CT measurements of central pulmonary vasculature as predictors of severe exacerbation in COPD

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Abstract

To identify a predictive value for the exacerbation status of chronic obstructive pulmonary disease (COPD) subjects, we evaluated the relationship between pulmonary vascular measurements on chest CT and severe COPD exacerbation.

Six hundred three subjects enrolled in the COPDGene population were included and divided into nonexacerbator (n = 313) and severe exacerbator (n = 290) groups, based on whether they had an emergency room visit and/or hospitalization for COPD exacerbation. We measured the diameter of the main pulmonary artery (MPA) and ascending aorta (AA) at 2 different sites of the MPA (the tubular midportion and bifurcation) on both axial images and multiplanar reconstructions. Using multiple logistic regression analyses, we evaluated the relationship between each CT-measured pulmonary vasculature and exacerbation status.

Axial and multiplanar MPA to AA diameter ratios (PA:AA ratios) at the tubular midportion and the axial PA:AA ratios at the bifurcation indicated significant association with severe exacerbation. The strongest association was found with the axial PA:mean AA ratio at the bifurcation (adjusted odds ratio [OR] = 12.53, 95% confidence interval [CI] = 2.35–66.74, P = .003) and the axial PA:major AA ratio at the tubular midportion (adjusted OR = 10.72, 95% CI = 1.99–57.86, P = .006). No differences were observed in the MPA diameter. Receiver operating characteristic analysis of these variables indicates that they may serve as a good predictive value for severe exacerbation (area under the curve, 0.77–0.78). The range of cut-off value for PA:AA ratio was 0.8 to 0.87.

CT-measured PA:AA ratios at either the bifurcation or the tubular site, measured either on axial or multiplanar images, are useful for identification of the risk of severe exacerbation, and consequently can be helpful in guiding the management of COPD. Although CT measurement was used at the level of pulmonary bifurcation in previous studies, we suggest that future studies should monitor the tubular site of the MPA for maximum diagnostic value of CT in pulmonary hypertension or severe COPD exacerbation, as the tubular site of the MPA remains relatively constant on CT images.

Abbreviations: AA = ascending aorta, CI = confidence interval, COPD = chronic obstructive pulmonary disease, MPA = main pulmonary artery, OR = odds ratio, PA:AA ratio = main pulmonary artery to ascending aorta diameter ratio.

Keywords: chest CT, chronic obstructive pulmonary disease, COPD exacerbation, pulmonary artery diameter, pulmonary hypertension

1. Introduction

There is an important association between pulmonary hypertension and chronic obstructive pulmonary disease (COPD). It has been shown that pulmonary hypertension in COPD patients is predictive of hospitalization for acute exacerbation.[1,2] Previous studies have found a moderate-to-strong correlation between the axial CT measurement of the main pulmonary artery (MPA) diameter and pulmonary hypertension.[3–8] Recently, the CT value

of pulmonary arterial enlargement (MPA to ascending aorta [AA] diameter ratio [PA:AA ratio] of >1) was to correlated with the presence of pulmonary hypertension in severe COPD and strongly predicted COPD exacerbation.[9–11] Most studies have measured the MPA at or close to its bifurcation.[3–18] However, the site of measurement varied substantially. At the bifurcation, the MPA is often splayed, so that it may be difficult to find a reproducible site for measurement. Due to the morphologically complex shape and axis of the MPA and its branches, measurements of the MPA at different sites may be discordant and fail to accurately predict pulmonary hypertension or COPD exacerbation. In fact, a study tried to develop a reliable geometrical method to measure the MPA diameter at 4 separate sites on axial CT images.[19] In addition, several recent studies evaluating pulmonary hypertension in many cardiopulmonary diseases have used multiplanar reconstructions images with or without a quantitative analysis of pulmonary artery (PA)[14,20–23]: segmental PA size in various pulmonary hypertension, cross-sectional area of small PA in severe emphysema, PA pulsatility in COPD, semiautomated quantification of PA in sickle cell disease and right PA distensibility in primary and secondary hypertension showed diagnostic value for pulmonary hypertension. In this study, we sought to establish an optimal method for MPA measurement in an effort to predict exacerbation status, particularly severe exacerbation. We used multiplanar reconstructions to deal with the complex morphology of the MPA and its branches. We hypothesized that multiplanar CT measurements of the true orthogonal diameter of the MPA from 3D datasets strongly predict exacerbations compared with axial CT of its transverse diameter.

2. Materials and methods

2.1. Study population

The institutional review board of the National Jewish Health approved this retrospective study (HS 2778). Subjects of this investigation were participants in the COPDGene study, a multicenter observational study designed to identify genetic factors associated with COPD which enrolled 10,192 smokers with and without COPD across the Global Initiative for Chronic Obstructive Lung Disease (GOLD) stages based on spirometry.[24] Enrolment criteria for COPDGene have been described previously.[24] From this population, we randomly selected 200 subjects without COPD exacerbation and another 200 subjects who had a severe exacerbation in the preceding year. Additionally, we studied 203 COPDGene subjects at one institution. In this group, 113 subjects had no exacerbations in the preceding year and 90 patients had at least one severe exacerbation. Thus, the entire study group included a total of 290 subjects, who had a history of severe exacerbations and 313 subjects, who had no exacerbations. We evaluated the indices of COPD severity, including forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), FEV1/FVC, 6-minute walk distance (6-MWD), St. George's Respiratory Questionnaire (SGRQ), as well as body mass index, airflow obstruction, dyspnea, and exercise capacity (BODE).

Exacerbation episodes were defined and quantified by response to a respiratory epidemiology questionnaire modified from the Epidemiology Standardization Project questionnaire (American Thoracic Society-Division of Lung Diseases [ATS-DLD]-78).[25] Severe exacerbation was defined by increased dyspnea, cough, or sputum production warranting Emergency Room evaluation and/or hospitalization.[11] Mild-to-moderate exacerbations were defined by similar symptoms that were treated with antibiotics or systemic glucocorticoids in the outpatient setting or during an emergency room visit.[11]

2.2. CT scan examination

CT scans were acquired as part of the COPDGene study using multidetector CT scanners (at least 16 detector channels) without intravenous contrast.[24] Volumetric CT acquisitions were obtained on full inspiration using the standardized COPDGene study imaging protocol with 120 kVp, 200 mAs, and 0.5 rotation time. The images were reconstructed using the standard algorithm at submillimeter slice thickness (0.75 or 0.9 mm) and submillimeter interval (0.45, 0.5, or 0.625 mm).

2.3. CT measurements of pulmonary vasculature

CT scans were reviewed on a radiology workstation (Aquarius iNtuition Edition; TeraRecon, San Mateo, CA) by a chest radiologist, with 12 years of chest CT experience, who was blinded to clinical data. Two skilled radiologists with similar experiences tried to measure the MPA diameter, but ultimately only 1 radiologist was employed to measure the diameter.

The pulmonary vasculature was measured on 2D axial images and 3D multiplanar reconstructions created from the volumetric dataset.

The MPA was measured at its bifurcation and in its tubular portion. The bifurcation measurement was obtained at the level where the right and left PAs appeared to show equal size. The tubular measurement was obtained at the midportion of the MPA, adjacent to the AA.

On axial images, the widest diameter perpendicular to the short-axis of the MPA was measured at the bifurcation (Fig. 1A) and tubular sites (Fig. 1B). The AA major and minor diameters were measured using the same image used to obtain the bifurcation measurement of the MPA (Fig. 1A). On multiplanar images, we performed coronal oblique reconstructions of the MPA, which appeared as an approximately circular or oval structure, and measured the MPA major and minor diameters of bifurcation (Fig. 2) and tubular (Fig. 3) sites. Similarly, the axial oblique reconstructions of the AA were adjusted perpendicular to the short axis on both coronal and sagittal reconstruction planes and the AA major and minor diameters were measured at the level of MPA bifurcation (Fig. 4). The major and minor diameters of the MPA and AA were measured on axial and multiplanar reconstructions, and the mean value was subsequently calculated. Finally, the PA:AA ratios were determined using each of these measurements.

2.4. Statistical analysis

The descriptive data between the exacerbation groups were compared using the t test, Wilcoxon rank sum test, and Chi-square test, as appropriate. Descriptive statistics were used to define the baseline data (mean and, standard deviation [SD] and N [%], as appropriate). Simple and multiple logistic regression analyses were performed to assess the association between the CT-measured pulmonary vascular parameters at different sites and between 2 exacerbation groups. Receiver operating characteristic (ROC) curves were constructed to assess the optimal cut-off value for CT-measured parameters representative of severe COPD exacerbation. To examine the difference in the diagnostic accuracy of each CT-measured parameter for
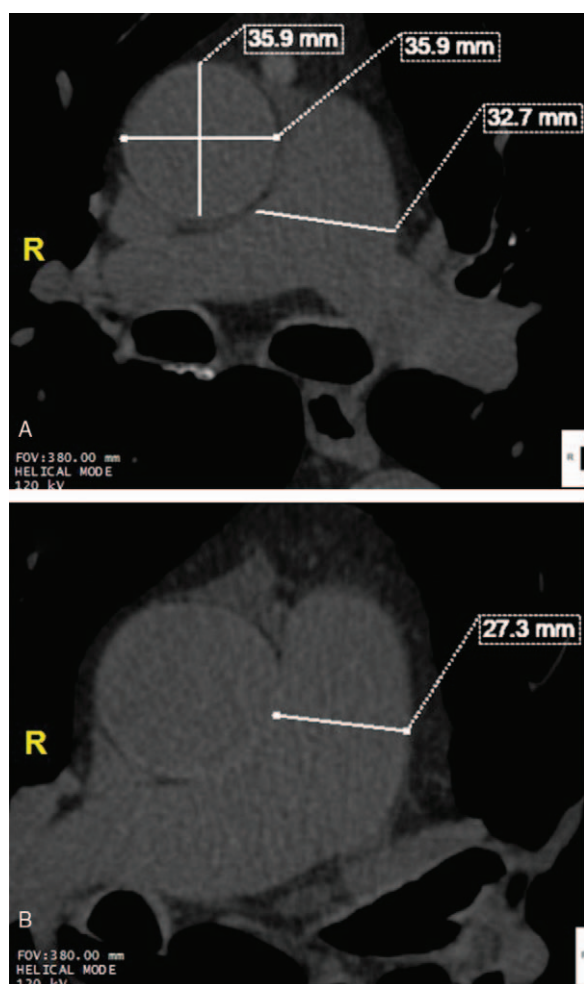
Figure 1. (A) Axial measurements of the MPA and AA diameters at the bifurcation site. The widest diameter perpendicular to the short axis of the MPA was measured. Using the same image of measured MPA, the AA major and minor diameters were measured. The AA showed a circular morphology with same major and minor diameters. (B) Axial measurement of the MPA diameter in the tubular site.

severe COPD exacerbation, we compared the area under the ROC curves (AUCs) by calculating a critical ratio proposed by Hanley and McNeil.[26] Statistical analysis was performed using SAS 9.3 (Carey, NC). *P* values less than .05 were considered statistically significant.

3. Results

3.1. Comparison of characteristics between nonexacerbator and severe exacerbator groups

The baseline demographic data of our patient population are summarized in Table 1. The severe exacerbator subjects had significantly lower FEV1, FVC, FEV1/FVC, and 6-MWD and significantly higher SGRQ score and BODE than the nonexacerbator group (*P* < .05). There were no significant differences in smoking history, age, male sex, and body mass index (*P* > .05).

3.2. Comparison of CT-measured pulmonary vascular parameters between nonexacerbator and severe exacerbator groups

A simple logistic regression analysis revealed significant differences in axial measurements of the MPA diameter at the tubular

site between the exacerbator groups (Table 2). Both axial and multiplanar CT measurements of PA:AA ratios at each site were significantly different between the exacerbator groups. The strongest associations with severe exacerbation were found with the axial PA:mean AA ratio at the bifurcation site (odds ratio [OR] = 12.14, 95% CI = 3.13–47.08, *P* = .0003) and the axial PA: major AA ratio at the tubular site (OR = 11.87, 95% CI = 3.00– 47.01, *P* = .0004) (Table 2).

A multiple logistic regression analysis adjusted for smoking duration, smoking pack years, age, male sex, FEV1/FVC, SGRQ score, and BODE indicated that MPA diameter was not significantly different between the groups. However, significant differences were found in the PA:AA ratio using axial measurements of the bifurcation and tubular sites and multiplanar measurements of the tubular site. The strongest associations with severe exacerbation were found with the axial PA:mean AA ratio at the bifurcation site (adjusted OR = 12.53, 95% CI = 2.35– 66.74, *P* = .003) and the axial PA:major AA ratio at the tubular site (adjusted OR = 10.72, 95% CI = 1.99–57.86, *P* = .006) (Table 2).

3.3. ROC curve analysis and optimal cut-off value for predicting severe COPD exacerbation

ROC curve analysis (using all the variables which were statistically significant in multiple logistic analyses) was used to assess the ability of CT-measured parameters in predicting severe COPD exacerbations (Table 3). All CT-measured parameters (axial PA:AA ratios at both sites and multiplanar PA:AA ratio at the tubular site) showed fair discriminatory ability to distinguish severe exacerbators from nonexacerbators (AUC range, 0.77–0.78). The axial PA:AA ratio at the tubular site was parameter with the highest AUC, with an optimal cut-off value ≥ 0.8. Notably, the AUC for this ratio was not significantly higher than that of the other ratios (axial PA:AA ratio at the bifurcation site and multiplanar PA:AA ratio at the tubular site). Logistic regression analyses were performed to examine the impact of the CT parameter ≥ the estimated optimal cut-off value for severe COPD exacerbation (Table 3). The PA:major AA ratio ≥ 0.8 measured on the axial CT scan at the tubular site and PA:major AA ≥ 0.87 measured by axial CT scan at the bifurcation site predicted the severe exacerbation status in COPD subjects. Multiplanar measurements of mean PA:major AA ratio ≥ 0.82 and mean PA:mean AA ratio ≥ 0.84 at the tubular site also predicted severe COPD exacerbation. The risk for severe COPD exacerbation associated with the axial PA:major AA ratio ≥ 0.80 at the tubular site was 1.72 (95% CI = 1.17–2.55, *P* = .006).

4. Discussion

COPD exacerbation is an important feature in the natural history of COPD and is associated with accelerated loss of lung function, poor quality of life, and substantial mortality risk.[27,28] Kessler et al[1] concluded that chronic hypercapneic respiratory insufficiency and pulmonary hypertension are predictive factors for hospitalization for acute exacerbation in a series of 64 patients with COPD. Severe pulmonary hypertension is an important complication of advanced COPD and predicts acute exacerbations, though pulmonary vascular abnormalities also occur early in the course of the disease.[11] Increased angiogenesis occurs in the lungs of patient with pulmonary hypertension, which is driven to a large extent by an exuberant proliferation of endothelial cells.[29,30] Angiogenesis is a complex process that
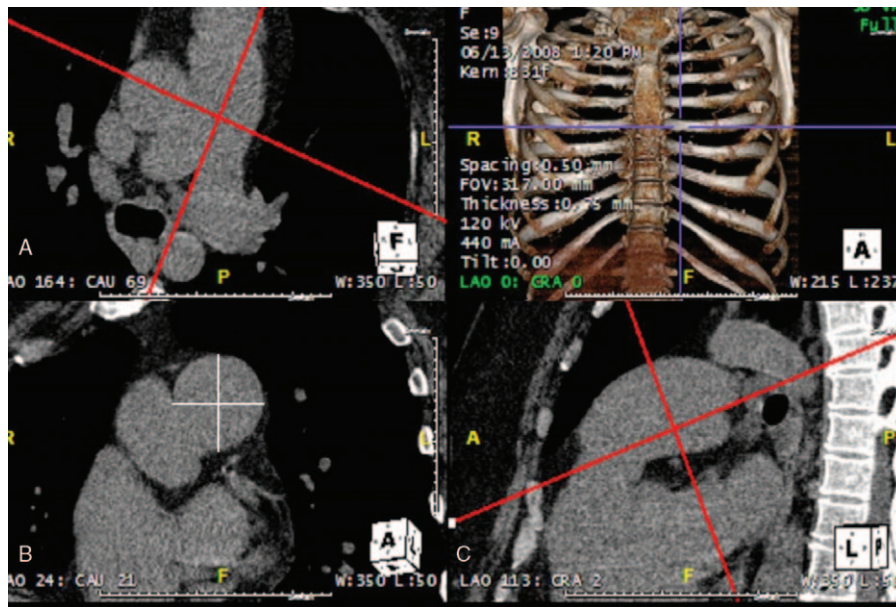
Figure 2. Multiplanar measurements of the MPA major and minor diameters at the bifurcation site. Coronal oblique reconstruction of the MPA (B) was adjusted perpendicular to the short axis of the axial (A) and sagittal (C) reconstruction planes at the bifurcation site.

leads to the formation of new blood vessels from a preexisting vasculature.[31,32] The angiogenesis in COPD is induced by different angiogenetic promoters such as tumor necrosis factor (TNF)-alpha, vascular endothelial growth factor (VEFG) or basic-fibroblast growth factor (B-FGF) released by inflamed, hypoxic, or injured tissues.[29,33]

Wells et al[11] concluded that axial CT-measured relative PA enlargement, defined as a PA:AA ratio > 1 at the bifurcation site, was associated with severe COPD exacerbation. Generally, the MPA diameter and PA:AA ratio, measured on axial 2D CT have been used to suggest the presence of pulmonary hypertension in various cardiopulmonary diseases[3–10] and the MPA diameter has generally been measured at the level of pulmonary bifurcation.[3–18] However, measurement at the bifurcation site of the MPA on CT images is sometimes more challenging due to the morphologically complex shape and axis of the MPA and its branches. In the present study, we evaluated the advantages of pulmonary vascular measurements on chest CT to identify a

Figure 3. Multiplanar measurements of the MPA major and minor diameters at the tubular site. Similar method to Fig. 2 (A and C), a coronal oblique reconstruction of the MPA (B) at the tubular site was obtained.
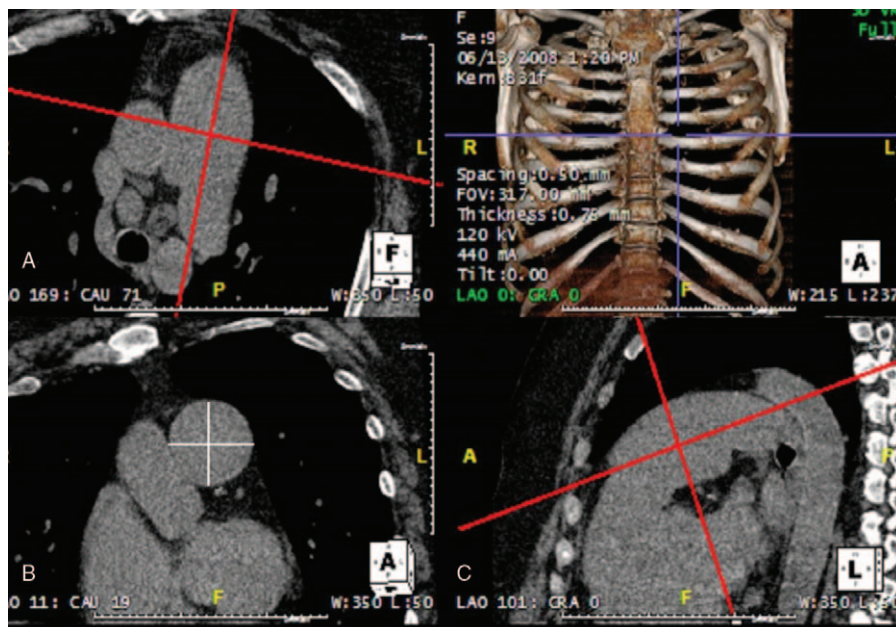
Figure 4. Multiplanar measurements of the AA major and minor diameters. Axial oblique reconstruction of the AA (A) was adjusted perpendicular to the short axis on both coronal (B) and sagittal (C) reconstruction planes and was obtained at the bifurcation site.
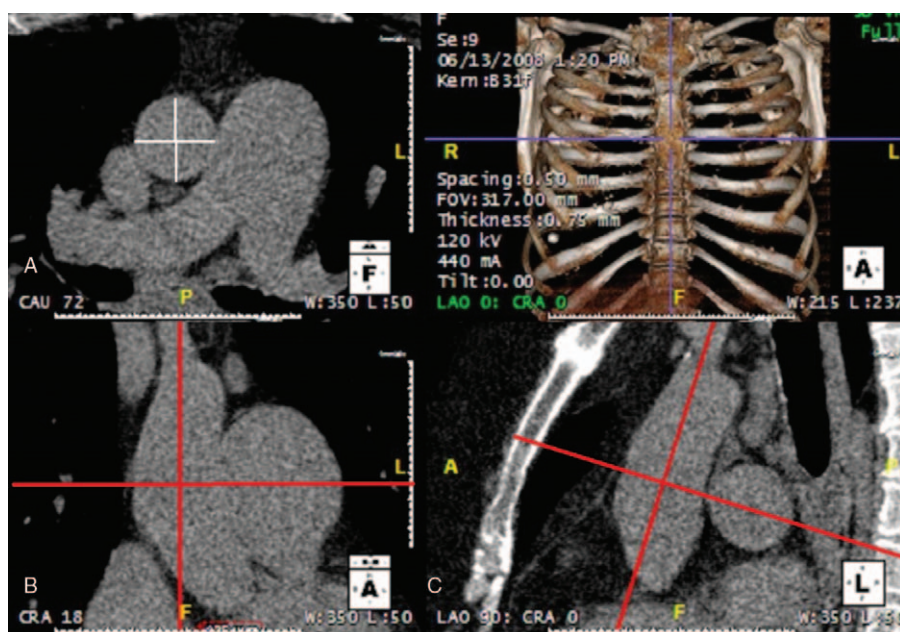
predictive value for severe COPD exacerbation. To overcome the limitations of the complex morphology of the MPA and its branches, we used multiplanar reconstructions to perform measurements and computed the MPA diameter at 2 different sites including the tubular portion and the bifurcation, in order to establish the optimal measurement technique for predicting pulmonary hypertension and severe COPD exacerbation.

Using simple logistic regression analysis, we found the strongest association with severe exacerbation between the axial PA:mean AA ratio at the bifurcation site and the axial PA:major AA ratio at the tubular site, which persisted after adjusting for potential confounders using multiple logistic regression analysis (Table 2). Our results indicate that the predictive value of multiplanar measurements for severe COPD exacerbation was not superior to that of axial measurements. This finding was

contrary to our initial hypothesis. It is possible that these discordant results may be due to a greater level of subjectivity and operator-dependence with multiplanar measurements. Further, the axial PA measurements somehow capture important information regarding the orientation of the PA, which is not apparent when a true transverse diameter of the PA is obtained.

Using the ROC curve analysis, we determined that the axial measurement of the PA:AA ratios at both sites and multiplanar measurement of the PA:AA ratio at the tubular site provided the fair discriminatory ability of AUC, which enabled us to distinguish severe exacerbators from nonexacerbators (Table 3). The axial PA:major AA ratio at the tubular site was the parameter with highest AUC. Our results indicate that CT-measured PA:AA ratios at either the bifurcation or the tubular site enable the risk assessment of severe COPD exacerbation. Mahammedi et al[19]

Table 1

Demographic data stratified by COPD exacerbation.

	Total (n=603)	Nonexacerbator (n=313)	Severe exacerbator (n=290)	P
Current smoker, N (%)	235 (38.97)	116 (37.06)	119 (41.03)	.32
Smoking duration, y	39.63 (9.22)	39.67 (9.17)	39.59 (9.29)	.97
Pack years	51.58 (26.70)	51.28 (25.56)	51.89 (27.91)	.99
Age	61.85 (8.78)	62.14 (8.84)	61.54 (8.73)	.39
Male, N (%)	299 (49.59)	160 (51.12)	139 (47.93)	.43
BMI	28.14 (6.75)	28.00 (6.12)	28.28 (7.37)	.84
FEV1 (% predicted)	49.66 (19.87)	53.96 (20.04)	45.03 (18.64)	<.001[*]
FVC (% predicted)	76.04 (17.97)	78.83 (17.62)	73.04 (17.90)	<.001[*]
FEV1/FVC	0.49 (0.15)	0.52 (0.15)	0.47 (0.15)	<.001[*]
6-MWD	1173.07 (393.56)	1293.38 (372.25)	1044.36 (375.17)	<.001[*]
SGRQ	44.62 (21.10)	35.68 (19.42)	54.28 (18.44)	<.001[*]
BODE	3.12 (2.01)	2.53 (2.02)	3.76 (1.79)	<.001[*]

Note: P values obtained by t test, Wilcoxon rank sum test, and Chi-square test, as appropriate.

6-MWD = 6-minute-walk distance, BMI = body mass index, BODE = body mass index, airflow obstruction, dyspnea, and exercise capacity index, FEV_1 = forced expiratory volume in the first second, FVC = forced vital capacity, SGRQ = St. George's Respiratory Questionnaire.

[*] Statistically significant (P < .05).

Table 2

Comparison of CT pulmonary vascular parameters between exacerbation groups.

CT pulmonary vascular parameters	Nonexacerbator (n=313)	Severe exacerbator (n=290)	Simple logistic regression			Multiple logistic regression		
			OR	95% CI	P	OR[†]	95% CI	P
MPA diameter								
Axial CT								
Tubular site								
Diameter	26.33 (4.22)	27.12 (4.31)	1.05	1.01–1.09	.023[*]	1.05	1.00–1.10	.065
Bifurcation								
Diameter	28.35 (4.63)	28.84 (4.83)	1.02	0.99–1.06	.209	1.03	0.99–1.07	.203
Multiplanar CT								
Tubular site								
Mean diameter	27.79 (4.04)	28.29 (4.16)	1.03	0.99–1.07	.132	1.03	0.98–1.08	.226
Bifurcation								
Mean diameter	28.64 (4.32)	28.98 (4.38)	1.02	0.98–1.06	.346	1.02	0.97–1.06	.512
PA:AA ratio								
Axial CT								
Tubular site								
PA:major AA	0.78 (0.11)	0.81 (0.13)	11.87	3.00–47.01	.0004[*]	10.72	1.99–57.86	.006[*]
PA:mean AA	0.85 (0.13)	0.88 (0.14)	4.18	1.30–13.46	.017[*]	4.88	1.19–20.00	.028[*]
Bifurcation								
PA:major AA	0.84 (0.13)	0.87 (0.15)	4.03	1.24–13.08	.021[*]	4.26	1.04–17.50	.044[*]
PA:mean AA	0.79 (0.12)	0.83 (0.13)	12.14	3.13–47.08	.0003[*]	12.53	2.35–66.74	.003[*]
Multiplanar CT								
Tubular site								
Mean PA:major AA	0.83 (0.11)	0.86 (0.12)	6.91	1.72–27.73	.006[*]	7.09	1.32–38.09	.022[*]
Mean PA:mean AA	0.84 (0.12)	0.87 (0.12)	6.79	1.74–26.43	.006[*]	6.75	1.30–35.01	.023[*]
Bifurcation								
Mean PA:major AA	0.86 (0.12)	0.88 (0.12)	4.27	1.13–16.13	.032[*]	4.13	0.83–20.60	.084
Mean PA:mean AA	0.87 (0.12)	0.89 (0.13)	4.25	1.16–15.53	.029[*]	3.99	0.83–19.21	.085

CI = confidence interval, major = major diameter, mean PA:major AA = the ratio of the main pulmonary artery mean diameter to ascending aorta major diameter, mean PA:mean AA = ratio of the main pulmonary artery mean diameter to ascending aorta mean diameter, mean = mean diameter, MPA = main pulmonary artery, OR = odds ratio, PA:major AA = the ratio of the main pulmonary artery diameter to ascending aorta major diameter, PA:mean AA = the ratio of the main pulmonary artery diameter to ascending aorta mean diameter.

[*] Statistically significant (P < .05).

[†] Odds ratios adjusting for smoking duration, smoking pack years, age, male sex, FEV1/FVC, and BODE.

attempted to standardize the diameter used for measuring the MPA diameter in 400 patients (including 27 with COPD) diagnosed with various cardiopulmonary diseases. The group measured the MPA diameter at 4 different sites (4 methods) based on the bifurcation site of the MPA, in order to establish the most reproducible method with the highest correlation to PA pressure. They found that all the methods correlated with mean PA pressure. The highest correlation coefficient with mean PA pressure was observed using method 1, the MPA diameter was measured along the line that originates at the center of the AA and

Table 3

ROC curve and optimal cut-off value for severe exacerbation of COPD.

CT-measured PA:AA ratios	Cut-off value	Sensitivity (%)	Specificity (%)	AUC ± SE	Logistic regression		
					OR[†]	95% CI	P
Axial CT							
Tubular site							
PA:major AA	0.80	51.8	64.6	0.78 ± 0.02	1.72	1.17–2.55	.006[*]
PA:mean AA	0.80	52.9	62.5	0.78 ± 0.02	1.19	0.80–1.77	.393
Bifurcation							
PA:major AA	0.87	48.5	67.4	0.77 ± 0.02	1.78	1.20–2.64	.004[*]
PA:mean AA	0.88	49.6	66.0	0.77 ± 0.02	1.41	0.90–2.20	.135
Multiplanar CT							
Tubular site							
Mean PA:major AA	0.82	60.7	55.0	0.77 ± 0.02	1.86	1.26–2.72	.002[*]
Mean PA:mean AA	0.84	57.7	57.7	0.77 ± 0.02	1.82	1.24–2.66	.002[*]

AUC = area under the receiver operating characteristic curve, CI = confidence interval, major = major diameter, mean PA:major AA = the ratio of the main pulmonary artery mean diameter to ascending aorta major diameter, mean PA:mean AA = ratio of the main pulmonary artery mean diameter to ascending aorta mean diameter, mean = mean diameter, OR = odds ratio, PA:major AA = the ratio of the main pulmonary artery diameter to ascending aorta major diameter, PA:mean AA = the ratio of the main pulmonary artery diameter to ascending aorta mean diameter, ROC curve = receiver operating characteristic curve, SE = standard error.

[*] Statistically significant (P < .05).

[†] Odds ratios adjusting for smoking duration, smoking pack years, age, male, FEV1/FVC, and BODE.

which passes perpendicular to the long axis of the PA at the bifurcation site. However, attempts to reproduce the MPA diameter measurements showed intraobserver and interobserver variability. In fact, most previous studies measured the widest MPA diameter on the axial image at the bifurcation site (method 2 mentioned in Mahammedi et al[19]).[3–18] However, sometimes it was difficult to determine the bifurcation site due to the morphologically complex shape and axis of the MPA and its branches. The MPA diameter was measured at the bifurcation site in a few studies, which focused on the tubular or bifurcation site of the right PA.[3,10,12,34] Truong et al[35] measured the MPA diameter at the bifurcation site of the right PA, although the images appeared to indicate the tubular site. Therefore, several studies reported conflicting conclusions regarding the diagnostic value of the MPA diameter or PA:AA ratio in pulmonary hypertension.[20,34,36–38] The potential advantage of the tubular segment of the MPA relates to its relatively constant diameter. Thus, we believe that measuring the MPA diameter at the tubular site is simpler and less subjective, potentially decreasing discordant measurements.

In addition, our results indicate that the range of cut-off values for PA:AA ratio was 0.8 to 0.87. Generally, at the level of pulmonary bifurcation, the AA is larger in diameter than the MPA in healthy individuals.[35] A PA:AA ratio >1 strongly correlated with pulmonary hypertension in various cardiopulmonary diseases.[8,9,11,19] Some authors reported that a PA:AA ratio >1 on CT scan indicated pulmonary hypertension in patients with COPD.[9,11] On the other hand, Truong et al[35] reported that using the 90th percentile, the sex-specific cut-off value for the PA:AA ratio was 0.9 for both sexes. Chan et al[12] also found that the optimal cut-off value >0.84 for the PA:AA ratio predicted pulmonary hypertension. In our view, minor differences in the cut-off value for identifying severe COPD exacerbation may be related to different study populations.

Except for prediction of COPD exacerbations,[11] the clinical implications of our results remain largely unknown. Ando et al[39] evaluated the role of quantitative CT in determining the effect of pulmonary vasodilators in COPD patients with pulmonary hypertension and concluded that quantitative CT analysis is a plausible and beneficial tool. If an elevated PA:AA ratio is a reliable surrogate for pulmonary hypertension, it may represent a useful parameter for the diagnostic screening of patients for right heart catheterization and before considering therapy with vasodilators or other treatments aimed at the disorder.[40,41] Additionally, a chest CT is performed the routine clinical work-up and follow-up of end-stage COPD patients being screened for lung transplantation.[42] Some authors suggested a crucial role of CT in the complex diagnostic algorithm after recognizing PA dilatation[43]: management of a dilated PA is individualized, however, the work-up usually begins with echocardiography, followed by right heart catheterization to confirm the diagnosis. Although the technological development of CT has reduced the radiation dosage, additional studies are needed to support routine CT evaluation of COPD patients at high risk of acute exacerbation in addition to screening for lung transplantation.

There were a few limitations of this study. First, CT measurements of the PA were subjective due to the use of manual techniques. Specifically, it may be difficult to create a reproducible multiplanar reconstruction plane from a volumetric dataset due to the need for technical expertise. Second, the PA margins may be difficult to delineate on a few noncontrast non-gated CT images, increasing the risk of inaccurate measurement of PA. Another study limitation relates to intervention by a single radiologist in the measurements, and no interobserver variability was determined. As a follow-up study, an investigation of interobserver reliability at the tubular site of the MPA is needed. Finally, we failed to investigate the relationship between CT-measured pulmonary vascular parameters and echocardiography or right heart catheterization. Right heart catheterization remains the gold standard for diagnosis of pulmonary hypertension, although it is an invasive test with recognized complications.[44] Echocardiography is a frequently used noninvasive tool that measures systolic PA pressure, however, in patients with advanced COPD it can lead to an under- or overestimation of systolic PA pressure due to lung hyperinflation and poor acoustic windows.[45,46] We studied the relationship between CT-measured pulmonary vasculatures and severe COPD exacerbation, assuming that the dilatation of the MPA on CT images was associated with a marker of increased mean PA pressure suggesting pulmonary hypertension. There may be potential bias suggesting the absence of true pulmonary hypertension because CT-measured PA:AA ratio dose not compare the pulmonary hypertension detected by right heart catheterization or echocardiography. However, the study correlating PA:AA ratio, echocardiography, and invasive hemodynamics in COPD reported that a PA:AA ratio >1 on CT scan outperforms echocardiography for diagnosis of resting pulmonary hypertension associated with severe COPD.[9] Furthermore, a combination of CT and echocardiographic markers of pulmonary hypertension is strongly related to mean PA pressure than either test in isolation.[14] Based on these reports, we believe that the PA:AA ratio can adequately predict pulmonary hypertension, although we failed to investigate the relationship between CT-measured pulmonary vascular parameters and echocardiography or invasive hemodynamics.

In conclusion, both axial and multiplanar CT-measured PA:AA ratios at both sites including the tubular and bifurcation are useful for predicting the severe COPD exacerbation and can be helpful in guiding the management of COPD treatment in patients with suspected severe exacerbation. In contrast to the bifurcation site, the tubular site of the MPA is relatively constant on CT images, rendering CT measurements simpler from a technical aspect. Although CT measurements at the level of pulmonary bifurcation have been frequently used in previous studies, we suggest that future studies consider measuring the MPA diameter at the tubular site to maximize the diagnostic value of CT measurement in pulmonary hypertension or severe COPD exacerbation.

5. Author contributions

All the authors were involved in study design, data acquisition, or data analysis/interpretation; all the authors were involved in manuscript drafting or revision for important intellectual content; all the authors approved the final version of the manuscript; all the authors consent to resolve any questions related to the works.

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Manuscript editing: Ji Young Rho, David A. Lynch.

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