CHEST

Imaging of Pulmonary Hypertension
Pictorial Essay

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Pulmonary hypertension (PH) is an end result of a diverse array of complex clinical conditions that invoke hemodynamic and pathophysiological changes in the pulmonary vasculature. Many patients' symptoms begin with dyspnea on exertion for which screening tests such as chest roentgenograms and more definitive noninvasive tests such as CT scans are ordered initially. It is imperative that clinicians are cognizant of subtle clues on these imaging modalities that alert them to the possibility of PH. These clues may serve as a stepping stone towards more advanced noninvasive (echocardiogram) and invasive (right heart catheterization) testing. On the CT scan, the signs are classified into mediastinal and lung parenchymal abnormalities. In addition to suspecting the diagnosis of PH, this paper provides a pictorial essay to guide health care professionals in identifying the etiology of PH. This paper also provides concrete definitions, wherever possible, of what constitutes abnormalities in PH, such as dilated pulmonary arteries, pruning of vessels, and increased thickness of free wall of the right ventricle. The sensitivities and specificities of each sign are enumerated. The common radiographic and clinical features of many different etiologies of PH are tabulated for the convenience of the readers. Some newer imaging modalities such as dual-energy CT of the chest that hold promise for the future are also described. CHEST 2019; 156(2):211-227

KEY WORDS: chronic thromboembolic pulmonary hypertension; dual-energy CT; ill-defined nodules; mosaicism; pulmonary hypertension

Pulmonary hypertension (PH) encompasses a composite of pulmonary and cardiac diseases that affect the pulmonary vasculature. It is defined by the European Society of Cardiology/European Respiratory Society guidelines as an elevation in the mean pulmonary artery pressure (mPAP) ≥25 mm Hg measured by right heart catheterization (RHC)[1]; however, this well-known definition is thought to inadequately capture patients with PH, specifically those with early PH. Additionally, it includes patients that may have postcapillary PH. The World Symposium on Pulmonary Hypertension Task Force recently proposed changing the definition of precapillary PH to an mPAP >20 mm Hg and pulmonary vascular

ABBREVIATIONS: CHP = chronic hypersensitivity pneumonitis; CTD = connective tissue disease; CTEPH = chronic thromboembolic pulmonary hypertension; DECT = dual-energy CT; ILD = interstitial lung disease; IPAH = idiopathic pulmonary arterial hypertension; IVS = interventricular septum; LDPA = left descending pulmonary artery; LV = left ventricle; mPAP = mean pulmonary artery pressure; PA = pulmonary artery; PA/Ao = pulmonary artery/aorta ratio; PAH = pulmonary arterial hypertension; PAVM = pulmonary arteriovenous malformations; PH = pulmonary hypertension; PVOD = pulmonary veno-occlusive disease; PVR = pulmonary vascular resistance; RHC = right heart catheterization; RHF = right heart failure; RPDA = right descending pulmonary artery; RV = right ventricle; RVH = right ventricular hypertrophy

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resistance ≥3 Woods unit.[2] The etiology of PH can be categorized into five groups (Table 1). Dividing PH into precapillary and postcapillary with RHC measurements can guide a clinician to pulmonary, systemic, or cardiac causes, but overlap between groups is common. The incidence of PH differs per group and the combined incidence is unknown. Approximately 200,000 hospitalizations occur annually with a diagnosis of primary or secondary PH.[3] It is widely accepted that left heart disease (group 2) is the most common cause of elevated pulmonary artery pressures in the United States,[1] whereas schistosomiasis is the most common cause of PH in the developing world.[3] Although the definitive diagnosis of PH is made with RHC, there are imaging clues to suggest PH and its causes. Although findings may be nonspecific, 90% of patients with idiopathic PAH (IPAH) will have an abnormal chest radiograph at the time of diagnosis.[1] CT imaging of the chest can not only suggest the diagnosis of PH, but also can evaluate vascular, cardiac, parenchymal, and mediastinal abnormalities that can help determine the etiology. The aim of this paper is to help provide a pictorial essay to guide pulmonologists when to suspect PH and to look for clues on imaging studies that may shed light on the underlying etiologies. In this approach, a close collaboration between clinicians and radiologists is imperative for optimal extraction and analysis of the data.

TABLE 1] Updated Clinical Classification of PH

1. PAH
   a. Idiopathic PAH
   b. Heritable PAH
   c. Drug- and toxin-induced PAH
   d. PAH associated with:
      i. CTD
      ii. HIV infection
      iii. Portal hypertension
      iv. Congenital heart disease
      v. Schistosomiasis
   e. PAH long-term responders to calcium channel blockers
   f. PAH with overt features of venous/capillaries (PVOD/PCH) involvement
   g. Persistent PH of the newborn syndrome
2. PH resulting from left heart disease
   a. PH from heart failure with preserved LVEF
   b. PH from heart failure with reduced LVEF
   c. Valvular heart disease
   d. Congenital/acquired cardiovascular conditions leading to postcapillary PH
3. PH from lung diseases and/or hypoxia
   a. Obstructive lung disease
   b. Restrictive lung disease
   c. Other lung disease with mixed restrictive/obstructive pattern
   d. Hypoxia without lung disease
   e. Developmental lung disorders
4. PH from pulmonary artery obstruction
   a. CTEPH
   b. Other pulmonary artery obstructions
5. PH with unclear and/or multifactorial mechanisms
   a. Hematological disorders
   b. Systemic and metabolic disorders
   c. Others
   d. Complex congenital heart disease

CTD = connective tissue disease; CTEPH = chronic thromboembolic pulmonary hypertension; ERS = European Respiratory Society; LVEF = left ventricular ejection fraction; PAH = pulmonary arterial hypertension; PCH = pulmonary capillary hemangiomatosis; PH = pulmonary hypertension; PVOD = pulmonary veno-occlusive disease. Adapted From ERS (2018).[2] Reproduced with permission of the © ERS 2019: European Respiratory Journal 53(1): 1801913; https://doi.org/10.1183/13993003.01913-2018. Published 24 January 2019.

Chest Radiograph Indicators Suggestive of PH

The chest radiograph is an easy and often overlooked investigation in the assessment of PH. The American College of Chest Physicians recommends obtaining a chest radiograph for the assessment of patients suspected of having PAH because of the clinical clues it can provide.[4]

Right Ventricular Hypertrophy

An enlarged right ventricle (RV) and right atrium are commonly associated with elevated pulmonary artery (PA) pressures and can be evaluated on chest radiography. The cardiothoracic ratio, defined as the ratio of the maximum transverse diameter of the heart to the maximal internal diameter of the thoracic cavity on a PA film, has long been used to assess cardiomegaly,[5] but it is important to understand which chambers form the border of the heart. The right heart border is formed by the right atrium[6] and, therefore, its enlargement will manifest as more than 44 mm from the midline to the prominent right heart border (Fig 1A).[7,8] The RV is better visualized on a lateral film; its dilation is suggested when there is filling of the retrosternal space (Fig 2).[6] A boot-shaped heart with upward tilt of the cardiac apex can represent RVH.[9]

Central Pulmonary Artery Dilation

A prominent main pulmonary artery, found just below and to the left of the aortic knob, is commonly seen in patients with PH.[10] Elevated PA pressures have also been associated with enlargement of the right descending pulmonary artery (RDPA) and left descending pulmonary artery (LDPA).

Normal Size of RDPA Is Affected by Sex, Age, Height, and Body Weight[11]: Matthay et al[12] assessed patients with severe COPD and PH, comparing the

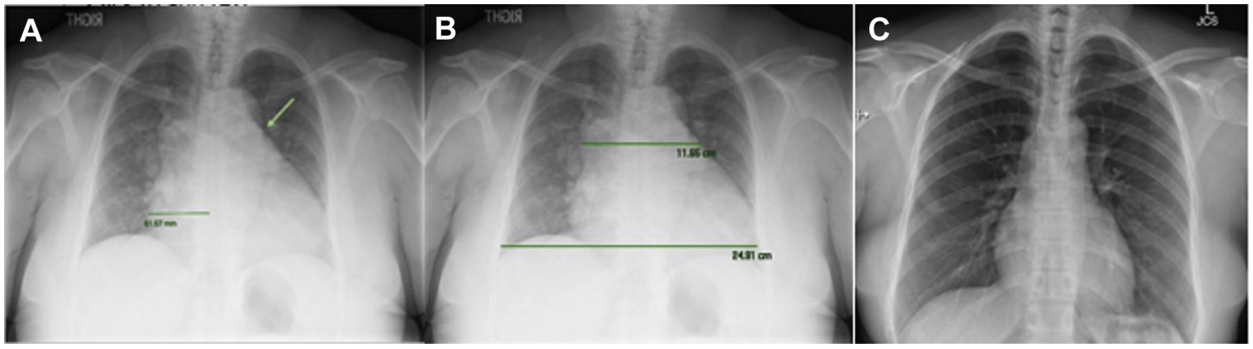

Figure 1 – *Frontal chest radiograph demonstrating right atrial enlargement. A, From the midline to the right heart border is measured to be 61 mm (>44 is abnormal). Also noted is oblique edge due to engorgement of the pulmonary artery (thin arrow) and left ventricular enlargement. B, Increase in the hilar to thoracic ratio of 0.47 (>0.44 is abnormal). This can be compared to a normal frontal chest radiograph (C).*

RDPA and LDPA size with measurement of mPAP. There is a statistically significant correlation with a RDPA ≥16 mm and LDPA ≥18 mm and the presence of PH. If both the LDPA and RDPA were enlarged on chest radiography, the positive predictive value of detecting PH was 93% (Fig 3).

RDPA and LDPA Not Always Visualized: The RDPA and LDPA are not always visualized easily on frontal and lateral films, but measurement of the hilum and the hilum to chest ratio may be more easily obtainable. An absolute measurement of the hilum ≥112 mm was associated with a sensitivity of 82% in detecting elevated pulmonary artery systolic pressure. A ratio of hilum to chest diameter ≥0.44 had an even greater sensitivity of 86% (Fig 1B).[7]

Pruning of Peripheral Pulmonary Vessels

The thinning out of vascular markings on a chest film also suggests elevation of pulmonary pressures and vascular remodeling, referred to as vascular pruning.[13] This is thought to be due to vascular remodeling of the pulmonary arteries (Fig 4).

CT Evidence of PH

Although chest radiograph can be useful for clinicians to pick up clues and suspect PH, there are many limitations and findings may be nonspecific. Clues to PH are better delineated on chest CT scan; chest CT scans should be evaluated in all patients suspected of having PH.

Pulmonary Artery

Static Measurements: Similar to chest radiograph, a dilated PA can be a clue to elevated PA pressures and is more easily measured on a CT scan. It is important to note that there are many causes for a dilated PA, and its presence does not confirm PH. For example, a dilated PA can be seen in conditions other than PH, such as high altitude, vasculitis, or idiopathic.[14-16] The best location to measure the PA is at the level of the PA bifurcation perpendicular to its long axis.[15,16] On CT angiograph, it is the vascular lumen that should be

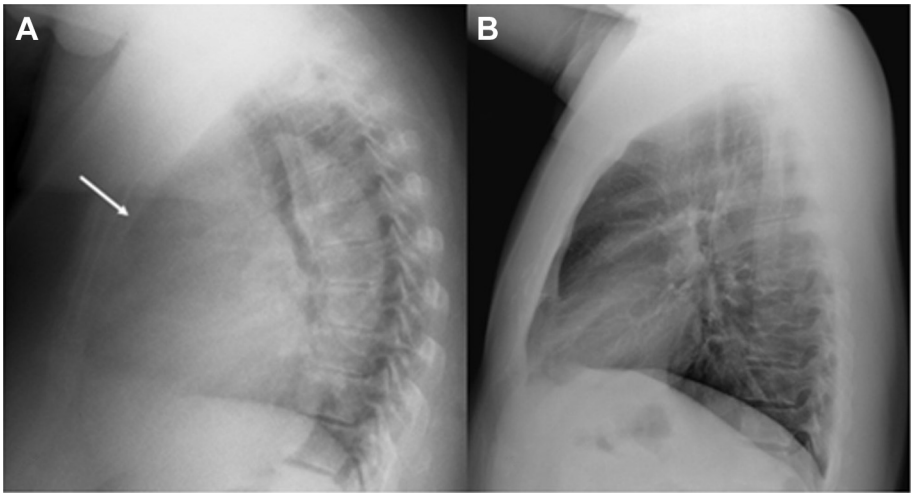

Figure 2 – *A, Lateral chest radiograph demonstrating fullness of the retrosternal space (arrow) commonly seen in right ventricular enlargement on the left. B, Normal lateral chest radiograph provided on the right for comparison.*

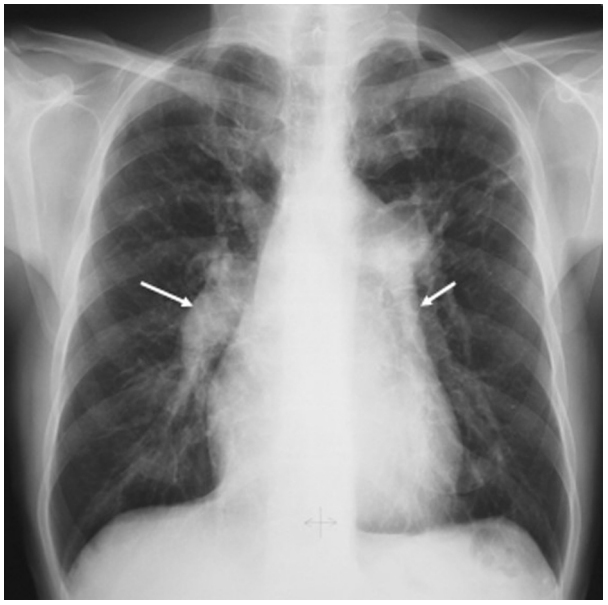

Figure 3 – *Frontal chest radiograph with enlargement of the right descending pulmonary artery (RDPA) and left descending pulmonary artery (LDPA) in a patient with pulmonary hypertension (arrows). RPDA >16 mm and LDPA >18 mm are considered abnormal and predictive of the presence of pulmonary hypertension. Note the additional presence of a focal infiltration in the left axillar region.*

measured; on non-contrast CT scans the vessel wall is included.[15] Many studies have assessed what a normal PA diameter is on chest CT.[15] It is generally accepted that a PA ≥29 mm in males and ≥27 mm in females is considered to represent abnormal dilation based on the results of the Framingham study.[16-19] Although the correlation may vary depending on the etiology of PH,

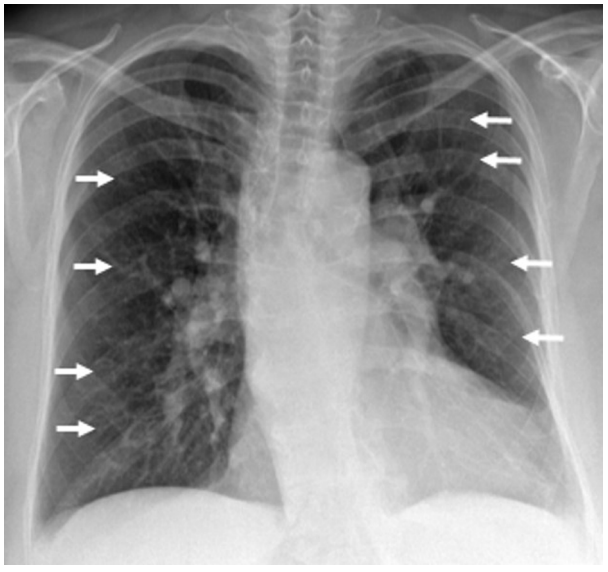

Figure 4 – *Frontal chest radiograph with plump pulmonary arteries seen coursing to the outer 1/3 of the lung with rapid tapering of vessels consistent with vascular pruning (arrows). The presence of vascular pruning is thought to be associated with vascular remodeling of the pulmonary arteries.*

there remains a moderate to strong correlation of PA diameter with PH[20]; however, the ability to determine a "cutoff" mark has been more difficult.[21] According to the Framingham study, a ratio of PA/aorta (PA/Ao) of 0.91 is found to be within the 90th percentile of healthy subjects. This suggests a ratio >.90 is associated with PH,[15] which was also confirmed by a retrospective study that found a ratio >1 correlated with mPAP >20 mm Hg, with a specificity of 96%[14,15] (Fig 5) and a positive predictive value of >95%.[18] For patients younger than age 50 years, the ratio of PA/Ao correlated more strongly with mean PA pressure than the diameter of the main PA, and vice versa for patients older than 50 years.[22] In fact, a ratio of PA/Ao diameter may be able to predict the mPAP by using the equation 3.7 + (24 × PA diameter/aortic diameter).[15] Average sensitivity and specificity for PH based on dilated PA is 71.9%.[14] This improves to nearly 100% if the main pulmonary artery is ≥29 mm and the segmental artery to bronchus ratio is >1:1 in three of four pulmonary lobes (Fig 6).[14,17,23] A normal PA diameter does not rule out the diagnosis of PH. The presence of PA/Ao ratio >1 on CT scan can also be helpful in patients who do not have adequate views on echocardiogram to screen for PA. For example, even patients with COPD, who not uncommonly have poor acoustic windows, have PH on RHC 83% of the time if they have a PA/Ao >1.[24] Although the size of the PA can be useful in diagnosing patients with PH, it has been found to continue increasing in size without relation to the pressure of the PA and should not be used for estimating PA pressure during routine follow-up.[25]

Dynamic Measurements: Whereas many studies have evaluated static findings on CT scan that suggest PH, some dynamic parameters are accessible on routine CT

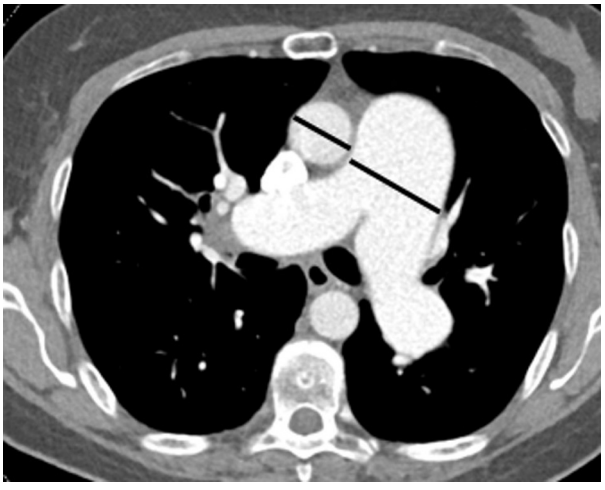

Figure 5 – *CT angiogram of the chest demonstrating a significantly enlarged pulmonary artery at the level of bifurcation with an increased pulmonary artery to aorta ratio >1:1 (black lines).*

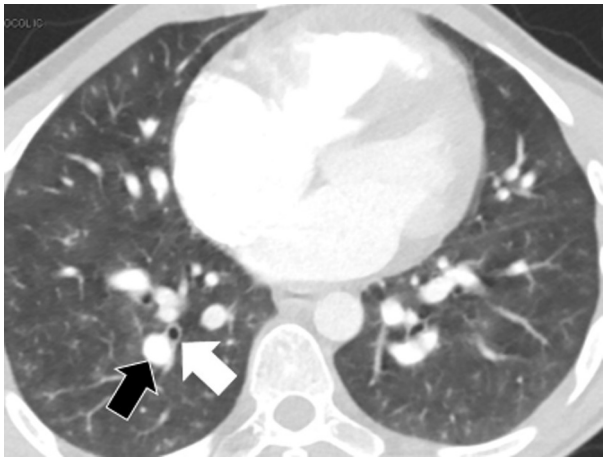

Figure 6 – *CT angiogram demonstrating increased segmental artery (black arrow) to bronchus ratio (white arrow).*

angiographic examinations. They are based on the fact that an elevated pulmonary pressure will lead to hemodynamic changes affecting IV contrast flow in central pulmonary arteries.[26]

- As pressures rise in pulmonary artery, back pressure will cause increased pooling of IV contrast at the prearteriolar level of the pulmonary bed, increasing density in the main pulmonary artery (Fig 7). Additionally, this can cause increased IV transit time, leading to relatively late aortic opacification and an elevated pulmonary artery/thoracic aorta ratio. These findings are only accessible for injection protocols triggering data acquisition with a region of-interest positioned within the pulmonary trunk.

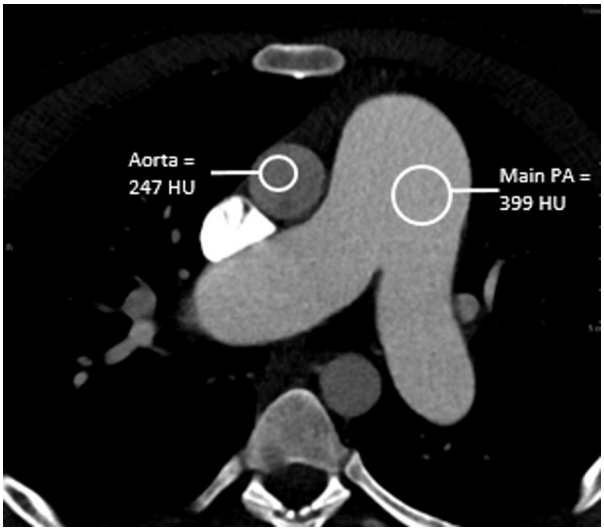

Figure 7 – *CT angiogram of the chest demonstrating a significantly enlarged pulmonary artery at the level of the pulmonary artery bifurcation with an increased pulmonary artery to aorta ratio >1:1. Increased contrast density in the main pulmonary artery is due to increased resistance at the pre-arteriolar level, leading to increased pooling of IV contrast relative to the aorta.*

- PA distensibility is reduced in patients with PH. This is calculated by the change in cross-sectional area of the right pulmonary artery during systole and diastole can but can only be measured using ECG-gated CT acquisitions.[27]

RV Size

In normal subjects, the RV is a thin-walled chamber that has a smaller diameter than the left ventricle (LV). As pulmonary pressures increase, the RV begins to hypertrophy to maintain stroke volume and cardiac output.[19] It can eventually dilate and fail. The changes in the RV on chest CT include the following.

Thickness of RV Free Wall: The RV muscle mass increase can be measured on CT scan. In general, the normal thickness of the RV free wall is <4 mm.[28] An RV free-wall thickness as measured in the mid-ventricle has been able to predict the presence of PH with a sensitivity of 81% and specificity of 91.9% when using a cutoff of ≥6 mm (Fig 8).[23,29]

RV/LV Lumen Ratio: Once RV dilation begins, the ratio between the RV's and LV's lumen will be significantly affected. RV dilation is considered when the RV/LV ratio is >1:1. A ratio of ≥1.28 was associated with a sensitivity and specificity of 85.7% and 86.1%, respectively (Fig 8).[29]

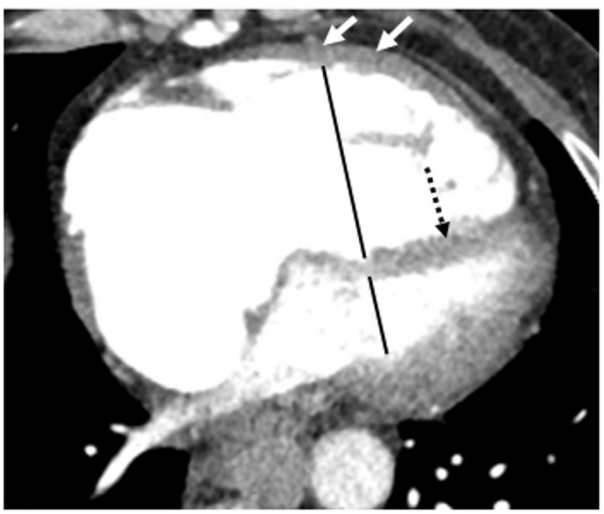

Figure 8 – *CT angiogram demonstrating increased right ventricle (RV) free wall thickness (white arrows), RV/left ventricle (LV) ratio >1 (black line), and bowing of the interventricular septum into the left ventricle (black dashed arrow) with an enlarged right atrium. RV and LV measurements are made perpendicular to the axis of the ventricular cavities from the endocardium to the interventricular septum. The widest diameter is used for each ventricle; of note, this may occur at different levels.*

Interventricular Septum:

- Straightening/bowing. In healthy patients, the interventricular septum (IVS) should have a convex shape with bowing into the RV. As the pressures on the right side of the heart rise, the IVS begins to flatten and even reverse its convexity (Fig 8).[23] Once the IVS begins impeding on the LV, cardiac output is compromised. Patients with an mPAP ≥30 mm Hg have been found to have leftward deviation of the IVS into the LV (Fig 8).[14]
- Septal angle. The septal angle, defined as the angle between the IVS and a line drawn from the sternum midpoint to thoracic spinous process, increases with RV overload.[14] In fact, a septal angle >135 can predict PH with a sensitivity of 100% and specificity of 79%.[30]

Pericardial Effusion

Pericardial effusions can also be seen with PH of any etiology, but remains a nonspecific finding.[16] Presence of a pericardial effusion in the setting of PH has been associated with a worse prognosis.[18] In patients with connective-tissue disease PAH, inflammatory etiology of pericardial effusion is also possible, as demonstrated by higher prevalence of moderately large pericardial effusions in this group of patients (Fig 9).[31]

Etiology of PH on CT Scans

In the context of suspected or confirmed PH, the clinician can begin to look for clues in an effort to suspect etiology of PH. Some of the common etiologies and their radiologic features are summarized (Table 2).

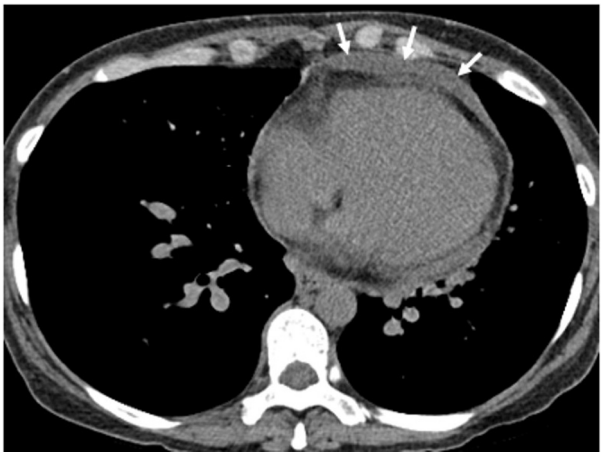

Figure 9 – *Transverse view of non-contrast chest CT scan demonstrating pericardial effusion in patient previously diagnosed with scleroderma (white arrows). While it is a nonspecific finding, a pericardial effusion in pulmonary hypertension (PH) is associated with poor prognosis. Additionally, pericardial effusion may be related to underlying connective tissue disease causing the PH.*

Mediastinal Images

The mediastinal images may help assess for vascular changes associated with chronic thromboembolic PH (CTEPH), PA obstruction, and cardiovascular causes.

Vascular Remodeling: The depiction of mural thrombi, webs, bands, and severely stenosed PAs allows diagnosis of chronic thromboembolic disease.[14] The thrombi can also cause pouch-like defects, or complete convex-shaped obstruction in the lumen of the vessels (Fig 10).[18] The more distal obstructions are apparent by narrowing and stenosis of the smaller branches of the pulmonary arteries. CT pulmonary angiogram shows the extent of the disease, allowing the clinician to determine if thrombi exist proximally and/or distally; this morphological information will help decide whether patients with CTEPH are candidates for surgical intervention.[14] Note that CTEPH is observed in the context of dilated PAs resulting from elevated PA pressures with the possibility of depicting calcified thrombi.[14] Neovascularity, described as small, serpiginous pulmonary vessels located in peripheral or centrilobular regions, can be seen in patients with PAH. Its presence, although not pathognomonic, has a much higher association with PAH resulting from congenital heart disease (72%) than patients with PAH (22%).[32] Portopulmonary hypertension appears similar to PAH on CT scan with a dilated PA, enlarged PA/Ao ratio, and a segmental artery to bronchus ratio >1. Esophageal varices may also be apparent on chest CT scan as enhancing nodular opacities that bulge into the esophagus (Fig 11).[33]

Systemic Collateral Supply: Patients are more likely to have bronchial artery collaterals to maintain vascular supply after chronic occlusion of the pulmonary arteries. Bronchial arteries with a diameter ≥1.5 mm are seen in 47% to 77% of patients with CTEPH.[18] Bronchial artery dilation is most often seen in the lower lung zones. In fact, bronchial and nonbronchial collaterals are present in 73% of patients with CTEPH, but only 14% of patients with idiopathic PH (Fig 12). [18]

Obstruction of the PA: PA Tumor: A PA sarcoma can be mistaken for acute or chronic thrombus. The filling defect can be shown as an enhancing mass; it is usually centrally located and can invade into the mediastinum, extending past the vessel walls (Fig 13).[18] Case series have shown diagnostic utility in performing a PET scan to differentiate tumor from embolism because, although pulmonary embolism has been seen to show PET

TABLE 2] Clinical Conditions Associated With PH and Their Corresponding Imaging Findings

Clinical Disease	PH WHO Classification	Findings on Imaging
Pulmonary arterial hypertension	Group 1	Patchy ill-defined nodules, RV dilation possible, deviated IVS, mosaic attenuation
Collagen vascular disorder	Group 1	Ill-defined micronodules, traction bronchiectasis, increased reticular markings
Portopulmonary hypertension	Group 1	Dilated pulmonary artery, esophageal varices, increased pulmonary to bronchus ratios
Atrial septal defect/ ventricular septal defect	Group 1	Direct visualization of septal defect, left to right intracardiac contrast shunting
Pulmonary arteriovenous malformations	Group 1	Rounded pulmonary opacities, feeding artery, and draining vein
Pulmonary veno-occlusive disease/PCH	Group 1	Diffuse ill-defined nodules, mediastinal lymph node enlargement, pleural effusions, and thickening of the interlobular septa
Pulmonary vein stenosis/ agenesis	Group 2	Narrowing of pulmonary vessels, abrupt obliteration/termination of pulmonary vasculature
COPD	Group 3	Dilation/destruction of small airways, centrilobular emphysema, increased radiolucency of lung on chest radiograph, flattening of diaphragmatic contour, bullae
Idiopathic pulmonary fibrosis	Group 3	Peripheral/basilar reticular opacities, honeycomb changes, traction bronchiectasis, typically pleura sparing
Chronic (fibrotic) hypersensitivity pneumonitis	Group 3	Ill-defined centrilobular nodules, diffuse mosaic perfusion, upper lobe predominant bronchocentric fibrosis, reticulation, traction bronchiectasis
CTEPH	Group 4	Endoluminal filling defects, vascular webs, mural thrombi, pulmonary segmental artery narrowing distal to obstruction, pouch-like defects, neovascularity, bronchial and nonbronchial collateral vessels, mosaic attenuation
Pulmonary artery sarcoma	Group 4	Endoluminal filling defect with invasion into and through the vessel wall; FDG avidity on PET scan is greater than PE
Sarcoidosis	Group 5	Hilar/mediastinal lymphadenopathy, ill-defined micronodules, possibly cysts, possibly fibrosis
Pulmonary Langerhans cell histiocytosis	Group 5	Diffuse cystic lung disease with a preference for upper and middle lung zones, nodules of varying size which may or may not cavitate
Fibrosing mediastinitis	Group 5	Soft tissue-attenuated mediastinal infiltrative mass that encases or invades nearby structures

IVS = interventricular septum; PE = pulmonary embolism; RV = right ventricle. See Table 1 legend for expansion of other abbreviations.

avidity,[34] the uptake is much less intense. The presence of PH in these cases is due to direct occlusion or obliteration of the pulmonary vessels.[18]

Fibrosing Mediastinitis: Symptoms develop with progressive fibrosis of mediastinal structures, including the pulmonary vasculature.[35] When obstruction of the pulmonary venous system occurs, patients develop secondary PH and cor pulmonale.[35] Less commonly, secondary PH can occur with obstruction of the PAs. Fibrosing mediastinitis will appear as a soft tissue-attenuated infiltrative mass that encases or invades nearby structures (Fig 14).[35] With pulmonary venous occlusion resulting from the fibrosing mass, patients will develop mosaic attenuation, ground-glass opacities, and thickening of the interlobular septa similar to what is seen with pulmonary veno-occlusive disease (PVOD) and pulmonary capillary hemangiomatosis (PCH), as discussed later.[35] Although these two entities were originally considered separate, they are now considered a common entity and are classified as a subgroup of PAH.[2]

Mediastinal and Hilar Lymphadenopathy: Mediastinal lymphadenopathy is a common radiologic finding and lacks sensitivity, but may be present in patients with PH resulting from multiple conditions. Bergin and Park[36] found that 45% of patients with CTEPH had mediastinal lymphadenopathy, possibly secondary to right-sided failure and increased lymphatic flow. This finding was more commonly seen in patients with pericardial and pleural effusions for the same reason. Sarcoidosis has

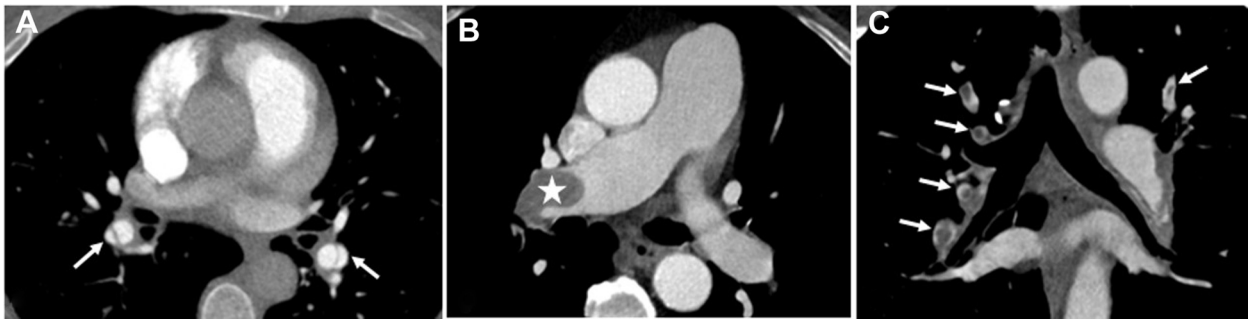

Figure 10 – *CT scan with contrast of different patients with evidence of pulmonary embolism. A, Axial image of patient with bilateral webs suggesting chronic thromboembolic pulmonary hypertension (white arrows). B, Axial image of patient with large pouch-like filling defect in the right main pulmonary artery (star). C, Coronal CT scan with multiple intraluminal filling defects in the segmental and subsegmental pulmonary arteries (white arrows).*

been frequently associated with PH, although the exact prevalence is unknown.[37] The etiology may be multifactorial, including vasculopathy and chronic hypoxia, but extrinsic compression of pulmonary vessels from enlarged lymph nodes is present in 21% of the PH patients with stage IV sarcoidosis.[37] Lymphadenopathy is another distinguishing feature of PVOD/PCH that is not as commonly seen in PAH. Limited data exist in evaluating mediastinal lymphadenopathy in PAH, but in one small study mediastinal lymphadenopathy was found in 20% of patients with IPAH with no other obvious cause,[38] whereas lymph node enlargement is seen in up to 80% of patients with PVOD/PCH.[39] A combination of centrilobular ground-glass opacities, septal lines, and lymph node enlargement is suggestive of PVOD/PCH. In fact, the presence of two or more

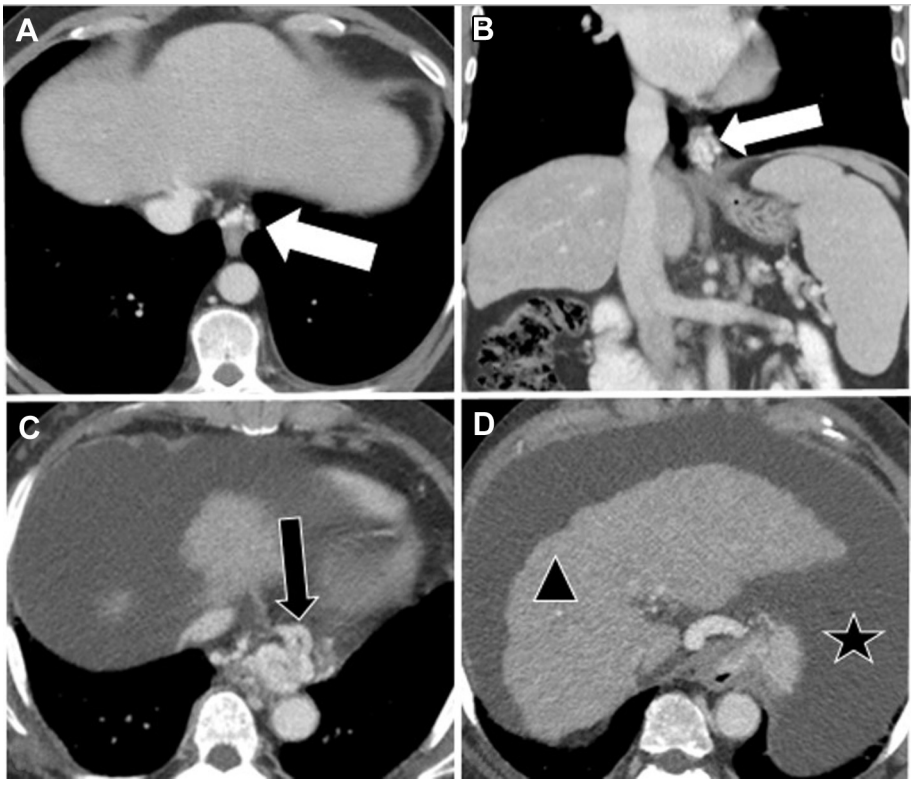

Figure 11 – *Axial and coronal contrast enhanced CT scan through lower chest demonstrating esophageal varices. A, B, Axial (A) and coronal (B) images of the same patient with esophageal varices. Serpiginous enhancing structures adjacent to distal esophagus, consistent with varices (white arrows). C, D, Axial contrast enhanced CT images through lower chest in different patient with portal hypertension. C, Serpiginous enhancing structures adjacent to distal esophagus, consistent with esophageal varices (black arrow). D, There is a shrunken liver with a nodular contour, consistent with cirrhosis of the liver (triangle). Large ascites is also present (star).*

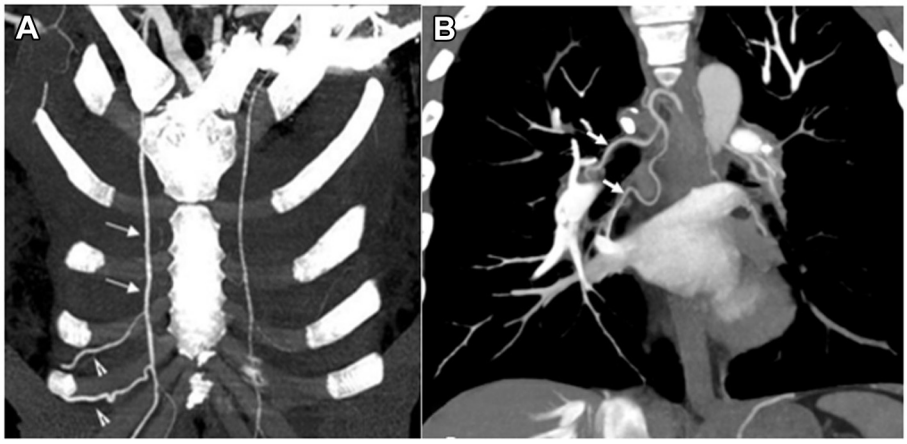

Figure 12 – *Bronchial and nonbronchial collaterals. A, Coronal maximum intensity projection (MIP) image demonstrating prominent internal mammary artery (arrows) and intercostal arteries (arrowheads). B, Coronal MIP image demonstrating prominent bronchial artery collaterals (arrows). Development of dilated collaterals suggests vascular collateral supply developed to overcome chronically obstructed pulmonary arteries.*

abnormalities on chest CT scan is highly associated with PVOD/PCH,[40] but the absence of radiographic findings cannot rule it out.

Cardiovascular Causes (Group 1/Group 2):

Intracardiac Defects, Systemic-to-Pulmonary Shunts: Chest CT scan can help in analyzing the shape and convexity of the IVS. Imaging of the IVS may demonstrate septal defects. These defects can cause a left to right shunt that, when left untreated, can lead to shunt reversal resulting in PAH (group 1). Large ventricular septal defects may be directly visualized or be seen as a focal jet of contrast into the RV.[16] Atrial septal defects have also been associated with PH, but are difficult for a pulmonologist to detect on CT chest (Fig 15). Other evidence of group 2 PH includes LV dilation, left atrium dilation and calcification of aortic or mitral valves.[16]

Pulmonary Arteriovenous Malformation (PAVM); Anomalous Pulmonary Venous Return: Pulmonary arteriovenous malformations are usually rounded pulmonary opacities in the lung parenchyma that are associated with a feeding artery and draining vein (Fig 16).[18] These patients can develop significant hyperdynamic circulatory compromise with shunting resulting in severe hypoxemia. PH is rare in this disease and is usually a contraindication to PAVM occlusion.[18] Less commonly, patients with hepatopulmonary syndrome can also be found to have PAVM.[33] Although most congenital cardiac defects present at an early age, partial anomalous pulmonary venous return is a rare cause of adult-onset PH (Fig 17).[41]

Pulmonary Vein Stenosis/Agenesis: Acquired pulmonary venous stenosis/agenesis in adults is rare, but important to detect on CT scan because of its high

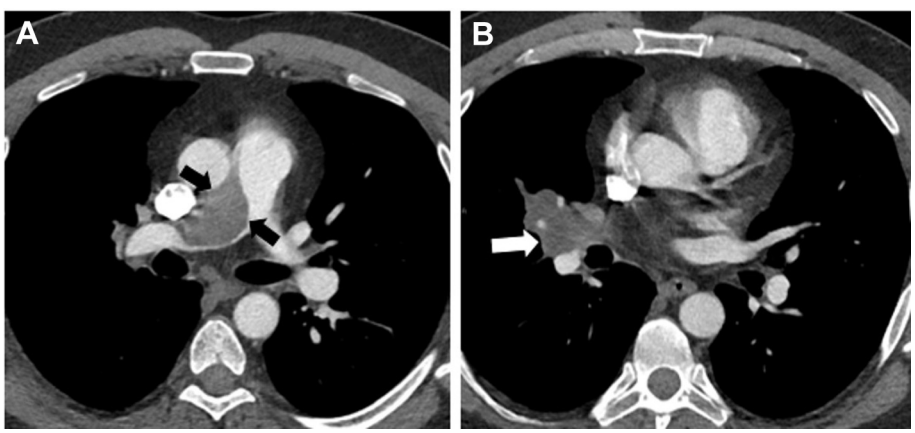

Figure 13 – *Axial images from CT angiogram of the chest through level of main pulmonary artery (A) and right hilum (B). A, Demonstrates a large filling defect in the right pulmonary artery. The filling defect extends beyond the lumen of the artery, into the mediastinum, distinguishing this mass from a large pulmonary embolism (black arrows). B, The presence of right hilar adenopathy also raises the suspicion of neoplasm (white arrows). Pathology report was consistent with a high-grade intimal sarcoma.*

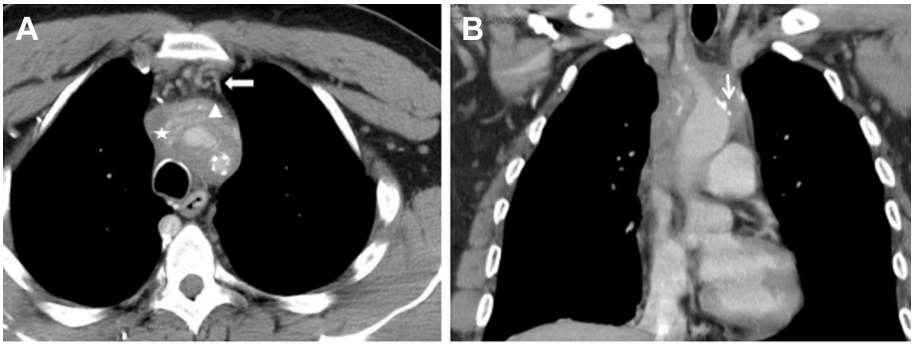

Figure 14 – *Axial (A) and coronal (B) contrast enhanced CT scan images demonstrate infiltrating soft tissue mass encasing the vessels in upper mediastinum. A, There is obstruction of the superior vena cava (star) and left brachiocephalic vein (triangle) with development of collateral vessels (thick white arrow) in anterior mediastinum. B, Portions of the mass contain calcification (thin white arrow).*

mortality rate. It may be due to extrinsic compression, infiltrative process, or ablation of the nearby atria in patients receiving ablation therapy for atrial fibrillation.[42] The pulmonary veins are best seen on CT scan with contrast and acquired stenosis may have narrowing of the vessels or an abrupt obliteration (Fig 18).[42]

Lung Images

Lung parenchymal findings can help pinpoint contributing factors to elevated PH and should be evaluated fully.

Mosaic Attenuation: Alternating patchy areas of hypo- and hyperattenuation can be seen in a variety of lung diseases associated with PH, including CETPH,

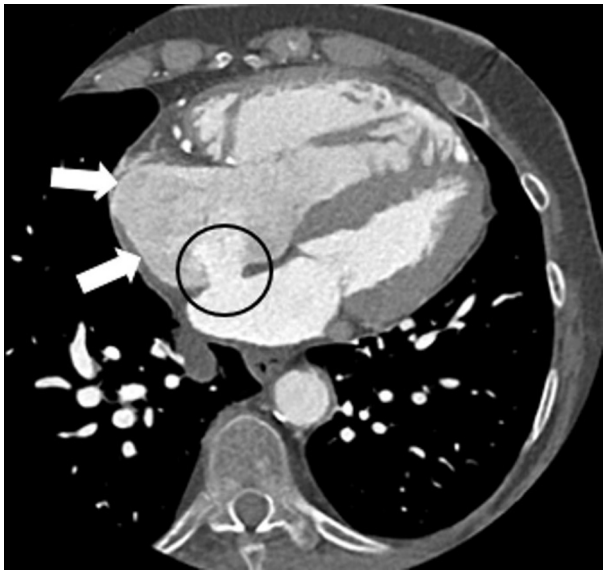

Figure 15 – *CT scan with contrast demonstrating defect within the wall of the atrial septum with evidence of contrast flow from left atrium to right consistent with a left to right shunt (circle) with an associated dilation of the right atrium (RA) (white arrows) consistent with volume and pressure overload of the RA due to shunting. Also notable is LV hypertrophy and RV dilation with an RV:LV ratio >1. See Figure 8 legend for expansion of other abbreviations.*

obstructive airway disease, PAH, and chronic hypersensitivity pneumonitis (CHP). If the mediastinal windows are more suggestive of vascular findings associated with CTEPH, the lung parenchyma will also have certain changes to support the diagnosis. The narrowing of pulmonary vessels leads to a mosaic-like pattern in the lung parenchyma[14] with areas of low attenuation correlating with hypoperfused areas.[16] The vessel diameter can be defined as narrow when its diameter is smaller than the corresponding bronchus diameter as they usually course through the lungs in a 1:1 diameter ratio.[18] The hyperdense areas are due to increased blood flow through open vessels. These regions of alternating attenuation usually follow a segmental or subsegmental pattern. Chronic infarcts resulting from thromboemboli will cause peripheral parenchymal opacities.[14] Although these changes are nonspecific on their own, the vascular evidence in conjunction with parenchymal evidence is highly suggestive of CTEPH. This is in contrast to the mosaic pattern that can been seen in idiopathic PAH that usually occurs in the perihilar or peripheral distribution (Fig 19).[18] Alternatively, hypersensitivity pneumonitis more commonly presents variably with diffuse mosaic perfusion in association with upper lobe predominant bronchocentric fibrosis and ill-defined centrilobular nodules.[43] The presence of mosaic attenuation in association with hypersensitivity pneumonitis is more common in patients without evidence of pulmonary fibrosis.[44]

Centrilobular Lucencies: Dilation and destruction of the small airways resulting in centrilobular lucencies are consistent with COPD. Mild to moderate centrilobular emphysema can progress to become confluent (spanning several secondary pulmonary lobules) and advanced destructive (hyperexpansion of secondary pulmonary

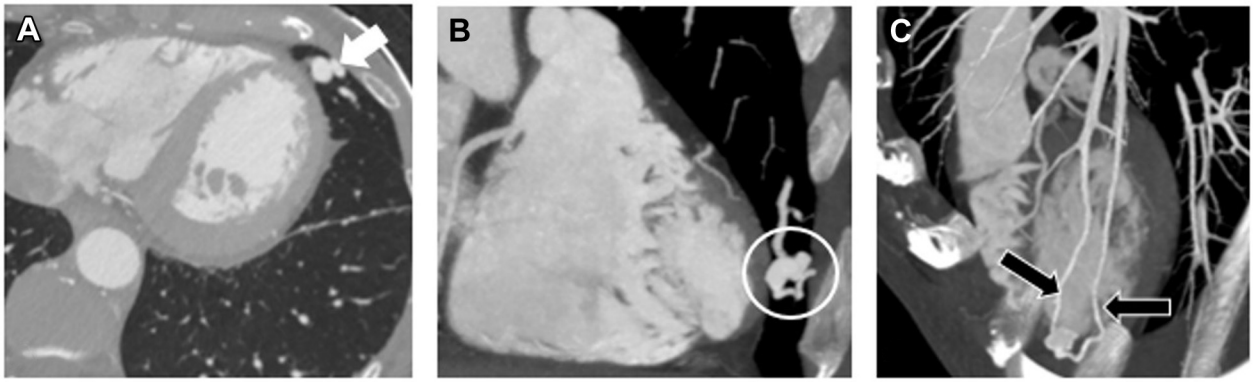

Figure 16 – *CT scan with contrast with a pulmonary arteriovenous malformation. A, B, Show the rounded, tortuous opacity within the lung periphery (white arrow, white circle). C, Shows the same rounded opacity with a feeding and draining vessel (black arrows).*

nodules and disruption of the pulmonary architecture) according to the most recent Fleischner Society guidelines (Fig 20).[45] Although PH can occur in any patient with COPD or emphysema, it is most common in those with severe obstructive airways disease. The prevalence of PH in patients with COPD is unknown, though studies have a reported a range of 30% to 70%.[46] Severe PH, defined as mPAP >45 is relative uncommon in patients with COPD and is reported in <5%.[47,48] If severe PH is present, 60% of such patients likely have comorbid disease that can jointly contribute to PH rather than emphysema alone.[46] COPD is also associated with exercise-induced PH and patients should be evaluated for PH if they are having worsening exercise tolerance or dyspnea on exertion.[49] The presence of coexistent emphysema in the upper lobes and pulmonary fibrosis in the lower lobes has correlated with a higher prevalence of PH, approaching almost 50%.[50]

Reticulation and Honeycombing: The presence of subpleural and basal predominance of reticular abnormalities associated with honeycombing is most consistent with a usual interstitial pneumonia pattern on CT scan (Fig 21). Traction bronchiectasis can be present and, although a craniocaudal gradient commonly exists, some upper lobe involvement is common.[43] Patients with (fibrotic) CHP may progress to develop a usual interstitial pneumonia-like pattern with patchy/random reticulation and traction bronchiectasis that typically spares the lung bases.[51] Patients with CHP can have comorbid PH with prevalence estimates ranging between 19% and 50%.[52,53] Because of the wide variety of disease processes in interstitial lung disease (ILD), the exact prevalence of PH associated ILD is unknown and varies from 8.1%[54] to 14%.[40] Although all chronic lung diseases may be associated with PH, idiopathic

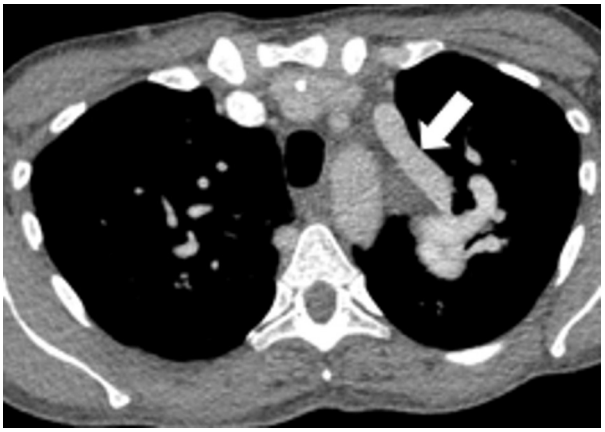

Figure 17 – *CT chest scan in the mediastinal window demonstrating partial anomalous pulmonary venous return (white arrow).*

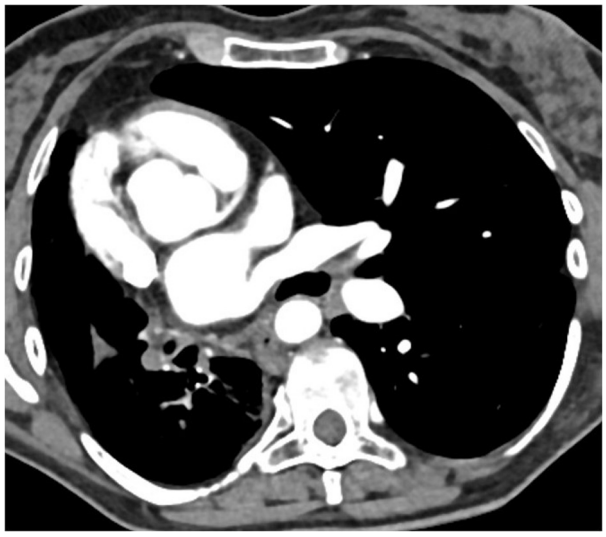

Figure 18 – *CT scan section obtained at the level of the left atrium in a patient with unilateral agenesis of pulmonary veins. Note the absence of pulmonary venous return at the level of the left atrium with no opacification of ipsilateral pulmonary arteries. Presence of small-sized vascular sections in the right hilum, suggestive of collateral vascular supply.*

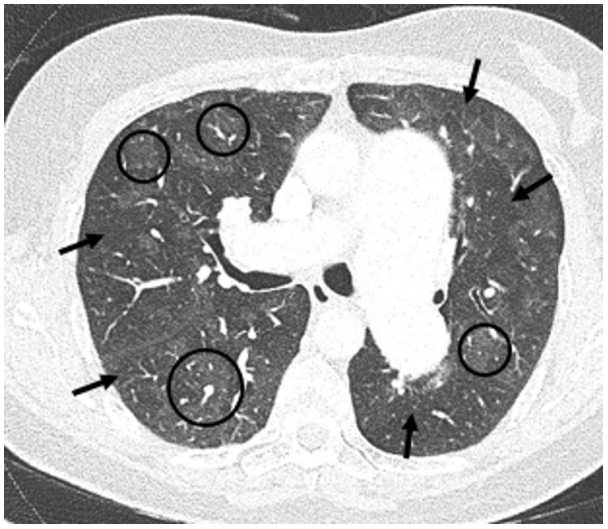

Figure 19 – *Axial CT scan of the chest showing alternating patchy areas of increased (circles) and decreased (arrows) attenuation. Mosaicism may be due to air trapping vs chronic thromboembolic disease or pulmonary arterial hypertension. Hypoattenuated areas due to both air trapping and vascular disease show decreased vasculature and may be difficult to differentiate. Occasionally, expiratory CT films may be helpful. If mosaicism is due to air trapping, the hypoattenuated areas will remain hypoattenuated on expiration. On the contrary, in vascular disease and pulmonary hypertension, the previously hypoattenuated areas will show an increase in attenuation and appear more gray.*

pulmonary fibrosis is the most prevalent cause of PH due to ILD.[55]

Ill-Defined Nodules: As mentioned previously, the presence of mosaic attenuation can be seen in CTEPH and PAH. Assessing lung parenchyma may allow differentiation between primary PAH and chronic lung disease. The presence of patchy, ill-defined nodules is seen in idiopathic PAH as frequently as 41%.[56] The distribution of these nodules is predominantly (>50%) centrilobular.[56] These nodules are most likely the result of cholesterol granulomas within small vessels.[16] PVOD/PCH can develop similar centrilobular nodules as seen in PAH. In PVOD/PCH, the presence of centrilobular nodules are significantly more frequent than in PAH; in one study, centrilobular ill-defined nodules were present in 87% of patients with PVOD/PCH vs 33% of patients with PAH.[39] The presence of smooth interlobular septal thickening located preferentially subpleural without a craniocaudal predominance can help distinguish PVOD/PCH from PAH.[16,39] Although it is a rare disease, it is important to be able to recognize features of PVOD/PCH because treatment with vasodilator therapy can result in morbidity and mortality resulting from pulmonary edema.[16,39] Despite the fact that PVOD/PCH is classified as World Health Organization group 1 PH and has many similarities to PAH on CT imaging, ill-defined nodules should not be confused with ground-glass opacities. Centrilobular nodules can also be seen in subacute (cellular) hypersensitivity pneumonitis, although it is more likely to be associated with diffuse ill-defined opacities and mosaic attenuation. CHP, which is more commonly linked with PH, usually demonstrates evidence of fibrosis as described previously, superimposed on poorly defined centrilobular nodules and bilateral ground-glass opacities.[51] Assessing the size and distribution of ill-defined micronodules in conjunction with other radiographic findings can be helpful in differentiating between PAH and PVOD/PCH (Table 3, Fig 22).

Pleural Effusion(s): The presence of pleural effusions is generally a nonspecific finding because they can be associated with many conditions, although it is most commonly associated with left heart failure; however, studies have shown that pleural effusions can also be seen with right heart failure (RHF). Approximately 21% of patients with IPAH or hereditary pulmonary arterial hypertension have been found to have pleural effusions, 14% of which had no other explanation for the development of an effusion and almost all had associated RHF.[57] Although there has been no notable hemodynamic differences between patients with RHF

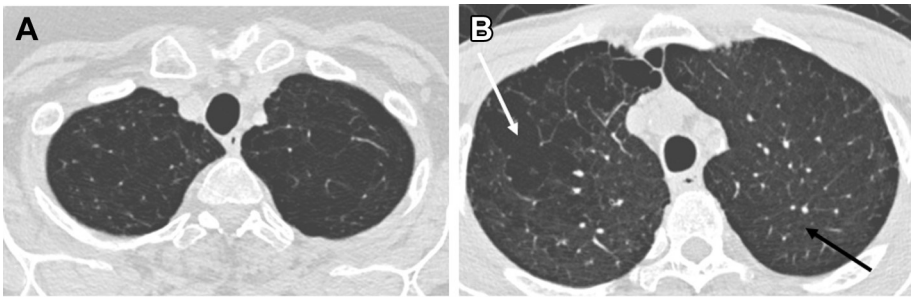

Figure 20 – *CT scan of the chest in a patient with advanced destructive emphysema (A, B). Both images demonstrate hyperlucency with complete disruption of the pulmonary architecture. Image (B) shows areas of destructive emphysema (white arrows) as well as areas of mild to moderate centrilobular lucencies (black arrow).*

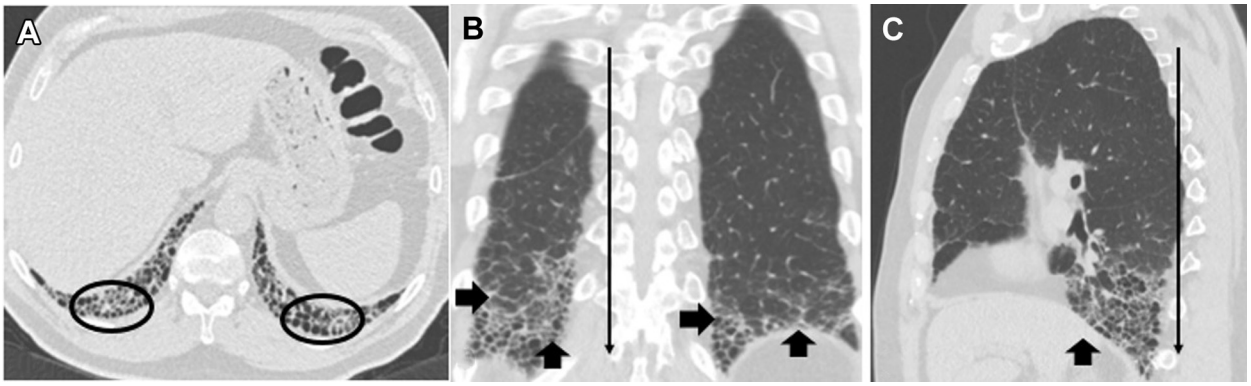

Figure 21 – *CT scan of the chest in axial (A), coronal (B), and sagittal (C) views in a patient with typical usual interstitial pneumonia pattern. A, honeycombing at bilateral bases in a craniocaudal gradient and predominantly reticular pattern (B, C).*

who have pleural effusions and those who do not, there has been a statistically significant increase in mortality in patients with effusions and RHF.[57] Pleural effusions are also seen in patients with PVOD/PCH, although the incidence is similar to IPAH and its presence cannot distinguish between the two.[39] It is more common to see pleural effusions with RHF when associated with PH resulting from connective tissue disease (CTD); in one study, 34% of patients with PH secondary to CTD had pleural effusions with no alternative explanation.[58] Although all CTD can be associated with pleural effusions, it is much more common in patients with systemic lupus erythematous, rheumatoid arthritis, and mixed CTD.[58] Pleural effusions resulting from hepatic hydrothorax are seen in 5% to 10% of patients with cirrhosis. These effusions are most commonly present on the right side, but can be seen on the left and, less commonly, bilaterally.[33]

Cysts: Although few cystic lung diseases have been associated with PH, the latter is frequently associated with advanced pulmonary Langerhans cell histiocytosis. The diagnosis is uncommon, but PH confirmed by RHC has been seen in 92% to 100% of patients with pulmonary Langerhans cell histiocytosis referred for lung transplantation.[59,60] This diffuse cystic lung disease is associated with bizarre-shaped, thick-walled cysts demonstrating a preference for upper and mid-lung zones. Associated findings include micronodules of varying size that may cavitate (Fig 23).[61]

Evolving Techniques for PH Imaging

Single-Energy CT Scan

There are two standard CT scan techniques that can be proposed for the evaluation of patients with PH, both based on single-energy CT scan. Noncontrast CT scan is sufficient for the evaluation of most lung diseases because it allows identification of structural changes in the airways and lung parenchyma. A variety of PH etiologies can be suspected, such as COPD, ILD, PAVM, and PVOD/PCH. It is noticeable that the nonvascular features of CTEPH are depictable on noncontrast scans, justifying the subsequent use of

TABLE 3] Common Causes of PH Associated With Lung Parenchymal Nodules

Diagnosis	Description	Distinguishing Features
Pulmonary arterial hypertension	Patchy, ill-defined centrilobular nodules[a]	Higher incidence of RV dilation and deviated IVS
Pulmonary veno-occlusive disease	Diffuse, ill-defined nodules	Interlobular septal thickening, mediastinal lymph node enlargement and pleural effusions[b]
Pulmonary capillary hemangiomatosis	Diffuse, larger ground-glass opacities	Basilar reticulonodular and micronodular opacities
Hypersensitivity pneumonitis	Ill-defined centrilobular nodules, diffuse mosaic perfusion, upper lobe predominant bronchocentric fibrosis	Reticulation, traction bronchiectasis which are predominately subpleural and peribronchovascular which typically spares lung bases

See Table 1 and 2 legends for expansion of abbreviations.
[a]Most common in PAH secondary to scleroderma.
[b]Can also be present in PCH, but less commonly so.

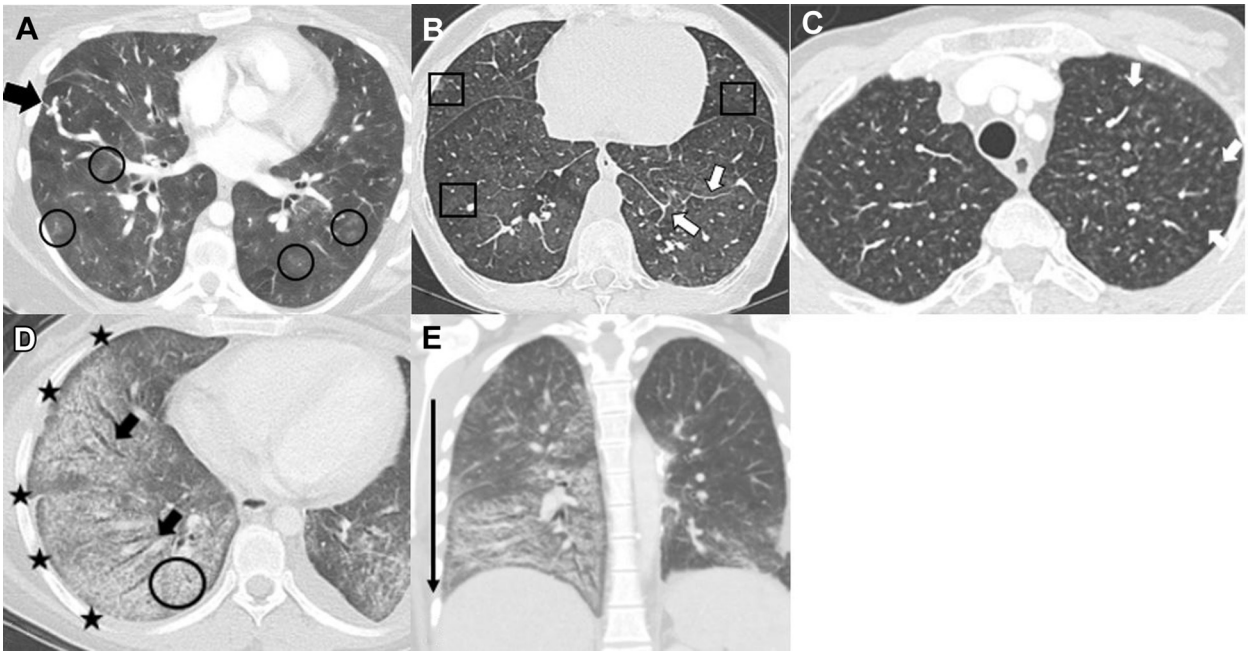

Figure 22 – *Examples of neovascularization and lobular ground-glass opacities in a patient with (A) heritable pulmonary arterial hypertension (PAH) with patchy and ill defined centrilobular nodules, thought to be due to cholesterol granulomas within small vessels. Also notable on this image is the presence of neovascularization with serpiginous peripheralpulmonary collaterals (black arrow). B, Pulmonary veno-occlusive disease with diffuse, ill-defined small pulmonary nodules (boxes) due to venous obstruction and associated with interlobular septal thickening (white arrows). C, PAH due to limited cutaneous scleroderma and ill-defined micronodules associated with CVD (white arrows). D, E, Nonspecific interstitial pneumonia (NSIP) with predominantly peripheral ground glass opacities (circle) with subpleural sparing (stars) and traction bronchiectasis (thick black arrows); E, Shows the same patient with NSIP in a coronal view highlighting the craniocaudal gradient seen with NSIP (long black arrow).*

chest CT angiography to assess for the diagnosis of chronic thromboembolic disease. This approach allows for evaluation of the differential causes of PAH, including CTEPH, and provides diagnostic information at the level of the cardiac cavities. The comprehensive evaluation of all anatomical compartments with CT scan has led to reconsideration of its use in the diagnostic workup of PH. Although the traditional schema relies on ventilation/perfusion scintigraphy aimed at differentiating CTEPH from other causes of PH, standard CT angiography is currently considered as an effective and reliable first-line imaging modality.[62,14,63]

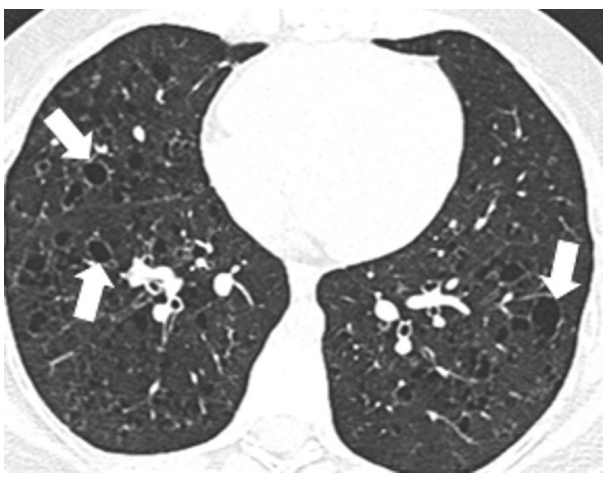

Figure 23 – *Transverse chest CT scan with diffuse bizarrely shaped thick-walled cysts of varying sizes consistent with pulmonary Langerhans cell histiocytosis.*

Dual-Energy CT Scan

The introduction of dual-energy CT (DECT) offers new perspectives by combining traditional cross-sectional imaging with the creation of iodine maps through which perfusion defects can be analyzed. Inclusion of CT pulmonary angiography allowed for visualization of endoluminal defects of the pulmonary vasculature. Lung scintigraphy allows for evaluation of the relationship between perfusion and ventilation within the lungs. With the advent of DECT, clinicians gained the ability to simultaneously evaluate both the physiology and anatomy of the lungs in detail and incorporate it into the diagnostic workup for PH. In the clinical context of PH, most attention has been directed toward the description of DECT perfusion changes in CTEPH.[64-66] The patterns of DECT perfusion changes have a high level of concordant findings with V/Q scintigraphy in the

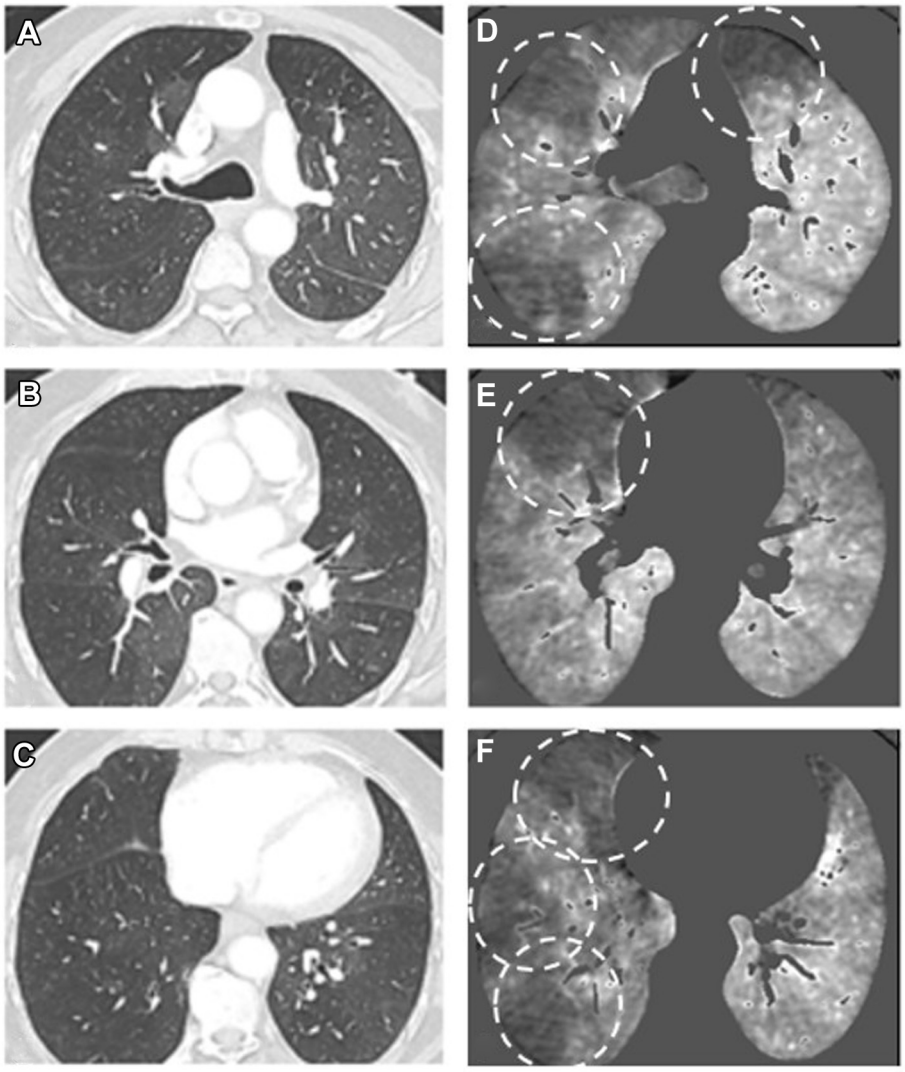

Figure 24 – *Morphologic and perfusion images generated from the same dual-energy CT scan acquisition of a patient with chronic thromboembolic pulmonary hypertension. Mosaic perfusion on lung images with CT features of peripheral chronic pulmonary embolism depictable in the right lower lobe (A, B, C). Corresponding perfusion images showing numerous triangular perfusion defects in both lungs, more important on the right side (white circles in D, E, F).*

differential diagnosis between PAH and peripheral forms of CTEPH.[67] In CTEPH patients, there is a combination of pulmonary edema-type perfusion defects, seen with the concurrent presence of patchy and/or more extensive perfusion defects (Fig 24). In PAH, DECT perfusion is either normal or shows patchy perfusion defects in the same proportion as that seen with scintigraphy. The excellent agreement between DECT perfusion and V/Q scintigraphy in the triage of patients with PH[68] and the strong diagnostic accuracy of DECT perfusion scans for the diagnosis of CTEPH[69] suggest an evolving diagnostic algorithm for PH patients. The main advantage of DECT is that it relies on the possibility of providing standard diagnostic information and lung perfusion from a single acquisition.[14]

Conclusions

Many diverse etiologies and complex diseases can result in PH, which necessitates distinct management strategies. The diagnosis of PH requires RHC, obtained in patients with a high echocardiographic suspicion for PH; however, the first step requires a high degree of clinical suspicion to diagnose this condition. Most patients will have chest imaging performed before undergoing advanced testing. Careful analysis of the images by pulmonologists, in conjunction with

radiologists, can help clinicians in determining both the presence of PH and its etiologies. Visualizing the lung parenchyma with CT scan may demonstrate specific signs associated with the various groups. New imaging modalities such as DECT may come to offer a noninvasive alternative to diagnose, prognosticate, and monitor patients with PH. Radiographic imaging cannot definitively diagnose PH, but using the signs discussed can give invaluable information to the pulmonologist approaching a patient with new-onset PH. This greater awareness can then translate into earlier detection and treatment, hopefully improving outcomes for patients.

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References

1. Galie N, Humbert M, Vachiery JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: the Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). *Eur Heart J*. 2016;37(1):67-119.
2. Simonneau G, Montani D, Celermajer DS, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. *Eur Respir J*. 2019;53(1). pii: 1801913.
3. Graham BB, Bandeira AP, Morrell NW, Butrous G, Tuder RM. Schistosomiasis-associated pulmonary hypertension: pulmonary vascular disease: the global perspective. *Chest*. 2010;137(6 Suppl): 20S-29S.
4. McGoon M, Gutterman D, Steen V, et al. Screening, early detection, and diagnosis of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest*. 2004;126(1 Suppl):14S-34S.
5. Mensah YB, Mensah K, Asiamah S, et al. Establishing the cardiothoracic ratio using chest radiographs in an indigenous Ghanaian population: a simple tool for cardiomegaly screening. *Ghana Med J*. 2015;49(3):159-164.
6. Boyars M. Chest roentgenography for pulmonary evaluation. In: Walker HK, Hall WD, Hurst JW, eds. *Clinical Methods: The History, Physical, and Laboratory Examinations*, 3rd ed. Boston: Butterworths; 1990.
7. Mirsadraee M, Nazemi S, Hamedanchi A, Naghibi S. Simple screening of pulmonary artery hypertension using standard chest x ray: an old technique, new landmark. *Tanaffos*. 2013;12(3):17-22.
8. Murphy JG, Lloyd MA, Clinic Mayo. *Mayo Clinic Cardiology: Concise Textbook*. 4th ed. Oxford: Mayo Clinic Scientific Press/ Oxford University Press; 2013.
9. Ferguson EC, Krishnamurthy R, Oldham SA. Classic imaging signs of congenital cardiovascular abnormalities. *Radiographics*. 2007;27(5):1323-1334.
10. Raoof S, Feigin D, Sung A, Raoof S, Irugulpati L, Rosenow EC III. Interpretation of plain chest roentgenogram. *Chest*. 2012;141(2):545-558.
11. Teichmann V, Jezek V, Herles F. Relevance of width of right descending branch of pulmonary artery as a radiological sign of pulmonary hypertension. *Thorax*. 1970;25(1):91-96.
12. Matthay RA, Schwarz MI, Ellis JH Jr, et al. Pulmonary artery hypertension in chronic obstructive pulmonary disease: determination by chest radiography. *Invest Radiol*. 1981;16(2):95-100.
13. Kasper DL. *Harrison's Principles of Internal Medicine. 19th ed.* New York: McGraw Hill Education; 2015.
14. Ascha M, Renapurkar RD, Tonelli AR. A review of imaging modalities in pulmonary hypertension. *Ann Thorac Med*. 2017;12(2): 61-73.
15. Raymond TE, Khabbaza JE, Yadav R, Tonelli AR. Significance of main pulmonary artery dilation on imaging studies. *Ann Am Thorac Soc*. 2014;11(10):1623-1632.
16. Lewis G, Hoey ET, Reynolds JH, Ganeshan A, Ment J. Multi-detector CT assessment in pulmonary hypertension: techniques, systematic approach to interpretation and key findings. *Quant Imaging Med Surg*. 2015;5(3):423-432.
17. Tan RT, Kuzo R, Goodman LR, Siegel R, Haasler GB, Presberg KW. Utility of CT scan evaluation for predicting pulmonary hypertension in patients with parenchymal lung disease. Medical College of Wisconsin Lung Transplant Group. *Chest*. 1998;113(5):1250-1256.
18. Grosse C, Grosse A. CT findings in diseases associated with pulmonary hypertension: a current review. *Radiographics*. 2010;30(7):1753-1777.
19. Pena E, Dennie C, Veinot J, Muniz SH. Pulmonary hypertension: how the radiologist can help. *Radiographics*. 2012;32(1):9-32.
20. Shin S, King CS, Brown AW, et al. Pulmonary artery size as a predictor of pulmonary hypertension and outcomes in patients with chronic obstructive pulmonary disease. *Respir Med*. 2014;108(11): 1626-1632.
21. Haimovici JB, Trotman-Dickenson B, Halpern EF, et al. Relationship between pulmonary artery diameter at computed tomography and pulmonary artery pressures at right-sided heart catheterization. Massachusetts General Hospital Lung Transplantation Program. *Acad Radiol*. 1997;4(5):327-334.
22. Truong QA, Massaro JM, Rogers IS, et al. Reference values for normal pulmonary artery dimensions by noncontrast cardiac computed tomography: the Framingham Heart Study. *Circ Cardiovasc Imaging*. 2012;5(1):147-154.
23. Barbosa EJ Jr, Gupta NK, Torigian DA, Gefter WB. Current role of imaging in the diagnosis and management of pulmonary hypertension. *AJR Am J Roentgenol*. 2012;198(6):1320-1331.
24. Iyer AS, Wells JM, Vishin S, Bhatt SP, Wille KM, Dransfield MT. CT scan-measured pulmonary artery to aorta ratio and echocardiography for detecting pulmonary hypertension in severe COPD. *Chest*. 2014;145(4):824-832.
25. Boerrigter B, Mauritz GJ, Marcus JT, et al. Progressive dilatation of the main pulmonary artery is a characteristic of pulmonary arterial hypertension and is not related to changes in pressure. *Chest*. 2010;138(6):1395-1401.
26. Siegel Y, Mirpuri T. Pulmonary hypertension detection using dynamic and static measurable parameters on CT angiography. *J Comput Assist Tomogr*. 2014;38(4):586-590.
27. Revel MP, Faivre JB, Remy-Jardin M, Delannoy-Deken V, Duhamel A, Remy J. Pulmonary hypertension: ECG-gated 64-section CT angiographic evaluation of new functional parameters as diagnostic criteria. *Radiology*. 2009;250(2):558-566.
28. Lin FY, Devereux RB, Roman MJ, et al. Cardiac chamber volumes, function, and mass as determined by 64-multidetector row computed tomography: mean values among healthy adults free of hypertension and obesity. *JACC Cardiovasc Imaging*. 2008;1(6):782-786.
29. Chan AL, Juarez MM, Shelton DK, et al. Novel computed tomographic chest metrics to detect pulmonary hypertension. *BMC Med Imaging*. 2011;11:7.
30. Hussain N, Capener D, Elliot C, et al. Interventricular septal angle can be used to predict which patients have combined postcapillary or precapillary pulmonary hypertension in left heart disease. *J Cardiovasc Magn Reson*. 2015;17(1):P338.
31. Fenstad ER, Le RJ, Sinak LJ, et al. Pericardial effusions in pulmonary arterial hypertension: characteristics, prognosis, and role of drainage. *Chest*. 2013;144(5):1530-1538.

32. Modolon C, Attina D, Buia F, et al. Lung neovascularity in pulmonary arterial hypertension associated with congenital heart defects and idiopathic pulmonary arterial hypertension: study of 198 patients. *Eur Radiol*. 2012;22(5):1059-1066.
33. Sureka B, Bansal K, Patidar Y, Kumar S, Arora A. Thoracic perspective revisited in chronic liver disease. *Gastroenterol Rep (Oxf)*. 2015;3(3):194-200.
34. Tueller C, Fischer Biner R, Minder S, et al. FDG-PET in diagnostic work-up of pulmonary artery sarcomas. *Eur Respir J*. 2010;35(2):444-446.
35. Rossi SE, McAdams HP, Rosado-de-Christenson ML, Franks TJ, Galvin JR. Fibrosing mediastinitis. *Radiographics*. 2001;21(3):737-757.
36. Bergin CJ, Park KJ. Lymph node enlargement in pulmonary arterial hypertension due to chronic thromboembolism. *J Med Imaging Radiat Oncol*. 2008;52(1):18-23.
37. Nunes H, Humbert M, Capron F, et al. Pulmonary hypertension associated with sarcoidosis: mechanisms, haemodynamics and prognosis. *Thorax*. 2006;61(1):68-74.
38. Moua T, Levin DL, Carmona EM, Ryu JH. Frequency of mediastinal lymphadenopathy in patients with idiopathic pulmonary arterial hypertension. *Chest*. 2013;143(2):344-348.
39. Resten A, Maitre S, Humbert M, et al. Pulmonary hypertension: CT of the chest in pulmonary venoocclusive disease. *AJR Am J Roentgenol*. 2004;183(1):65-70.
40. Montani D, Achouh L, Dorfmuller P, et al. Pulmonary veno-occlusive disease: clinical, functional, radiologic, and hemodynamic characteristics and outcome of 24 cases confirmed by histology. *Medicine (Baltimore)*. 2008;87(4):220-233.
41. Sears EH, Aliotta JM, Klinger JR. Partial anomalous pulmonary venous return presenting with adult-onset pulmonary hypertension. *Pulm Circ*. 2012;2(2):250-255.
42. Galizia M, Renapurkar R, Prieto L, et al. Radiologic review of acquired pulmonary vein stenosis in adults. *Cardiovasc Diagn Ther*. 2018;8(3):387-398.
43. Raghu G, Remy-Jardin M, Myers JL, et al. Diagnosis of idiopathic pulmonary fibrosis. An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline. *Am J Respir Crit Care Med*. 2018;198(5):e44-e68.
44. Chung JH, Zhan X, Cao M, et al. Presence of air trapping and mosaic attenuation on chest computed tomography predicts survival in chronic hypersensitivity pneumonitis. *Ann Am Thorac Soc*. 2017;14(10):1533-1538.
45. Lynch DA, Austin JH, Hogg JC, et al. CT-definable subtypes of chronic obstructive pulmonary disease: a statement of the Fleischner Society. *Radiology*. 2015;277(1):192-205.
46. Minai OA, Chaouat A, Adnot S. Pulmonary hypertension in COPD: epidemiology, significance, and management: pulmonary vascular disease: the global perspective. *Chest*. 2010;137(6 Suppl):39S-51S.
47. Thabut G, Dauriat G, Stern JB, et al. Pulmonary hemodynamics in advanced COPD candidates for lung volume reduction surgery or lung transplantation. *Chest*. 2005;127(5):1531-1536.
48. Burrows B, Kettel LJ, Niden AH, Rabinowitz M, Diener CF. Patterns of cardiovascular dysfunction in chronic obstructive lung disease. *N Engl J Med*. 1972;286(17):912-918.
49. Hoeper MM, Barbera JA, Channick RN, et al. Diagnosis, assessment, and treatment of non-pulmonary arterial hypertension pulmonary hypertension. *J Am Coll Cardiol*. 2009;54(1 Suppl):S85-S96.
50. Caminati A, Cassandro R, Harari S. Pulmonary hypertension in chronic interstitial lung diseases. *Eur Respir Rev*. 2013;22(129):292-301.
51. Silva CI, Churg A, Muller NL. Hypersensitivity pneumonitis: spectrum of high-resolution CT and pathologic findings. *AJR Am J Roentgenol*. 2007;188(2):334-344.
52. Koschel DS, Cardoso C, Wiedemann B, Hoffken G, Halank M. Pulmonary hypertension in chronic hypersensitivity pneumonitis. *Lung*. 2012;190(3):295-302.
53. Oliveira RK, Pereira CA, Ramos RP, et al. A haemodynamic study of pulmonary hypertension in chronic hypersensitivity pneumonitis. *Eur Respir J*. 2014;44(2):415-424.
54. Hamada K, Nagai S, Tanaka S, et al. Significance of pulmonary arterial pressure and diffusion capacity of the lung as prognosticator in patients with idiopathic pulmonary fibrosis. *Chest*. 2007;131(3):650-656.
55. Andersen CU, Mellemkjaer S, Hilberg O, Nielsen-Kudsk JE, Simonsen U, Bendstrup E. Pulmonary hypertension in interstitial lung disease: prevalence, prognosis and 6 min walk test. *Respir Med*. 2012;106(6):875-882.
56. Rajaram S, Swift AJ, Condliffe R, et al. CT features of pulmonary arterial hypertension and its major subtypes: a systematic CT evaluation of 292 patients from the ASPIRE Registry. *Thorax*. 2015;70(4):382-387.
57. Tang KJ, Robbins IM, Light RW. Incidence of pleural effusions in idiopathic and familial pulmonary arterial hypertension patients. *Chest*. 2009;136(3):688-693.
58. Luo YF, Robbins IM, Karatas M, Brixey AG, Rice TW, Light RW. Frequency of pleural effusions in patients with pulmonary arterial hypertension associated with connective tissue diseases. *Chest*. 2011;140(1):42-47.
59. Dauriat G, Mal H, Thabut G, et al. Lung transplantation for pulmonary Langerhans' cell histiocytosis: a multicenter analysis. *Transplantation*. 2006;81(5):746-750.
60. Fartoukh M, Humbert M, Capron F, et al. Severe pulmonary hypertension in histiocytosis X. *Am J Respir Crit Care Med*. 2000;161(1):216-223.
61. Brauner MW, Grenier P, Mouelhi MM, Mompoint D, Lenoir S. Pulmonary histiocytosis X: evaluation with high-resolution CT. *Radiology*. 1989;172(1):255-258.
62. Freed BH, Collins JD, Francois CJ, et al. MR and CT imaging for the evaluation of pulmonary hypertension. *JACC Cardiovasc Imaging*. 2016;9(6):715-732.
63. McCann C, Gopalan D, Sheares K, Screaton N. Imaging in pulmonary hypertension, part 1: clinical perspectives, classification, imaging techniques and imaging algorithm. *Postgrad Med J*. 2012;88(1039):271-279.
64. Hoey ET, Mirsadraee S, Pepke-Zaba J, Jenkins DP, Gopalan D, Screaton NJ. Dual-energy CT angiography for assessment of regional pulmonary perfusion in patients with chronic thromboembolic pulmonary hypertension: initial experience. *AJR Am J Roentgenol*. 2011;196(3):524-532.
65. Nakazawa T, Watanabe Y, Hori Y, et al. Lung perfused blood volume images with dual-energy computed tomography for chronic thromboembolic pulmonary hypertension: correlation to scintigraphy with single-photon emission computed tomography. *J Comput Assist Tomogr*. 2011;35(5):590-595.
66. Le Faivre J, Duhamel A, Khung S, et al. Impact of CT perfusion imaging on the assessment of peripheral chronic pulmonary thromboembolism: clinical experience in 62 patients. *Eur Radiol*. 2016;26(11):4011-4020.
67. Giordano J, Khung S, Duhamel A, et al. Lung perfusion characteristics in pulmonary arterial hypertension (PAH) and peripheral forms of chronic thromboembolic pulmonary hypertension (pCTEPH): dual-energy CT experience in 31 patients. *Eur Radiol*. 2017;27(4):1631-1639.
68. Masy M, Giordano J, Petyt G, et al. Dual-energy CT (DECT) lung perfusion in pulmonary hypertension: concordance rate with V/Q scintigraphy in diagnosing chronic thromboembolic pulmonary hypertension (CTEPH). *Eur Radiol*. 2018;28(12):5100-5110.
69. Dournes G, Verdier D, Montaudon M, et al. Dual-energy CT perfusion and angiography in chronic thromboembolic pulmonary hypertension: diagnostic accuracy and concordance with radionuclide scintigraphy. *Eur Radiol*. 2014;24(1):42-51.