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Research article

Performance of computed tomography-derived pulmonary vasculature metrics in the diagnosis and haemodynamic assessment of pulmonary arterial hypertension

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ABSTRACT

Background: Few studies have addressed the value of combining computed tomography-derived pulmonary vasculature metrics for the diagnosis and haemodynamic evaluation of pulmonary arterial hypertension (PAH).
Materials and methods: We measured three computed tomography parameters for the pulmonary artery, peripheral vessels, and pulmonary veins: the ratio of the diameter of the pulmonary artery to the aorta (PA/Ao), the cross-sectional area of small pulmonary vessels $< 5\ mm^2$ as a percentage of total lung area ($\%CSA_{<5}$), and the diameter of the right inferior pulmonary vein (PVD). The measured quantities were compared between patients with PAH (n = 45) and control subjects (n = 56), and their diagnostic performance and associations with PAH-related clinical indices, including right heart catheterization measurements, were examined.
Results: PA/Ao and $\%CSA_{<5}$ were significantly higher in patients with PAH than in controls. Receiver-operating characteristic curve analysis for ability to diagnose PAH showed a high area under the curve (AUC) for PA/Ao (0.95) and modest AUCs for $\%CSA_{<5}$ (0.75) and PVD (0.56). PA/Ao correlated positively with mean pulmonary arterial pressure and PVD correlated negatively with pulmonary vascular resistance. The $\%CSA_{<5}$ correlated negatively with mean pulmonary arterial pressure and pulmonary vascular resistance and positively with cardiac index. Notably, the PA/Ao and PVD values divided by $\%CSA_{<5}$ correlated better with right heart catheterization indices than the non-divided values.
Conclusion: PA/Ao, $\%CSA_{<5}$, and PVD are useful non-invasive pulmonary vasculature metrics, both alone and in combination, for diagnosis and haemodynamic assessment of PAH.

1. Introduction

Treatment for pulmonary arterial hypertension (PAH) has improved dramatically in recent years [1,2]. Early and accurate diagnosis of PAH has thus become critically important. Right heart catheterization (RHC) is mandatory for diagnosis of pulmonary hypertension (PH), and the current guidelines for PH recommend that RHC should be performed by well-trained physicians in high-volume PH centres [3].

Chest computed tomography (CT) is a less invasive and widely available imaging modality. To date, studies have reported the diagnostic value of plain CT-derived parameters, such as the diameter of the main pulmonary artery (PA) [4–6], the ratio of the diameter of the pulmonary artery to that of the aorta (PA/Ao) [7–10], and the segmental artery-to-bronchus ratio [11] in PH. In addition, recent studies have shown that the cross-sectional area of small pulmonary vessels $< 5\ mm^2$ as a percentage of total lung area ($\%CSA_{<5}$) reflects mean pulmonary arterial pressure (PAP) and is useful for diagnosis of PH in patients with emphysema or chronic obstructive pulmonary disease (COPD) [12–15]. However, the clinical relevance of $\%CSA_{<5}$ has not been examined in subjects without emphysema or COPD. The ostial diameter of the pulmonary vein (PVD) is another CT-derived metric that reflects PV pressure and flow [16] and is used in the field of

Abbreviations: AUC, area under the curve; BMI, body mass index; CI, cardiac index; $\%CSA_{<5}$, cross-sectional area of small pulmonary vessels $< 5\ mm^2$ as a percentage of total lung area; CT, computed tomography; HU, Hounsfield units; ICC, intraclass correlation coefficient; ILD, interstitial lung disease; LOA, limit of agreement; PA/Ao, ratio of the diameter of the pulmonary artery to that of the aorta; PAH, pulmonary arterial hypertension; PAP, pulmonary arterial pressure; PH, pulmonary hypertension; PVD, ostial diameter of the right inferior pulmonary vein; PVR, pulmonary vascular resistance; RHC, right heart catheterization; ROC, receiver-operating characteristic curve; SSc, systemic sclerosis

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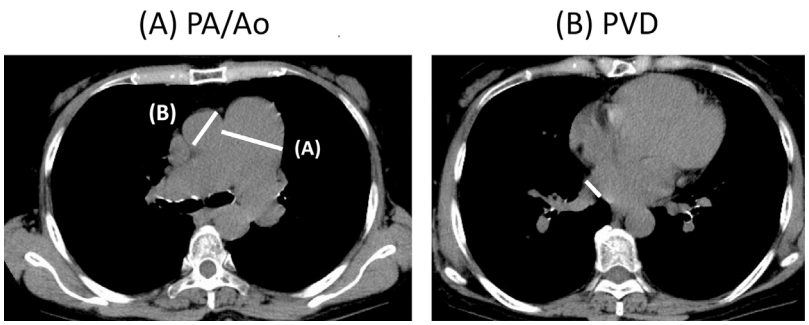

Fig. 1. Measurement of PA, Ao, and PVD.
(A) The interpreter measured the diameter of the main pulmonary artery at the level of its bifurcation (pulmonary artery) and the diameter of the ascending aorta in its maximum dimension (Ao) using the same images.
(B) We chose a short-axis computed tomography image that showed the ostium of the right inferior pulmonary vein at its widest diameter, and then measured the PVD.
Abbreviations: Ao, aorta; PA, pulmonary artery; PA/Ao, ratio of the diameter of the pulmonary artery to that of the aorta; PVD, ostial diameter of the right inferior pulmonary vein.

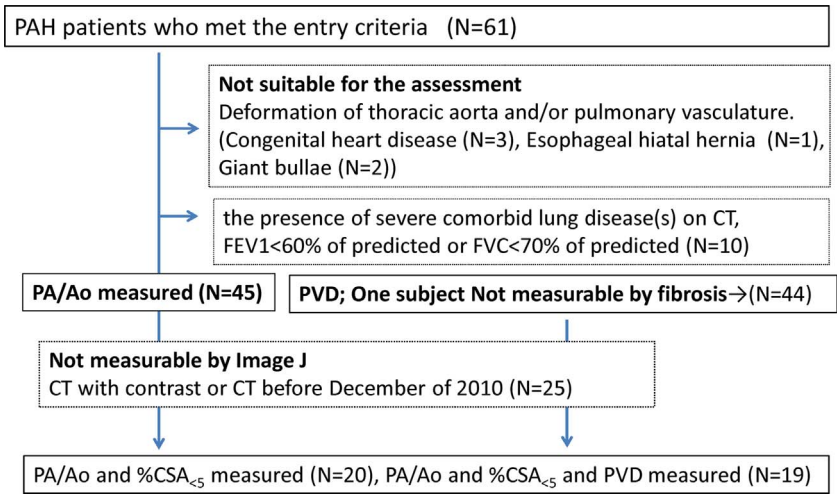

Fig. 2. Selection of patients with PAH.
We measured the diameters of the PA, Ao, and PVD and calculated the PA/Ao in 45 subjects (PAH group). PVD was not measurable in one patient because of distortion caused by parenchymal fibrosis. %CSA $_{<5}$ was calculated in only 20 of these 45 subjects (%CSA $_{<5}$ group), because of use of contrast medium or inadequate CT acquisition parameters in the remaining 25 subjects.
Abbreviations: %CSA $_{<5}$cross-sectional area of small pulmonary vessels < 5 mm2 as a percentage of total lung area; CTcomputed tomography; FEV_1forced expiratory volume in 1 s; FVCforced vital capacity; PA/Aoratio of the diameter of the pulmonary artery to that of the aorta; PAHpulmonary arterial hypertension; PVDostial diameter of the right inferior pulmonary vein.

Table 1
Demographics of patients with PAH and controls.

Characteristics	PAH		Control
	PA/Ao group	%CSA $_{<5}$ group	
Patients, n	45	20	56
Age, years	46.7 ± 14.8	49.0 ± 14.9	50.5 ± 12.8
Sex, male/female	3/42	1/19	1/19
Height, cm	156.0 ± 7.5	155.9 ± 7.9	156.9 ± 6.3(N = 48)
Weight, kg	57.0 ± 11.6	55.5 ± 11.0	56.0 ± 9.8 (N = 48)
Body mass index, kg/m^2	23.4 ± 4.3	22.7 ± 4.1	22.8 ± 4.0 (N = 48)

Data are shown as the mean ± standard deviation. Abbreviations: %CSA $_{<5}$, cross-sectional area of small pulmonary vessels < 5 mm^2 as a percentage of total lung area; PAH, pulmonary arterial hypertension.

interventional treatment for cardiac arrhythmias [17,18]. However, its clinical application in PH has not been investigated to date.

In the current study, we sought to examine the clinical value of three plain CT-derived indices of the pulmonary vasculature, i.e., PA/Ao, %CSA $_{<5}$, and PVD, in the diagnosis of PAH. Notably, these three indices reflect different parts of the pulmonary vasculature, and we hypothesised that combined use of these indices may be useful for the diagnosis and haemodynamic assessment of PAH.

2. Material and methods

2.1. Subjects

The protocol used in this retrospective study was approved by the ethics committee at Hokkaido University Hospital. All patients with PAH gave informed consent for their data to be included in the study. Our ethics committee gave permission for inclusion of the data for controls on the condition that online details of our study protocol are available in the public domain via the Hokkaido University Hospital website. The inclusion criteria for the PAH group were as follows: (1) a resting mean PAP ≥ 25 mmHg and a pulmonary arterial wedge pressure ≤ 15 mmHg on RHC; (2) a diagnosis of PAH according to the 2015 guidelines for PH [3]; and (3) CT with/without contrast and RHC performed within 3 months of each other, during which time the patient's condition remained stable. The exclusion criteria were (1) any cardiovascular, respiratory, or other comorbidity that might affect the geometry of the thoracic aorta and/or pulmonary vasculature, (2) a forced expiratory volume in 1 s < 60% of predicted, and (3) a forced vital capacity < 70% of predicted [18]. We also studied controls matched for age and sex who fulfilled the following criteria: (1) no cardiac, respiratory, or other disease that might affect the geometry of the thoracic aorta and/or pulmonary vasculature, and (2) having chest CT data without contrast after December 2010 for screening or evaluation of lung nodules.

2.2. CT scanning

In this study, several types of scanners were used to capture the CT images, including Somatom Sensation 64 (Siemens, Munich, Germany), VCT (GE Healthcare, Little Chalfont, UK), Aquilion 64, Aquilion Prime, and Aquilion ONE ViSION Edition (Toshiba Medical Systems Corporation, Tochigi, Japan), and Brilliance iCT (Philips, Amsterdam, The Netherlands). The acquisition parameters and contrast media injection conditions were as follows: 100 kV, 0.5 s/rot, automatic exposure control (AEC), 450 mgI/kg, and injection 50 s for Somatom Sensation 64 and VCT; 120 kV, 0.5 s/rot, AEC, 480 mgI/kg, and injection 50 s for Aquilion 64; 120 kV, 0.5 s/rot, AEC, 450 mgI/kg, injection 50 s for Aquilion Prime; 120 kV, 0.4 s/rot, AEC, 480 mgI/kg, and injection 50 s for Aquilion ONE ViSION Edition; and 120 kV, 0.4 s/rot, AEC, 500 mgI/kg, and injection 50 s for Brilliance iCT.