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#### Research paper

## Left Atrial Area and Right Ventricle Dimensions in Non-gated Axial Chest CT can Differentiate Pulmonary Hypertension Due to Left Heart Disease from Other Causes



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#### ABSTRACT

*Background:* It is unknown whether axial non-gated CT can distinguish World Health Organization Group 2 pulmonary hypertension (pulmonary hypertension due to left heart disease) from non-Group 2 pulmonary hypertension.

*Objective*: The study was performed to identity imaging parameters in non-gated chest CT that differentiate Group 2 from non-Group 2 pulmonary hypertension.

Methods: Among 158 patients who underwent right heart catheterization for evaluation of pulmonary hypertension, 112 had sufficient data and chest CT for review. Invasive hemodynamic data and numerous variables obtained from axial CT images (maximum diameters of main, right, left pulmonary arteries, ascending aorta, main pulmonary artery to ascending aorta diameter ratio, right atrial diameter, left atrial area and right ventricular size) were collected. CT variables were validated against hemodynamic data to identify parameters that would allow to differentiate pulmonary hypertension due to left heart disease (Group 2) from non-Group 2 pulmonary hypertension.

Results: Based on right heart catheterization data, we identified 53 patients with Group 2 pulmonary hypertension, 50 patients with non-Group 2 pulmonary hypertension, and 9 subjects with no pulmonary hypertension. In patients with a dilated pulmonary artery (n=84), the ROC curve for left atrial area (area under the ROC curve  $0.76 \pm 0.06$ ) independently distinguished patients with Group 2 pulmonary hypertension (n=42) from patients with non-Group 2 pulmonary hypertension (n=42). A dilated left atrium (>20 mm²) in combination with a normal right ventriuclar size had a sensitivity of 77% and specificity of 94% for Group 2 pulmonary hypertension.

Conclusions: In patients with a dilated pulmonary artery on chest CT, left atrial area and right ventricular dimensions may aid to diagnose pulmonary hypertension and to distinguish underlying cardiac disease from other causes.

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#### 1. Introduction

Pulmonary hypertension is a condition that carries significant morbidity and mortality, characterized by enhanced pulmonary vascular pressures, vascular constriction, and vascular remodeling. <sup>1,2</sup> The most common cause of pulmonary hypertension is left heart

failure, classified as World Health Organization (WHO) Group 2 pulmonary hypertension.<sup>3,4</sup> While Group 2 pulmonary hypertension is predominantly pulmonary *venous* hypertension, non-Group 2 pulmonary hypertension is pulmonary arterial hypertension, with major differences in therapy and outcomes between the two.<sup>5</sup>

In contemporary practice, when pulmonary hypertension is suspected, transthoracic echocardiography is performed as a screening test. By providing a fair estimation of pulmonary artery, left and right atrial pressures and comprehensive evaluation of the cardiac chamber morphology and function, echocardiography may serve not only as an initial diagnostic test in pulmonary

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hypertension but may also be useful to assess subsequent therapeutic response. <sup>6,7</sup> However, right heart catheterization is the gold standard test used to diagnose and distinguish Group 2 from non-Group 2 pulmonary hypertension. <sup>1,8</sup>

Currently, non-gated CT chest with or without contrast is routinely used in the diagnostic evaluation of pulmonary hypertension to assess parenchymal lung disease and suspected pulmonary thromboembolic disease. The utility of chest CT to diagnose and make a distinction between Group 2 and non-Group 2 pulmonary hypertension is unknown. However, prior studies indicate that a dilated pulmonary artery on an axial non-gated chest computer tomography (CT) may be suggestive of pulmonary hypertension. In addition, some studies demonstrated that an enlarged left atrium on CT is suggestive of elevated left atrial pressure. In the present work, we sought to identify cardiac parameters that can be used to identify and differentiate Group 2 from non-Group 2 pulmonary hypertension solely based on axial nongated chest CT (with or without contrast).

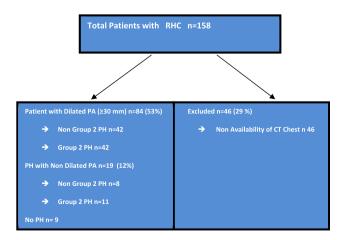
#### 2. Methods and materials

#### 2.1. Study population

Institutional review board approval was obtained. We identified 158 patients who were referred for right heart catheterization (Jan 2009 through Dec 2013) due to suspected pulmonary hypertension (Fig. 1). We included patients who underwent axial non-gated CT chest (with or without contrast) within 3 months of right heart catheterization, either as work up for suspected pulmonary hypertension or evaluation of other pulmonary pathology. Study population was divided into those with and without pulmonary arterial dilatation (>30 mm), as the dilated pulmonary artery was typically used as the primary screening imaging parameter for pulmonary hypertension. Patients with a chest CT who had no pulmonary hypertension based on right heart catheterization were used as the control group.

#### 2.2. CT measurements

CT imaging was performed on a 64-slice CT scanner. Axial CT variables examined were the maximum cross sectional diameters of the main pulmonary artery (immediately proximal to the bifurcation), proximal right and left pulmonary arteries as well as ascending aorta (at the level of the main pulmonary artery bifurcation); the ratio of the main pulmonary artery to ascending aorta



**Figure 1.** Flow diagram – Study population RHC: right heart catheterization, PA: pulmonary artery, PH: pulmonary hypertension, n: number.

diameter; right atrial diameter; left atrial area; and right ventricular size. The right atrial diameter was measured as the maximum distance between the septum and lateral wall on an axial 4 chamber view (Fig. 2). The maximum left atrial area (Fig. 2) was measured in an axial view at the level of the left ventricular outflow tract, as described in a previous study. Hight ventricular size was qualitatively assessed visually in an axial 4 chamber view (Fig. 2) and noted as dilated when it appeared to be larger than the left ventricle.

## 2.3. Comparison of CT variables with right heart catheterization hemodynamic data

The normal values for pulmonary artery and left atrial sizes were established based on previous studies. 14–16 Group 2 versus non-Group 2 distinction on right heart catheterization was defined based on the universal WHO definition of Group 2 pulmonary hypertension.<sup>3,4</sup> Group 2 included patients with a mean pulmonary arterial pressure (PAP) > 25 mm Hg, a pulmonary capillary wedge pressure (PCWP) > 15 mm Hg and a trans-pulmonary gradient (TPG) < 12 mm Hg. Patients with a PCWP > 15 mm Hg and elevated TPG (>12 mm Hg) are considered as a Group 2 with reactive pulmonary hypertension. We examined the differences of various CT parameters among Group 2, non-Group 2 pulmonary hypertension patients, and control groups. We further analyzed if a composite of 3 CT variables including main pulmonary artery diameter, left atrial size, and right ventricular size, can distinguish Group 2 from non-Group 2 pulmonary hypertension when compared to right heart catheterization hemodynamic data. We defined CT criteria as follows: 1) as a combination of main pulmonary artery size >30 mm with normal left atrial area (<20 mm<sup>2</sup>) and dilated right ventricle; and 2) as a pulmonary artery diameter > 30 mm in combination with a dilated left atrium (area >20 mm<sup>2</sup>) and normal right ventricular size.

The investigators that determined the CT parameters were blinded to right heart catheterization hemodynamic data.

#### 3. Statistical analysis

Continuous are were expressed as means ± SD or median (interquartile range), depending on their distribution. Categorical variables are indicated as numbers (percentage). Mean values of CT parameters were compared using 1-way ANOVA for paired samples. P values < 0.05 were considered statistically significant. Dichotomous variables were compared by univariate analysis using the Chi Square method. Multivariable logistic regression analysis was performed to identify independent predictors among CT parameters to differentiate Group 2 from non-Group 2 pulmonary hypertension. Sensitivity and specificity of the predefined CT parameters (criteria 1 and 2) to distinguish Group 2 versus non-Group 2 pulmonary hypertension patients, along with their negative and positive predictive values were determined. The receiver operator characteristic (ROC) curve for left atrial area was calculated to determine the area under the curve (AUC) to distinguish Group 2 from non-Group 2 pulmonary hypertension.

#### 4. Results

#### 4.1. Patient characteristics

Among a total of 158 patients referred for right heart catheterization (January 2009 through Dec 2013), 84 (53%) patients with pulmonary hypertension had a dilated pulmonary artery ( $\geq$ 30 mm) on axial non-gated chest CT (50(60%) with contrast; 34 (40%) without contrast). Among these, there were 42 patients (50%) with

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