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Original Research Article

A study to determine how accurately various measures of the PA, as viewed on HRCT, predict right heart catheterisation (RHC)-confirmed pulmonary hypertension

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Abstract
Aim: We aimed to determine how accurately various measures of the PA, as viewed on HRCT, predict right heart catheterisation (RHC)-confirmed pulmonary hypertension.
Methods: The present study was conducted in department of radiology and 500 patients were included in the study. Patients with a CT scan within 90 days of MRI and RHC were included. In order to meet inclusion criteria, a diagnostic quality CT pulmonary angiogram (CTPA) with a slice thickness of less than 5 mm was required.
Results: We included 500 scans from 500 patients; 300 (60%) had RHC-confirmed pulmonary hypertension, with mPAP ⩾25 mmHg. Compared with the non-pulmonary hypertension group, the group with pulmonary hypertension had greater MPAD, RPAD, LPAD and PA:Ao in both respiratory cycles, whereas the PA angle was greater in the non-pulmonary hypertension group. In the subgroup with pulmonary hypertension, the median MPAD was 34.60 mm in inspiration and 34.65 mm in expiration, while in the non-pulmonary hypertension group it was 30.00 mm in inspiration and 30.50 mm in expiration. For the cohort as a whole, the areas under the receiver operating characteristic curves (AUCs) for inspiratory MPAD and inspiratory PA:Ao (for RHC-confirmed pulmonary hypertension defined as Mpap ⩾25 mmHg) were 0.741 and 0.750, respectively. For the cohort as a whole, the cut-offs MPAD ⩾32.5 mm and PA:Ao ⩾0.94 yielded the most favourable diagnostic profiles.
Conclusion: Findings on HRCT may assist in the diagnosis of RHC-confirmed pulmonary hypertension. MPAD ⩾29 mm had high sensitivity and PA:Ao ⩾1.0 had high specificity. Compared with the entire cohort, MPAD had greater sensitivity in ILD and PA:Ao had higher specificity in COPD.
Keywords: interstitial lung disease, computed tomography (CT) scanning, right heart catheterisation, pulmonary artery diameter, pulmonary hypertension

Introduction

Pulmonary hypertension (PH) is defined on right heart catheterisation (RHC), as a resting mean pulmonary artery pressure (mPAP) greater than or equal to 25 mmHg [1, 2]. PH commonly complicates lung disease and chronic hypoxia, such as interstitial lung disease (ILD). When present in lung disease, PH is associated with a poor outcome [3]. CT is used to diagnose and phenotype suspected ILD, and is often part of the workup of patients with unexplained breathlessness and suspected PH [4]. Dilatation of the main pulmonary artery (PA) or major branch vessels has been identified as markers of the presence of PH and is often the first imaging finding to suggest the diagnosis [5-9]. As CT is commonly used in the investigation of patients with ILD, it would be useful to use the pulmonary arterial size to screen for the presence of pulmonary hypertension. Routine CT pulmonary angiography is performed without ECG gating. Pulmonary arterial size changes during the cardiac cycle. MRI is typically gated to the cardiac cycle and allows assessment of pulmonary arterial size at both systole and diastole. Some authors have suggested that in the presence of established

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lung fibrosis, the main PA diameter is not accurate for estimation of mean pulmonary arterial pressure as dilatation of the main PA develops in patients with pulmonary fibrosis in the absence of PH [5, 10].

Computed tomography (CT) chest scans have largely supplanted chest x-rays in patients with PH, partly due to its ability to detect thromboembolism in some cases, but also to identify any diffuse parenchymal lung diseases that may not be evident in 15% of chest x-rays [11, 12]. With advances in CT technology and its wide availability, there have been attempts to address the utility of CT to predict the presence of PH. The pulmonary artery (PA) is a more compliant vessel than the systemic arterial system, and is thus more sensitive to changes in pressure and volume. As a result, an increase in mean pulmonary arterial pressure (MPAP) should correlate with pulmonary artery diameter. A variety of PA dimensions have been explored to see if there is any association with both the presence and severity of PH, including the PA diameter, the cross-sectional area, the ratio of the diameter to the bronchus, the ratio of the diameter to the pulmonary vein, the ratio of diameter to the aortic diameter, and multiple regression methods assessing dimension of the main and branching pulmonary arteries [13-15].

We aimed to determine how accurately various measures of the PA, as viewed on HRCT, predict right heart catheterisation (RHC)-confirmed pulmonary hypertension.

Materials and Methods

The present study was conducted in department of radiology and 500 patients were included in the study. Patients with a CT scan within 90 days of MRI and RHC were included. In order to meet inclusion criteria, a diagnostic quality CT pulmonary angiogram (CTPA) with a slice thickness of less than 5 mm was required. Patients underwent systemic evaluation as part of their routine clinical workup, which included clinical review, multi-modality imaging and lung function testing.

Radiographic evaluation

All patients underwent volumetric CT imaging on a multidetector row helical CT scanner (Siemens Definition AS+ or Siemens Sensation 64; Siemens, Forchheim, Germany) at full-inspiration and end-expiration. CT scans were reconstructed with a slice thickness of 0.75 mm. Scans were acquired at 50–200 mAs and 120 kV peak. Vessel dimensions were measured using mediastinal windows. A radiologist and pulmonologist decided on, reviewed and practised the protocol for measurements: MPAD was measured at the widest portion of the main PA perpendicular to the wall abutting the Ao. The Ao was also measured at this level to establish PA:Ao. Left and right PA diameters (LPAD and RPAD, respectively) were measured at their widest points after the bifurcation. The angle between the main PA at the bifurcation (PA angle) was also measured. We used various cut-offs, including the conventional values MPAD $\geqslant$29 mm and PA:Ao $\geqslant$1.0, to assess diagnostic accuracy of HRCT measures for RHC-confirmed pulmonary hypertension [16-18]. All HRCT scans were reviewed by a pulmonologist (P.R.) blinded to the presence of pulmonary hypertension and results of the RHC. To assess the validity of measurements made by the pulmonologist, 50 randomly selected scans were also reviewed by a chest radiologist (A.O.) who was also blinded to the presence of pulmonary hypertension and results of the RHC.

RHC haemodynamics

All pressure measurements were performed at end-expiration while patients were in the supine position and breathing spontaneously. We defined pulmonary hypertension as mean PA pressure (mPAP) $\geqslant$25 mmHg [19]. In certain analyses, we used the newly proposed criterion (mPAP $\geqslant$20 mmHg) from the 6th World Symposia on Pulmonary Hypertension [20].

Statistical analysis

Because data were not normally distributed, we report median values (interquartile range) for continuous variables. Differences between groups were evaluated using Chi-squared or Wilcoxon rank sum tests as appropriate. We used intraclass correlation and Bland–Altman

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analyses to assess inter-rater reliability and agreement between measurements made by the radiologist and pulmonologist. To assess the diagnostic performance of HRCT-derived measures for RHC-derived measures, we generated 2×2 contingency tables and calculated the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). We conducted separate analyses for subjects who had HRCT and RHC within 7, 14, 30 or 60 days of each other. Spearman correlation was used to examine associations between HRCT- and RHC-derived measures. We considered $p<0.05$ to represent statistical significance. All analyses were conducted using Stata version 11.

Results

Table 1: Demographic and clinical characteristics

	Total n=500	**Pulmonary hypertension group n=300**	**Non-pulmonary hypertension group n=200**	**p-value**
Age years	70.01±15.15	71.09±15.67	70.96±14.54	0.760
Male	250	144	100	0.550
Height cm	168.00±14.50	167.10±14.20	169.00±14.99	0.180
Weight kg	83.00±30.71	84.37±30.46	78.47±29.99	0.002
BMI kg·m−2	29.31±9.42	30.03±9.97	28.20±8.46	<0.001
Smoking history				
Nonsmoker	210	120	88	0.160
Current smoker	15	9	4	
Ex-smoker	275	171	108	
Underlying disease				
COPD	200	72	36	0.033
ILD	190	108	80	0.384
Embolism	30	18	16	0.432
Heart disease	280	180	100	0.010
Haemodynamics				
mPAP mmHg	27±13	33±12	20±5	<0.001
CO (TD) L·min−1	4.69±1.93	4.60±2.06	4.80±1.80	0.065
CO (Fick) L·min−1	4.60±1.75	4.59±1.81	4.65±1.63	0.458
PVR (TD) WU	3.02±2.69	4.09±3.28	2.11±1.11	<0.001
PVR (Fick) WU	3.10±2.64	4.00±3.26	2.18±1.31	<0.001
RAP mmHg	7±5	9±6	5±4	<0.001
PCWP mmHg	12±6	14±7	10±5	<0.001
Inspiratory HRCT median (IQR)				
MPAD mm	32.75 (7.35)	34.60 (7.10)	30.00 (6.50)	<0.001
PA:Ao	0.95 (0.22)	1.01 (0.23)	0.87 (0.16)	<0.001
RPAD mm	25.95 (5.35)	27.00 (4.90)	24.30 (5.10)	<0.001
LPAD mm	25.20 (4.80)	26.15 (4.50)	24.10 (4.70)	<0.001
PA angle deg	84.45 (29.57)	80.17 (28.83)	90.67 (30.62)	<0.001
Expiratory HRCT median (IQR)				
MPAD mm	32.80 (7.20)	34.65 (7.05)	30.50 (6.00)	<0.001
PA:Ao	0.94 (0.21)	0.99 (0.22)	0.86 (0.16)	<0.001
RPAD mm	25.50 (5.35)	26.60 (5.00)	23.80 (4.70)	<0.001
LPAD mm	25.60 (4.90)	26.10 (4.90)	24.20 (4.70)	<0.001
PA angle deg	94.44 (23.02)	92.99 (22.46)	98.56 (25.96)	<0.001

We included 500 scans from 500 patients; 300 (60%) had RHC-confirmed pulmonary

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hypertension, with mPAP ⩾25 mmHg. Compared with the non-pulmonary hypertension group, the group with pulmonary hypertension had greater MPAD, RPAD, LPAD and PA:Ao in both respiratory cycles, whereas the PA angle was greater in the non-pulmonary hypertension group. In the subgroup with pulmonary hypertension, the median MPAD was 34.60 mm in inspiration and 34.65 mm in expiration, while in the non-pulmonary hypertension group it was 30.00 mm in inspiration and 30.50 mm in expiration.

Table 2: Diagnostic performance of various high-resolution computed tomography-derived measures for pulmonary hypertension defined as mean pulmonary artery (PA) pressure ⩾25 mmHg on right heart catheterisation for subgroups with chronic obstructive pulmonary disease (COPD) or interstitial lung disease (ILD)

	Subjects n	Sensitivity %	Specificity %	PPV	NPV
COPD					
Inspiration					
MPAD ⩾29 mm	200	88.17	41.86	0.77	0.62
PA:Ao ⩾1.0	200	50.54	88.37	0.90	0.45
MPAD and PA:Ao	200	50.54	88.37	0.90	0.45
MPAD or PA:Ao	200	88.17	41.86	0.77	0.62
Expiration					
MPAD ⩾29 mm	195	90.11	37.50	0.77	0.63
PA:Ao ⩾1.0	195	50.55	85.00	0.88	0.43
MPAD and PA:Ao	195	49.45	85.00	0.88	0.43
MPAD or PA:Ao	195	91.21	37.50	0.77	0.65
ILD					
Inspiration					
MPAD ⩾29 mm	190	91.24	37.76	0.67	0.76
PA:Ao ⩾1.0	190	52.55	80.61	0.79	0.55
MPAD and PA:Ao	190	50.36	84.69	0.82	0.55
MPAD or PA:Ao	190	93.43	33.67	0.66	0.79
Expiration					
MPAD ⩾29 mm	185	91.97	32.98	0.67	0.74
PA:Ao ⩾1.0	185	45.99	78.72	0.76	0.50
MPAD and PA:Ao	185	45.99	79.79	0.77	0.50
MPAD or PA:Ao	185	91.97	31.91	0.66	0.73

For the cohort as a whole, the areas under the receiver operating characteristic curves (AUCs) for inspiratory MPAD and inspiratory PA:Ao (for RHC-confirmed pulmonary hypertension defined as Mpap ⩾25 mmHg) were 0.741 and 0.750, respectively. For the cohort as a whole, the cut-offs MPAD ⩾32.5 mm and PA:Ao ⩾0.94 yielded the most favourable diagnostic profiles.

Table 3: Spearman correlation coefficients showing the relationship between various high-resolution computed tomography-derived measures for pulmonary hypertension defined as mean pulmonary artery (PA) pressure ⩾25 mmHg on right heart catheterization

	Inspiration			Expiration		
	All	ILD	COPD	All	ILD	COPD
MPAD	0.479	0.456	0.574	0.444	0.415	0.534
RPAD	0.335	0.295	0.462	0.327	0.327	0.327
LPAD	0.339	0.323	0. 405	0.273	0.254	0.183
(RPAD+LPAD)/2	0.360	0.329	0.463	0.297	0.269	0.265
PA:Ao	0.507	0.489	0.579	0.488	0.461	0.564
PA angle	−0.241	−0.212	−0.246	−0.241	−0.327	−0.316

There were weak positive correlations between RHC-measured mPAP and inspiratory MPAD, RPAD, LPAD and (RPAD+LPAD)/2. There was moderate positive correlation between mPAP and PA:Ao. There was weak negative correlation between mPAP and the PA

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angle. In general, compared with inspiration, correlations were not as strong between mPAP and HRCT measurements taken in expiration. Compared with the ILD subgroup, in the subgroup with COPD, correlations were generally stronger between HRCT measures and mPAP.

Discussion

Although there have been significant advances in the treatment of pulmonary hypertension (PH), there remains significant morbidity and mortality [21-23] With increasingly more effective and safer pharmacological therapy for pulmonary arterial hypertension (PAH), outcomes may be improved by earlier detection of PH [23]. Screening algorithms have been proposed to facilitate the timely and accurate diagnosis of PH, utilizing a combination of echocardiographic, physiologic (lung function), and radiologic non-invasive techniques [24, 25], before proceeding to a definitive right heart catheterization (RHC) for confirmation.

In a meta-analysis of 20 publications, CT-measured MPAD had a mean sensitivity of 79% and a mean specificity of 83% for identifying RHC-confirmed pulmonary hypertension, and PA:Ao had a mean sensitivity of 74% and a mean specificity of 81% [7]. On balance, in each study of HRCT included in the meta-analysis, diagnostic performance of HRCT was not as good as standard CT or CTA, and our results suggest the same [26].

A wide range of cut-off values for identifying RHC-confirmed pulmonary hypertension have been proposed for MPAD (from 25 to 38 mm) and PA:Ao (from 0.84 to 1.4) [26]. We elected to use the cut-offs proposed in the European Society of Cardiology/European Respiratory Society pulmonary hypertension guideline for our main analyses [18, 27]. But also ran analyses using a range of values, and found that alternative cut-off values performed better. We also conducted analyses for a lower threshold for mPAP (20 mmHg), as that may be adopted as the threshold for pulmonary hypertension in the future [20]. Reassuringly, on balance, results were similar whether we considered scans within 1 week or out to within 2 months of the RHC.

Results for the subgroups with COPD or ILD were similar to those for the cohort as a whole: MPAD was highly sensitive (>90% for the ILD subgroup) but poorly specific and PA:Ao was poorly sensitive but highly specific for each of the two subgroups. For subjects with COPD, cut-offs of MPAD 32.5 mm and PA:Ao 0.90 yielded the most favourable diagnostic profile. For subjects with ILD, cut-offs of MPAD 32.5 mm and PA:Ao 0.92 yielded the most favourable diagnostic profiles. Because HRCT is used most often in patients with ILD, we propose these as cut-offs values for these patients. Of course, our work will require validation. ALHAMAD et al. [28] found MPAD $\geqslant$25 mm had a sensitivity of 86%, a specificity of 41% and yielded the largest AUC (0.65) among 100 subjects with various forms of ILD. Among 34 subjects without ILD, including eight with COPD, they found MPAD $\geqslant$31.6 mm had a sensitivity of 47%, a specificity of 93% and yielded the largest AUC (0.73).

Conclusion

Measurements of the PA taken on HRCT scan may suggest the presence or absence of pulmonary hypertension; these measures may be highly sensitive (MPAD) or specific (PA:Ao), but not both. In ILD, the sensitivity of MPAD was higher, while in COPD, the specificity of PA:Ao was higher. Among patients in whom HRCT is performed, inspiratory measures for MPAD and PA:Ao may raise or lower the level of concern for pulmonary hypertension. A MPAD $\geqslant$32.5 mm in a patient with ILD or COPD has high sensitivity for RHC-confirmed pulmonary hypertension.

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