

Diagnostic evaluation of Imaging findings, Causes of Pulmonary Hypertension and its correlation with 2D Echocardiography: A CT Pulmonary Angiogram based study

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PWG SK conceived idea, PG PWG SN drafted the study, PWG TY collected data, PG SK GJ did statistics analysis and interpretation, PWG SK critical review manuscript, All approved final version to be published

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The authors declare that there is no conflict of interest.

Abstract

Background: Pulmonary arterial hypertension (PAH) is a common health problem resulting in morbidity and mortality. It is much more common than previously thought due to improved imaging techniques.. Diagnosing PAH is important for the prognosis and treatment planning in PH patients.

Objective: Objective of the present study was to systematically evaluate the signs and causes of PAH on CT Pulmonary angiography (CTPA) and its correlation with 2D echocardiography.

Methodology: The study was conducted at Bolan Medical Complex Hospital over a time duration of 9 months. In this study, 40 patients underwent CTPA for evaluation of their pulmonary vasculature, pulmonary parenchyma and mediastinal structures to detect different diagnostic criteria, causes and associations of pulmonary arterial hypertension. All 40 patients underwent echocardiography.

Results: Total 40 patients underwent non ECG gated pulmonary angiography. 20 were males and 20 were females. 18 patients out of total 40 were positive for PAH on CTPA. Out of these 8 had mild PAH, 8 had moderate and 2 had severe PAH. Out of total 40 patients 10 were normal on echocardiography, 11 had mild pulmonary hypertension, 7 had moderate pulmonary hypertension, 12 had severe hypertension. Combined CTPA and echo results showed that findings of only 28 patients out of 40 were positive for PH and correlated on both modalities including patients with and without PAH.

2D echocardiography is operator, machine and patient body habitus dependent therefore it can over estimate results. Sensitivity and specificity of echo is higher for negative cases. PA:AA ratio correlated well with Pulmonary hypertension.

Conclusion: Echocardiography is usually more commonly carried out for PAH however it can also substantially lead to an underestimation or overestimation of pulmonary arterial hypertension. Using CTPA and Echocardiography in combination is more reliable in determining PAH. In our study echocardiography over estimated patients for PH which were subsequently not positive on CTPA.

Key Words: Pulmonary arterial hypertension; Pulmonary artery; Echocardiography

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Introduction

Pulmonary arterial hypertension is one of the common health damaging disease resulting in morbidity and mortality. It is much more common than previously thought due to improved imaging techniques.¹ Pulmonary hypertension (PH) is caused by multiple factors. The latest hemodynamic definition of pulmonary hypertension as proposed by the 6th World Symposium on PH Task Force is mPAP >20 mmHg along with pulmonary vascular resistance ≥3 Wood Units.² The combination of clinical history, physical examination and electrocardiogram findings may suspect PH however imaging especially Computed tomography pulmonary angiogram (CTPA) is usually central to confirming the diagnosis and even guiding towards the cause for PAH.¹

Echocardiography is one of the common method used to screen patients with suspected PH. One meta-analysis recently published suggested that the sensitivity and specificity of echocardiography were 83% and 72%, respectively. However, the diagnostic accuracy of echocardiography can be operator dependent and can be affected by heart rate, patient body habitus and detectable tricuspid regurgitation.^{3,4} The gold standard for the diagnosis of PH is Right heart catheterization (RHC). But it is invasive, with some morbidity and mortality even when performed by experienced doctors. Therefore, non ECG gated CT PA is a non-invasive technique to detect PH.² CT PA can help in making diagnosis of PAH in patients presenting with breathlessness and can rule out other causes of dyspnea. Few of the features on CT PA which helps to diagnose PAH are an increased pulmonary artery (PA) to ascending aorta (AA) diameter ratio. The sensitivity of PA/AA ratio for diagnosis of PAH is 58–87 %. Diagnostic sensitivity is further increased by adding the ratio of the transverse diameter of left ventricle (LV) and right ventricle (RV) measured on the reconstructed four chamber (4CH) view. The literature states that RV/LV diameter ratio

has a sensitivity of 86 % for diagnosis of PAH. It is stated that there is improvement in the predictive value of precapillary PH by CTPA when RV/ LV and PA/AA-ratio are combined.⁵ Another parameter which is closely related to PAH is the segmental artery-to-bronchus ratio (SA: B). The PA/AA ratio and the segmental artery-to-bronchus ratio were associated with mPAP but showed no added benefits as compared with the ratio PA/AA alone.⁶

Objective of our study was to do the systemic evaluation of the signs and causes of PAH on CT PA, and its correlation with 2D echocardiography.

Objective

The study was aimed to evaluate the signs of pulmonary hypertension shown by CTPA and correlate the data obtained with echocardiography in patients with suspected pulmonary hypertension in a tertiary care hospital.

Methodology

The study was conducted at Bolan Medical Complex Hospital over a time period of 9 months. The study was conducted after approval by the Ethical review committee of Bolan medical complex hospital.

In this study, 40 patients did CT pulmonary angiography using a 128 slice multidetector CT, (Toshiba prime aquilion) scanner for evaluation of their pulmonary vasculature, pulmonary parenchyma and mediastinal structures to detect different diagnostic criteria, causes and associations of pulmonary arterial hypertension. All the 40 patients underwent echocardiography. Patients were mainly referred from medicine, cardiology and pulmonology departments.

Patient underwent a kidney function test (urea and serum creatinine). The scans were acquired with bolus tracking software at pulmonary artery at the level of carina at maximum inspiration after intravenous injection of a 70 to 90ml of non-ionic, low-

Table 1. Echocardiography and CT PA results in all (40) cases

Echocardiography results	Men (Mi, Mo, Se)	Women (Mi, Mo, Se)	Total
Positive	Mi(3), Mo(5), Se(6)	Mi(8), Mo(2), Se(6)	30
Negative	6	4	10
CT PA results	Men (Mi, Mo, Se)	Women (Mi, Mo, Se)	Total
Positive	Mi(3), Mo(3), Se(1)	Mi(5), Mo(5), Se(1)	18
Negative	13	9	22

(Positive = PAH, Negative = No PAH). Mi (Mild), Mo (Moderate), Se (Severe)

osmolar contrast agent with dual phase injector followed by saline chase of 15 – 30ml. Contrast rate was 4ml/sec. 18g cannula was used in the right forearm or antecubital vein. CTPA studies were reviewed by two consultant radiologists. The diameters of the main pulmonary artery and ascending aorta were obtained at the level of the the pulmonary trunk bifurcation. PA and AA were measured on the same image in the axial view (Figure 1). Th PA/AA ratio was calculated afterwards.

Maximum transverse diameters of the LV and RV was defined as the widest distance of the endocardium to the interventricular septum measured in the axial

plane perpendicular to the long axis of the heart. Maximum diameters of the LV and RV necessarily were not obtained from the similar image. Subsequently the RV/LV ratio was measured. (Figure 2)

Further, we compared the measurement of the segmental pulmonary artery with its neighboring bronchus in lower lobes which is normally 1 : 1. When the pulmonary blood pressure increases, this ratio also increases .

Length of Right atrium was measured from the center of tricuspid annulus to the superior right atrial margin.

Table 2. Relationship between PA to Aorta Ratio and adjacent AA in all CT PA positive cases (Total 18)

Ratio of PA to Aorta	Men	Women	Total
Normal <1:1, 1:1	13	9	22
Increased > 1:1	7	11	18

Contrast reflux into the inferior vena cava (IVC) (Figure 3) was also included which represented right heart strain. It was further divided into three categories as (A) no reflux into IVC, (B) reflux into IVC (C) reflux into IVC and hepatic veins.

Other parameters seen were carina cross over sign (CCO), egg and banana sign, calcification of PA, signs of chronic pulmonary embolism, shift of the interventricular septum towards left, dilatation of IVC and hepatic veins, parenchymal changes such as pulmonary infarcts, centrilobular nodules, mosaic attenuation, fibrosis, pleural effusions, mediastinal lymphadenopathy.

CCO sign was defined as positive when the right pulmonary artery had already crossed anterior to the carina, on the most cephalad axial 2.5mm section on which the carinal division was visible 22. The egg and banana sign (Figure 4) can be seen in patients with severe pulmonary arterial hypertension (PAH). It is identified by the presence of the pulmonary artery lateral to the aortic arch with the aortic arch being described as the banana and the PA as the egg 23 Transthoracic echocardiography was performed by the consultant cardiologist at Bolan Medical Complex Hospital.

Results

Total 40 patients underwent non ECG gated pulmonary angiography. Age range of male patients was between 25 to 85 years with mean age of 55 and that of females was between 20 to 76 years with mean age of 48.18 (45%) patients out of total 40 were positive for PAH on CT PA. Out of these 8 (44.4%) had

mild PAH, 8 (44.4%) had moderate and 2 (11.1%) had severe PAH. Out of total 40 patients 10 (25%) were reported normal on echocardiography, 11 (27.5%) had mild pulmonary hypertension, 7 (17.5%) had moderate pulmonary hypertension, 12 (30%) had severe hypertension. Combined CT PA and echo results showed that findings of only 28 patients out of 40 correlated with one another including patients with and without PAH (Table 1) .

18 patients had PA: AA ratio > 1 (Table 2). Right ventricle to left ventricular ratio (RV/LV) was > 1 in 9 (50%) patients. However 9 (50%) patients showed right ventricle to left ventricular ratio of either 1:1 or < 1 despite of increased pulmonary artery to aortic ratio. Patients which had ratio of less than <1 were few in number and had underlying left heart disease. Right ventricular enlargement is the most clinically relevant long-term complication that affects survival in patients with PAH which was seen in only 50% of cases as most of the our PH positive patients had either mild or moderate PAH. 33 (82.5%) patients showed segmental artery to bronchus ratio (SA: B) of >1. Six (15%) patients showed SA:B ratio of 1:1 and 1 (2.5%) patient showed ratio of <1 as patient had bronchiectasis. Right atrial enlargement was seen in 15 (83.3%) cases out of 18 CT positive cases. 3 (16%) cases had no atrial enlargement and had mild PH.

Reflux of the contrast was seen in IVC in 28 (70%) patients out of which only 13 were positive for pulmonary hypertension. Reflux was also seen in patients who were negative for pulmonary hypertension on CTPA and Echocardiography. Reflux into hepatic veins was seen in 9 (22.5%) patients out of

which 6 had pulmonary hypertension on CT PA. 3 patients had reflux into hepatic veins however no pulmonary hypertension was seen. Shift of the interventricular septum was seen in 9 (22.5%) patients and all of these patients had either mild, moderate or severe pulmonary hypertension with RV:LV ratio of more than 1 and also had reflux into either IVC or IVC and hepatic veins both.

In summary patients which were positive of CT PA proved to be positive on echocardiography however patients which were not positive on CT PA also proved to be positive on echocardiography, showing that results are of two modalities can differ from one another keeping in mind that echocardiography is operator/machine and patient body habitus dependent. Cases of mild and moderate pulmonary hypertension on CTPA showed severe PH on echocardiography. It was observed that echo overestimated the findings. However cases which were negative on echo were also negative on CT PA concluding that the sensitivity and specificity of echo is higher for negative cases. PA: AA ratio correlated well with Pulmonary hypertension. Whereas RV: LV ratio was > 1 in moderate and severe cases of PAH. Findings of segmental artery to bronchus ratio was > 1 in positive cases but were also more than > 1 in negative cases making it a less reliable sign for pulmonary hypertension. Reflux of contrast into IVC and hepatic veins was mostly seen in all positive cases of moderate and severe pulmonary hypertension but was also seen in some negative cases making us think of the fact that reflux may be associated with rate of the contrast administration in addition to right heart strain. Shift of the

interventricular septum was again seen mostly in positive cases and in moderate and severe cases of PAH and was not associated with negative cases making it a more reliable sign of right heart strain rather than reflux of the contrast.

Table 3 shows frequency of pulmonary findings in positive cases of PAH. Further positive cases were divided into 4 groups based on the causes of PAH. Groups included Patients as having PAH due to lung disease (group A), cardiac disease (group B), Idiopathic cases (group C) and thromboembolism (group D). Out of 18 positive cases 9 (50%) were due to lung diseases, 4 (22%) were due to cardiac diseases, 3 (16%) had PAH due to unknown cause and 2 (11.1%) patients had pulmonary embolism. Only 1 patient with severe PAH showed egg and banana sign (Figure 4).

Discussion

Pulmonary hypertension is a devastating condition leading to morbidity and mortality. Early detection of PH can significantly improve the clinical outcome.⁵ If pulmonary hypertension is left untreated, it can result in right-heart dysfunction and death.^{7,10}

Previous study has reported that Pulmonary artery caliber of greater than 29 mm as measured 2 cm from the pulmonary valve has sensitivity of 84%, specificity 75% and positive predictive value of 97% for PAH as confirmed with invasive imaging. If the PA has a maximum transverse diameter greater than that of the thoracic aorta, it has a sensitivity of 70%, specificity 92%, and positive predictive value of 96% for the presence of PAH. However care should be taken to rule out aortic ectasia/aneurysm.⁸ The aorta is the largest artery in the body and normally the MPA is

Table 3. Different CT findings in all positive cases

Findings	Frequency of Presentation
Mosaic attenuation/ground glass opacities	10
Centrilobular ground glass nodules	4
Emphysematous changes	2
Subsegmental atelectasis/	2
fibrotic changes/honey combing/interstitial changes	3
Neovascularity	0
Coarse reticulation/bronchiectasis	3
Consolidation/subpleural opacities/infarcts	8
Mediastinal nodes (calcified/non calcified)	11
Cardiomegaly	11
Pulmonary artery filling defects	4
Pleural effusions	5

smaller in diameter than the ascending aorta. When there is an increase in the pulmonary arterial pressure, the main PA artery diameter may become larger than that of the aorta and the relationship becomes more than 1:1.1

It has been reported that CTPA using only the PA/AA calculations had an accuracy of near around 90.1% in differentiating patients with PH from the other ones without PH. When they added the ratio of right and left ventricular diameter to the PA/AA ratio, the accuracy was noted to be improved to more than 98%. If the PA/AA ratio is higher or equal to 1 or a RV/LV ratio is higher or near to 1.20, it is indicative of PH and the patient should be further evaluated to confirm the diagnosis. It is although emphasized that only CTPA should not be used as a primary screening tool for pulmonary hypertension, but rather used as a predictive tool that needs further evaluation by an echocardiography.⁵

Another CT chest finding that is suggestive of pulmonary arterial hypertension when the segmental arteries ratio is greater than 1.25 times the adjacent bronchus. The combination of these findings increases the diagnostic confidence. Moreover, the finding of an enlarged MPA of greater than 29 mm and associated enlargement of few segmental arteries (arterial-to-bronchial diameter ratio of greater than 1.25) has 100% specificity for PAH.⁸ In our study we

found that patients with normal diameter of PA also showed segmental artery ratio to bronchus of > 1 which proved it to be a less sensitive sign of PAH. The ratio of PA/AA is considered the most common feature of pulmonary hypertension on CTPA.⁵ Although echocardiography is used frequently as a screening tool which is noninvasive and gives an estimate of systolic PAH. However, sometimes this measurement is difficult to make, moreover, it may be less accurate, especially in patients with diffuse lung disease.^{6,9}

Chan et al calculated the ratio of RV/LV in the axial plane and reported that a RV/LV of greater than 1.28 predicted PH with a sensitivity of 85.7 and 86.1%.¹¹ In our study RV/LV ratio was > 1 in moderate and severe PAH and was mostly normal in cases of mild PAH. The severity grading system for PH has been given in the literature. Cut points for PA/AA ratio were defined as normal less than or equal to 0.9; mild less than 0.9 to 1.0; moderate more than 1.0 to 1.1 and severe more than 1.1.¹²

In PAH, CT can not only give diagnosis but can help in determining the prognostic factors. The Right ventricular function is a prognostic marker which can be determined by the interventricular (IV) shift of the septum and dilatation of RV and thus help in predicting the failing RV. The diameter of the vena cava reflects the pressure in the RA, which is an

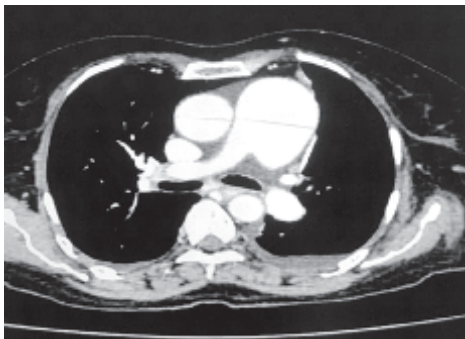


Fig 1: increased PA : AA ratio

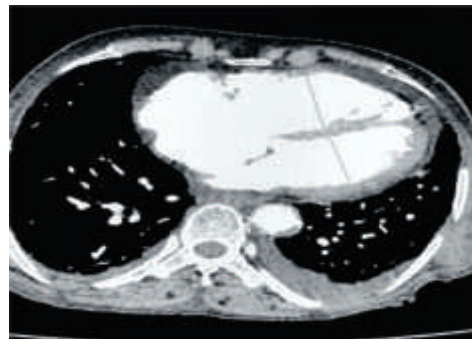


Fig 2: RV/ LV ratio

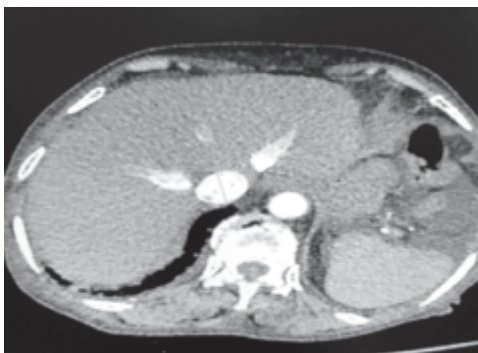


Fig 3: Reflux of the contrast into IVC and hepatic veins



Fig 4: Egg and banana sign in severe PAH

important prognostic determinant in PAH.¹³ In our study shift of IV septum was seen in all cases of moderate and severe PAH. Dilatation of the IVC, hepatic veins and pericardial effusion are also mentioned as signs of right-sided heart failure.⁵

Although echocardiography can be used to measure pulmonary arterial pressure, but to get precise measurement right ventricular catheterization is required.¹⁴ CTPA is a noninvasive valuable imaging modality in the workup of PH and best method for evaluating the pulmonary parenchyma.¹⁵ PH can be due to pulmonary embolism. Acute pulmonary embolism is an uncommon cause of pulmonary hypertension, 16 however chronic pulmonary thromboembolism is more commonly associated with PH.¹⁷ CTPA can very well differentiate acute and chronic pulmonary thromboembolic disease.¹⁸

A combination of CT and echocardiographic measures of PH is closely associated with mean pulmonary arterial pressure (mPAP) than either in isolation and the presence of PA/AA ratio was a better predictor of the PH as compared to bronchus to segmental artery ratio. The study conducted by Devaraj et al showed that a combination of CT and echocardiographic markers of PAH in the form of a composite index is more strongly related to mPAP than either test in isolation.⁶ The ratio of the diameter of the main PA to the diameter of the proximal descending thoracic aorta, the segmental artery diameter and the ratio of segmental artery-to-bronchus were related to mPAP but did not enhance correlations compared with the ratio of the diameter of the main PA to the diameter of the proximal descending ascending aorta in isolation.⁶

CT being a noninvasive test has the potential to provide the first pointer toward the diagnosis of the condition.¹⁹

Moreover “carina cross-over sign” and egg and banana sign” are newly proposed highly specific morphological criterion for the CT diagnosis of PH present in a significant number of such patients.^{20,21} Combination of echocardiography and CT chest is better than either imaging technique alone in diagnosing patients with PH in a heterogeneous population and helps to exclude PAH.²² To make accurate and easy diagnostic evaluation of Pulmonary hypertension by noninvasive methods will be of great help in facilitating the treatment of PH.²³

Conclusion

The gold standard for the measurement of pulmonary artery pressure is right heart catheterization, but this is an invasive procedure with recognized complications even in experienced hands. CTPA can be used

for diagnosis of suspected pulmonary hypertension with high accuracy and can also diagnose the cause for pulmonary hypertension, It can help in diagnosis of other disease conditions mimicking clinically as pulmonary hypertension.

Echocardiography is usually more commonly carried out for PAH however it can also substantially lead to an overestimation or underestimation of systolic pulmonary arterial pressure. Using CTPA and Echocardiography in combination is more reliable in determining PAH. In our study echocardiography over estimated patients for PAH which were subsequently not positive on CTPA.

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