Imaging of Chronic Thromboembolic Pulmonary Hypertension

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KEYWORDS

• CTEPH • Pulmonary embolism • Pulmonary hypertension • CT • Perfusion • Dual energy

KEY POINTS

- CT pulmonary angiography (CTPA) can be highly sensitive for detecting CTEPH, but the diagnosis is frequently missed by radiologists.
- Imaging findings of chronic thromboembolic pulmonary disease (CTEPD) differ from those of acute pulmonary embolism, though both chronic and acute disease may coexist on CTPA.
- Hypoperfusion can help pinpoint areas of CTEPD, a process that may be enhanced by spectral imaging techniques.
- Preoperative imaging aims to assess the extent of disease and identify other factors that could impact treatment decisions.
- Conditions that can mimic CTEPH include acute pulmonary embolism, in situ thrombus, pulmonary artery sarcoma, vasculitis, and fibrosing mediastinitis.

INTRODUCTION

Chronic thromboembolic pulmonary hypertension (CTEPH) is a form of pulmonary hypertension caused by prolonged obstruction of the pulmonary arteries by organized thromboemboli.[1] Each year, approximately 600,000 Americans experience an acute pulmonary embolism. While the majority of cases resolve, about 1% to 5% result in persistent thromboembolism and CTEPH.[2–4] Although a relatively rare disease, CTEPH is frequently missed both clinically and on imaging, particularly on CT pulmonary angiogram (CTPA). A recent position paper by the Fleischner Society highlighted the educational gap contributing to this underdiagnosis.[5] CTEPH is a treatable condition with surgical, endovascular, and medical interventions that can improve both survival and quality of life, making it crucial for radiologists to recognize the imaging findings of this disease.

This article will discuss imaging of CTEPH, with particular emphasis on CTPA. We will first discuss the clinical presentation and pathophysiology of CTEPH, followed by a review of normal pulmonary arterial anatomy and CTPA technique. Finally, we will describe the imaging features of CTEPH and its mimics.

CLINICAL PRESENTATION AND PATHOPHYSIOLOGY

The most common presenting symptoms of CTEPH are dyspnea on exertion and fatigue, which are nonspecific, likely contributing to underdiagnosis.[6,7] In the setting of right heart failure, patients may additionally experience related symptoms including lower extremity swelling, abdominal distension, chest pressure, and syncope, but these are less common presenting symptoms.[8] Similarly, hemoptysis related to

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bronchial artery hypertrophy is a less-frequent presenting symptom.

Risk factors for CTEPH partially overlap with those for acute pulmonary embolism and include malignancy, chronic inflammatory states (eg, chronic infection from indwelling catheters), prior splenectomy, and hypothyroidism.[1] While antiphospholipid antibodies and lupus anticoagulant and coagulopathies related to elevated factor VIII, von Willebrand factor, and abnormal fibrinogen are associated with CTEPH, the most common inherited thrombotic risk factors such as protein C deficiency and protein S deficiency interestingly are not.[9]

Approximately 75% of patients with CTEPH have a history of acute pulmonary embolism, suggesting that most cases arise from the failure of acute emboli to resorb. While acute pulmonary embolism primarily consists of red blood cells, platelets, and fibrin, failure to resolve leads to infiltration by inflammatory cells, which organize the clot and deposit extracellular matrix proteins such as fibrin and elastin. This process results in a chronic thrombus that is inherently different in composition from acute pulmonary embolism.[10] In addition to obstructive thrombi, patients with CTEPH also develop a microvasculopathy, likely due to prolonged exposure to elevated pressures and associated shear stress.[6] In unobstructed pulmonary arteries, this is simply due to pulmonary hypertension, and in obstructed pulmonary arteries, it results from bronchial collateral vessels with systemic pressure.

CTEPH specifically refers to patients with chronic thromboembolism and pulmonary hypertension. Recent guidelines from the European Respiratory Society have proposed the term chronic thromboembolic pulmonary disease (CTEPD) to describe patients with chronic thromboembolism, with or without pulmonary hypertension at rest.[11] However, the term chronic thromboembolic disease (CTED) is still frequently used to describe patients with chronic thromboembolism without pulmonary hypertension.

NORMAL ANATOMY

Accurate knowledge of the pulmonary arterial tree is essential for identifying and characterizing thromboembolic disease. In patients with CTEPH, occluded or diminutive pulmonary arteries can easily be overlooked if not specifically included in the search pattern.

The main pulmonary artery (PA) bifurcates into the right and left pulmonary arteries. The right PA continues as the interlobar artery beyond the first branch to the right upper lobe PA, usually the truncus anterior. Variable terminology has been used to describe the segment of the left PA distal to the first left upper lobe PA, with some still describing it as the left PA, and others using the term left descending or interlobar PA.

Segmental pulmonary arteries are named according to the bronchopulmonary segments they supply and usually run parallel to the segmental bronchi. However, many anatomic variations exist.[12–14] For accurate identification of segmental pulmonary arteries, it can be useful to first locate a bronchopulmonary segment and then trace the course of its dominant pulmonary arterial supply.

The right upper lobe consists of 3 segments supplied by the apical (A1), posterior (A2), and anterior (A3) segmental arteries. The apical and anterior segmental arteries most often share a common trunk, called the truncus anterior, while the posterior segmental artery arises separately from the interlobar artery. The right middle lobe has 2 segments supplied by lateral (A4) and medial (A5) segmental branches, which may have a common trunk. The right lower lobe superior segmental artery (A6) typically originates at or proximal to the takeoff of the right middle lobe arteries.[12] After giving off these branches, the interlobar artery continues as the right lower lobe basal trunk, which supplies the medial basal (A7), anterior basal (A8), lateral basal (A9), and posterior basal (A10) segmental arteries. The medial and anterior basal arteries (A7 + A8) usually arise from one trunk, while the lateral and posterior basal arteries (A9 + A10) arise from another.

The left upper lobe consists of the apicoposterior (A1–A2) and anterior (A3) segments, which may arise from separate segmental arteries or a common trunk. The superior (A4) and inferior (A5) lingular arteries typically share a common trunk but may arise separately. Similar to the right side, the left lower lobe superior segmental artery (A6) may arise at or proximal to the takeoff of the lingular pulmonary arteries. Beyond the A6 takeoff, the basal segmental arteries vary in their branching patterns, but most commonly, there are 2 trunks: one supplying the anteromedial basal segments (A7–A8) and the other supplying the lateral basal (A9) and posterior basal (A10) segments.

CT IMAGING TECHNIQUE

CTPA technique for CTEPH is similar to that used for acute pulmonary embolism. Typically, 75 to 100 mL of iodinated contrast is injected at 4 to 6 mL/s with adjustments based on patient body mass index.[15–18] A test bolus or automated bolus triggering is used to determine the scan delay with the region of interest usually placed in the

main PA. In cases of slow flow due to pulmonary hypertension or left-sided heart failure, placing the region of interest in the left atrium may help ensure better opacification of the distal pulmonary arteries. Electrocardiogram (ECG)-gating is generally not required. Scanning is performed in a caudocranial direction, as the lower lobes are more prone to motion artifacts due to greater respiratory excursion compared to the upper lobes. This approach also reduces streak artifacts caused by contrast inflow into the superior vena cava (SVC).[17,19]

A key aspect of CTPA for CTEPH is using the thinnest possible slice thickness, typically 0.625 to 1.0 mm, to avoid the partial volume averaging that can obscure linear chronic thromboemboli. At our institution, we also reconstruct 3 plane maximum intensity projection (MIP) images at a thickness of 7 to 10 mm, which are useful for identifying small or occluded vessels.

When available, spectral imaging techniques, that is, dual-energy CT or photon counting CT, should be used for the identification of perfusion defects. At our institution, source iodine map images are used to generate 3 plane colorized post-processed iodine maps reconstructed at a thickness of 12 mm. Although most institutions perform a single-phase CT, some have suggested the use of dual-phase CT for patients with known CTEPH to better evaluate collateral vessels, which can help differentiate acute from chronic disease.[20] Additionally, this technique may help distinguish between artifacts such as contrast "smoke" and true thromboembolic disease.

IMAGING FINDINGS/PATHOLOGY

V/Q Scan

V/Q is currently the screening modality of choice to exclude CTEPD.[11] While V/Q scan is reported to have a sensitivity of 96% to 97% and specificity of 90% to 95%,[13,14] V/Q scan may underestimate the extent of disease in cases of nonocclusive thromboembolism.[15] When available, single photon emission computed tomography - computed tomography (SPECT-CT) is preferred over planar imaging, as planar imaging has limitations such as overlapping pulmonary segments, adjacent lung shine-through, and challenges in assessing the size of defects.[5,16–18]

The interpretation of V/Q scans for CTEPD follows a similar approach to V/Q scans for acute pulmonary embolism, using the modified prospective investigation of pulmonary embolism diagnosis II (PIOPED II) criteria. While small mismatched perfusion defects do not exclude CTEPH, most CTEPH cases display moderate (25%–75% of a bronchopulmonary segment) or large (>75%) mismatched perfusion defects (**Fig. 1**). When mismatches in both ventilation and perfusion are detected, further

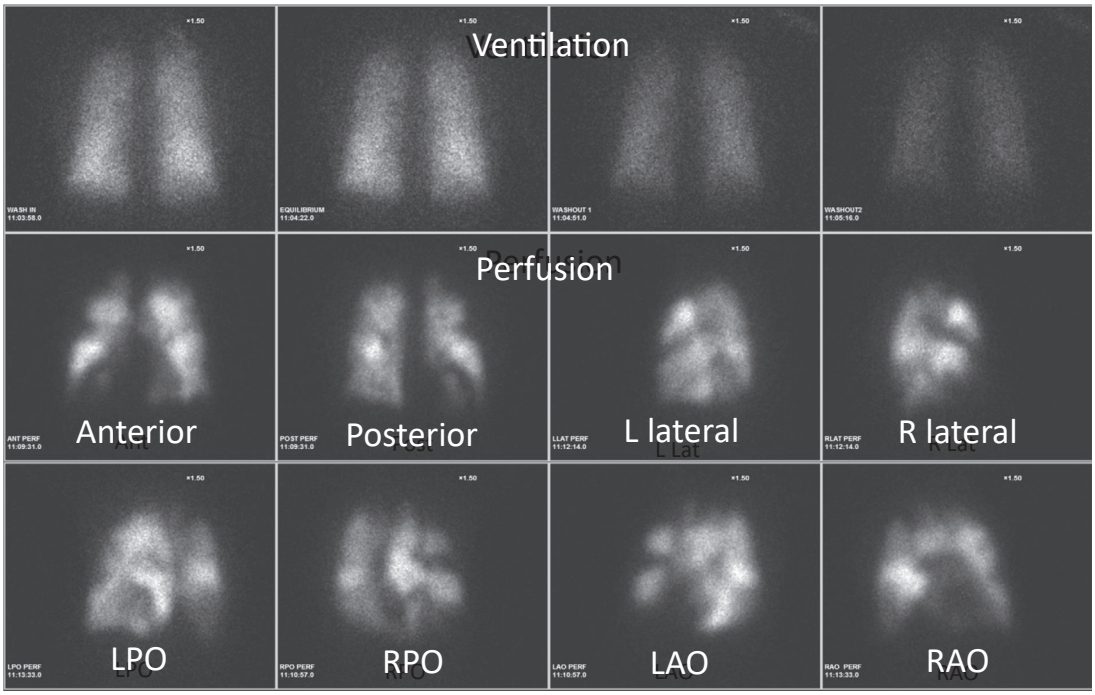

Fig. 1. V/Q scan of a 59 year old man with CTEPH. Large, bilateral mismatched perfusion defects are seen in all lobes, greater in the lower lobes.

evaluation with anatomic imaging is essential to assess the full extent of the disease, evaluate lung parenchyma abnormalities, or identify potential CTEPH mimics. Several other conditions can cause vascular obstruction with preserved airflow, further discussed in the CTEPH mimics section.

CT Pulmonary Angiogram

The pulmonary arterial filling defects of CTEPD on CTPA can often be distinguished from acute pulmonary embolism based on their morphology. Linear filling defects called "bands" are indicative of chronic rather than acute pulmonary embolism. Multiple bands joining together are called "webs" (**Fig. 2**A). Chronic thromboemboli are usually eccentrically positioned within the vessel, abutting the vessel wall, in contrast to the more centrally located acute emboli[15] (**Fig. 2**B, C). The margins of chronic emboli are usually concave, whereas acute emboli tend to have convex margins (**Fig. 3**A, B). Consequently, chronic thromboemboli form an obtuse angle with the vessel wall, while acute emboli form an acute angle.

In all cases of CTEPH, occluded vessels with decreased caliber are observed (**Fig. 2**C, D). In some cases, such vessels may be so diminutive that they appear to be "absent"; in this situation, it can be helpful to use lung windows and trace the bronchi to infer the presence of occluded vessels. In contrast, pulmonary arteries affected by occlusive acute pulmonary embolism will have a normal or increased caliber (**Fig. 3**C). CT imaging can underestimate thromboembolic disease because organized thrombus may be contracted and strongly adherent to the vessel wall, making it difficult to visualize (**Fig. 4**A, B). In fact, some cases of CTEPH will demonstrate no obvious pulmonary arterial filling defects, and it is solely the observation of reduced vessel caliber and distal occlusions, which suggests the diagnosis. This is particularly true in patients with prior splenectomy, who often only have isolated segmental and subsegmental disease (**Fig. 5**A–C). The presence of splenectomy in a patient being evaluated for CTEPH should prompt scrutiny of subsegmental vessel caliber, even if no obvious defects are visible on initial review.

The presence of acute pulmonary embolism does not rule out concurrent chronic disease. Many patients with CTEPH have repeated acute pulmonary embolism events, and CT can reveal findings of acute, subacute, and CTED simultaneously (**Fig. 6**). Retrospective review of CTPA at the time of initial acute pulmonary embolism diagnosis in patients with CTEPH often shows evidence of chronic thromboembolism, which is a common reason for missed diagnoses.[3]

Compensatory bronchial artery hypertrophy is often seen in patients with CTEPH. These arteries most often arise from the aorta but can also arise from the great vessels, intercostal arteries, and occasionally the coronary arteries. Large bronchial arteries can lead to retrograde perfusion of the

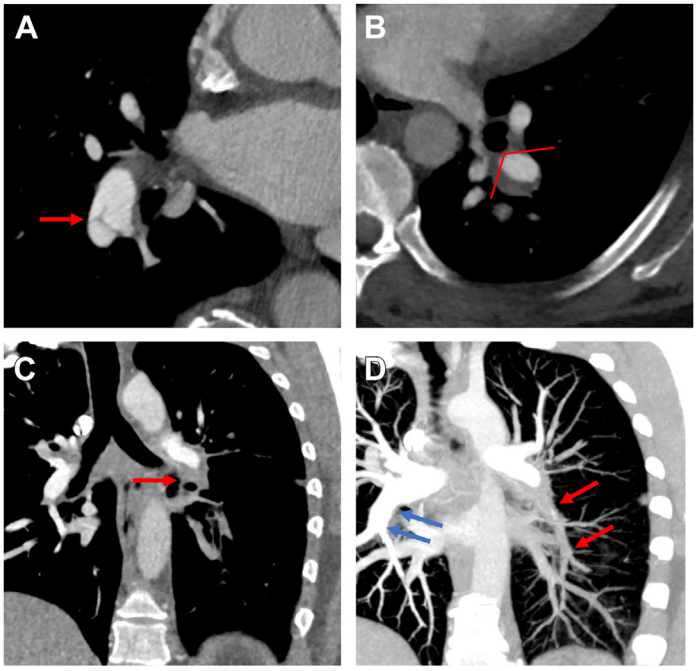

Fig. 2. Findings of CTEPD. (*A*) Axial CTPA image with multiple linear bands joining together to form a web in the right lower lobe basal trunk. (*B*) Axial CTPA image demonstrating eccentric thrombus with concave margin forming an obtuse angle with the vessel wall in the common trunk of the left lower lobe lateral and basal segmental arteries. (*C*) Coronal CTPA image demonstrating occlusive thrombus in the left descending pulmonary artery with concave margin. (*D*) Corresponding maximum intensity projection (MIP) image demonstrates diminutive caliber of the downstream pulmonary arteries (*red arrows*) relative to the contralateral side (*blue arrows*).

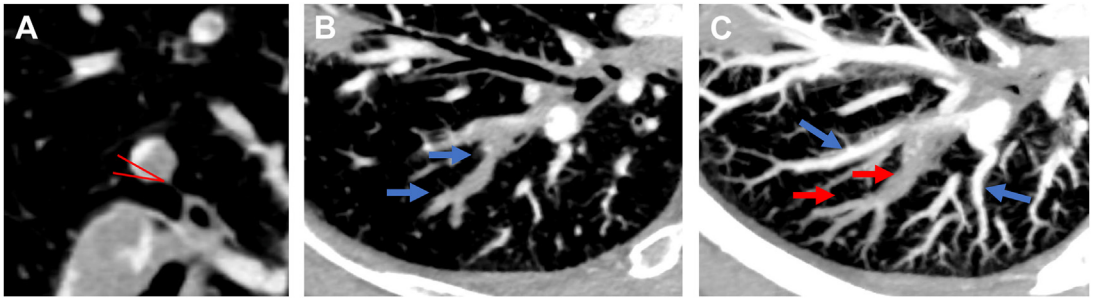

Fig. 3. Acute pulmonary embolism. (*A*) Acute pulmonary embolism has a convex margin, which forms an acute angle relative to the vessel wall. (*B*) In acute pulmonary embolism, the pulmonary artery is normal or increased in size. (*C*) Axial MIP image demonstrating enlarged caliber of the occluded pulmonary artery (*red arrows*) relative to adjacent patent subsegmental vessels (*blue arrows*).

pulmonary arteries, resulting in "smoke artifact" from unopacified blood if contrast does not sufficiently opacify the systemic arteries. The identification of large bronchial arteries is important because retrograde blood flow into the pulmonary arteries during cardiopulmonary bypass can obscure the surgical field during pulmonary thromboendarterectomy (PTE) surgery.[21]

Evaluation of the lung parenchyma can be useful to identify chronic thromboembolism. Mosaic perfusion is often pronounced in cases of CTEPH, and areas of hypoperfused lung can help direct attention to chronic thromboemboli in the corresponding pulmonary arteries (**Fig. 7**A, B). Even without dedicated iodine maps, mosaic perfusion can still be observed on single-energy CT images. Areas of normal or hyperperfusion may also be seen in regions without thromboembolic disease due to blood flow redistribution. Mosaic perfusion in CTEPD needs to be distinguished from mosaic perfusion due to small airways disease and hypoxic vasoconstriction. In such cases, the presence of large airways disease, as suggested by bronchial wall thickening or mucus plugging, along with the absence of thromboemboli, suggests airways disease as the cause of mosaic perfusion. However, bronchiectasis can occur with both CTEPH and airways disease, and its presence alone is not useful for differentiation. Mosaic perfusion is common in CTEPH, but in patients with CTEPD without pulmonary hypertension, it may be less conspicuous, particularly in nonobstructive cases. Finally, infarcts or peripheral scarring representing sequelae of infarcts are frequently observed in patients with CTEPH and an unexpected finding in patients with small airways disease.

Although right heart catheterization is required for a definitive CTEPH diagnosis, most patients with CTEPH will demonstrate CT evidence of pulmonary hypertension (**Fig. 8**A, B). According to the Fleischner Society, a PA diameter greater than 32 mm or a PA-to-aorta diameter ratio greater than 1 should raise suspicion for pulmonary hypertension in intermediate-risk patients, including those with a prior history of acute pulmonary embolism.[5] An increased ratio of right ventricle (RV) to left ventricle (LV) transverse diameter greater than 1 with flattening of the interventricular septum

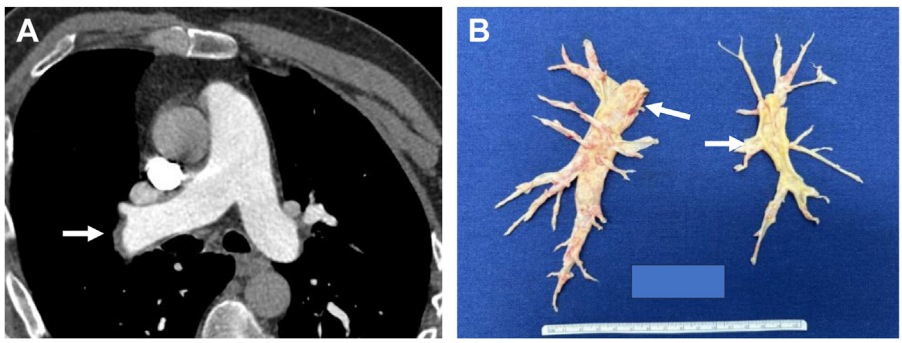

Fig. 4. Underestimation of disease extent on CTPA of a 72 year old man with CTEPH. (*A*) Preoperative CTPA demonstrated lining thrombus in the interlobar artery (*arrow*), but no conclusive disease in the main pulmonary arteries. (*B*) Surgical specimen following pulmonary thromboendarterectomy demonstrates lining thrombus in both main pulmonary arteries (*arrows*) in addition to the remainder of the pulmonary arterial tree.

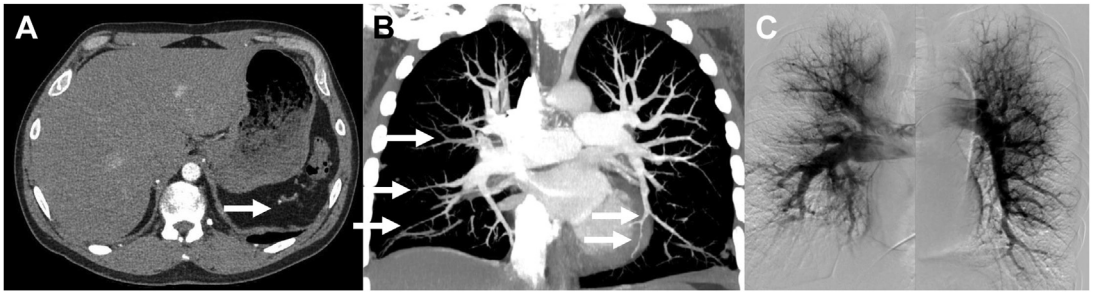

Fig. 5. Distal CTEPH in a 42 year old man with history of splenectomy in the setting of hereditary spherocytosis. (*A*) Axial image from CTPA through the upper abdomen demonstrates evidence of prior splenectomy. (*B*) Coronal MIP image demonstrates abnormal distal tapering of segmental and subsegmental pulmonary arteries, a typical pattern seen in postsplenectomy patients. (*C*) Anteroposterior images from digital subtraction angiography catheter angiography confirm evidence of segmental and subsegmental disease.

also suggests elevated right heart pressure. Thus, the finding of an elevated RV:LV ratio in a patient with acute pulmonary embolism can be equivocal for acute right heart strain in patients with underlying pulmonary hypertension. Right ventricular hypertrophy may be helpful for suggesting long-standing pulmonary hypertension, but the assessment can be difficult on a non-ECG-gated CT. Additionally, comparing current imaging with prior studies can also help determine chronicity of RV enlargement.

Preoperative Imaging

The first-line treatment of CTEPH is PTE. Suction thrombectomy is ineffective and potentially dangerous for chronic thromboembolism due to the strong adhesion of clots to the vessel wall. PTE involves removing the intimal lining of the pulmonary arteries along with the organized clot by dissecting along a plane in the media layer of the vessel wall. At experienced centers, it is possible to even remove disease at the subsegmental level through PTE, but expertise varies between institutions. Balloon pulmonary angioplasty (BPA) is a catheter-based technique used for patients who are not surgical candidates for PTE. BPA dilates stenotic or occluded vessels and may sometimes be combined with PTE. Finally, medical therapy employs various types of vasodilators, usually acting on smooth muscle cells, to alleviate pulmonary hypertension. Currently, riociguat is the only FDA-approved medication for inoperable or recurrent CTEPH, but medical therapy can be used in conjunction with PTE or BPA.

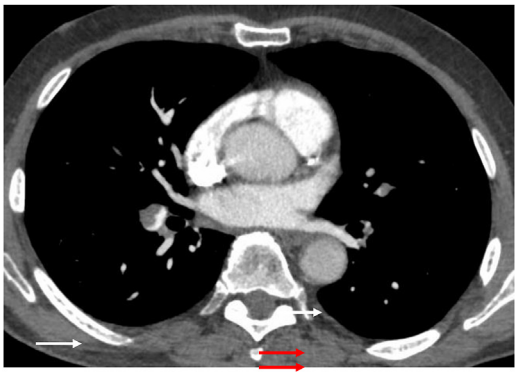

Fig. 6. Acute on chronic pulmonary embolism in a 73 year old man with acute dyspnea. Acute pulmonary embolism is present in the right lower lobe basal trunk and the inferior lingular pulmonary artery (*white arrows*). Note the convex borders of the right lower lobar pulmonary embolism and the expansile filling defect in the inferior lingular artery. The proximal left lower lobe segmental arteries (*red arrows*) are diminutive and contain webs, compatible with chronic thromboembolism.

In addition to identifying CTEPH, radiologists can contribute to preprocedural planning through surgical classification. The University of California, San Diego (UCSD) surgical classification system assigns levels of disease based on the location of the most proximal thrombus in the right and left pulmonary arteries.[22] Level 1 involves the main pulmonary arteries, level 2 involves the lobar arteries, level 3 involves the segmental arteries, and level 4 involves the subsegmental arteries. Levels are assigned to both left and right sides. All levels of disease, including level 4 disease, can potentially be treated surgically at expert centers, but local surgical expertise, patient comorbidities, and degree of pulmonary hypertension may influence whether a patient is deemed operable. BPA is generally considered more suitable for level 3 and 4 disease.[23] Although CT can underestimate the extent of disease, it remains essential for determining surgical candidacy. Radiologists should describe the most proximal level of disease, with the understanding that surgical staging may reveal additional disease.

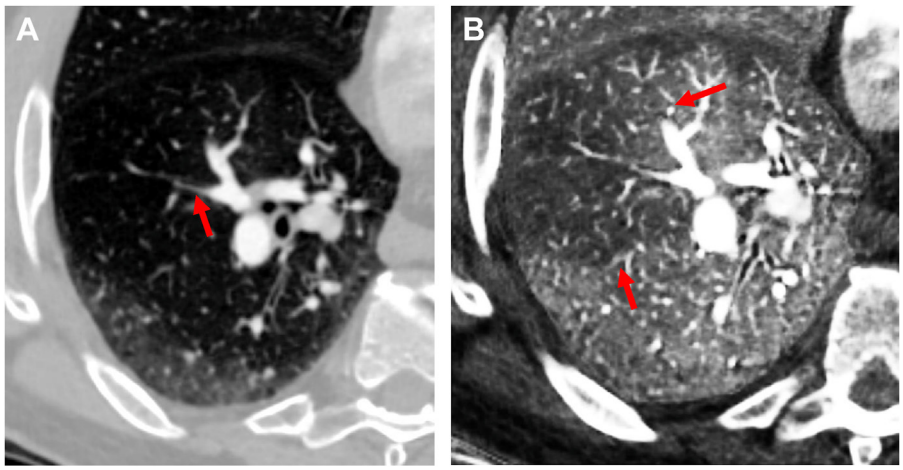

Fig. 7. Dual-energy CTPA of a 55 year old man with CTEPH. (*A*) Axial CTPA image demonstrates a diminutive subsegmental pulmonary artery in the right lower lobe anterior basal segment. (*B*) This abnormality is more apparent after observing a subsegmental perfusion defect on the corresponding iodine map, directing one's attention to the supplying pulmonary artery.

Additional findings on CT that may require concurrent repair during PTE include shunt lesions contributing to pulmonary hypertension, such as patent foramen ovale, atrial septal defect, or partial anomalous pulmonary venous return. Pulmonary hypertension can cause right-to-left flow through these lesions, resulting in an atypical appearance that may be easily missed. Chronic thrombus in the right atrium or ventricle should also be noted, as surgical removal may be required. This can be challenging to identify due to the mixing of opacified blood from the SVC and nonopacified blood from the inferior vena cava in the right atrium. Additionally, the presence of breast implants should be noted in patients undergoing minimally invasive PTE, as they may interfere with port placement. Finally, coronary artery disease, particularly in younger patients aged under 50 years, may prompt additional preoperative evaluation and possible revascularization.

Additional Modalities

Some institutions have explored the use of MR angiography for evaluating CTEPH, but its lower spatial resolution compared to CT reduces its sensitivity, particularly for detecting subsegmental disease.[24,25] However, MR offers several advantages, including the absence of ionizing radiation, the ability to assess pulmonary arterial flow, and detailed evaluation of the right ventricle.[26] MR perfusion techniques may perform similarly to

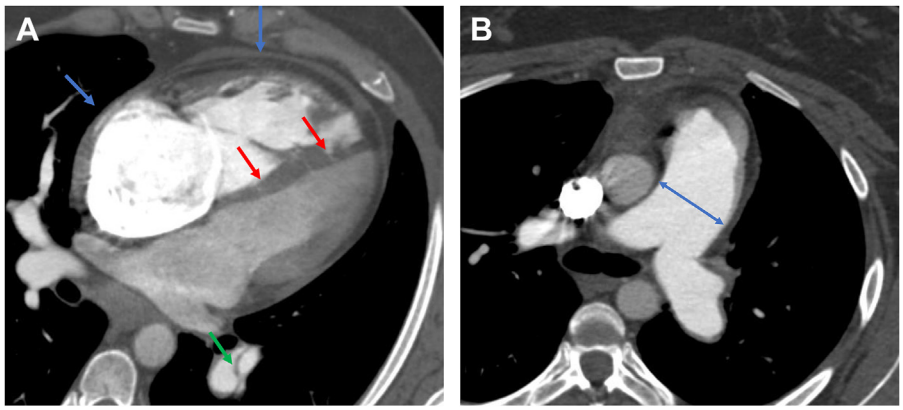

Fig. 8. CT findings of pulmonary hypertension. (*A*) Four chamber reformation from CT pulmonary angiogram demonstrates enlargement of the right atrium and right ventricle (*blue arrows*) with flattening of the interventricular septum (*red arrows*). The right ventricle is hypertrophied. Note the band in the left lower lobe basal trunk in this patient with CTEPH (*green arrow*). (*B*) Enlargement of the main pulmonary artery relative to the ascending aorta.

scintigraphy.[27] For now, MR imaging is generally considered an ancillary imaging modality rather than a primary one at most institutions, but its role may expand in the future.

Echocardiography, right heart catheterization, and catheter angiography are commonly performed in the CTEPH workup but are rarely interpreted by radiologists. Echocardiography remains the preferred noninvasive modality for the assessment of pulmonary hypertension in patients with persistent dyspnea following acute pulmonary embolism.[11] Right heart catheterization provides definitive hemodynamic characterization of pulmonary hypertension. Digital subtraction pulmonary angiography is commonly performed in the workup of CTEPH. In addition to demonstrating findings seen on CT such as pulmonary artery webs/bands, stenoses, and occlusions, it offers 2 key advantages: (1) it allows for better visualization of global vascular structure compared to CT pulmonary angiography, where overlapping pulmonary arteries and veins can make assessment challenging, and (2) it enables dynamic assessment of blood flow by showing vessel opacification over time.

DIAGNOSTIC CRITERIA

Diagnosis of CTEPH requires the identification of both CTEPD and pulmonary hypertension. CTEPD is typically identified through CT pulmonary angiography or catheter-based pulmonary angiography. While CT can suggest the presence of pulmonary hypertension, confirmation requires right heart catheterization. Pulmonary hypertension is defined as a mean pulmonary artery pressure greater than 20 mm Hg.[28] Patients with CTEPH specifically have precapillary hypertension, defined by a pulmonary artery wedge pressure of less than 15 mm Hg, and pulmonary vascular resistance of greater than 2 Wood units.

All CTEPH cases should be discussed by a multidisciplinary team consisting of pulmonologists, cardiothoracic surgeons, cardiologists, and radiologists to confirm the diagnosis and discuss treatment.[29,30] In some patients, CTEPD may contribute to pulmonary hypertension without being its primary cause, making it a less attractive target for treatment. In other cases, patients may have symptomatic CTEPD without resting pulmonary hypertension and could still benefit from treatment.

DIFFERENTIAL DIAGNOSIS

Conditions that can mimic CTEPH include acute pulmonary embolism, in situ thrombus, vasculitis, pulmonary artery sarcoma, and fibrosing mediastinitis. Acute pulmonary embolism was discussed earlier, and we will focus our discussion on the other entities. Although these conditions are relatively rare, it is important to recognize them, as their treatment differs significantly from that of CTEPH.

In Situ Thrombus

In situ thrombus refers to thrombus forming within the pulmonary arteries rather than embolizing from a deep vein. Similar to thrombus formation in other parts of the body, Virchow's triad of altered blood flow, endothelial injury, and hypercoagulability can lead to thrombus formation in the pulmonary arteries. For example, stump thrombus following pneumonectomy may result from endothelial injury and stasis of blood.

In the setting of CTEPH imaging, the most common differential consideration is pulmonary arterial hypertension with in situ thrombus, which can mimic CTEPH due to the presence of eccentric filling defects in the central pulmonary arteries (**Fig. 9**A–C).[31,32] However, extension of in situ thrombus into the segmental or subsegmental pulmonary arteries and vascular occlusions is rare, which typically distinguishes it from CTEPH. Additionally, in PAH, the "pruning" of pulmonary arteries tends to affect the entire arterial tree rather than specific areas corresponding to occluded vessels, a distinction often more evident when reviewing MIP images. Accordingly, mismatched defects on V/Q scan are generally smaller in patients with pulmonary arterial hypertension (PAH) and in situ thrombus, and hypoperfusion of the lung parenchyma generally involves smaller territories than those seen in CTEPH. Furthermore, PAH may demonstrate periarteriolar blushing,[33] which is atypical of CTEPH.

Other indirect findings can also help distinguish between PAH with in situ thrombus and CTEPH. Bronchial artery hypertrophy may be present in PAH but is generally less pronounced compared to CTEPH. Calcifications of the pulmonary arterial wall are uncommonly seen in CTEPH but occur in PAH due to significantly elevated pulmonary arterial pressure and development of atherosclerosis. However, calcification of thrombus itself is not useful for determining the underlying cause. Finally, infarcts and peripheral scarring are atypical in PAH.

Although in situ thrombus is more commonly seen in PAH, it can occur in any form of pulmonary hypertension (**Fig. 10**A, B), likely due to endothelial injury in the setting of high pressure. Interestingly, many patients with CTEPH have no history of deep vein thrombosis or acute pulmonary embolism,

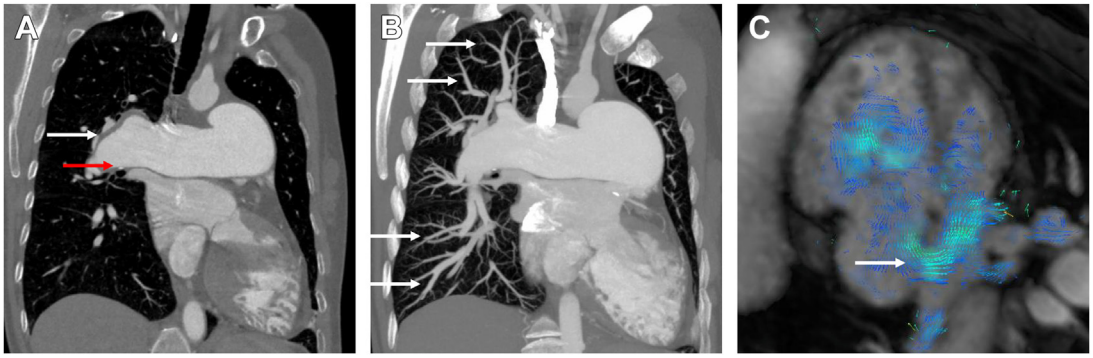

Fig. 9. A 43 year old man with in situ thrombus in the setting of unrepaired secundum atrial septal defect. (*A*) Coronal oblique image demonstrates massively dilated central pulmonary arteries. Lining thrombus is seen in the interlobar artery and proximal right upper lobe basal trunk (*white arrow*). Mural atherosclerotic calcification is present (*red arrow*), which is atypical of CTEPH. (*B*) Maximum intensity projection image from the same patient demonstrates patency of the distal segmental/subsegmental arteries, further confirming a non-CTEPH diagnosis. (*C*) A 4 chamber 4D flow MR image demonstrating marked enlarged of the right heart in keeping with pulmonary hypertension with right to left flow through the ASD in this still frame. Due to bidirectional flow, the pulmonary-to-systemic blood flow ratio (Qp/Qs) was 1.1.

suggesting that in situ thrombus could contribute to the pathophysiology of CTEPH.[34]

Pulmonary Artery Sarcoma

Intimal sarcoma of the pulmonary arteries is rare, but its imaging findings can overlap with those of CTEPH. Pulmonary artery sarcomas typically present as large filling defects in the central pulmonary arteries (**Fig. 11**A–C), with convex margins that often help distinguish them from chronic pulmonary embolism. Additional findings suggestive of a tumor include lung parenchymal or nodal metastatic disease, extravascular extension, or contrast enhancement.

However, there are cases where the imaging features of pulmonary artery sarcoma and CTEPH overlap. Pulmonary artery sarcomas may show concurrent bland thromboembolic disease, including occluded or diminished distal vessels and bronchial artery hypertrophy. While most central thrombus in CTEPH tends to be more peripheral, chronic or concurrent in situ thrombus can occasionally appear more space-occupying, complicating the differentiation.

PET-CT is reported to have a sensitivity of approximately 90%.[35] Alternatively, follow-up CT after 4 weeks may help identify enlarging filling defects, though care must be taken when assessing changes as bland thrombus may retract while tumor continues to grow. MR imaging may also be useful for identifying contrast enhancement, further aiding in the distinction between thrombus and tumor.

Vasculitis

Pulmonary arterial involvement of vasculitis has been described in large vessel vasculitis including Takayasu arteritis, giant cell arteritis, and Behçet disease (**Fig. 12**A–D). In most patients with

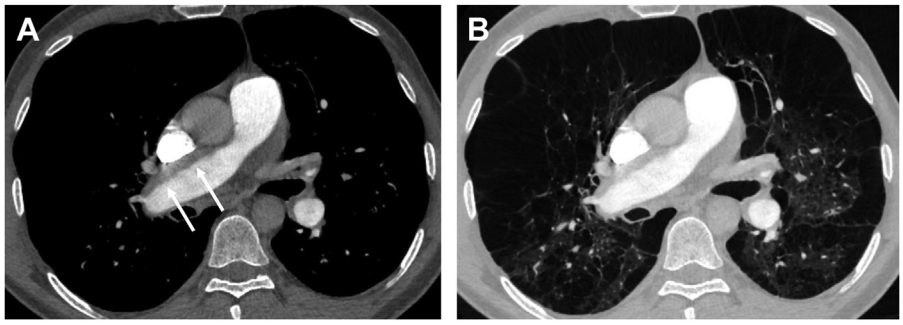

Fig. 10. A 55 year old man with in situ thrombus in the setting of smoking-related lung disease. (*A*) Axial CTPA image demonstrates lining thrombus of the right and interlobar pulmonary arteries. No thromboembolism was seen in segmental or subsegmental pulmonary arteries. (*B*) Corresponding lung windows demonstrate extensive centrilobular emphysema.

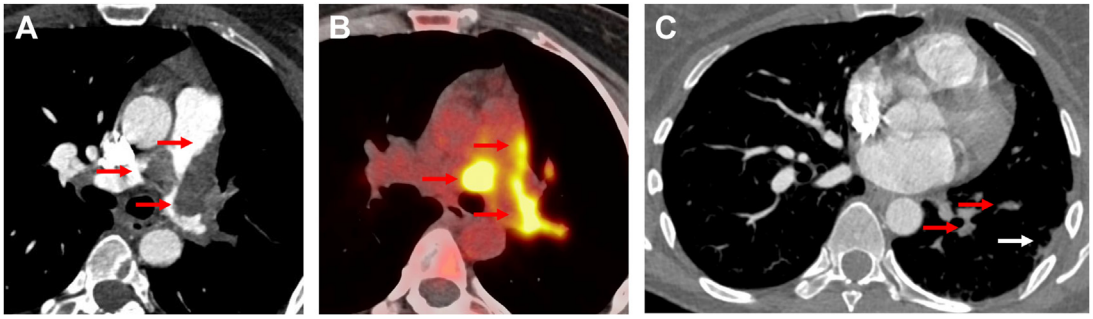

Fig. 11. A 43 year old woman with history of Lynch syndrome, dyspnea, and chest pain. (*A*) Axial oblique CTPA images demonstrate central pulmonary artery masses with convex margins which were initially interpreted as acute pulmonary embolism. (*B*) Subsequent PET-CT demonstrated heterogeneous fluorodeoxyglucose (FDG) uptake of the mass which may be due to admixed bland thrombus or non-FDG avid tumor. (*C*) Left lower lobe segmental arteries are occluded and diminutive (*red arrows*) relative to right-sided pulmonary arteries with associated infarct (*white arrow*), mimicking CTEPH. This may have been due to tumor, bland thrombus, or a combination of both.

Takayasu arteritis and giant cell arteritis, there will be concurrent evidence of systemic arterial involvement; however, in rare instances, pulmonary arterial involvement may occur in isolation. Overt wall thickening or enhancement is suggestive of arteritis, but other cases can mimic CTEPH with diminished vessel caliber and occluded distal pulmonary arteries. However, certain features can help distinguish vasculitis from CTEPH, such as the presence of "beading" in the pulmonary arteries, characterized by sequential stenosis and dilatation, which is atypical for CTEPH.

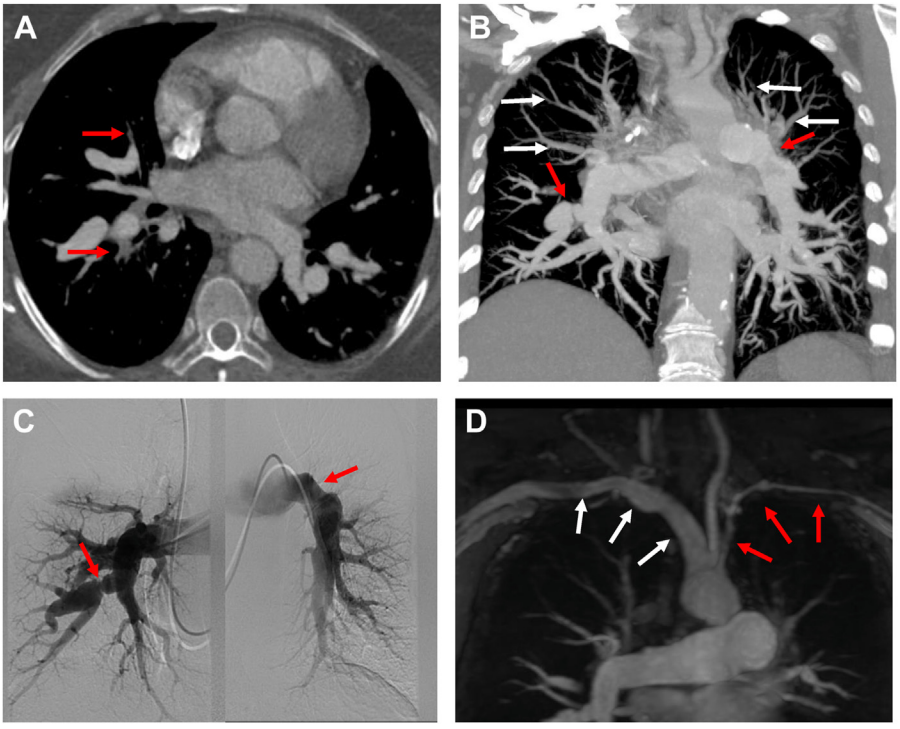

Fig. 12. A 59 year old woman with large vessel vasculitis. (*A*) Axial CT pulmonary angiogram image demonstrating diminutive medial segmental artery of the right middle lobe and proximal occlusion at the origin of the right lower lobe lateral and posterior basal segmental arteries (*arrows*). (*B*) Coronal oblique MIP image demonstrates unusual areas of vessel narrowing with beading of the anterior basal segmental artery of the right lower lobe and focal narrowing of the left descending pulmonary artery (*red arrows*). The upper lobe pulmonary arteries are occluded. These findings and distribution would be atypical of CTEPH and are more suggestive of vasculitis. (*C*) Digital subtraction angiography confirmed CT findings with redemonstrated areas of focal narrowing (*arrows*) and occluded upper lobe pulmonary arteries. (*D*) Subsequent MRA demonstrates segmental narrowing of the left axillosubclavian artery (*red arrows*) relative to the right axillosubclavian artery (*white arrows*).

Additionally, CTEPH shows greater involvement of the pulmonary arteries in the lower lobes, so predominant upper lobe involvement should raise suspicion for an alternative diagnosis.

Hughes–Stovin syndrome, which may represent a limited form of Behçet disease, is marked by focal pulmonary artery aneurysms or pseudoaneurysms. These aneurysms are usually more localized compared to the generalized arterial abnormalities seen in vasculitis affecting larger segments. Pulmonary artery aneurysms with lining thrombus are also uncommon in CTEPH.

Fibrosing Mediastinitis

Fibrosing mediastinitis is due to an exaggerated immune response to an antigen, most commonly from *Histoplasma capsulatum*. It is usually easy to distinguish from CTEPH, as pulmonary artery occlusions in fibrosing mediastinitis result from extrinsic compression by a mediastinal mass, rather than an intravascular process. Calcifications within the mediastinal mass are suggestive of a granulomatous origin, and splenic calcifications are often present.

Fibrosing mediastinitis more commonly affects the pulmonary veins, whereas CTEPH exclusively involves the pulmonary arteries. The distribution of pulmonary artery involvement in fibrosing mediastinitis can also differ from CTEPH. While CTEPH typically presents with bilateral, lower lung-predominant disease, fibrosing mediastinitis may show upper lobe predominance or unilateral involvement.

SUMMARY

CTEPH is an underdiagnosed but treatable condition, and radiologists play a critical role in improving patient care by recognizing CTED, particularly on CTPA. While chronic and acute pulmonary embolism have different imaging characteristics, distinguishing between the two can be challenging, especially when they coexist. Accurate imaging-based classification of CTEPH and identification of any additional pathology requiring surgical intervention are crucial in preoperative evaluation. Lastly, CTEPH has several mimics, but these conditions usually have distinct imaging features that help differentiate them.

CLINICS CARE POINTS

- The first-line screening for CTEPH is currently a V/Q scan, with SPECT-CT preferred when available.
- CT pulmonary angiography (CTPA) can be highly sensitive for detecting CTEPH, but the diagnosis is frequently missed by radiologists.
- Imaging findings of CTEPD differ from those of acute pulmonary embolism, though both chronic and acute disease may coexist on CTPA.
- Hypoperfusion can help pinpoint areas of CTEPD, a process that may be enhanced by spectral imaging techniques.
- Preoperative imaging aims to assess the extent of disease and identify other factors that could impact treatment decisions.
- Conditions that can mimic CTEPH include acute pulmonary embolism, in situ thrombus, pulmonary artery sarcoma, vasculitis, and fibrosing mediastinitis.

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