CT of the chest in the evaluation of idiopathic pulmonary arterial hypertension

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Learning objectives

1. To describe the characteristic histologic features of idiopathic pulmonary arterial hypertension (IPAH) and the related morphologic changes seen at CT.
2. To discuss CT features allowing differentiation of IPAH from other obstructive disorders of the pulmonary arteries including chronic thromboembolic pulmonary hypertension (CTEPH).
Background

Idiopathic pulmonary arterial hypertension (IPAH), previously known as primary pulmonary hypertension is the idiopathic subset of a range of disease characterized by high pulmonary arterial pressures. Although occurrences have been reported in patients with widely varying ages, IPAH is generally considered a disease of young adulthood, occurring most often in those between the ages of 20 and 45 years. Women are more commonly affected than men.

Although the pathogenesis of the disease remains unclear, histological changes include medial hypertrophy of the pulmonary arteries, intimal proliferation, small-vessel occlusion and plexiform lesions. These have the combined effect of gradually increasing the pulmonary vascular resistance, with the resultant increase in the right ventricular pressure eventually leading to right-sided heart failure and death.

As IPAH is a diagnosis of exclusion, CT is primarily performed to exclude other cause of pulmonary hypertension such as pulmonary embolism, parenchymal lung disease and cause of venous hypertension. However, previous studies have highlighted several intrapulmonary and extrapulmonary abnormalities suggestive of IPAH. In this exhibit, we will present radiological features consistently seen in patients with IPAH, and describe the findings that are helpful for differentiating IPAH from other disease entities such as CTEPH.
Imaging findings OR Procedure details

1. The characteristic histologic features of IPAH and the related morphologic changes seen at CT

A. Extrapulmonary findings

a. Central pulmonary arterial enlargement

Regardless of the underlying pathologic changes, central pulmonary arterial enlargement is the characteristic morphologic CT feature of chronic pulmonary arterial hypertension. The diameter of the pulmonary artery trunk frequently exceeds that of the ascending aorta (Fig. 1a). Dilatation of the right and left main pulmonary arteries and abrupt narrowing and tapering of the peripheral pulmonary vessels have been described as a frequent finding in patients with pulmonary arterial hypertension. In adult patients, the distal main pulmonary artery with exceeding the diameter of the ascending aorta has specificity and positive predictive value of greater than 90% 6). The ratio of the right and left pulmonary arteries to right and left main bronchi is greater than 1.1 4, 6). However, the degree of pulmonary arterial dilatation has a nonlinear correlation with the mean pulmonary arterial pressure 7).

In a recently published study, the measurement of right pulmonary artery wall distensibility at ECG-gated CT may help improve the accuracy of CT-based diagnosis of pulmonary hypertension and the measurement of diastolic right ventricular outflow tract wall thickness, which correlates with the mean pulmonary artery pressure and is potentially reversible, may be useful inpatients referred for CT evaluation of pulmonary hypertension 8).

In patients with IPAH, characteristic vascular features depicted at CT are central pulmonary artery dilatation, usually in the absence of detectable intraluminal thrombi and an abrupt decrease in the caliber of segmental and subsegmental arteries. Wall-adherent apposition thrombi may form in the central pulmonary arteries in severe cases of IPAH and usually are accompanied by massive enlargement of the pulmonary artery trunk and the right and left main pulmonary arteries 1).

b. Right-sided cardiac enlargement

Regardless of the underlying pathologic changes, findings of adaptation and failure of the right side of the heart that may be seen at ECG-gated CT include right ventricular hypertrophy, which is defined as wall thickness of more than 4mm; straightening or leftward bowing of the interventricular septum; right ventricular dilatation (as a right ventricle-to-left ventricle diameter ratio of more than 1:1 at the midventricular level on
axial images); decreased right ventricular ejection fraction; dilatation of the inferior vena cava and hepatic veins; and pericardial effusion 9) (Fig.1b.c).

c. Mediastinal lymphadenopathy

Lymphnode enlargement is a relatively uncommon finding in patients with IPAH, in whom it is seen more consistently with pulmonary capillary hemangiomatosis (PCH) and pulmonary veno-occlusive disease (PVOD).

d. Dilatation of bronchial arteries

Dilatation of bronchial and nonbronchial systemic arteries is more commonly seen in patients with CTEPH (73%) than in those with idiopathic pulmonary arterial hypertension (14%), and, in case with inconclusive imaging findings, CT evidence of dilated bronchial arteries may help distinguish between these two disease entities 10).

B. Intrapulmonary findings

a. Small tortuous peripheral vessels

Plexogenic arteriopathy is considered the histologic hallmark of IPAH. This manifests in small to medium-sized muscular pulmonary arteries as intimal cellular proliferation with focal disruption of the internal elastic lamina and media by glomeruloid small vascular channels, which ramify into alveolar septal capillaries 2). Plexogenic arteriopathy can occasionally be detected at CT, manifesting as small, tortuous peripheral arteries without a significant connection to pulmonary veins such as that seen in an arteriovenous shunt 1)(Fig.2).

b. Centrilobular ground-glass nodules

Centrilobular ground-glass nodules are a feature of pulmonary hypertension and are especially common in patients with IPAH (Fig.3). Pathologically, they represent cholesterol granulomas, which are caused by ingestion of red blood cells by pulmonary macrophages, a result of repeated episodes of pulmonary hemorrhage. Centrilobular ground-glass nodules are also seen in patients with pulmonary capillary hemangiomatosis; however, in these patients, the pathologic substrate is thought to result from profuse proliferation of capillaries 9).

c. Mosaic pattern of attenuation in lung parenchyma

A mosaic pattern of attenuation caused by regional variations in lung perfusion is a frequent finding in patients with IPAH (Fig.4). Unlike the segmental and subsegmental
patterns of variable attenuation typically seen in chronic thromboembolic pulmonary hypertension (CTEPH), the pattern seen in IPAH often is characterized by focal perivascular hypertension areas in a peripheral or perihilar distribution or small, scattered, well-defined areas of low attenuation corresponding to the anatomic unit of a secondary pulmonary lobule with adjacent areas of increased attenuation in a patchy and diffuse distribution 1).

2. CT features allowing differentiation of IPAH from other obstructive disorders of the pulmonary arteries

A. Chronic thromboembolic pulmonary hypertension (CTEPH)

CTEPH occurs as a complication in 4% of cases of acute symptomatic pulmonary embolism. However, since the initial thromboembolic event is asymptomatic in most patients, CTEPH is likely more common than previously thought. Patients with CTEPH become symptomatic only when at least 60% of the pulmonary arterial bed is obstructed 9).

It is important to understand that CTEPH may be successfully treated with pulmonary thromboendarterectomy. CT may be used to assess whether patients will benefit from surgery. Patients are considered for resection if disease is present in the main, lobar, or proximal segmental arteries, a finding that is easily identifiable at CT. Patients with distal disease usually undergo medical treatment.

Intramural thrombi, webs and bands in central or peripheral pulmonary arteries are the vascular CT findings with the highest specificity for a diagnosis of CTEPH 1) (Fig.5). In IPAH, apposition thrombus is demonstrated only in severe cases, and localized in the central pulmonary arteries, associated with massive central pulmonary artery enlargement. Findings of disparity in the size of segmental vessels and mosaic lung attenuation reliably distinguish CTEPH from nonthromboembolic pulmonary arterial hypertension. Lymph node enlargement is common and corresponds histologically to vascular transformation of the lymph node sinus with various degree of sclerosis (Fig.6). Owing to the increased bronchial artery blood flow secondary to chronic obstruction of the pulmonary arteries, dilated bronchial arteries are seen and nonbronchial systemic collaterals (notably, inferior phrenic, intercostal, and internal mammary arteries) are visible in as many as 45% cases of CTEPH 10) (Fig.6.7). In a study by Remy-Jardin et al, enlarged bronchial and nonbronchial systemic arteries were found in 73% of patients with CTEPH and in only 14% of patients with idiopathic pulmonary arterial hypertension 10).

The parenchymal findings in patients with CTEPH are nonspecific but often helpful toward achieving a definite diagnosis in the appropriate clinical setting. Mosaic lung perfusion is the key imaging feature produced by CTEPH-related parenchymal changes (Fig.8). Mosaic lung perfusion is characterized by sharply demarcated regions of hypoattenuation...
with reduced vessel size and without air trapping, interspersed with adjacent areas of normal attenuation or relative hyperattenuation. Region of CTEPH-related hypo-and hyperattenuation are typically segmental or subsegmental in distribution.

Other frequent parenchymal findings in CTEPH include peripheral opacities caused by previous infarction, and cylindrical bronchial dilatation (Fig.9).

**B. Pulmonary arterial hypertension associated with connective tissue disease**

Pulmonary arterial hypertension associated with connective tissue disease is most commonly observed in systemic sclerosis, notably in its limited variant previously defined as CREST syndrome. Pulmonary arterial hypertension in this patients group is related to interstitial fibrosis, which is most commonly manifested histologically as nonspecific interstitial pneumonia, pulmonary vascular disease, or both (Fig.10.11).

Histopathologic changes in this condition are generally indistinguishable from those of IPAH, except for scleroderma-associated vasculopathy, which is characterized histologically by medial and intimal hyperplasia with a marked absence of plexiform lesions 1). In comparison with IPAH, patients with this condition are mainly women, are older, have a significantly lower cardiac output, and show a trend toward a shorter survival.

**C. Pulmonary arterial hypertension in HIV infection**

HIV-associated pulmonary arterial hypertension is a life-threatening complication of HIV infection. The mechanism leading to the development of pulmonary arterial hypertension in the setting of HIV infection is unknown, although indirect action of the virus through second messengers such as cytokines and growth factors is strongly suspected. Because of considerable overlap between HIV-associated and idiopathic IPAH with regard to their clinical, pathological, and radiologic manifestations, HIV testing should be considered in patients with CT evidence of pulmonary arterial hypertension without another identifiable cause1).

**D. Pulmonary capillary hemangiomatosis (PCH) and pulmonary veno-occlusive disease (PVOD)**

PCH and PVOD are rare causes of pulmonary arterial hypertension and are characterized by specific pathologic changes that lead to obliteration of the postcapillary veins. They most commonly affect children or young adults. Its etiology is unknown. Clinical associations with high estrogen levels during pregnancy, oral contraceptive use, viral infection, bone marrow transplantation, and drug toxicity have been described. A definite diagnosis of PCH or PVOD requires histologic analysis. However, it is important for radiologist to recognize the CT findings of PCH and PVOD, because patients with
these conditions may develop fatal pulmonary edema if they are treated with vasodilator agents 9). At CT, the combination of features of pulmonary arterial hypertension with interstitial and alveolar edema is virtually diagnostic of these conditions (Fig.12). CT shows markedly small central pulmonary veins, interlobular septal thickening, and patchy centrilobular ground-glass opacities representing interstitial and alveolar edema 1). Additional CT findings include a normal-sized left atrium and mediastinal lymphadenopathy.
Fig. 1: Vascular and cardiac features of chronic pulmonary arterial hypertension. a. Axial multidetector CT angiogram shows dilatation of the pulmonary artery trunk exceeding that of the ascending aorta. b. Axial multidetector CT angiogram shows right ventricular myocardium (large arrow) is more than 4mm thick. Right ventricular dilatation and straightening of the interventricular septum (small arrow) also are seen. c. Axial multidetector CT angiogram shows reflux of contrast material into the inferior vena cava, which is dilated, and hepatic veins (arrow).

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Fig. 2: IPAH in a 39-year-old woman (a) and a 44-year-old man (b). a. b. HRCT shows corkscrewlike peripheral pulmonary arteries (arrows), findings indicative of plexogenic arteriopathy.

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Fig. 3: IPAH in a 39-year-old woman. HRCT shows diffuse centrilobular ground-glass nodules findings indicative of cholesterol granulomas.

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**Fig. 4**: IPAH in a 42-year old woman. HRCT shows multiple perivascular areas of hyperattenuation (mosaic pattern). Unlike the segmental and subsegmental patterns of variable attenuation typically seen in CTEPH, this shows small, scattered, well-defined areas of low attenuation corresponding to the anatomic unit of a secondary pulmonary lobule with adjacent area of increased attenuation in a pathy and diffuse distribution. Note the dilatation of the pulmonary artery trunk and the left main pulmonary artery.

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**Figure 5.**

*Fig. 5:* CTEPH in a 72-year old woman. 

a. Axial contrast-enhanced CT scan shows an eccentric wall-adherent thrombus (large arrow) in the right interlobar pulmonary artery producing an irregular contour of the intimal surface. An intraluminal band (small arrow) in left lower lobe pulmonary artery is also seen. 

b. Axial contrast-enhanced CT scan shows right ventricular dilatation and straightening of the interventricular septum (arrow).

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Figure 6: CTEPH in a 77-year old woman. a. b. Axial contrast-enhanced CT shows bronchial artery collateral vessels (arrows) and multiple enlargement of lymphnodes.

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Fig. 7: CTEPH in a 63-year old woman. Axial contrast-enhanced CT shows dilated bronchial artery (large arrow) and intercostal arteries (small arrows) as collateral vessels.

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Fig. 8: CTEPH in a 61-year-old woman (a) and a 71-year-old woman (b). a. HRCT shows a common pattern of mosaic lung attenuation with segmental perfusion defects. b. HRCT shows a common pattern of mosaic lung attenuation with mainly subsegmental perfusion defects.

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**Fig. 9:** CTEPH in a 60-year old woman. 

a. Axial contrast-enhanced CT scan shows an eccentric wall-adherent thrombus (large arrow) in the right main pulmonary artery and extending interlobar pulmonary artery. An intramural thrombus (small arrow) in left lower lobe pulmonary artery is also seen.

b. HRCT shows cylindrical bronchial dilatation (arrow) in the right upper lobe.

c. HRCT shows a small peripheral opacity (arrow) caused by previous infarction in the right middle lobe.

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Fig. 10: Pulmonary arterial hypertension associated with systemic sclerosis in a 12-year old girl. a.Axial CT scan shows dilatation of the pulmonary artery trunk exceeding that of the ascending aorta. b.Axial CT scan shows right ventricular dilatation and a small amount of pericardial effusion (arrow). c.HRCT shows multiple perivascular areas of hyperattenuation (mosaic pattern).

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Fig. 11: Pulmonary arterial hypertension associated with systemic sclerosis in a 68-year old man. HRCT shows diffuse interstitial fibrosis consistent with histologically nonspecific interstitial pneumonia. Traction bronchiectasis (arrow) is also demonstrated.

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**Fig. 12:** Pulmonary veno-occlusive disease in a 59-year-old man (by clinical diagnosis and not confirmed by histologic analysis) a. Axial contrast-enhanced CT scan shows right ventricular dilatation and straightening of the interventricular septum. Dilatation of segmental pulmonary arteries and normal sized pulmonary vein are also seen. b. HRCT shows interlobular septal thickening and patchy centrilobular ground-glass opacities representing interstitial and alveolar edema.

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Conclusion

Although diseases that can induce pulmonary hypertension display a wide spectrum of partially overlapping CT features, CT represents a useful non-invasive modality in the evaluation of IPAH.
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