumor, interstitial lung disease, or obstructive sleep apnea hypopnea syndrome). Respiratory symptoms were assessed using the modified British Medical Research Council (mMRC) dyspnea scale and COPD Assessment Test (CAT) score.[16] Acute respiratory events or exacerbations were defined as new onset or aggravation of at least two of the following five symptoms: cough, sputum production, purulent sputum, wheezing, and dyspnea persisting for at least 48 h, excluding left and right heart insufficiency, pulmonary embolism, pneumothorax, pleural effusion, and arrhythmia.[17,18] The severity of acute exacerbations of COPD was assessed and recorded by well-trained staff according to the following categories. Mild exacerbations were defined as those resulting in domiciliary management with COPD medications alone. Moderate exacerbations were defined as those resulting in outpatient or emergency department visits and the need for COPD medication. Severe exacerbations were defined as those resulting in hospitalization.

Spirometry

Spirometry was performed following the normative operation methods and standard quality-control principles recommended by the American Thoracic Society and Europe Respiratory Society.[19,20] We used a MasterScreen Pneumo PC spirometer (CareFusion, Yorba Linda, CA, USA) for spirometry measurements. Each subject needed to fit at least three acceptable measurement values and two repeatable measurement values (i.e., maximum and sub-maximum of forced vital capacity [FVC] and forced expiratory volume in 1 s [FEV_1] within 150 mL or 5%). The post-bronchodilator test was performed 20 min after inhalation of a bronchodilator (400 μg salbutamol [Ventolin; GlaxoSmithKline, UK]). We defined spirometry-defined COPD and airflow limitation severity according to the GOLD Report.[1] Subjects with a post-bronchodilator FEV_1/FVC of ≥0.70 and FEV_1% predicted of ≥80% were defined as having normal spirometry, and subjects with a post-bronchodilator FEV_1/FVC of <0.70 were defined as having spirometry-defined COPD. We used the reference values of the European Coal and Steel Community 1993 for the FEV_1% predicted, adjusted using conversion factors for the Chinese population (men, 0.95 and women, 0.93).[21,22] The airflow limitation severity was classified as GOLD stages 1 to 4 using the post-bronchodilator FEV_1% predicted (≥ 80%, ≥ 50% to < 80%, ≥ 30% to < 50%, and < 30%, respectively).[1]

Statistical analyses

Continuous variable with a normal distribution was expressed as mean ± standard deviation, and continuous variable with a non-normal distribution was expressed as median (interquartile range). Discontinuous variable was expressed as n (%). We evaluated the differences between the two groups using a two-sample t-test, chi-square test, or Fisher's exact test as required. Multivariate linear regression analyses were used to assess the PMA and airflow limitation severity, respiratory symptoms, lung function, emphysema, and air trapping after adjusting for confounding factors (i.e., age, sex, BMI, smoking status, smoking index, biomass exposure, family history of respiratory disease, and occupational history of dusts/gasses/fumes). Meantime, the GOLD ABE classification was used to assess the association of PMA and disease severity as a sensitivity analysis.[1] Multivariate linear regression analysis was used to evaluate the PMA and the annual decline in lung function after adjustment. Cox proportional hazards analysis and Poisson regression analysis were used to evaluate the PMA and acute respiratory events/exacerbations adjusted by confounding factors. We repeated the above analyses for the pectoralis major muscle area and pectoralis minor muscle area. Statistical analyses were performed using SPSS 25.0 software (IBM Corp., Armonk, NY, USA). Two-sided P values of <0.05 indicated statistical significance.

Results

Table 1 shows the subjects' baseline characteristics (normal spirometry, n=667; spirometry-defined COPD, n=685).

PMA was associated with airflow limitation severity

Table 2 shows the association of the PMA with airflow limitation severity. The PMA was monotonically lower with progressive airflow limitation severity after adjusting for confounding factors (vs. normal spirometry; GOLD 1: β=−1.27, 95% confidence interval [CI], −2.41 to −0.14, P=0.028; GOLD 2: β=−2.29, 95%CI, −3.48 to −1.11, P<0.001; GOLD 3: β=−4.88, 95%CI, −6.94 to −2.83,

Table 1 Clinical characteristics of the subjects at baseline.

Variable	Normal spirometry (n=667)	Spirometry-defined COPD (n=685)	P Value
Age, years	58.0±7.7	64.8±7.1	<**0.001**
Male, no. (%)	400 (60.0)	631 (92.1)	<**0.001**
Body mass index, kg/m^2	23.5±3.1	22.3±3.3	<**0.001**
Smoking status, no. (%)			<**0.001**
Never smoker	352 (52.8)	89 (13.0)	
Ex-smoker	86 (12.9)	218 (31.8)	
Current smoker	229 (34.3)	378 (55.2)	
Smoking index, pack-years	18.9±28.3	35.0±30.4	<**0.001**
Biomass exposure, n (%)	266 (39.9)	287 (41.9)	0.31
Occupational history of dusts/gasses/fumes, n (%)	116 (17.4)	216 (31.5)	<**0.001**
Family history of respiratory diseases, n (%)	69 (10.4)	145 (21.3)	<**0.001**
Previous medication for respiratory disease, n (%)	73 (10.9)	351 (51.2)	<**0.001**
Previous diagnosis of COPD, n (%)	17 (2.3)	252 (36.8)	<**0.001**
mMRC dyspnea scale score	0.2±0.5	0.5±0.7	<**0.001**
CAT score	3.9±4.3	5.7±5.6	<**0.001**
Post-bronchodilator FEV_1, L	2.52±0.55	1.96±0.61	<**0.001**
Post-bronchodilator FEV_1 % of predicted value, %	100.9±12.5	75.3±19.8	<**0.001**
Post-bronchodilator FVC, L	3.19±0.73	3.36±0.78	<**0.001**
Post-bronchodilator FEV_1/FVC, %	79.3±5.6	58.0±9.7	<**0.001**
GOLD ABE classification, no. (%)			
GOLD stage A	–	595 (86.9)	
GOLD stage B	–	57 (8.3)	
GOLD stage E	–	33 (4.8)	
Airflow reversibility, n (%)	37 (5.5)	122 (17.8)	<**0.001**
Inspiratory LAA_{-950},%	0.3 (0.1−0.7)	2.0 (0.7−5.9)	<**0.001**
Expiratory LAA_{-856},%	3.6 (1.1−8.4)	25.9 (11.7−45.2)	<**0.001**

Data are mean ± standard deviation, n (%), or median (interquartile range).
Abbreviations: **COPD**, chronic obstructive pulmonary disease; **mMRC**, modified British Medical Research Council dyspnea score; **CAT**, COPD assessment test; **FEV_1**, forced expiratory volume in one second; **FVC**, forced vital capacity; **GOLD**, Global Initiative for Chronic Obstructive Lung Disease; **LAA_{-950}**, low-attenuation area of the lung with attenuation values below −950 Hounsfield units on inspiratory; **LAA_{-856}**, low-attenuation area of the lung with attenuation values below −856 Hounsfield units on expiratory.

P<0.001; GOLD 4: β=−6.47, 95%CI, −11.61 to −1.33, P=0.014). Age, sex, BMI, and smoking index were respectively associated with the PMA (all P<0.05). A similarly negative association was found in the pectoralis major muscle area and pectoralis minor muscle area, and in the GOLD ABE classification (Supplementary Table 1).

PMA was associated with respiratory symptoms and lung function

Table 3 shows the associations of the PMA with respiratory symptoms and lung function. Among all subjects, the PMA was negatively associated with the mMRC score (β=−0.005, 95%CI, −0.009 to −0.001, P=0.026) and CAT score (β=−0.06, 95%CI, −0.09 to −0.02, P=0.001) after adjusting for confounding factors. The PMA was positively associated with pre-bronchodilator or post-bronchodilator lung function including the FEV_1, FEV_1% predicted, FVC, and FEV_1/FVC (all P<0.05). A similarly positive association was found for the pectoralis major muscle area and pectoralis minor muscle area.

PMA was associated with emphysema and air trapping

Table 3 shows the association of the PMA with CT imaging. The PMA was negatively associated with emphysema (inspiratory LAA_{-950}: β=−0.07, 95%CI, −0.10 to −0.04, P<0.001) and airflow trapping (expiratory LAA_{-856}: β=−0.24, 95%CI, −0.35 to −0.12, P<0.001) in CT-quantitated imaging adjustment for confounding variables. The addition of the adjustment for confounding factors did not substantively alter the association between emphysema or air trapping and the pectoralis major or minor muscle area.

PMA and 1-year respiratory outcomes

Of 685 subjects with spirometry-defined COPD, 593 had 1-year of spirometry measurements (follow-up rate, 87%) and 618 had 1-year of complete exacerbation assessment data (follow-up rate, 90%). Of 667 subjects with normal spirometry, 563 had 1-year of follow-up spirometry measurements (follow-up rate, 84%) and 622 had 1-year follow-up acute respiratory event assessment data (follow-up rate, 93%).

Table 2 Multivariate linear regression model for muscle measurements with airflow limitation severity (n=1352).

Parameter	Pectoralis muscle area*			Pectoralis major muscle area*			Pectoralis minor muscle area*		
	Unstandardized $\beta^{\dagger}$	95% CI	P Value	Unstandardized $\beta^{\dagger}$	95% CI	P Value	Unstandardized $\beta^{\dagger}$	95% CI	P Value
Age (per 1 year)	−0.28	(−0.33, −0.22)	<**0.001**	−0.22	(−0.26, −0.18)	<**0.001**	−0.06	(−0.08, −0.04)	<**0.001**
Sex (male vs. female)	12.09	(10.52, 13.67)	<**0.001**	9.78	(8.56, 11.00)	<**0.001**	2.31	(1.75, 2.87)	<**0.001**
Body mass index (per 1 kg/m^2)	0.93	(0.79, 1.06)	<**0.001**	0.65	(0.55, 0.76)	<**0.001**	0.27	(0.23, 0.32)	<**0.001**
Ex-smoker (vs. never smoker)	1.58	(−0.31, 3.47)	0.10	1.12	(−0.34, 2.58)	0.13	0.47	(−0.21, 1.14)	0.18
Current smoker (vs. never smoker)	1.19	(−0.45, 2.82)	0.15	0.60	(−0.67, 1.86)	0.36	0.59	(−0.01, 1.18)	**0.046**
Smoking index (per 1 pack-year)	−0.03	(−0.05, −0.01)	**0.002**	−0.02	(−0.03, −0.01)	**0.003**	−0.007	(−0.013, −0.001)	**0.029**
Biomass exposure (yes vs. no)	0.13	(−0.71, 0.97)	0.76	0.23	(−0.42, 0.88)	0.48	−0.10	(−0.40, 0.20)	0.51
Occupational history of dusts/gasses/fumes (yes vs. no)	0.12	(−0.87,1.11)	0.81	−0.01	(−0.75, 0.78)	0.98	0.11	(−0.28, 0.53)	0.55
Family history of respiratory diseases (yes vs. no)	0.21	(−0.93,1.35)	0.72	0.08	(−0.80, 0.97)	0.85	0.12	(−0.31, 0.49)	0.55
GOLD 1 (vs. normal spirometry)	−1.27	(−2.41, −0.14)	**0.028**	−0.78	(−1.66, 0.10)	0.08	−0.49	(−0.89, −0.09)	**0.017**
GOLD 2 (vs. normal spirometry)	−2.29	(−3.48, −1.11)	<**0.001**	−1.51	(−2.42, −0.59)	**0.010**	−0.79	(−1.21, −0.36)	<**0.001**
GOLD 3 (vs. normal spirometry)	−4.88	(−6.94, −2.83)	<**0.001**	−3.68	(−5.27, −2.09)	<**0.001**	−1.21	(−1.94, −0.48)	**0.001**
GOLD 4 (vs. normal spirometry)	−6.47	(−11.61, −1.33)	**0.014**	−4.87	(−8.85, −0.89)	**0.017**	−1.60	(−3.43, 0.23)	0.09

Abbreviations: **GOLD**, Global Initiative for Chronic Obstructive Lung Disease; **CI**, confidence interval.

* Multiple linear regression models included for age, sex, body mass index, smoking status, smoking index, biomass exposure, occupational history of dusts/gasses/fumes, family history of respiratory diseases, and GOLD stage.

† Unstandardized β was the regression coefficient in multiple linear regression analysis that represented the extent of the independent variable's influence on the dependent variable.

Table 3 Association between muscle measurements and lung function, respiratory symptoms, and computed tomography imaging (n=1352).

Parameter	Pectoralis muscle area			Pectoralis major muscle area			Pectoralis minor muscle area		
	Unstandardized $\beta^{\dagger}$	95% CI	P Value	Unstandardized $\beta^{\dagger}$	95% CI	P Value	Unstandardized $\beta^{\dagger}$	95% CI	P Value
Respiratory Symptoms*									
mMRC	−0.005	(−0.009, −0.001)	**0.026**	−0.006	(−0.012, −0.001)	**0.030**	−0.009	(−0.022, 0.003)	0.13
CAT	−0.06	(−0.09, −0.02)	**0.001**	−0.06	(−0.11, −0.02)	**0.009**	−0.19	(−0.28, −0.09)	<**0.001**
Pre-bronchodilator Lung Function*									
FEV_1, L	0.010	(0.007, 0.014)	<**0.001**	0.012	(0.007, 0.017)	<**0.001**	0.026	(0.016, 0.036)	<**0.001**
FEV_1 % of predicted value, %	0.29	(0.16, 0.43)	<**0.001**	0.35	(0.18, 0.53)	<**0.001**	0.63	(0.25, 1.01)	**0.001**
FVC, L	0.007	(0.002, 0.011)	**0.002**	0.008	(0.002, 0.013)	**0.004**	0.015	(0.003, 0.026)	**0.015**
FEV_1/FVC, %	0.20	(0.13, 0.28)	<**0.001**	0.23	(0.14, 0.33)	<**0.001**	0.50	(0.29, 0.71)	<**0.001**
Post-bronchodilator Lung Function*									
FEV_1, L	0.010	(0.007, 0.014)	<**0.001**	0.012	(0.007, 0.016)	<**0.001**	0.03	(0.02, 0.04)	<**0.001**
FEV_1 % of predicted value, %	0.28	(0.15, 0.41)	<**0.001**	0.35	(0.18, 0.51)	<**0.001**	0.58	(0.22, 0.94)	**0.002**
FVC, L	0.005	(0.002, 0.009)	**0.007**	0.006	(0.001, 0.012)	**0.014**	0.013	(0.002, 0.024)	**0.022**
FEV_1/FVC, %	0.21	(0.14, 0.29)	<**0.001**	0.25	(0.15, 0.34)	<**0.001**	0.5	(0.3, 0.7)	<**0.001**
Computed Tomography Imaging*									
Inspiratory LAA_{-950}, %	−0.07	(−0.10, −0.04)	<**0.001**	−0.09	(−0.14, −0.05)	<**0.001**	−0.12	(−0.21, −0.02)	**0.014**
Expiratory LAA_{-856}, %	−0.24	(−0.35, −0.12)	<**0.001**	−0.28	(−0.43, −0.13)	<**0.001**	−0.57	(−0.90, −0.24)	**0.001**

Abbreviations: **CI**, confidence interval; **mMRC**, modified British Medical Research Council dyspnea score; **CAT**, COPD assessment test; **FEV_1**, forced expiratory volume in one second; **FVC**, forced vital capacity; **LAA_{-950}**, low-attenuation area of the lung with attenuation values below −950 Hounsfield units on inspiratory; **LAA_{-856}**, low-attenuation area of the lung with attenuation values below −856 Hounsfield units on expiratory.

* Multiple linear regression models adjusted for age, sex, body mass index, smoking status, smoking index, biomass exposure, occupational history of dusts/gasses/fumes, and family history of respiratory diseases.

† Unstandardized β was the regression coefficient in multiple linear regression analysis that represented the extent of the independent variable's influence on the dependent variable.

Table 4 Association between muscle measurements and lung function annual decline (n=1156).

Parameter	Pectoralis muscle area		
	Unstandardized β[†]	95% CI	P Value
Pre-bronchodilator Lung Function[*]			
FEV_1, L	0.00005	(−0.00008, 0.00017)	0.46
FEV_1 % of predicted value, %	0.002	(−0.003, 0.007)	0.48
FVC, L	0.00003	(−0.00020, 0.00025)	0.83
FEV_1/FVC, %	0.002	(−0.002, 0.005)	0.33
Post-bronchodilator Lung Function[*]			
FEV_1, L	0.00002	(−0.00009, 0.00013)	0.71
FEV_1 % of predicted value, %	0.022	(0.008, 0.035)	**0.002**
FVC, L	−0.00006	(−0.00026, 0.00014)	0.53
FEV_1/FVC, %	0.002	(−0.001, 0.002)	0.16

Abbreviations: **CI**, confidence interval; **FEV_1**, forced expiratory volume in one second; **FVC**, forced vital capacity.
[*] Multiple linear regression models adjusted for age, sex, body mass index, smoking status, smoking index, biomass exposure, occupational history of dusts/gasses/fumes, family history of respiratory diseases.
[†] Unstandardized β was the regression coefficient in multiple linear regression analysis that represented the extent of the independent variable's influence on the dependent variable.

Table 5 Association between muscle measurements and exacerbations (n=1240).

	Pectoralis muscle area					
	RR[*]	95%CI	P Value	HR[†]	95%CI	P Value
All subjects						
Total acute respiratory events or exacerbations	0.994	(0.980−1.009)	0.43	0.994	(0.977−1.011)	0.48
Moderate-to-severe acute respiratory events or exacerbations	0.989	(0.971−1.007)	0.24	0.990	(0.969−1.012)	0.38
Spirometry-defined COPD Patients						
Total exacerbations	0.987	(0.969−1.005)	0.16	0.984	(0.963−1.006)	0.15
Moderate-to-severe exacerbations	0.984	(0.963−1.006)	0.16	0.982	(0.956−1.009)	0.18

Abbreviations: **RR**, risk ratio; **CI**, confidence interval; **HR**, hazard ratio; **COPD**, chronic obstructive pulmonary disease.
[*] Poisson regression models adjusted for age, sex, body mass index, smoking status, smoking index, biomass exposure, occupational history of dusts/gasses/fumes, family history of respiratory diseases.
[†] Cox proportional hazards regression models adjusted for age, sex, body mass index, smoking status, smoking index, biomass exposure, occupational history of dusts/gasses/fumes, family history of respiratory diseases.

The results are displayed in Table 4. A multivariable linear regression analysis model was used to explore the relationship between the PMA and the annual decline in lung function. The PMA was associated with a reduced annual decline of post-bronchodilator FEV_1% predicted (β=0.022, 95%CI, 0.008 to 0.035, P=0.002) after adjusting for confounding factors. After the 1-year follow-up, the PMA was not associated with the annual rate of exacerbations (Table 5).

Discussion

Our study demonstrated that the PMA was significantly associated with airflow limitation severity, respiratory symptoms, lung function, emphysema, and air trapping after adjusting for confounding factors. Similar associations were discovered in the pectoralis major and minor muscle area. During the 1-year follow-up, the PMA was associated with an annual decline of the post-bronchodilator FEV_1% predicted.

Previous studies have only revealed reduced pectoral muscle in patients with severe and very severe airflow limitation compared with controls.[10,23] To our knowledge, this is the first study to show a reduced PMA in patients with mild or moderate airflow limitation, thus expanding the knowledge base in this field. Patients with mild or moderate airflow limitation have a reduced PMA, indicating not only worse lung function than individuals with normal spirometry but also extrapulmonary changes. We adjusted for age, sex, BMI, smoking status, smoking index, biomass exposure, family history, and occupational history using multivariate multiple linear regression when exploring the association between the PMA and airflow limitation severity. Therefore, the results of this study are convincing.

In the cross-sectional analysis, we consistently found that the PMA was associated with various aspects of COPD assessment, including airflow limitation severity, respiratory symptoms, lung function, emphysema, and air trapping. These results suggest that measurement of the PMA can assist with COPD assessment. However, the current

measurement of the PMA still requires doctors to manually import CT images into software. Thus, if the number of measurements is large, the workload will be large. This measurement method is not suitable for routine assessment of COPD. Automated cutting, extraction, and measurement of pectoralis muscles based on deep learning techniques are currently in development.[24] These techniques are expected to further incorporate pectoralis muscles into the routine assessment of COPD.

We also found that the PMA was associated with one indicator of the annual decline in lung function. This result indicates that the PMA is a potential prognostic marker in patients with COPD. We found no association between the PMA of community-based patients with COPD and exacerbations in 1-year follow-up results, possibly because of their lower occurrence of exacerbations than the hospital-based patients with COPD. Previous studies showed that severe exacerbations in patients with COPD were associated with respiratory muscle weakness.[25,26]

Another innovative aspect of this study is the sensitivity analysis of the pectoralis major and minor muscles. Our results indicated that either the pectoralis major muscle or pectoralis minor muscle is an important indicator of the patients' nutritional status, and their reductions are synchronous.

This study had several strengths. The major strength is that it was a prospective, large-sample, population-based study including subjects with normal spirometry and patients with COPD. A population-based study is better suitable for investigation of the initiation of disease than studies involving hospital-sourced patients. Additionally, participants who had never smoked were included in this study. Therefore, the conclusions of this study can be better extrapolated than the results of previous studies involving only heavy smokers.

This study also had some potential limitations. First, 3D Slicer software was used to measure the PMA in this study, but not the pectoralis muscle density. We did not have pectoralis muscle density measurements and could not assess the association between pectoralis muscle density and airflow limitation severity. However, a previous phantom study showed that measures of muscle area were more reliable than measures of muscle density.[27] Therefore, the absence of pectoral muscle density measurements is unlikely to have affected the clinical significance of our study findings. Second, the follow-up period of this study was 1 year, which may have been insufficient to assess the association of the PMA with lung function decline and exacerbation. Finally, the number of patients with GOLD stage 3 and 4 COPD was limited because of the enrollment of subjects from the community.

Conclusion

In summary, patients with mild or moderate airflow limitation had a reduced PMA. The PMA was associated with airflow limitation severity, respiratory symptoms, lung function, emphysema, and air trapping. Similar results were found for the pectoralis major and minor muscle areas. The PMA was associated with the annual decline in lung function but not with exacerbation. Further studies are needed to clarify that relationship.

Ethical approval and consent to participate

The study was approved by the Ethics Committee of The First Affiliated Hospital of Guangzhou Medical University (No. 2018-53), and written informed consent was obtained from all participants.

Data sharing statement

With the permission of the corresponding authors, we can provide participant data without names and identifiers. The corresponding authors have the right to decide whether to share the data based on the research objectives and plan provided.

Declaration of Competing Interest

All of the authors declare no competing interests.

CRediT authorship contribution statement

K. Zhou: Conceptualization, Supervision, Formal analysis, Data curation, Writing – review & editing, Writing – original draft. **F. Wu:** Conceptualization, Supervision, Formal analysis, Data curation, Writing – review & editing, Writing – original draft. **N. Zhao:** Writing – review & editing, Writing – original draft. **Y. Zheng:** Writing – review & editing, Writing – original draft. **Z. Deng:** Writing – review & editing, Writing – original draft. **H. Yang:** Writing – review & editing, Writing – original draft. **X. Wen:** Writing – review & editing, Writing – original draft. **S. Xiao:** Writing – review & editing, Writing – original draft. **C. Yang:** Writing – review & editing, Writing – original draft. **S. Chen:** Writing – review & editing, Writing – original draft. **Y. Zhou:** Conceptualization, Supervision, Formal analysis, Data curation, Writing – review & editing, Writing – original draft. **P. Ran:** Conceptualization, Supervision, Formal analysis, Data curation, Writing – review & editing, Writing – original draft.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.pulmoe.2023.02.004.

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