CHEST

Original Research

PULMONARY VASCULAR DISEASE

CT Scan-Measured Pulmonary Artery to Aorta Ratio and Echocardiography for Detecting Pulmonary Hypertension in Severe COPD

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Background: **COPD is associated with significant morbidity primarily driven by acute exacerbations. Relative pulmonary artery (PA) enlargement, defined as a PA to ascending aorta (A) diameter ratio greater than one (PA:A > 1) identifies patients at increased risk for exacerbations. However, little is known about the correlation between PA:A, echocardiography, and invasive hemodynamics in COPD.**

Methods: **A retrospective observational study of patients with severe COPD being evaluated for lung transplantation at a single center between 2007 and 2011 was conducted. Clinical characteristics, CT scans, echocardiograms, and right-sided heart catheterizations were reviewed. The PA diameter at the bifurcation and A diameter from the same CT image were measured. Linear and logistic regression were used to examine the relationships between PA:A ratio by CT scan and PA systolic pressure (PASP) by echocardiogram with invasive hemodynamics. Receiver operating characteristic analysis assessed the usefulness of the PA:A ratio and PASP in predicting resting pulmonary hypertension (PH) (mean pulmonary artery pressure [mPAP] > 25 mm Hg).**

Results: **Sixty patients with a mean predicted FEV_1 of 27% ± 12% were evaluated. CT scan-measured PA:A correlated linearly with mPAP after adjustment for multiple covariates ($r = 0.30$, $P = .03$), a finding not observed with PASP. In a multivariate logistic model, mPAP was independently associated with PA:A > 1 (OR, 1.44; 95% CI, 1.02-2.04; $P = .04$). PA:A > 1 was 73% sensitive and 84% specific for identifying patients with resting PH (area under the curve, 0.83; 95% CI, 0.72-0.93; $P < .001$), whereas PASP was not useful.**

Conclusions: **A PA:A ratio > 1 on CT scan outperforms echocardiography for diagnosing resting PH in patients with severe COPD.**

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Abbreviations: A = aorta; dPAP = diastolic pulmonary artery pressure; mPAP = mean pulmonary artery pressure; PA = pulmonary artery; PASP = pulmonary artery systolic pressure; PVR = pulmonary vascular resistance; RHC = right-sided heart catheterization; ROC = receiver operating characteristic; sPAP = systolic pulmonary artery pressure; UAB = University of Alabama at Birmingham

COPD is the third leading cause of death in the United States and is associated with significant morbidity and health-care-related expenditures mostly due to acute exacerbations.[1,2] Patients with COPD may develop subclinical or overt pulmonary vascular disease, and the presence of pulmonary hypertension (PH) is an important predictor of both COPD and exacerbation-related morbidity and mortality, particularly in patients with severe disease.[3-8] Although PH can occur in patients with mild to moderate COPD because of pulmonary inflammation and endothelial or cardiac dysfunction, it more commonly occurs and becomes clinically apparent when airflow limitation is severe and is believed to be primarily due to hypoxic vasoconstriction of small pulmonary arteries that result in intimal hyperplasia as well as smooth muscle hypertrophy and hyperplasia.[9-11]

Right-sided heart catheterization (RHC) remains the gold standard for diagnosis of pulmonary vascular disease.[12] Although noninvasive strategies, such as Doppler echocardiography, allow the measurement of pulmonary artery systolic pressure (PASP), this modality is often problematic in patients with COPD because of lung hyperinflation and difficulty in obtaining clear

acoustic windows.[13] CT scanning has been used to assess the mean pulmonary artery (PA) diameter, the cross-sectional area of small pulmonary vasculature, and the PA to ascending aorta (A) ratio, and each has demonstrated varying associations with RHC data. However, most of these studies were conducted in heterogeneous populations with various underlying lung diseases, thus, limiting their application to patients with COPD.[14-20]

We showed that CT image-measured relative PA enlargement, defined as a PA:A ratio > 1, identifies patients at increased risk of COPD exacerbation and hospitalization[21]; however, the mechanism underlying relative PA enlargement has not been clearly elucidated.[16,22] Although increases in the PA:A ratio could represent resting PH, other factors may contribute, including left ventricular dysfunction and hyperinflation due to emphysema. We hypothesized that the PA:A ratio would correlate with mean PA pressure (mPAP) by RHC and that the presence of PA:A > 1 could serve as a more useful screening test than echocardiography for identifying PH in patients with severe COPD.

Materials and Methods

Study Design and Patient Selection

Records for patients who underwent lung transplant evaluation between 2007 and 2011 at the University of Alabama at Birmingham (UAB) were analyzed. Men and women were eligible if they were > 40 years of age; had a history of COPD at the time of evaluation; lacked coexisting lung diseases such as cystic fibrosis, bronchiectasis, diffuse interstitial lung disease, or lung cancer; and had RHC, echocardiogram, and CT scan performed within 4 months of each other. The study was approved by the Institutional Review Board at the UAB (X120803011).

Clinical Characterization

Sociodemographic, clinical, and laboratory data were abstracted from medical records and the UAB Transplant Database at the time of transplant evaluation. RHC data collected included systolic PA pressure (sPAP), diastolic PA pressure (dPAP), mPAP, and mean pulmonary capillary wedge pressure, as well as mean right and left ventricular end-diastolic pressures, mean right atrial pressure, cardiac output by thermodilution, cardiac index, peripheral vascular resistance, and systemic vascular resistance. Echocardiography data collected included left ventricular ejection fraction, right ventricular ejection fraction, and PASP. Pulmonary hypertension was defined as a resting mPAP > 25 mm Hg by RHC.[12] Severe COPD was defined as airflow obstruction of < 50% defined by postbronchodilator FEV_1 in the setting of an FEV_1:FVC ratio of < 0.70.

Measuring the PA:A Ratio

One reviewer, blinded to hemodynamic information, analyzed CT scans using Philips iSite Enterprise Software (Koninklijke Philips N.V.). The PA diameter was measured at the level of the PA bifurcation, and the A diameter was averaged from two perpendicular measurements taken from the same CT image as previously reported (Fig 1).[21] A second blinded reviewer measured the PA and A diameters to assess interobserver agreement. Cohen κ was 0.82 (95% CI, 0.68-0.97) for interobserver agreement in CT scan measurement of the PA:A ratio.

Statistical Analysis

Baseline data were expressed as means with SD for normally distributed values. Continuous variables were compared using two-sided Student *t* tests, and categorical variables were examined by χ^2 testing as well as Fisher exact test as appropriate. Pearson correlation coefficients were determined for the relationships between the PA diameter, A diameter, and PA:A ratio, as well as echocardiography-measured PASP and hemodynamic parameters. Multiple linear regression, including demographic and clinical covariates, was used to examine the relationship between CT image metrics (PA, A, and PA:A ratio) as well as PASP and hemodynamic parameters. Univariate and multivariate logistic

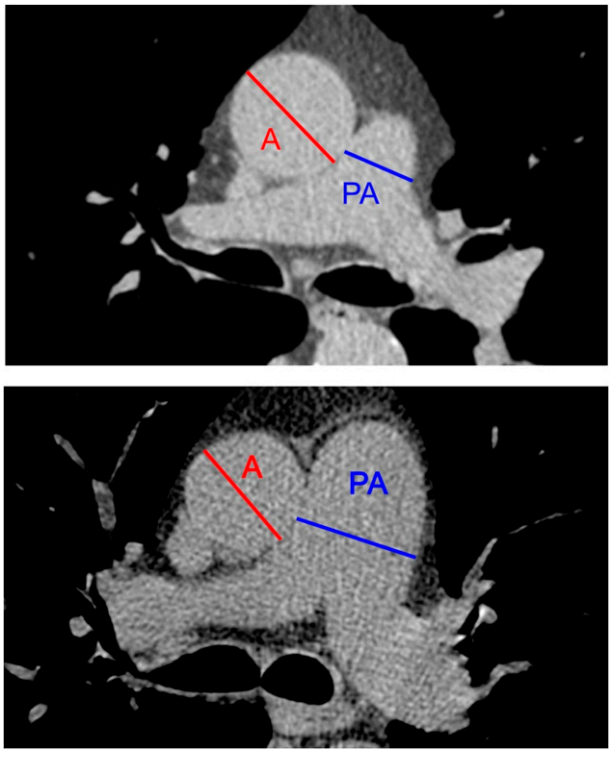

Figure 1. Measurement of the PA and A diameters at the PA bifurcation. A = aorta; PA = pulmonary artery.

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regression were used to determine the relationship between hemodynamic measurements and the presence of a PA:A > 1. Steiger Z-test was calculated to compare correlations between echocardiography-measured PASP and CT scan-measured PA:A with mPAP. Receiver operating characteristic (ROC) analysis assessed the usefulness of the PA:A ratio and PASP in predicting the presence of mPAP > 25 mm Hg. Cohen κ measured interobserver variability in CT scan diameter measurements for the cohort. SPSS for Windows version 20 (IBM) was used for all analyses. All statistical tests were two-sided, with significance assigned to tests with P values < .05.

Results

Between 2007 and 2011, 134 of 690 patients referred for lung transplant evaluation had COPD, and 74 subjects were excluded on the basis of not having matched CT scan, echocardiography, or RHC data. The current analysis included 60 patients who were separated into groups based on a PA:A ratio > 1 (n = 22) and a PA:A ratio ≤ 1 (n = 38). Participants had a mean (± SD) age of 55 (± 7) years; 50 were white (83%), and 34 were women (57%). Mean predicted FEV_1 was 27% (± 12%). The mean (± SD) number of days between RHC and CT scan was 18 (± 50) days and 1 (± 23) day between RHC and echocardiography. Of these patients, 22 (38%) had mPAP > 25 by RHC.

Differences in the PA:A ratio between both groups were driven by the PA diameter (27.3 ± 3.2 mm in PA:A < 1 vs 34.3 ± 4.1 mm in PA:A > 1, $P < .001$), as no differences were detected between aortic diameters (31.8 ± 2.7 mm vs 31.1 ± 3.2 mm, respectively; $P = .42$; Table 1). There were no significant differences between the PA:A < 1 and PA:A > 1 groups regarding

Table 1—*Baseline Characteristics of Participants*

Characteristic	PA:A < 1 (n = 38)	PA:A > 1 (n = 22)	*P* Value
Age, y	55 (± 7.9)	57.5 (± 5.9)	.21
Female sex	22 (58)	12 (55)	.80
White	34 (90)	16 (73)	.09
FEV_1 % predicted	26.3 (± 11.3)	29.1 (± 14.8)	.40
FEV_1:FVC ratio	37.3 (± 12.1)	38.4 (± 14.3)	.76
6-min walk distance, ft	915 (± 214)	776 (± 191)	.07
Coronary artery disease	4 (10)	4 (18)	.41
Hyperlipidemia	9 (24)	4 (18)	.63
Congestive heart failure	2 (5)	5 (23)	.04
Hypertension	18 (47)	11 (50)	.85
Diabetes mellitus	1 (3)	4 (18)	.04
OSA	4 (10)	6 (27)	.10
Currently smoking	1 (3)	0 (0)	.45
Smoking, pack-y	45 (± 21)	54 (± 31)	.23
Heart rate, beats/min	91 (± 12)	94 (± 19)	.46
Percent oxygen saturation by pulse oximetry	95 (± 3)	91 (± 6)	.004
BMI, kg/m^2	23.1 (± 3.9)	25.8 (± 5.5)	.04
pH	7.41 (± 0.03)	7.41 (± 0.03)	.94
P_{CO_2}	45 (± 8)	50 (± 14)	.14
P_{O_2}	65 (± 11)	54 (± 13)	.003
P_{HCO_3}	27.9 (± 3.9)	29.9 (± 5.4)	.16
Systolic PAP by RHC, mm Hg	31 (± 6)	46 (± 14)	< .001
Diastolic PAP by RHC, mm Hg	14 (± 5)	21 (± 8)	< .001
Mean PAP by RHC, mm Hg	21 (± 4)	31 (± 10)	< .001
Mean PCWP by RHC, mm Hg	11 (± 4)	13 (± 6)	.11
Mean LVEDP by RHC, mm Hg	11 (± 6)	15 (± 6)	.08
Mean RVEDP by RHC, mm Hg	8 (± 4)	11 (± 4)	< .001
Mean RAP by RHC, mm Hg	6 (± 3)	9 (± 4)	.009
Cardiac output, L/min	5.0 (± 0.9)	5.3 (± 1.1)	.26
Cardiac index, $L/min/m^2$	2.9 (± 0.4)	2.9 (± 0.5)	.72
Pulmonary vascular resistance, mm Hg × min/L	2.1 (± 0.8)	4.5 (± 3.8)	< .001
Systemic vascular resistance, mm Hg × min/L	18.4 (± 4.4)	17.1 (± 5.4)	.37
PA diameter by CT scan, mm	27.3 (± 3.2)	34.3 (± 4.1)	< .001
Ascending aortic diameter by CT scan, mm	31.8 (± 2.7)	31.1 (± 3.2)	.42
LVEF by echocardiography, %	54 (± 5)	55 (± 1)	.51
RVEF by echocardiography, %	54 (± 2)	49 (± 12)	.009
PASP by echocardiography, mm Hg	34 (± 11, n = 25)	49 (± 21, n = 13)	< .001

Data are presented as No. (%) or mean (± SD). A = aorta; LVEDP = left ventricular end-diastolic pressure; LVEF = left ventricular ejection fraction; PA = pulmonary artery; PAP = pulmonary artery pressure; PASP = pulmonary artery systolic pressure; PCWP = pulmonary capillary wedge pressure; P_{HCO_3} = partial pressure of bicarbonate; RAP = right atrial pressure; RHC = right-sided heart catheterization; RVEDP = right ventricular end-diastolic pressure; RVEF = right ventricular ejection fraction.

age, sex, race, smoking status, lung function, or prevalence of coronary artery disease, hyperlipidemia, hypertension, and OSA. Those with PA:A > 1 had higher BMIs and comorbid diabetes (18% vs 3%, $P = .04$), as well as lower percutaneous oxygen saturation (91% vs 95%, $P = .004$) and lower arterial oxygen tension (PaO_2, 54 mm Hg vs 65 mm Hg; $P = .003$) (Table 1). The sPAP, dPAP, and mPAP were all higher in those with PA:A > 1 as compared with those with PA:A < 1. No difference in pulmonary capillary wedge pressure was observed despite the PA:A > 1 group having more patients with comorbid congestive heart failure (23% vs 5%, $P = .04$) (Table 1). Echocardiography-measured PASP was higher in the group with PA:A > 1 than in those with PA:A < 1 (49 ± 21 mm Hg vs 34 ± 11 mm Hg, $P < .001$), and the right ventricular ejection fraction was reduced (49% ± 12% vs 54% ± 2%, $P = .009$) as seen in Table 1.

CT scan-measured PA diameter correlated linearly with sPAP ($r = 0.62$, $P < .001$), dPAP ($r = 0.53$, $P < .001$), and mPAP ($r = 0.60$, $P < .001$) (Fig 2, Table 2). In contrast, the aortic diameter was not associated with any measure of PA pressure (Table 2). The PA:A ratio also demonstrated a significant linear correlation with sPAP ($r = 0.60$, $P < .001$), mPAP ($r = 0.56$, $P < .001$), and dPAP ($r = 0.47$, $P < .001$) by RHC and remained significant after multiple linear regression analysis for sPAP ($r = 0.40$, $P = .005$) and mPAP ($r = 0.30$, $P = .03$) adjusting for age, race, sex, BMI, resting oxygen saturation, sleep apnea, congestive heart failure, and diabetes mellitus (Fig 2, Table 2). Measuring the PA diameter at a more proximal location yielded a similar correlation between the PA:A ratio and mPAP (e-Table 1).

Echocardiography-measured PASPs were available on 38 patients (63%) and in that subgroup correlated linearly with sPAP ($r = 0.42$, $P = .009$), mPAP ($r = 0.33$, $P = .043$), dPAP ($r = 0.35$, $P = .03$), and pulmonary vascular resistance (PVR) ($r = 0.49$, $P = .002$) (Fig 2, Table 3). In the 22 other patients, PASP was not measured because of the absence of a tricuspid regurgitant

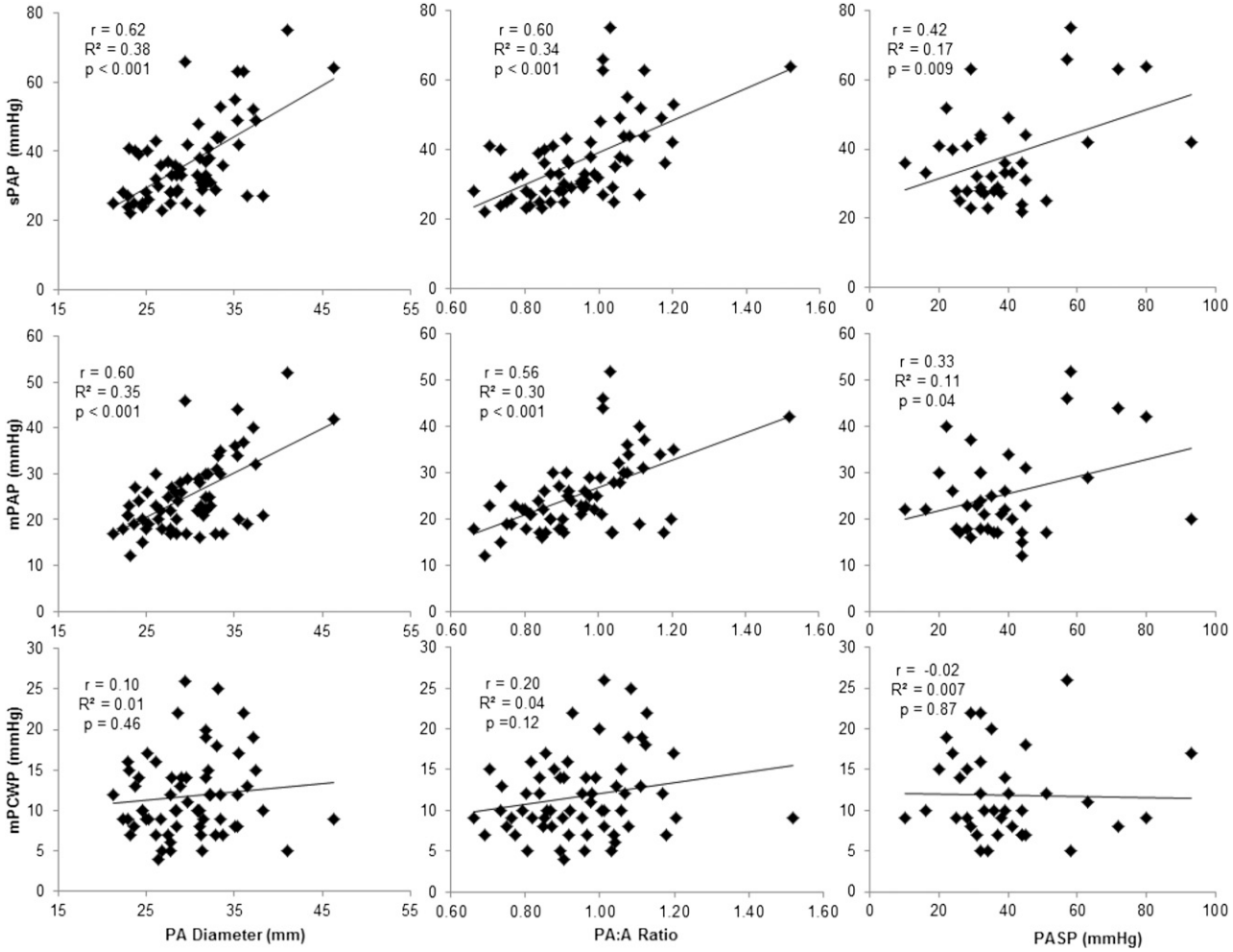

FIGURE 2. Linear relationships between invasive hemodynamics, PA diameter and PA:A ratio from CT scan as well as PA systolic pressure by echocardiography. mPAP = mean PA pressure; mPCWP = mean pulmonary capillary wedge pressure; PASP = echocardiographic PA systolic pressure; sPAP = systolic PA pressure. See Figure 1 legend for expansion of other abbreviations.

Table 2—*Univariate and Multiple Linear Regression Comparisons Between Invasive Hemodynamics and PA Diameter, A Diameter, and PA:A*

	Univariate Linear Regression						Multiple Linear Regression[a]	
Measure	PA	*P* Value	A	*P* Value	PA:A	*P* Value	PA:A	*P* Value
sPAP	0.62	< .001	0.07	.59	0.60	< .001	0.40	.005
mPAP	0.60	< .001	0.09	.50	0.56	< .001	0.30	.03
dPAP	0.53	< .001	0.10	.46	0.47	< .001	0.33	.06
LVEDP	0.23	.10	0.05	.97	0.27	.06	0.20	.35
RVEDP	0.37	.004	−0.09	.48	0.42	.001	0.23	.22
RAP	0.27	.03	−0.13	.32	0.36	.005	0.12	.56
PVR	0.45	< .001	0.04	.79	0.45	< .001	0.49	.003
PCWP	0.10	.46	−0.19	.15	0.20	.12	0.20	.37

dPAP = diastolic PA pressure; mPAP = mean PA pressure; PVR = pulmonary vascular resistance; sPAP = systolic PA pressure. See Table 1 legend for expansion of other abbreviations.

[a]Variables in the multiple linear regression model: PA:A value, age, race, sex, BMI, resting oxygen saturation, sleep apnea, congestive heart failure, and diabetes mellitus.

jet or an inadequate window. In a multiple linear regression model adjusting for age, race, sex, BMI, resting oxygen saturation, sleep apnea, congestive heart failure, and diabetes mellitus, the correlation between PASP and PVR remained significant ($r = 0.34$, $P = .02$) (Table 3), but the correlations between PASP and sPAP, dPAP, or mPAP were lost (Table 3). The correlation coefficients between PA:A ratio and echocardiography-measured PASP with sPAP were not statistically different, but the correlation of the PA:A ratio with mPAP was significantly stronger than the correlation between echocardiography-derived PASP and mPAP ($z = 2.01$, $P < .05$). In a multivariate logistic model, mPAP was independently associated with the presence of PA:A > 1 (OR, 1.44; 95% CI, 1.02-2.04; $P = .04$) adjusting for age, sex, race, BMI, resting oxygen saturation, sleep apnea, congestive heart failure, and diabetes (Table 4).

ROC curves were performed to evaluate the sensitivity and specificity of both the PA:A ratio and echocardiography-measured PASP for diagnosing PH defined by an mPAP > 25 mm Hg. The area under the curve for the PA:A ratio was 0.83 (95% CI, 0.72-0.93; $P < .001$) with an mPAP > 25 mm Hg (Fig 3A). The sum of sensitivity and specificity between the PA:A ratio and an mPAP > 25 mm Hg was greatest at a PA:A ratio > 1 (73% sensitivity and 84% specificity) when compared in a range of PA:A ratio from > 0.70 to > 1.20 (Table 5). The area under the curve between PASP and an mPAP > 25 mm Hg did not achieve statistical significance (0.60; 95% CI, 0.39-0.80; $P = .33$) (Fig 3B), corresponding to a significant difference from the area under the ROC curve for the PA:A ratio and an mPAP > 25 mm Hg ($P = .045$). The sum of sensitivity and specificity between the PASP and mPAP > 25 mm Hg was greatest at a PASP > 55 mm Hg (36% sensitivity and 96% specificity) (e-Table 2). We also evaluated the usefulness of the PA:A ratio and echocardiography-measured PASP for diagnosing severe PH, defined by an mPAP > 35 mm Hg.[23] The area under the ROC curve for the PA:A ratio was 0.85 (95% CI, 0.75-0.95; $P = .003$), whereas the area

Table 3—*Univariate and Multiple Linear Regression Comparisons Between Invasive Hemodynamics and Echocardiographic PA Systolic Pressure*

	Univariate Linear Regression		Multiple Linear Regression[a]	
Measure	PASP	*P* Value	PASP	*P* Value
sPAP	0.42	.009	0.16	.23
mPAP	0.33	.04	0.01	.91
dPAP	0.35	.03	0.16	.34
PVR	0.49	.002	0.34	.02

See Table 1 and 2 legends for expansion of abbreviations.

[a]Variables in the multiple linear regression model: PASP, age, race, sex, BMI, resting oxygen saturation, sleep apnea, congestive heart failure, and diabetes mellitus.

Table 4—*Relationship Between Invasive Hemodynamics and PA:A > 1 by Multivariate Logistic Regression*

Measure	OR	95% CI	*P* Value
sPAP	1.50	1.02-2.20	.04
mPAP	1.44	1.02-2.04	.04
dPAP	1.38	0.94-2.05	.10
RAP	1.12	0.80-1.57	.52
LVEDP	1.09	0.92-1.29	.33
RVEDP	1.21	0.88-1.66	.25
PVR	1.04	1.004-1.09	.03
PCWP	1.08	0.86-1.37	.50
Cardiac output	0.33	0.05-2.28	.26
Cardiac index	0.58	0.02-16.8	.75

Variables in the multivariate logistic model: age, race, sex, BMI, resting oxygen saturation, sleep apnea, congestive heart failure, and diabetes mellitus, and the hemodynamic measurement of interest. A separate multivariate logistic regression model was used for each hemodynamic metric. See Table 1 and 2 legends for expansion of abbreviations.

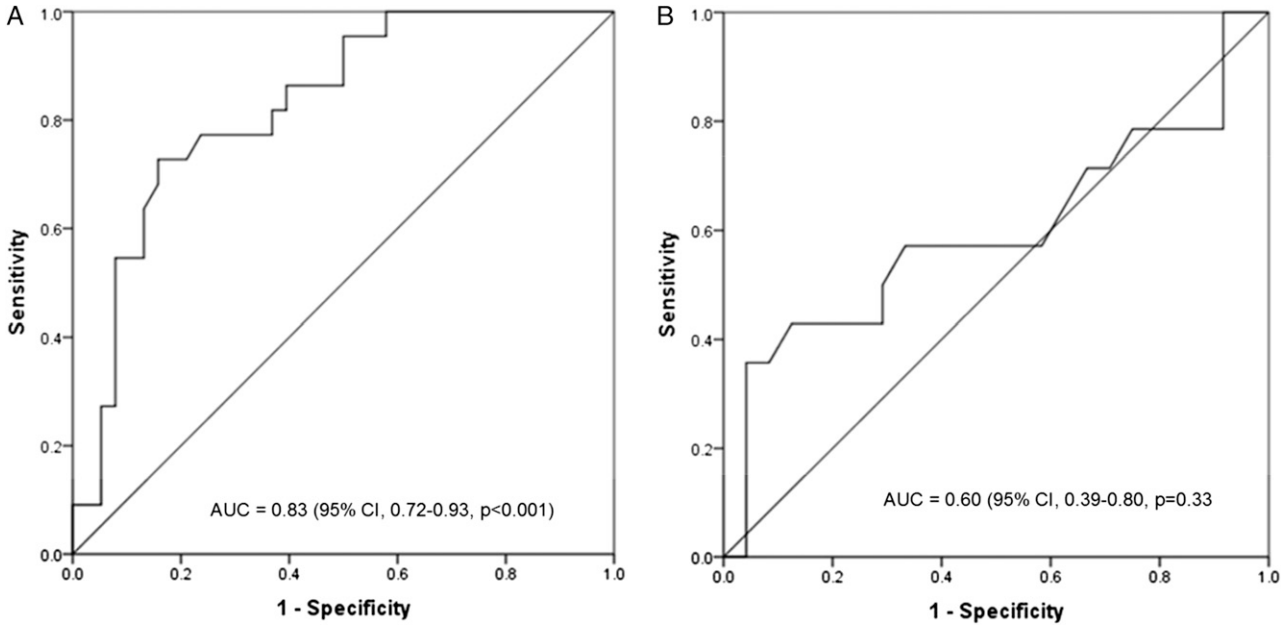

FIGURE 3. A, Receiver operator characteristic curve with the PA:A ratio at identifying mPAP > 25 mm Hg. B, Receiver operating characteristic curve with the echocardiographic PA systolic pressure at identifying mPAP > 25 mm Hg. AUC = area under the curve. See Figure 1 and 2 legends for expansion of other abbreviations.

under the ROC curve for the PASP was again nonsignificant (0.70; 95% CI, 0.39-0.99; $P = .13$).

Discussion

We have demonstrated that the CT scan-measured PA:A ratio correlates with pulmonary arterial pressures as determined by RHC in patients with severe COPD. This is the first study, to our knowledge, to specifically examine this relationship in a cohort consisting exclusively of well-characterized patients with severe COPD and provides a plausible mechanism for the development of relative pulmonary artery enlargement on CT scan, which has in turn been linked to the risk of exacerbation.[21] Defining the relationship between the PA:A ratio and PH is important given the implications of comorbid COPD and PH on exacerbation risk, exacerbation-related mortality, and all-cause mortality.[24,25] These findings also strengthen the pathophysiologic link between an elevated PA:A ratio and exacerbations.[21] Measurement of the PA:A ratio is reproducible, requires minimal training, and performs better than echocardiography for the identification of PH in patients with severe COPD.[11,16,26,27]

Estimates of the prevalence of PH in COPD vary widely from as low as 10% to as high as 85% depending on the severity of the underlying lung disease and the diagnostic criteria as well as approach used.[11,28-30] Accurate estimates have also been problematic, because RHC is not routinely used in patients with COPD, particularly in those with moderate disease.[11] In our population of patients with severe COPD, we found a 37% prevalence of PH using an mPAP ≥ 25 mm Hg and a 37% prevalence using a PA:A > 1. Overall, the presence of PA:A > 1 was reproducible and 83% accurate in predicting resting PH as defined by RHC. We also explored the relationship between measurement of the PA diameter and invasive hemodynamics at a location more proximal to the bifurcation and found that the correlations with RHC data were similar. The interobserver agreement and anatomic consistency of the PA:A ratio support its clinical usefulness.

Table 5—*Sensitivity and Specificity for PA:A Ratio in Identifying mPAP > 25*

Measure	> 0.70	> 0.75	> 0.80	> 0.85	> 0.90	> 0.95	> 1.00	> 1.05	> 1.10	> 1.15	> 1.20
Sensitivity	1.00	1.00	1.00	1.00	0.86	0.77	0.73	0.50	0.27	0.14	0.09
Specificity	0.05	0.13	0.21	0.39	0.53	0.66	0.84	0.92	0.92	0.95	1.00
PPV	0.38	0.40	0.42	0.49	0.51	0.57	0.73	0.79	0.67	0.60	1.00
NPV	1.00	1.00	1.00	1.00	0.87	0.83	0.84	0.76	0.69	0.65	0.66

NPV = negative predictive value; PPV = positive predictive value. See Table 1 and 2 legends for expansion of other abbreviations.

Doppler echocardiography can provide an estimate of right ventricular systolic pressure (believed to reflect PASP[13]); however, this technique can be problematic in patients with COPD due in part to difficulties in obtaining adequate acoustic windows, a factor that does not impact the use of CT imaging.[13,31-33] PA pressures by echocardiography were only measured in 60% of the patients, a value not dissimilar from the 44% Arcasoy et al[13] reported in a heterogeneous population with advanced lung disease undergoing lung transplant evaluation. Furthermore, our analysis showed that the correlation between CT scan-measured relative PA enlargement and invasive hemodynamics was more robust than echocardiography-measured PASP, thus, supporting CT scan as the preferred modality for the identification of PH in patients with severe COPD.

Although the correlation between relative PA enlargement and PA pressures is driven most by changes in PA diameter rather than changes in aortic diameter, relative PA enlargement is only partially explained by intrinsic PH itself, as indicated by the modest *r* value we report. Other mechanisms could contribute, including changes to pulmonary arterial distensibility,[34] redistribution of blood flow from peripheral capillary loss,[35] or left ventricular systolic or diastolic dysfunction,[36-38] although we observed no clear correlation with capillary wedge pressures, cardiac output, or left ventricular ejection fraction in those with PA:A $>$ 1 and PA:A $<$ 1.

Prior studies have characterized the relationship between CT scan metrics and hemodynamics; however, these have been conducted in heterogeneous populations with various lung diseases and included a small number of patients with COPD.[17,39-41] In contrast, our study focuses on well-characterized patients with severe COPD and, thus, allows a better understanding of the relationship between the PA:A ratio, hemodynamics, and echocardiography in this population. This is of significant importance, as the correlation between PA diameter and the PA:A ratio varies based on the included patients' lung disease and the mechanisms leading to PA enlargement.[42]

This study confirms our previous findings that an elevated PA:A ratio is associated with higher BMI, a greater requirement for oxygen, and lower arterial saturation, as well as a higher prevalence of congestive heart failure.[21] These factors each contribute to or are a consequence of PH, thus, supporting the biologic plausibility that the PA:A ratio could serve as an integrated measure of intrinsic and secondary pulmonary vascular disease in COPD.

Our study is limited by its small size, single-center experience, and retrospective design, although we did observe robust and clinically relevant associations between the CT image-measured PA:A ratio and hemodynamics. The modest sample size may account for the lack of association between echocardiography-derived PASP and hemodynamic metrics in multiple regression analyses. However, the relationships between the PA:A ratio and invasive metrics remained significant when controlled for other variables, highlighting the robust relationship between the PA:A ratio and hemodynamic measurements. Also, the association between mPAP and PA:A $>$ 1 in patients with severe COPD may not be generalizable to those with more moderate disease in whom PH would be less prevalent. However, in a population of moderate to severe COPD (GOLD [Global Initiative for Chronic Obstructive Lung Disease] stage II-IV),[21] the prevalence of PA:A $>$ 1 was 24% compared with 37% in the current study, suggesting that this process also occurs in milder disease. Last, we cannot account for exacerbations or other events that may have occurred between CT scan and RHC; however, the potential for confounding was minimized by the short time between the two measurements.

In conclusion, the PA:A ratio and the presence of a PA:A $>$ 1 correlate with invasive measurements of pulmonary arterial pressure and the presence of PH, respectively. These measurements are readily available, require minimal training, and show more robust linear correlation than echocardiography with invasive hemodynamics in patients with advanced COPD. CT scan-measured relative PA enlargement should be the preferred screening tool for PH in this patient population.

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Dr Iyer: contributed as co-first author and to study design, vessel measurement, manuscript writing, and manuscript editing.
Dr Wells: contributed as co-first author and to study design, vessel measurement, data analysis, manuscript writing, and manuscript editing.
Dr Vishin: contributed to data collection, manuscript writing, and manuscript editing.
Dr Bhatt: contributed to manuscript writing and manuscript editing.
Dr Wille: contributed to study design, data collection, and manuscript editing.
Dr Dransfield: contributed as senior author and to study design, data analysis, manuscript writing, and manuscript editing.
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Additional information: The e-Tables can be found in the "Supplemental Materials" area of the online article.

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