CT measurement of central pulmonary arteries to diagnose pulmonary hypertension (PHTN): more reliable than valid?

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Authors: S. Terpenning\textsuperscript{1}, L. Ketai\textsuperscript{1}, C. T. Lin\textsuperscript{2}, S. J. Kiglerman\textsuperscript{2}, J. Jeudy\textsuperscript{2}; \textsuperscript{1}Albuquerque, NM/US, \textsuperscript{2}Baltimore, MD/US
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Aims and objectives

Main pulmonary artery (MPA) measurement has shown to have a wide range of variability among the radiologists. Main pulmonary artery (MPA) diameter greater than 3 cm is commonly used to diagnose pulmonary hypertension (PHTN) (1) on Computed Tomography (CT) of the chest, however there is substantial overlap between normal subjects and patients with pulmonary artery hypertension based on the size of main pulmonary artery alone.

Clinical practice suggests that the specificity of this measurement is low and reader variability may be high. It is uncertain if additional measurement of the right pulmonary artery (RPA) and left pulmonary artery (LPA) may increase specificity or decrease reader variability.

The purposes of this study are to verify the accuracy of different cut-off values of the size of MPA in diagnosis PHTN, to determine the inter-rater agreement for this measurement and determine whether addition of RPA and LPA measurement can improve the accuracy.

Methods and materials

The study was approved by the IRB and the informed consent was waived.

Subject selection

We divided the patients into 2 groups, normal pulmonary artery pressure (< or = 25 mmHg) and pulmonary hypertension (>25 mmHg), based on the mean pulmonary artery pressure (2) documented from right heart catheterization performed by the University of Maryland cardiology service between January 2010 and December 2012.

Patients with prior cardiac surgery, congenital heart disease, pericardial disease, severe lung disease and critically ill patients documented on CT examinations were excluded from the study.

A total of 95 patients with available CT examinations, 45 patients with normal pulmonary artery pressure and 50 patients with PHTN were included and their CT examinations were retrospectively reviewed.
Axial CT examinations of the chest were performed using various CT parameters depending on the patient's factors such as Body Surface Area (BSA)), clinical indications and available CT scanners (40, 64 or 256 detector scanners).

CT scan of the chest without contrast enhancement includes routine CT chest without contrast and High Resolution CT Chest. The following CT parameters were used 1.25-4@1.3-3 Thickness/Increment, 100-120 kVp, 200-250 mAs, 2-128 x 0.625 collimation, 0.824-0.993 Pitch, 0.5 s rotation time and 350-400 Scan FOV.

CT scan of the chest with contrast includes routine CT chest with intravenous contrast, Computed Tomography Pulmonary Artery Angiography, Computed Tomography Coronary Angiography and Cardiac Computed Tomography. The following CT parameters were used 0.9-4@ 0.45-3 Thickness/Increment, 120 kVp, 250-400 mAs, 40-128 x 0.625 collimation, 0.703-0.993 Pitch, 0.27-0.5 s rotation time and 220-400 Scan FOV. The tube current, voltage and scan FOV were also adjusted accordingly to the patient's BMI who underwent CT Pulmonary Angiogram, CT Coronary Angiogram and Cardiac CT.

Three radiologists (CTL, SJK, JJ) with 1, 5 and 8 years experience in cardiothoracic imaging measured the main pulmonary artery diameter on axial images using an electronic ruler on 3D work-station (Terarecon/Aquarius net). Radiologists chose the key images to measure MPA, RPA and LPA independently but were not allowed to magnify the images or to view the images on sagittal or coronal reformats. Adjusting the window and level was permitted. The radiologists were also blinded to the patient clinical symptoms, diagnosis and each other's measurement to prevent bias. The measurement then was documented for future data analysis.

Data Collection

We collected the patient's demographic data such as age, gender, body weight (kg) and height (cm). Body surface area (BSA, m2) was calculated from the weight and height by the DuBois formula (BSA (m2)=0.007184 x Height (cm) 0.725 x Weight (Kg) 0.425). Clinical parameters such as pulmonary artery systolic and diastolic pressure were also recorded. Mean pulmonary artery pressure (MPAP) was calculated from systolic pressure (SP) and diastolic pulmonary pressure (DP). MPAP (mmHg) is equivalent to DP + 1/3 (SP-DP). This information was collected from right cardiac catheterization.
The size and the distance from the pulmonary artery bifurcation of measured MPA were measured in centimeters. This data was acquired from the 3D CT workstation using axial multiplanar reformatted images (Fig. 1 on page 4).

**Statistical analysis**

For patients with normal PAP and PHTN:

We tested the normality of the main pulmonary artery diameter (MPAD) by the Saphiro-Wilk test.

To analyze the statistical significance of MPAD and patients' profiles such as age, height, weight and body surface area, linear regression was used. Student T-test was used for the gender. The analysis was performed for both normal PAP and PHTH groups.

To evaluate inter-observer agreement of using 3.15 cm as a cut off value to diagnose PHTN, we used Cohen's kappa test. We also evaluated the inter-rater variation of the measured MPAD in terms of size and its relationship to the bifurcation by one-way ANOVA test.

To determine whether the addition of RPA and LPA measurements improve the accuracy in diagnosing PHTN, we added RPA and/or LPA diameter greater than 2.2 cm to the diagnostic criteria. Studies showing either an enlarged MPAD (≥ 3.15 cm) or an enlarged RPA or LPA were considered positive and the differences between controls and PHTN patients computed using Chi-Square test.

To verify the accuracy of different cut off values of MPAD at 3.15 cm to diagnose PHTN, we calculated the statistical values and demonstrated the data in the formats of histograms and ROI curves.

**Images for this section:**
Fig. 1: Measurement of MPAD and the distance from the measured MPAD to the bifurcation (Blue line= 19.62 mm). The distance was measured perpendicularly to the measured MPAD (Red line=16.38 mm).
Results

Demographics

None of the demographic data or patients' factors were related to the size of MPAD.

There is no significant relationship between the gender and MPAD of 45 patients (16 females and 29 males) with normal pulmonary artery pressure (p-value=0.17) or 50 patients (22 females and 28 males) with PHTN (p-value=0.16).

Pulmonary Artery measurements

The distribution of the main pulmonary artery diameter was normal in both groups (Fig. 2 on page ) (p=0.71 for normal PAP patients and 0.67 for PHTN patients by Shapiro-Wilk test). There was extensive overlap between normal controls and patients with pulmonary HTN (Fig. 3 on page 7).

Using 3.15 cm main MPA diameter as a threshold, reader sensitivities for PHTN were 76%, 74% and 74 % and specificities of 60 %, 62% and 71%) Areas under the ROC curves were similar for all three readers and per-case inter-rater agreement was good, kappa values > 0.65 (Fig. 4 on page 8). Body surface area did not differ between false positive (2.1± 0.4) and true negative patients (2.0±0.3).

ROC curves for RPA (Fig. 5 on page 9) or LPA (Fig. 6 on page 10) size demonstrated smaller areas under the curves for all readers and incorporation of RPA or LPA diameter > 2.2 cm to detect PHTN increased the sensitivities to 90%, 90% and 94% but degraded specificities to 36%, 29% and 33%.

Neither the distance from the measured MPA to the pulmonary artery bifurcation nor the measured size of MPA differed significantly among 3 radiologists (p-value=0.65 and 0.76 respectively).

Images for this section:
Fig. 1: Measurement of MPAD and the distance from the measured MPAD to the bifurcation (Blue line= 19.62 mm). The distance was measured perpendicularly to the measured MPAD (Red line=16.38 mm).
**Fig. 3:** The histogram demonstrated the overlapping of MPAD between normal controls and PHTN patients.
Fig. 4: The ROC curve shows similar trends of specificity and sensitivity of 3 radiologists in MPAD measurement using the cut-off value at 3.15 cm (black arrows). The area under curve of the reader 1, 2 and 3 are not different (0.740, 0.764 and 0.760 respectively).

<table>
<thead>
<tr>
<th>Test Result Variable(s)</th>
<th>Area</th>
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<tr>
<td>Reader1MPA</td>
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<tr>
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<td>0.764</td>
</tr>
<tr>
<td>Reader3MPA</td>
<td>0.760</td>
</tr>
</tbody>
</table>

Main Pulmonary Artery Diameter

\[ \downarrow = 3.15 \text{ cm} \]
Fig. 5: Using RPAD with the cut-off value at 2.2 cm to diagnose PHTN had slightly increased the sensitivity but had markedly degraded the specificity (black arrows).

<table>
<thead>
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<th>Test Result Variable(s)</th>
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<td>Reader1RPA</td>
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<tr>
<td>Reader2RPA</td>
<td>.643</td>
</tr>
<tr>
<td>Reader3RPA</td>
<td>.681</td>
</tr>
</tbody>
</table>

Diagonal segments are produced by ties.

Right Pulmonary Artery Diameter

\[ = 2.2 \text{ cm} \]
Fig. 6: Using LPAD with the cut-off value at 2.2 cm to diagnose PHTN had slightly increased the sensitivity but had markedly degraded the specificity (black arrows).
Conclusion

MPAD in our study has normal distribution similar to Shirin and Sinem et al (3,4).

We did not find any correlation between patient's demographic data or patient factors and the size of MPA while prior works have shown mixed results. Previously published data had shown that pulmonary artery pressure, patient's age, height, weight and BSA were correlated with the size of main pulmonary artery while the patient's gender was not. (4-8).

There is no statistical significance among 3 radiologists with different years of experience in cardiothoracic imaging in measuring MPA, RPA and LPA size and the distance of measured MPA to the pulmonary artery bifurcation. From this we infer measurement accuracy does not depend upon experience. When using 3.15 cm as a cut-off value to diagnose PHTN, per case inter-rater agreement was good, kappa value > 0.65. Our results were similar to Mohammedi et al and PD Edwards et al (7,9).

The higher cut-off values had more increase in sensitivity and more decrease in specificity. Incorporating RPA and/or LPA measurement to diagnose PHTN improved the sensitivity but markedly degraded the specificity. We found this to be disadvantageous in the diagnosis of PHTN.

To establish the cut-off value to diagnose PHTN, the trade-off of misdiagnosis of PHTN and sensitivity/specificity calculated from different cut off values must be weighed.

The size of central pulmonary arteries, specifically dilated MPA may imply presence of PHTN but is not diagnostic. PHTN patients can have normal sized MPA (Fig. 7 on page 13) and conversely, normal PAP patients can have dilated MPA (Fig. 8 on page 13). The latter, the false positive diagnosis of PHTN did not appear to be related to patient size (BSA) in our data.

In conclusion, measurements of MPA on CT examinations of the chest are reproducible. Cut-off values that are widely used are moderately sensitive relatively nonspecific. Incorporation or RPA and LPA measurement can improve sensitivity but severely degrade specificity. Diagnosis of PHTN based solely on CT examinations of the chest may not be sufficiently accurate for clinical use.
Fig. 7: An axial CT scan of the chest without contrast of a 68 years old man with normal mean PAP (21 mmHg) presenting with pleural effusion and shortness of breath showed mildly dilated main pulmonary artery (3.4 cm).
**Fig. 8:** An axial CT scan of the chest of a 63 years old man with PHTN (mean PAP = 35 mmHg) presenting with cough and pulmonary nodules demonstrated normal size main pulmonary artery (2.8 cm).
Personal information

Silanath Terpenning: An assistant professor at the department of radiology, division of cardiothoracic imaging, University of New Mexico, Albuquerque, NM, USA.

Loren H Ketai: A professor at the department of radiology University of New Mexico, division of cardiothoracic imaging, Albuquerque, NM, USA

Cheng Tin Lin: An assistant professor at the department of radiology, The Johns Hopkins University, division of cardiothoracic imaging, Baltimore, MD, USA

Seth J Kligerman: An assistant professor at the department of radiology, division of cardiothoracic imaging, University of Maryland, Baltimore, MD, USA

Jean Jeudy: An associated professor at the department of radiology, division of cardiothoracic imaging, University of Maryland, Baltimore, MD, USA

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Susie Hong-Zolman: An assistant professor at the department of internal medicine, division of cardiology, University of Maryland, Baltimore, MD, USA

Jason Mitchell: An assistant professor at the department of radiology, division of interventional radiology, University of Maryland, Baltimore, MD, USA

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