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Multidisciplinary Approach to Chronic Thromboembolic Pulmonary Hypertension: Role of Radiologists

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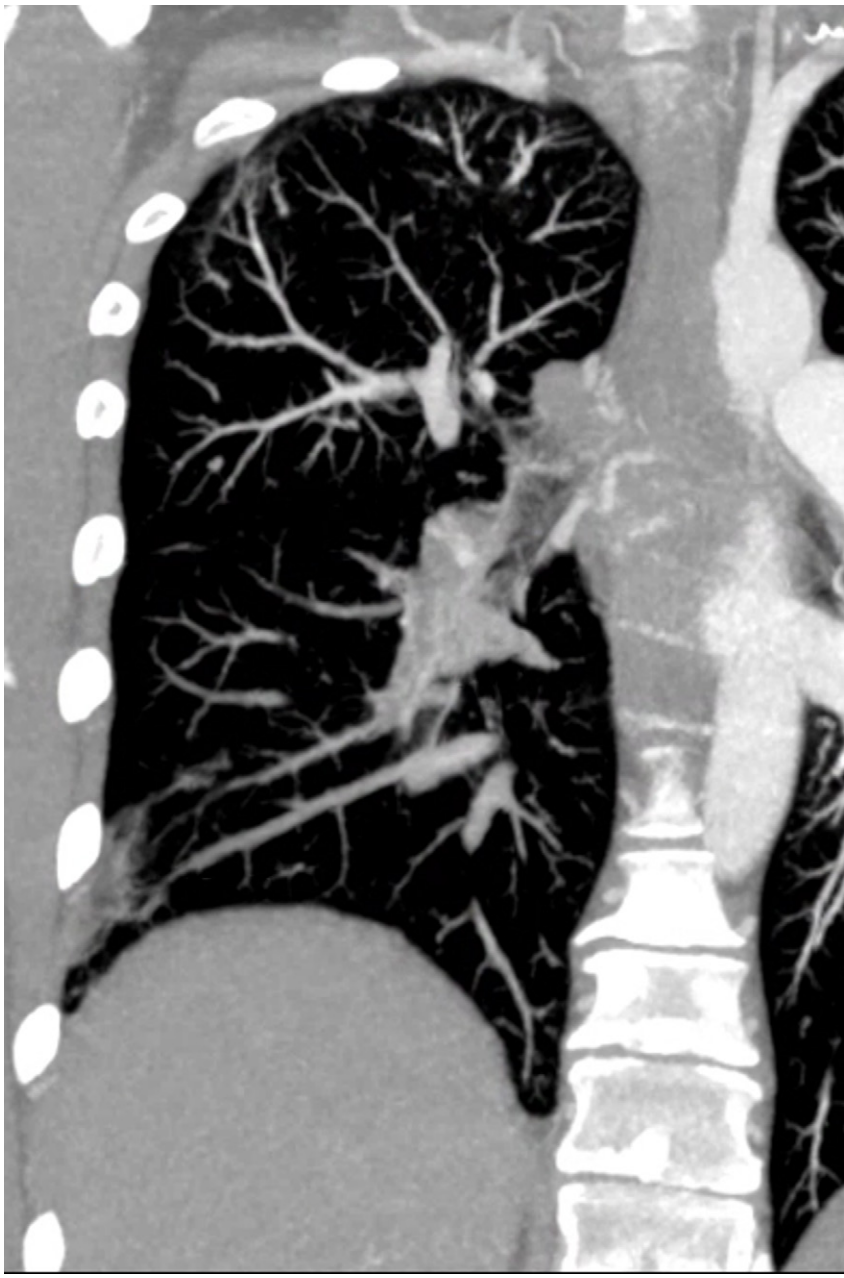
Management of chronic thromboembolic pulmonary hypertension (CTEPH) should be determined by a multidisciplinary team, ideally at a specialized CTEPH referral center. Radiologists contribute to this multidisciplinary process by helping to confirm the diagnosis of CTEPH and delineating the extent of disease, both of which help determine a treatment decision. Preoperative assessment of CTEPH usually employs multiple imaging modalities, including ventilation-perfusion (V/Q) scanning, echocardiography, CT pulmonary angiography (CTPA), and right heart catheterization with pulmonary angiography. Accurate diagnosis or exclusion of CTEPH at imaging is imperative, as this remains the only form of pulmonary hypertension that is curative with surgery. Unfortunately, CTEPH is often misdiagnosed at CTPA, which can be due to technical factors, patient-related factors, radiologist-related factors, as well as a host of disease mimics including acute pulmonary embolism, in situ thrombus, vasculitis, pulmonary artery sarcoma, and fibrosing mediastinitis. Although V/Q scanning is thought to be substantially more sensitive for CTEPH compared with CTPA, this is likely due to lack of recognition of CTEPH findings rather than a modality limitation. Preoperative evaluation for pulmonary thromboendarterectomy (PTE) includes assessment of technical operability and surgical risk stratification. While the definitive therapy for CTEPH is PTE, other minimally invasive or noninvasive therapies also lead to clinical improvements including greater survival. Complications of PTE that can be identified at postoperative imaging include infection, reperfusion edema or injury, pulmonary hemorrhage, pericardial effusion or hemopericardium, and rethrombosis.



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Abbreviations: BPA = balloon pulmonary angioplasty, CTEPD = chronic thromboembolic pulmonary disease, CTEPH = chronic thromboembolic pulmonary hypertension, CTPA = CT pulmonary angiography, DSPA = digital subtraction pulmonary angiography, MIP = maximum intensity projection, PAH = pulmonary arterial hypertension, PTE = pulmonary thromboendarterectomy, V/Q = ventilation-perfusion

TEACHING POINTS

- Although V/Q scanning is thought to be substantially more sensitive for CTEPH compared with CTPA, this is likely due to lack of recognition of CTEPH findings rather than a modality limitation.
- The diagnosis of CTEPH is commonly missed at CTPA, which can be the result of technical, patient-related, or radiologist-related factors.
- Mimics of CTEPH include acute pulmonary embolism, in situ thrombus, vasculitis, pulmonary artery sarcoma, and fibrosing mediastinitis.
- Preoperative evaluation for PTE includes assessment of technical operability and surgical risk stratification.
- Complications of PTE in the perioperative period include hypoxemia due to V/Q mismatch or reperfusion pulmonary edema, hemorrhage, pericardial effusion or hemopericardium, infection, and death.

Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) is the long-term result of organized thromboembolic material obstructing the pulmonary arteries. While the true prevalence of CTEPH has not been firmly established, it is clearly underdiagnosed, likely owing to its nonspecific symptoms and limited disease awareness (1,2). The rate of CTEPH after acute pulmonary embolism has been estimated to be 1%–5% (1–3). Based on this, an epidemiologic projection suggests that the incidence may exceed 15 000 per year in the United States, with less than 30% actually diagnosed (4). While relatively rare, CTEPH has the important distinction of being the only surgically curable form of pulmonary hypertension. Owing to advances in surgical technique, even distal disease in segmental and subsegmental pulmonary arteries is now routinely treated at high-volume centers (5).

CTEPH guidelines and consensus statements recommend patient evaluation at referral centers (6,7). The goal is to have each case of CTEPH addressed by a multidisciplinary team consisting of pulmonologists, cardiothoracic surgeons, cardiologists, and radiologists with expertise in the field. The contribution of radiologists in this process is integral, given that both ventilation-perfusion (V/Q) scintigraphy and CT pulmonary angiography (CTPA) are fundamental components of the initial workup. This includes verification of findings consistent with CTEPH at imaging, identification of potential alternative diagnoses, as well as quantifying the extent and topography of disease. Moreover, radiologists also help identify additional vascular, mediastinal, or lung parenchymal abnormalities that may affect treatment decisions.

In this article, we discuss multidisciplinary preoperative imaging assessment of CTEPH with particular attention to CTPA, at which the diagnosis is frequently missed (8). As part of this discussion, we describe mimics of CTEPH. We also address treatment of CTEPH, including pulmonary thromboendarterectomy (PTE), balloon pulmonary angioplasty (BPA), and medical therapy, as well as imaging of complications after PTE and BPA.

Terminology

There is variability in the literature on the nomenclature for CTEPH. Current guidelines from the European Respiratory Society use the term *chronic thromboembolic pulmonary disease* (CTEPD) to describe patients with chronic thromboembolism, with or without pulmonary hypertension at rest (5). The term *chronic thromboembolic pulmonary hypertension* is used for patients with CTEPD and pulmonary hypertension at rest. However, some still use the term *chronic thromboembolic disease* to refer to patients with chronic thromboembolism without pulmonary hypertension.

Preoperative Imaging of CTEPH

Echocardiography

Echocardiography has been suggested as the screening examination for pulmonary hypertension in patients with a history of acute pulmonary embolism and persistent dyspnea after 3–6 months of effective anticoagulation (9). In addition to providing qualitative information on both the right and left heart, echocardiography can be used to assess the probability of pulmonary hypertension (primarily based on the tricuspid regurgitant jet peak velocity) and prompt further workup for moderate- to high-probability cases (6). However, this finding is not specific for CTEPH and may result in exclusion of patients with symptomatic CTEPD without pulmonary hypertension who may benefit from surgical treatment (5).

Hence, performing V/Q scanning in addition to echocardiography is recommended in persistently symptomatic patients despite 3 months of anticoagulation after an acute pulmonary embolism (10) (Fig E1). In the preoperative setting, echocardiography also enables assessment of valvular regurgitation or shunts (using contrast material), such as a patent foramen ovale, which may require repair during surgery (11). Moderate to severe tricuspid regurgitation is often present in the setting of an enlarged right ventricle, but this usually resolves owing to postoperative remodeling of the right ventricle (11,12).

V/Q Scanning

Along with echocardiography, V/Q scanning is the initial imaging modality recommended for evaluation of patients with suspected CTEPH (Fig E1). Given its sensitivity of 96%–97% and specificity of 90%–95% (13), V/Q scanning with normal results allows exclusion of the diagnosis of CTEPH in most instances (14). Most cases of CTEPH demonstrate a moderate mismatched perfusion defect (25%–75% of a bronchopulmonary segment) or a large mismatched perfusion defect (>75%) (Fig 1A). However, since perfusion defects relate to occlusive disease, the degree of obstruction can be underestimated with V/Q scanning in the setting of nonocclusive chronic thromboembolic disease (15).

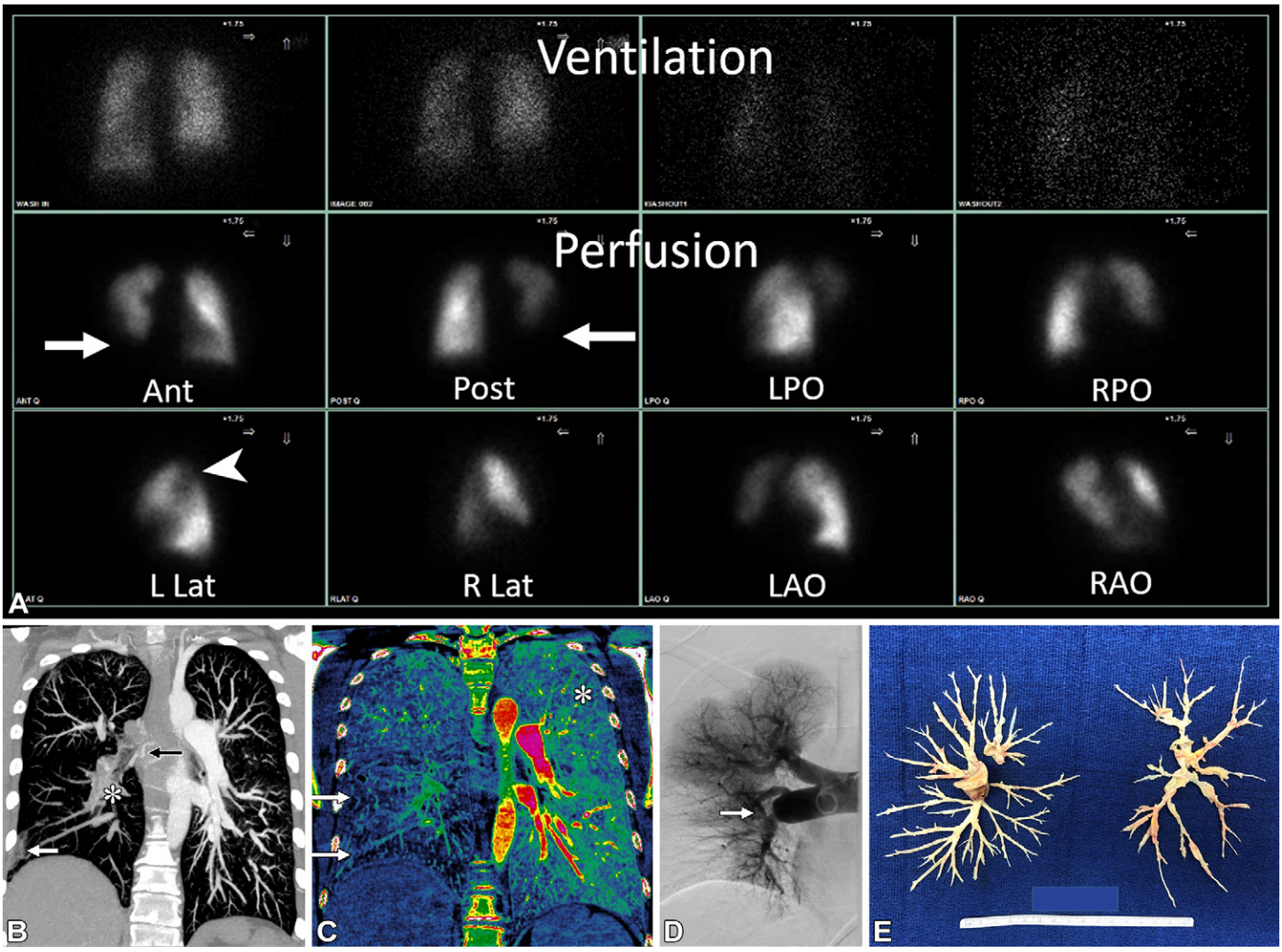


Figure 1. Multimodality imaging of a 32-year-old woman with CTEPH. **(A)** Images from V/Q scanning show large mismatched perfusion defects bilaterally, including absent perfusion to the right lower lobe (arrows) and a large apicoposterior left upper lobe defect (arrowhead). Ventilation (top row) is preserved. *ANT* = anterior, *LAO* = left anterior oblique, *L Lat* = left lateral, *LPO* = left posterior oblique, *Post* = posterior, *RAO* = right anterior oblique, *R Lat* = right lateral, *RPO* = right posterior oblique. **(B)** Coronal 5-mm-thick maximum intensity projection (MIP) image from CTPA shows occlusive thrombus (*) in the basal trunk pulmonary artery of the right lower lobe and diminutive pulmonary arteries distally. Note the subpleural opacity (white arrow) in the right lower lobe, representing scar from a prior infarct, and conspicuous bronchial artery hypertrophy (black arrow). **(C)** Coronal iodine map from dual-energy CT shows absent perfusion to the right lower lobe (arrows) and reduced perfusion in the left upper lobe (*). **(D)** Image from catheter angiography shows markedly reduced perfusion to the right lower and middle lobes with a pouch defect (arrow) in the right lower lobe basal trunk. Given the imaging evidence of disease beginning at the lobar pulmonary arteries (University of California San Diego classification level 2) and the absence of significant comorbidities or lung parenchymal abnormalities, the patient underwent PTE. **(E)** Photograph shows the PTE specimens.

Numerous other pathologic conditions can lead to vascular obstruction with preserved airflow and are discussed in the section on mimics of CTEPH. If both ventilation and perfusion mismatches are observed, further evaluation with anatomic imaging is necessary to determine the full extent of disease, assess for abnormalities of the lung parenchyma, or identify CTEPH mimics that could be a contraindication to surgery. As a tomographic technique, V/Q SPECT circumvents potential pitfalls of planar imaging related to overlap of pulmonary segments, shine-through from adjacent lung, and difficulties in assessing defect size. In CTEPH imaging specifically, V/Q SPECT has shown improved sensitivity relative to planar imaging and is preferred at many institutions (5,16–18).

CT Pulmonary Angiography

CTPA is an essential part of the workup in CTEPH patients. After V/Q scanning, CTPA allows confirmation of the diagnosis while excluding mimics. If CTEPH is confirmed, CTPA is used to identify the extent of disease in addition to other factors that would influence surgical assessment, such as lung parenchymal disease. At CTEPH referral centers, CTPA may need to be repeated if outside CTPA results are suboptimal. Our institutional protocol is non–electrocardiographically gated dual-energy CTPA reconstructed into 0.625-mm sections with three-plane postprocessed colorized iodine maps reconstructed at a thickness of 12 mm and three-plane maximum intensity projection (MIP) reconstructed at a thickness of 7–10 mm.

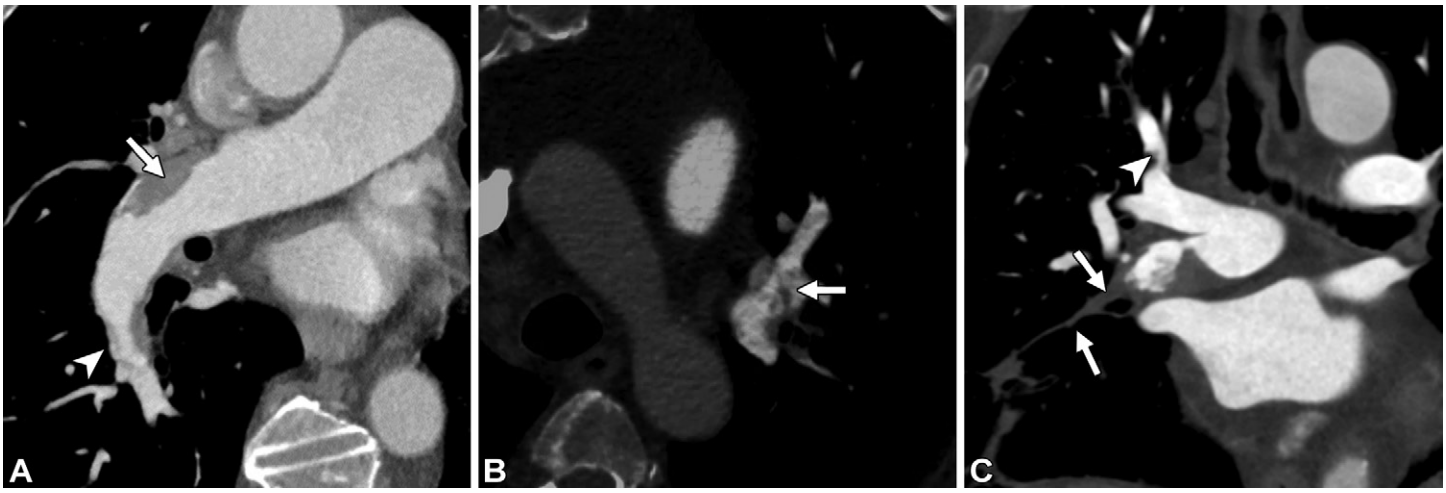


Figure 2. Common findings in CTEPD. **(A)** Axial oblique CT image shows a nonocclusive linear band (arrowhead) in the right lower lobe superior segment pulmonary artery branch. In addition, there is a larger focus of adherent thrombus (arrow) in the interlobar pulmonary artery. Even though these lesions are nonocclusive, they still cause impairment of blood flow, which can lead to increased pulmonary pressures. **(B)** Axial CT image through the left upper lobe anterior segment shows numerous interweaving bands of chronic clot (arrow), creating a web. **(C)** Coronal oblique CT image shows a chronic occlusive thrombus (arrows), which leads to vascular contraction and obliteration. Compared with acute pulmonary embolism, where thrombus leads to vascular dilatation, in chronic disease vessels rapidly taper and may seem to disappear. Also note the waistlike narrowing (arrowhead) in the apical segmental artery of the right upper lobe.

Diagnosis of CTEPH requires identification of both CTEPD and pulmonary hypertension. CTEPD can be occlusive or nonocclusive. Nonocclusive thrombi can appear as linear filling defects that create bands across the pulmonary arteries, which often intertwine to form webs, or as eccentric thrombi forming an obtuse vessel wall margin (19) that may taper into occlusive thrombi more distally (Fig 2). Occlusive chronic thrombus obstructs the vessel lumen and leads to vascular contraction, in contrast to acute thrombus, which distends the vessel.

In some instances, ostial occlusion of a vessel with distal contraction can be missed at CTPA, as the vessel appears absent. Use of lung windows to identify mosaicism or hypoperfusion and the expected location of pulmonary arteries, based on the accompanying bronchus, may assist in identification of such arteries. MIP images can be helpful for identification of abnormal vessel tapering and enlarged bronchial arteries.

Many CTEPH cases involve the central vasculature, but other cases are isolated to the segmental or subsegmental vasculature. This distribution of disease can make subtle findings even more inconspicuous, particularly with a large section thickness. However, correct identification is essential, as patients with isolated segmental or subsegmental disease remain surgical candidates at referral centers (5). This can be facilitated by use of a section thickness no greater than 1 mm.

It is also important to note that some patients with CTEPH may have hypercoagulable states that lead to repeated episodes of thromboembolism even with therapeutic anticoagulation. Therefore, the presence of acute pulmonary embolism should not exclude CTEPD (Fig 3), and one should carefully examine the entire pulmonary vasculature for signs of coexistent chronic disease.

Patients with CTEPH may demonstrate findings of pulmonary hypertension at CT. On axial images, evidence of elevated right heart pressure includes a right ventricle–to–left ventricle transverse diameter ratio of greater than 1 (Fig E2), often with flattening of the interventricular septum (20). When septal flattening or right ventricle–to–left ventricle diameter ratio is equivocal on axial images, it can be useful to reformat CT images in a cardiac short-axis plane or four-chamber plane. While right heart strain can occur in acute pulmonary embolism, development of right ventricular hypertrophy requires long-standing pulmonary hypertension (21). Right atrial dilatation coexists in many patients with CTEPH (12) owing to both elevated right heart pressures as well as functional tricuspid regurgitation due to right ventricular dilatation.

Additional findings of pulmonary hypertension are described in Table E1 (22–24). When findings of pulmonary hypertension are combined with evidence of chronic thrombus, the diagnosis of CTEPH can be suggested. However, hemodynamic evaluation with right heart catheterization is required to confirm the diagnosis and may help with management decisions.

The diagnosis of CTEPH can be supported by lung parenchymal findings. A pattern of mosaic attenuation with well-defined areas of lobar, segmental, or subsegmental hypoattenuation due to proximal occlusion is common (Fig 4). In many instances, this can help confirm the presence of distal disease when occlusion is questionable owing to limitations in spatial resolution or respiratory motion. A similar pattern of mosaicism can occur in patients with small airways disease (SAD) owing to hypoxic vasoconstriction, although there are ways to differentiate the two (25). Specifically, patients with mosaicism due to SAD often demonstrate large airway wall thickening in areas of hypoattenuation, a finding less commonly demonstrated in CTEPH.

Bronchiectasis has been reported in both CTEPH and SAD and in itself does not allow clear distinction between the two (26,27). While areas of mosaicism in SAD can involve larger subsegmental, segmental, or lobar territories,

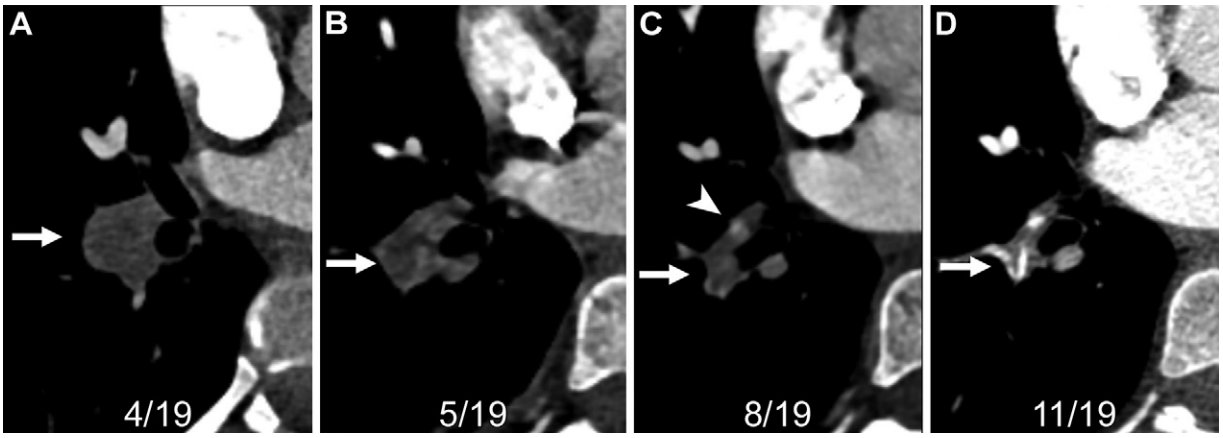


Figure 3. Evolution of thrombus from acute to chronic on axial images from CTPA in a 44-year-old woman. **(A)** Image from the initial CT study in April 2019—when the patient presented to the emergency department with chest pain—shows an expansile thrombus (arrow) in the right lower lobe basal trunk. The patient started anticoagulation therapy and underwent repeat CTPA owing to a repeat episode of chest pain; the repeat CTPA showed no acute pulmonary embolism. **(B)** Image from the repeat CTPA in May 2019 shows reduced extent and contraction of the thrombus (arrow). Follow-up CTPA was performed owing to continued symptoms. **(C)** Image from the follow-up CTPA in August 2019 shows further contraction and organization of the thrombus (arrow) with early recanalization (arrowhead). Note that the caliber of the pulmonary artery itself has also decreased. **(D)** Image from follow-up CTPA in November 2019 shows further recanalization (arrow) of the chronic thrombus.

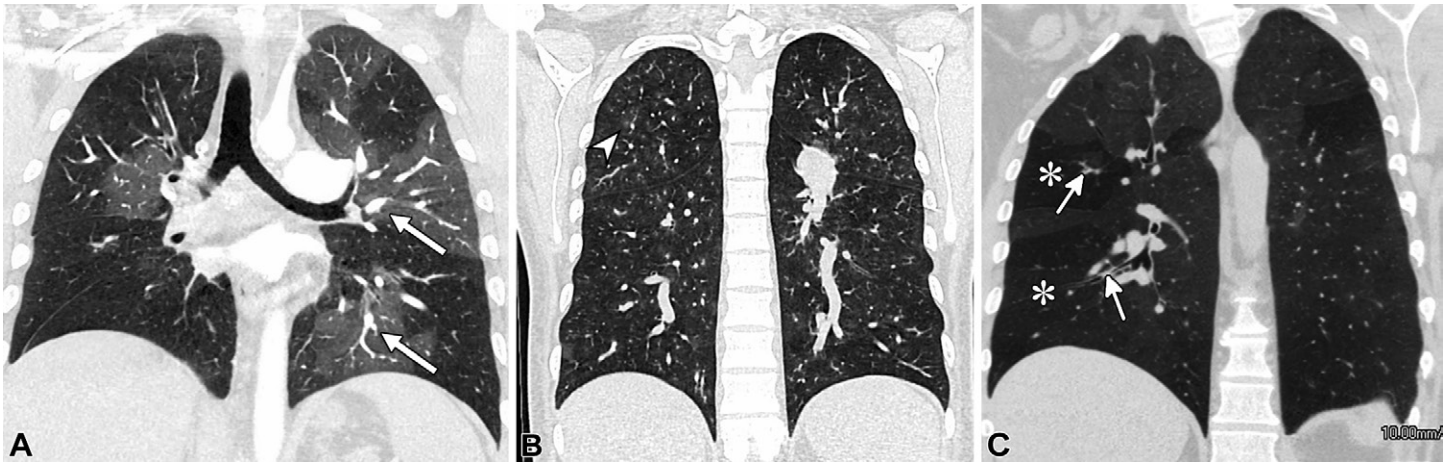


Figure 4. Comparison of patterns of mosaic attenuation in CTEPH, pulmonary arterial hypertension (PAH), and SAD on coronal CT images. **(A)** In CTEPH, well-defined geographic regions of hypoattenuation correspond to proximally obstructed pulmonary artery branches. The geographic mosaicism may be enhanced by juxtaposition of hyperperfused regions of lung containing engorged pulmonary arteries (arrows) next to lucent lung with decreased size of vasculature due to proximal obstruction. **(B)** By contrast, the boundaries of mosaic attenuation in PAH are less well defined, and upstream vascular occlusion is absent. Peri-arteriolar ground-glass opacities (arrowhead) are common and have been attributed to various entities, including cholesterol granulomas, periarteriolar hemorrhage, and plexiform arteriopathy. **(C)** In SAD, there is often accompanying evidence of large airways disease, such as bronchial wall thickening, bronchiectasis, and/or endobronchial mucus plugging (arrows). Areas of hyperlucent lung (*) are related to hypoxic vasoconstriction.

they often involve varying lobules not corresponding to vascular territories. Moreover, CTEPH cases may exhibit areas of subsegmental and segmental hyperperfusion with engorged pulmonary vasculature in areas free of chronic clot. Cardiac and pulmonary arterial findings of pulmonary hypertension, while sometimes prominent, are often absent or less conspicuous in SAD compared with in CTEPH. Lastly, patients with CTEPH may demonstrate peripheral scarring related to prior infarction, which is not characteristic of SAD (Fig 1B).

Collateral circulation develops in CTEPH, likely owing to elevated vascular resistance and blood flow obstructions. Therefore, it is common to encounter enlarged and tortuous bronchial artery collaterals coursing through the mediastinum into the hila in regions of corresponding obstruction (Fig 1B). Similarly, intercostal collaterals from the lung periphery and coronary artery collaterals may be visualized, although the latter are inconspicuous at CTPA (28) (Fig E3). Large bronchial collaterals may cause extensive retrograde blood flow into the pulmonary arteries after the patient begins cardiopulmonary bypass, reducing visibility of the surgical field during PTE and increasing operative difficulty (29).

Although V/Q scanning is thought to be substantially more sensitive for CTEPH compared with CTPA, this is likely due to lack of recognition of CTEPH findings rather than a modality limitation. An oft-cited early work that demonstrated superior sensitivity of V/Q scanning compared with CTPA was based on radiology reports rather than on evaluation of the images themselves (13). Findings

of CTEPH are often not recognized at CTPA likely owing to lack of awareness or ability to perceive subtle findings of CTEPH; however, adequate education, understanding, and use of a correct protocol including thin-section imaging can rectify this issue and dramatically increase sensitivity of CTPA for CTEPH.

In a recent study that reviewed outside imaging reports in patients with CTEPH, only 26% of outside radiologists made the correct diagnosis (8). When reviewed by expert radiologists explicitly for CTEPH, CTPA has been reported to have sensitivity of 88%–99% (26,30,31). Moreover, CT enables identification of alternative causes of perfusion deficits and lung parenchymal abnormalities, which is important for surgical assessment.

One strategy that may be superior to both V/Q scanning and CTPA is dual-energy CTPA, which can simultaneously provide a snapshot of perfusion while also allowing identification of direct evidence of thrombus (Fig 1C) (32). Dual-energy CTPA can improve detection of small subsegmental pulmonary emboli (33). While in some cases it may be difficult to distinguish between perfusion defects due to small airways disease (SAD) versus chronic thrombus, clues from evaluation of the pulmonary arteries and airways can be helpful, as discussed earlier for mosaic attenuation. Perfusion maps from dual-energy CTPA have sensitivity for CTEPH comparable to that of V/Q scanning using planar imaging (34,35).

The combination of anatomic and functional information enables comprehensive analysis of both proximal and distal vessels, unavailable from either technique alone. In addition, electrocardiographic gating can be added to the dual-energy technique, allowing evaluation of anatomic occlusions, pulmonary perfusion, coronary arteries, and right ventricular volumes or function. Hence, one study may provide comparable information to that of V/Q scanning, left heart catheterization, catheter-based pulmonary angiography, and echocardiography, excluding flow assessment. In select cases, such a study could reduce cost, radiation, and patient risk associated with redundant or invasive testing (Fig E4) (32) but would require clinical validation, high-quality results, and interpretation training.

MR Imaging

MR angiography has been studied in evaluation of CTEPH but is slightly less sensitive for findings of CTEPH than CTPA, particularly at the subsegmental level, owing to its lower spatial resolution (30,36). While this was a lesser issue in the early days of PTE, the current ability to intervene at a subsegmental level makes the resolution of MR angiography suboptimal for preoperative assessment.

However, MRI has the advantage of not requiring ionizing radiation while providing more complete assessment of right ventricular size and function and of pulmonary artery flow. This may be useful for monitoring changes in the postoperative period (37). MRI perfusion techniques have reported accuracy similar to that of perfusion scintigraphy in identifying patients with CTEPH (38). The role of MRI in CTEPH evaluation is currently in evolution and may expand in the future.

Right Heart Catheterization with Pulmonary Angiography

The standard of reference for hemodynamic and anatomic assessment in evaluation of CTEPH is right heart catheterization combined with digital subtraction pulmonary angiography (DSPA). Hemodynamic characterization of precapillary pulmonary hypertension, which includes CTEPH, is defined by a mean pulmonary artery pressure (mPAP) greater than 20 mm Hg, a pulmonary artery wedge pressure (PAWP) of less than or equal to 15 mm Hg, and a pulmonary vascular resistance (PVR) of greater than or equal to 240 dynes · sec · cm^{-5} or 3 Wood units (39,40). Similar to CTPA, DSPA enables visualization of pulmonary artery webs or bands, intimal irregularities, rapid narrowing, and complete obstruction (41). The latter is often described as a "pouch defect" (Fig 1D), in which thrombus organizes in a concave configuration, resulting in a perceived blind-ending pouch, although many such defects also demonstrate recanalized channels stemming from the pouch.

Of note, while the spatial resolution of DSPA is higher than that of CTPA and provides a cine view of vessels filling with contrast material over time, it may be limited by overlapping vessels. In some cases, left heart catheterization may also be performed concurrently with right heart catheterization on the basis of the cardiac risk profile. In the presence of flow-limiting disease, combined coronary artery bypass grafting and PTE can be performed (11).

Missed Diagnosis of CTEPH at CTPA

The diagnosis of CTEPH is commonly missed at CTPA, which can be the result of technical, patient-related, or radiologist-related factors (Fig 5).

Technical Factors

Technical factors overlap with those for diagnosing acute pulmonary embolism but are arguably even more essential for CTEPD, owing to the potential subtlety of findings. Inappropriate selection of peak kilovoltage (kVp) and tube current or a poorly timed contrast material bolus may make chronic thrombus difficult to visualize, particularly in large patients. While a large section reconstruction thickness can reduce image noise, the loss of spatial resolution can render thrombus inconspicuous or imperceptible.

In some cases, chronic thromboembolism may be mistakenly identified owing to "smoke," which is related to contrast-enhanced blood mixing with nonopacified blood coming from a bronchial collateral or stagnating in the setting of slow flow. Increasing contrast material volume, injection duration, and corresponding acquisition delay in the presence of known left heart or lung disease or when performing delayed phase imaging may be useful to distinguish smoke from true thromboembolism.

Patient-related Factors

CTEPD may also be missed or misinterpreted owing to factors related to the patient. Respiratory motion must be mitigated through clear instructions to the patient. Obesity, which occurs in nearly 50% of patients with CTEPH (42), can result in excessive image noise. Right heart failure due to long-standing

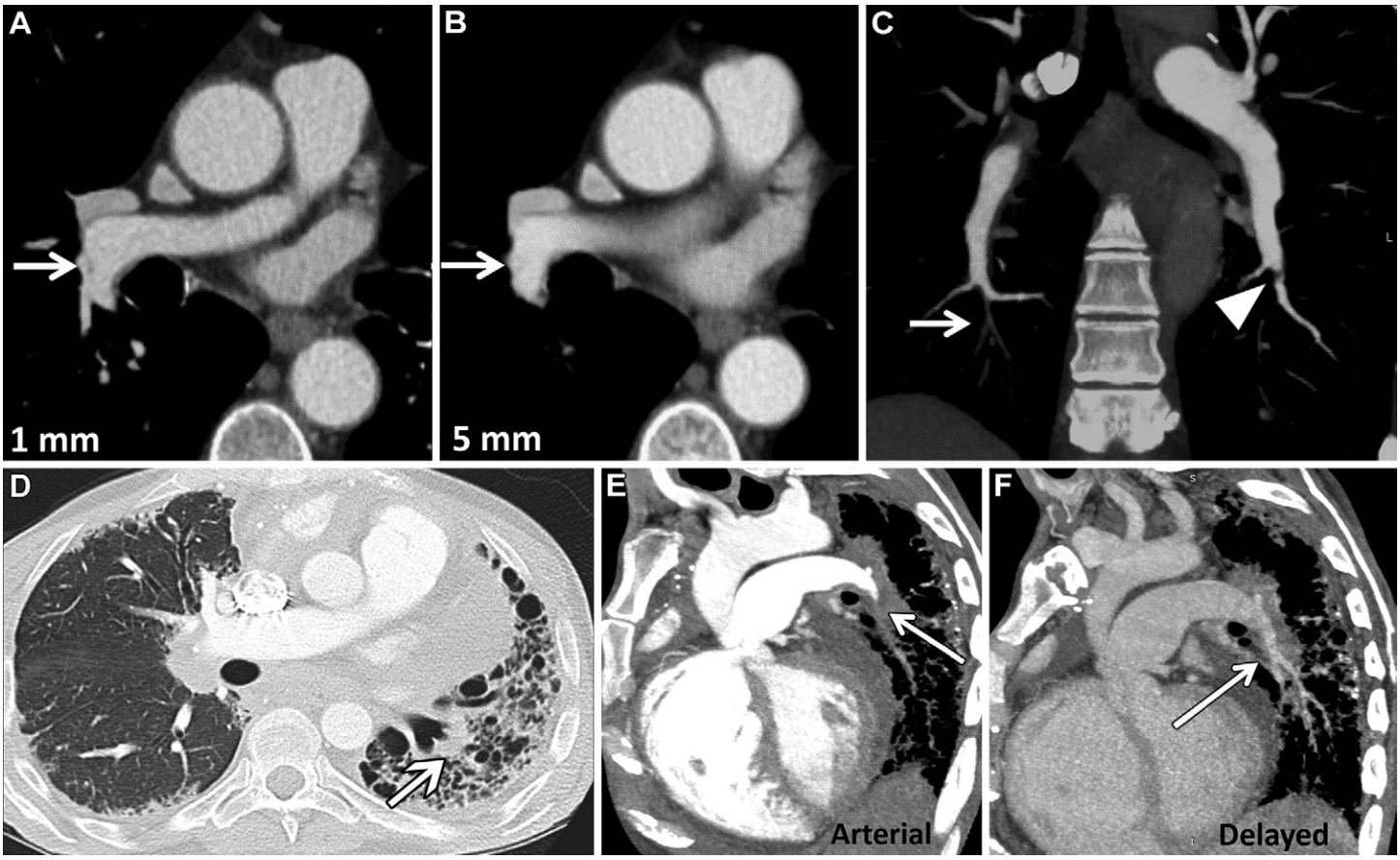


Figure 5. Reasons for misdiagnosis of CTEPD and CTEPH. **(A, B)** There are numerous technical factors that can lead to false-negative interpretations in patients with CTEPD. Axial CTPA image with 1-mm section thickness **(A)** shows a subtle band (arrow in **A**) in the right lower lobe. On an axial CTPA image with 5-mm section thickness **(B)**, the band (arrow in **B**) is invisible owing to partial volume averaging. Given the subtlety of the findings, we recommend using a section thickness of 1 mm or less to interpret these studies. **(C)** Isolated segmental and subsegmental disease in patients with CTEPH is common and may be missed owing to lack of radiologist knowledge of some of the subtle imaging findings. Coronal CTPA image shows extensive but inconspicuous occlusive (arrow) and nonocclusive (arrowhead) disease in the segmental and subsegmental vasculature, leading to severe pulmonary hypertension. However, the outside CT study was interpreted as normal. **(D–F)** In addition to disease being missed, disease can be overcalled in certain situations. Axial CT image of the lungs **(D)** shows asymmetric usual interstitial pneumonia (arrow in **D**). Sagittal CTPA image **(E)** shows lack of filling of the left lower lobe pulmonary artery branches (arrow in **E**), which was misinterpreted as chronic clot on multiple occasions. On review, this finding was recognized as likely being related to slow flow from pulmonary fibrosis. On the basis of this suspicion, the patient was brought back for repeat imaging, which was performed with a 60-second delay. Sagittal CTPA image **(F)** from repeat imaging with a 60-second delay shows that the pulmonary artery opacifies normally (arrow in **F**).

pulmonary hypertension or parenchymal fibrosis can lead to incomplete opacification of distal pulmonary arteries, mimicking pulmonary embolism.

Radiologist-related Factors

Finally, radiologists may simply miss the subtle findings of CTEPD or CTEPH owing to the rarity of the disease, lack of knowledge of the imaging findings, and ever-increasing study volumes. In many CTPA cases, radiologists prioritize identification of acute pulmonary embolism and either misinterpret chronic disease as acute or miss it altogether. Isolated disease involving the segmental or subsegmental vasculature in particular may be less conspicuous and easier to miss, especially in conjunction with a section thickness greater than 1 mm. In some cases, radiologists lack the experience or knowledge to discern the difference between acute thrombus and chronic thrombus, an educational gap that was recognized in a recent Fleischner Society statement (23). Finally, radiologists may also mistake mimics of CTEPH, such as in situ thrombus, for CTEPH.

Mimics of CTEPH in Imaging Studies

Mimics of CTEPH include acute pulmonary embolism, in situ thrombus, vasculitis, pulmonary artery sarcoma (PAS), and fibrosing mediastinitis (Table 1).

Acute Pulmonary Embolism

Acute pulmonary emboli are more likely to be located in the central portion of a pulmonary artery compared with chronic thromboembolism, which is more often eccentrically located (19). For acute pulmonary emboli in contact with a vessel wall, the angle formed by the opacified lumen between an eccentric acute pulmonary embolism and the pulmonary wall should be acute, whereas this angle is obtuse in chronic disease. The pulmonary artery containing an acute pulmonary embolism will be normal in size or expanded, differing from the contracted vessels in CTEPH secondary to clot organization and fibrosis (Fig 3).

A particular difficulty in CTEPH is that patients are prone to repeat thromboembolism, which can result in thrombus of variable ages. As noted earlier, other findings can be used to

Table 1: Distinguishing Imaging Findings of CTEPH Mimics at CTPA

CTEPH Mimic	Features More Suggestive of a CTEPH Mimic	Features More Suggestive of CTEPH or CTEPD
Acute PE	Filling defects at center of vessels Vessel expanded Acute margin between clot and PA wall Main PA does not dilate in response to acute PE nor does RV hypertrophy	Contracted vessels, webs, and bands Obtuse margin between clot and PA wall Main PA often dilated and RV is hypertrophied in CTEPH
In situ thrombus	Peripheral thrombus in a central PA without segmental or subsegmental disease PA wall calcifications Bronchial artery collaterals uncommon in PAH Diffuse peripheral vascular pruning	Significant segmental or subsegmental thromboembolic disease, with focal areas of vascular attenuation in regions of disease
Vasculitis	Systemic arterial involvement Wall thickening Pseudoaneurysms Thin beaded vessels Upper lung predominance	Intraluminal filling defects (however, may be present within PA aneurysms [eg, in Hughes-Stovin syndrome])
Pulmonary artery sarcoma	Central filling defect with convex margin extending toward pulmonary valve or into contralateral PA (sausage sign) Expansile beaded filling defect that grows despite anticoagulation Extravascular invasion or enhancement within the intravascular component Nodal or parenchymal metastatic disease Lack of bronchial collaterals Outside of direct extension, bilateral disease uncommon	Absence of expansile clot with convex margins Bilateral disease common Bronchial collaterals Presence of chronic clot does not exclude sarcoma
Fibrosing mediastinitis	Extrinsic soft tissue compressing vessel Findings of granulomatous disease elsewhere, including nodal calcifications and granulomas Occlusions of other structures, such as ipsilateral pulmonary veins	Only intraluminal filling defects

Note.—There is overlap in imaging features, and CTEPD can coexist with its mimics. PA = pulmonary artery, PE = pulmonary embolism, RV = right ventricle.

establish the chronicity of a case, including chronic-appearing thrombus, pulmonary artery occlusion, right ventricular hypertrophy, and bronchial artery formation. On the other hand, recurrent pulmonary embolism that resolves is not synonymous with chronic pulmonary embolism. Additionally, patients with CTEPD or CTEPH often have evidence of prior infarcts, resulting in peripheral scarring.

In Situ Thrombus

In situ thrombus is the result of de novo intravascular thrombus formation rather than an embolic event. This most commonly occurs in pulmonary arterial hypertension (PAH) or congenital heart disease (CHD) with left-to-right shunting (43) (Fig 6). While proinflammatory states have been attributed to this phenomenon (44), other possible causes include slow flow or stasis in the often very enlarged central pulmonary arteries. Distinction between in situ thrombus and CTEPH can be difficult, as both can show pruning of distal vessels and central pulmonary artery enlargement.

However, in situ thrombus is mostly wall lining and rarely occlusive, primarily involves the central vasculature, and the associated peripheral vascular pruning (if present) often involves the entire pulmonary artery tree without the localized vascular occlusions seen in CTEPH. Calcification of the pulmonary artery walls is exceedingly uncommon in CTEPH but can occur with the other two entities owing to atherosclerotic development from the severely elevated right heart pressures. While calcification of the clot is also subjectively more common for in situ thrombus in PAH and CHD, this can sometimes occur with CTEPH, particularly in patients with renal failure, and should not be used as a method of distinction.

At V/Q scanning and dual-energy CTPA, patients with PAH and in situ thrombus demonstrate few if any subsegmental perfusion defects, which are far less extensive than the perfusion defects seen in patients with CTEPH with central disease. Distinguishing between in situ thrombus and CTEPH is vital, as in situ thrombus is not treated with PTE.

Mosaic perfusion of the lungs can also be seen in PAH and CHD with left-to-right shunting. Compared with the well-defined segmental or subsegmental distribution of hypoperfusion in CTEPH, cases of PAH often exhibit periarteriolar ground-glass opacity or "blushing" (Fig 4) (45). However, patients with CHD can demonstrate regional perfusion abnormalities similar to those seen in CTEPH. Close examination of the heart and vasculature should allow distinction if the diagnosis is unknown. While bronchial artery dilatation can occur in PAH, it is often absent or less pronounced than in CTEPH. Lastly, areas of subpleural parenchymal scarring secondary to prior infarcts are common in CTEPH but not associated with PAH or CHD.

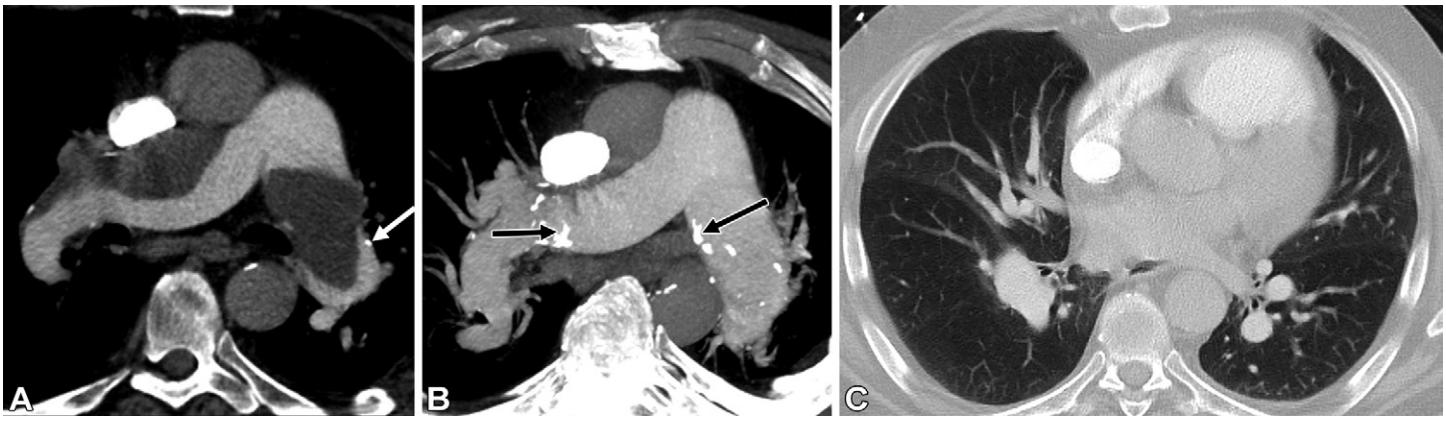


Figure 6. In situ thrombus in a 47-year-old-man with PAH. **(A)** Axial oblique CTPA image through the central pulmonary arteries shows a large volume of thrombus. Additionally, there are fine linear calcifications (arrow) along the pulmonary artery walls, both adjacent to and remote from the layering thrombus. **(B)** Axial 10-mm-thick MIP CTPA image at the same level better shows the extent of the pulmonary artery atherosclerotic calcifications (arrows) from the systemic pulmonary artery pressures. While clot can occasionally calcify in patients with CTEPH, linear wall calcifications are rare. **(C)** Axial CTPA image of the lungs in the expiratory phase shows no mosaic perfusion. Together with lack of vascular occlusion at CTPA, these findings suggest the diagnosis of PAH and layering in situ thrombus.

Vasculitis

Large-vessel vasculitis of the pulmonary arteries can be a manifestation of Takayasu arteritis, giant cell arteritis, or Behçet disease (46). While giant cell arteritis is the most common large-vessel vasculitis, Takayasu arteritis more frequently involves the pulmonary arteries. Many causes of pulmonary vasculitis will demonstrate coexistent abnormalities of the systemic arteries, with wall thickening or enhancement, sequential dilatation and stenosis (beading), aneurysms, and dissections.

However, vasculitis may be localized solely to the pulmonary arteries and can be difficult to differentiate from CTEPH, as both demonstrate areas of narrowing with poststenotic dilatation and occlusion. Mosaic attenuation can be present with either entity. The presence of thickened and enhancing pulmonary artery walls heavily favors vasculitis. Additionally, webs, bands, and visible thrombus are not typical of vasculitis.

Abnormal distribution of the areas of occlusion can be a helpful clue. Upper lobe–predominant disease, which is rare in CTEPH, may occur in vasculitis and should prompt reassessment of the appearance of the vasculature. Whereas CTEPH tends to demonstrate distal occlusions, the pulmonary arteries in vasculitis generally demonstrate thin elongated vessels with sequential foci of dilatation and narrowing (Fig 7). In cases of suspected vasculitis, multiplanar reconstruction can help better elucidate the abnormal characteristics of the vessels when compared with axial imaging.

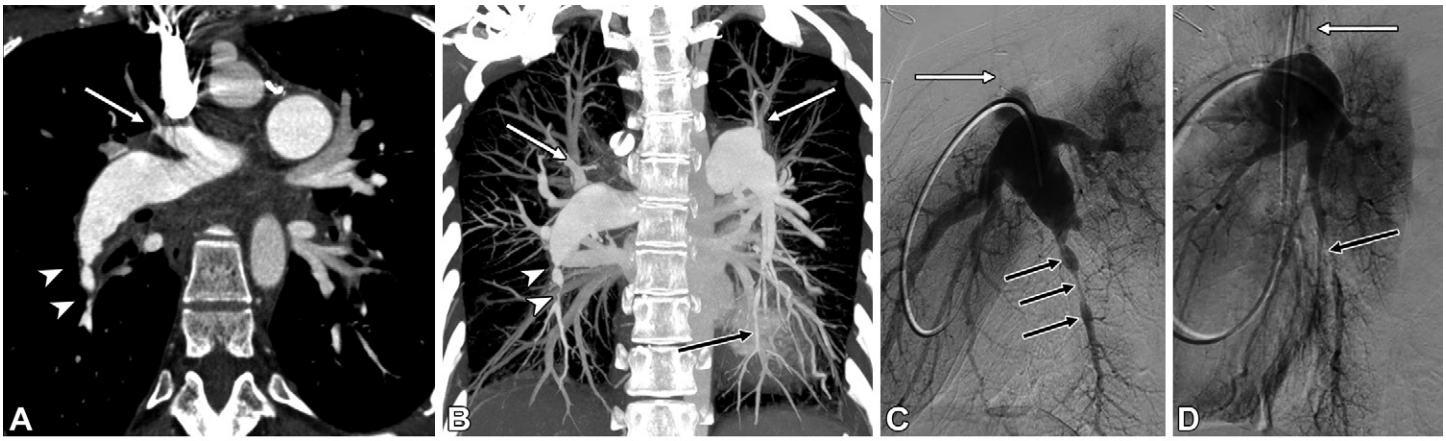
Hughes-Stovin syndrome is characterized by pulmonary artery aneurysms and vascular thrombosis and is considered by some to represent an incomplete manifestation of Behçet disease (47). The focal aneurysms or pseudoaneurysms of Hughes-Stovin syndrome seen at the lobar or segmental level have an appearance that is usually distinct from the more gradual and long-segment dilatation seen in CTEPH. Thrombus may be present in pulmonary artery aneurysms, but as stated earlier, cases of CTEPH will additionally demonstrate diminutive or occluded distal segmental or subsegmental arteries. Ground-glass opacity adjacent to a pulmonary artery aneurysm or pseudoaneurysm often represents hemorrhage and should be concerning for impending rupture.

Pulmonary Artery Sarcoma

Pulmonary artery sarcoma (PAS) can mimic CTEPH by similarly demonstrating moderate to large mismatched perfusion deficits at V/Q scanning and large pulmonary artery filling defects at CTPA (18,48) (Fig 8). These filling defects generally demonstrate convex margins with a smooth, lobulated, or irregular border (49), most commonly in the central pulmonary arteries (48). In PAS, tumor is often centered in and fills the right main or left main pulmonary artery and can extend centrally toward the pulmonary valve or cross the midline into the contralateral pulmonary artery, termed the *wall-eclipsing sign* by some (50) and the *sausage sign* by the authors. Vasculature distal to the tumor can be contracted, mimicking CTEPH, and the parenchyma can show subpleural scarring suggestive of a prior infarct as well as mosaic attenuation. Bronchial artery collaterals and right ventricular dilatation or hypertrophy can also be present.

Findings of CTEPH in the contralateral segmental and subsegmental vessels—such as webs and bands—are uncommon in PAS but can occur (51). Soft tissue in the main pulmonary artery extending to the pulmonary valve is uncommon in CTEPH and should raise concern for PAS. Overt invasion through the pulmonary wall or intratumor enhancement is the most helpful for clearly distinguishing PAS from CTEPH, although many cases of PAS show no or limited enhancement (49). Pulmonary metastases also suggest the diagnosis and may be solid or cavitary.

In some cases, distinction can be difficult at CTPA. In ambiguous cases, PET (which shows increased fluorodeoxyglucose [FDG] uptake in 90% of cases of PAS) or MRI (which can show intratumor first-pass perfusion and postcontrast enhancement not seen at pulmonary arterial phase CT) can be performed (49). In lieu of PET or MRI, 4-week follow-up CTPA can be performed; if the lesion does not change or even grows in the interim, the diagnosis of sarcoma should be suggested



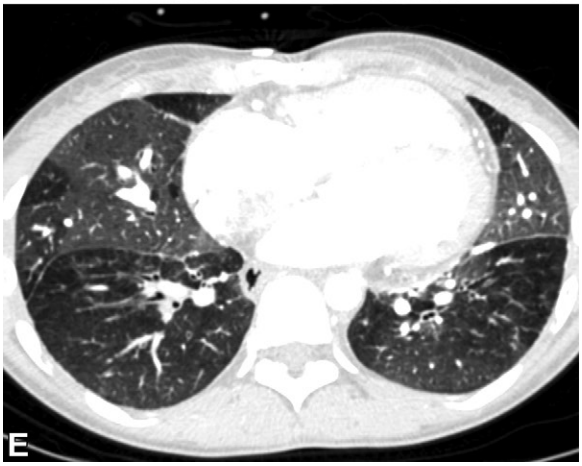


Figure 7. Vasculitis in a 25-year-old woman with dyspnea. **(A, B)** On coronal oblique multiplanar reformation **(A)** and 20-mm-thick MIP **(B)** CTPA images, there is beading of lobar and segmental pulmonary arteries, most pronounced in the right lower lobe (arrowheads). The upper lobe pulmonary arteries are proximally occluded (white arrows), and many of the lower lobe arteries appear thin and elongated (black arrow in **B**). No discrete thrombus is visualized. **(C, D)** On right lateral **(C)** and left lateral **(D)** still images from catheter angiography, there is no flow in the upper lobe pulmonary arteries (white arrow). There is conspicuous beading of the right lower lobe posterior branch (black arrows in **C**) and long-segment narrowing of the same vessel in the left lower lobe (black arrow in **D**). The lower lobe vessels overall appear thin and elongated. **(E)** Axial CTPA image of the lungs shows mosaic perfusion, which appears similar to cases of CTEPH. Distinction between vasculitis and CTEPH can be difficult. If vasculitis is suspected, careful inspection of the systemic vessels should be performed, as involvement would make the diagnosis vasculitis. However, this is often absent. Other clues include elongated often beaded vessels without clear signs of thrombus, as well as upper lobe–predominant disease. In this case, the multidisciplinary diagnosis was vasculitis, and the treatment decision was medical therapy. This is an essential distinction, as PTE will provide no benefit to patients with vasculitis and can be particularly dangerous, given the presence of inflamed or friable vessels.

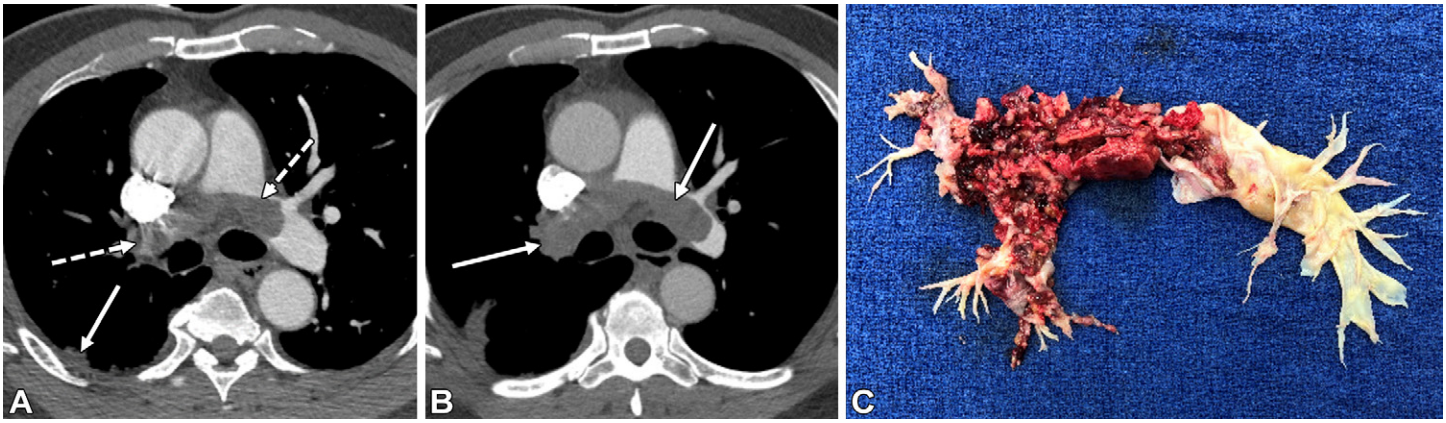


Figure 8. PAS in a 52-year-old man with an outside referral for CTEPH. He initially presented to the emergency department with chest pain and shortness of breath. **(A)** Axial oblique CT image in October shows a "sausagelike" mass (dashed arrows) filling the right pulmonary artery and extending across the midline into the left pulmonary artery. A healing infarct (solid arrow) is present in the right lower lobe. The patient was diagnosed with acute pulmonary embolus and treated with anticoagulation. **(B)** Axial oblique CT image obtained 2 months later owing to continued symptoms shows growth of the filling defect (arrows) despite anticoagulation. Although the patient was referred for PTE for CTEPH, the diagnosis of PAS was made during multidisciplinary review. **(C)** Photograph shows the endarterectomy specimen of the PAS. Differentiation between PAS, acute pulmonary embolism, and CTEPH can be difficult. While findings such as invasion beyond the confines of the pulmonary artery wall, neovascularity in the filling defects, and metastatic disease can help make the diagnosis, they are often absent. If there is concern for sarcoma at initial imaging, MRI, PET, or short-term interval follow-up after initiation of anticoagulation can be performed.

(49). However, a shrinking filling defect must be interpreted with caution, as thrombus and sarcoma can coexist.

Fibrosing Mediastinitis

Fibrosing mediastinitis can mimic CTEPH at V/Q scanning by obstructing the central pulmonary arteries, resulting in a large mismatched perfusion defect. Whereas CTEPH is more typically bilateral, a unilateral abnormality at V/Q should raise this possibility and prompt cross-sectional imaging with CT (18). In most cases, fibrosing mediastinitis is due to an overzealous immune response to histoplasmosis.

At CT, the findings of fibrosing mediastinitis are usually distinct from those of CTEPH (Fig 9), characterized by a large soft-tissue mass infiltrating the mediastinum and encasing

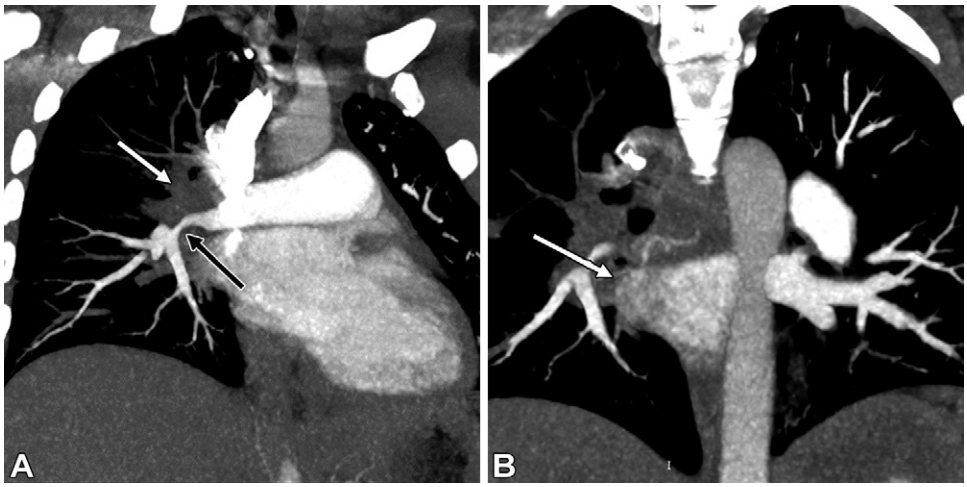


Figure 9. Fibrosing mediastinitis in a 28-year-old woman with progressive dyspnea diagnosed with CTEPH at an outside institution. This outside referral was reviewed at a multidisciplinary conference. **(A)** Coronal oblique MIP CTPA image shows confluent soft tissue (white arrow) in the right hilum occluding the right upper lobe and right middle lobe pulmonary arteries. The interlobar pulmonary artery appears extrinsically narrowed (black arrow). **(B)** Coronal MIP CTPA image obtained slightly more posterior shows occlusion (arrow) of the right superior pulmonary vein. The patient was diagnosed with fibrosing mediastinitis, and medical therapy was recommended. A confluent soft-tissue mass in the hilum or mediastinum compressing and occluding surrounding vasculature can mimic CTEPH. Compression and occlusion of the pulmonary veins are common findings in fibrosing mediastinitis and can help differentiate it from CTEPH. Calcifications in the mass can also help diagnose fibrosing mediastinitis but may not be present, as in this case.

or invading adjacent structures (52). Fibrosis due to prior granulomatous infection is usually focal or masslike and often associated with areas of calcification. Calcifications are apparent at CT but can be missed at MRI. Any of the surrounding structures can be narrowed or occluded, including the pulmonary veins, pulmonary arteries, bronchi, superior vena cava, and esophagus.

Treatment Options for CTEPH

The main treatment options for CTEPH include PTE, BPA, and medical treatment. Of these, PTE is the treatment of choice (6), as it is potentially curative and most patients with CTEPH are good surgical candidates (42). Patients who undergo PTE have a 3-year survival rate of 83%–91% after surgery versus 69%–70% without surgery (53–55), in addition to experiencing improved symptoms and activity levels (56). For patients who are inoperable owing to disease location, comorbidities, or other complicating factors, BPA and medical therapy with PAH-targeted medications may result in improved hemodynamics and exercise capacity (57). Although PTE, BPA, and medical therapy are often discussed separately, patients often benefit from a combination of therapies.

Pulmonary Thromboendarterectomy

PTE, also referred to as pulmonary endarterectomy (PEA), was pioneered at the University of California San Diego (58). After cardiopulmonary bypass and deep hypothermic circulatory arrest, the pulmonary artery is exposed between the aorta and superior vena cava and mobilized. The aorta is cross-clamped, and cold cardioplegia is administered. The pulmonary artery is then incised, and any visible thrombus is removed (Fig E5).

Endarterectomy is initiated by identifying a plane between the intima and media. Forceps are then used to longitudinally dissect along this plane and circumferentially excise the pulmonary artery intima, which—in the hands of an expert surgeon—can extend into the subsegmental vasculature. The intima is then pulled out (Figs 1E, E6). It is important to note that this procedure is not an embolectomy, which is not possible owing to strong adherence of organized thrombus to the vessel wall. Perfusion resumes, the arteriotomy is closed, then the process is repeated on the contralateral side.

Balloon Pulmonary Angioplasty

In BPA (Fig 10), central venous access is most often achieved via the femoral vein (45). A sheath is introduced into the main pulmonary trunk, and selective pulmonary angiography is performed to locate and assess target thromboembolic lesions. A wire (typically 0.014 inch) is passed across the target lesions, and vessels are then dilated (typical balloon size 2–5 mm in diameter). Within 1–3 weeks after angioplasty, treated lesions tend to further remodel, often corresponding to reduction of mean pulmonary artery pressure (59). In general, at least two to six sessions are required to treat all affected territories, with subsequent treatments spaced at 1–3-month intervals.

Medical Treatment

In inoperable patients or cases of residual pulmonary hypertension after PTE, PAH-targeted medical therapy with or without BPA may have therapeutic value; the rationale is based on evidence of PAH-like small-vessel arteriopathy in the unobstructed pulmonary vascular beds of patients with CTEPH (60). The only medication with a current U.S. Food and Drug Administration (FDA)–approved indication

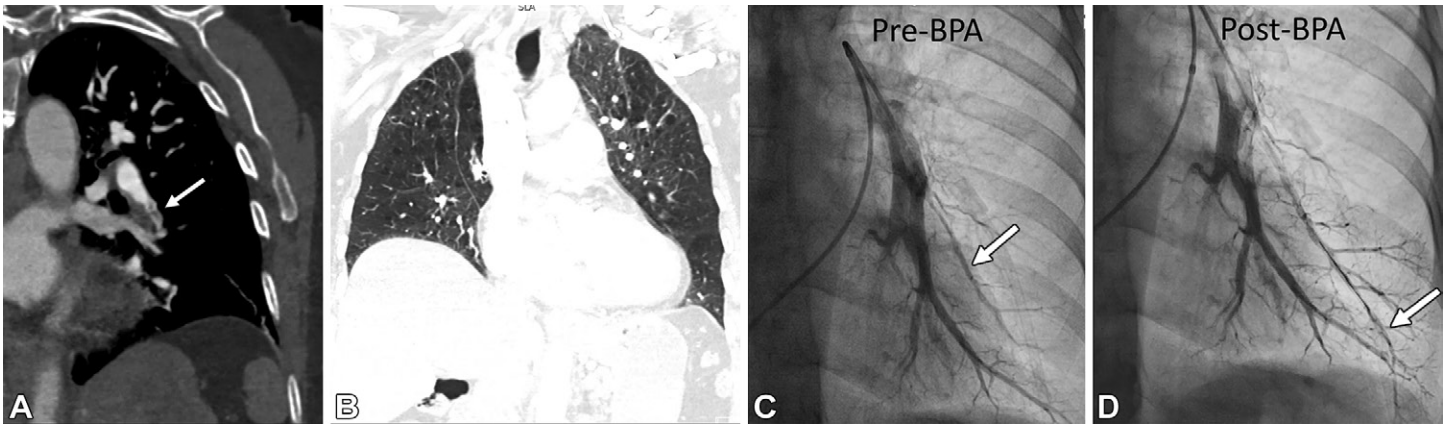


Figure 10. BPA in an 83-year-old woman with chronic obstructive pulmonary disease (COPD), ischemic cardiomyopathy, and a history of squamous cell carcinoma of the lung. **(A)** Coronal oblique image from CTPA shows scattered segmental and subsegmental webs and bands in the left lower lobe anteromedial basal segmental artery (arrow). These finding were identified bilaterally. **(B)** Coronal CTPA image (lung window) shows emphysema, scarring, and findings of prior right middle lobectomy. Given the surgical risk and the location of disease, the multidisciplinary consensus was to pursue BPA. **(C)** Catheter angiogram shows chronic disease in the form of diffuse narrowing (arrow) of the anteromedial basal segmental artery and its branches. **(D)** Catheter angiogram after BPA shows restored perfusion (arrow) to distal subsegmental branches.

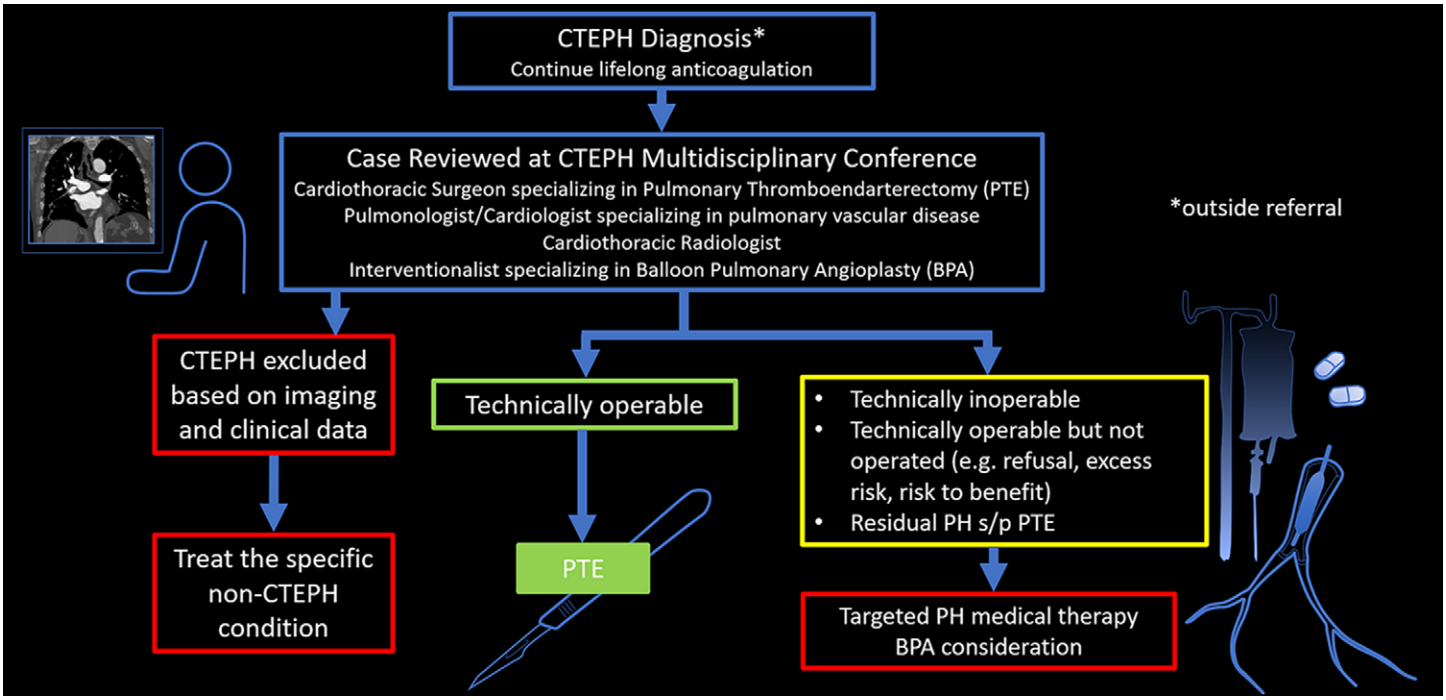


Figure 11. Proposed CTEPH treatment algorithm of the World Symposium on Pulmonary Hypertension. After initial diagnosis of CTEPH, the patient is evaluated at a referral center by a multidisciplinary team including a cardiothoracic surgeon, pulmonologist, cardiologist, and cardiothoracic radiologist. Together, this team first confirms or excludes the diagnosis of CTEPH and determines treatment. If a patient is ineligible for potentially curative PTE, BPA or medical therapy may be pursued. *PH* = pulmonary hypertension, *s/p* = status post. (Adapted and reprinted, with permission, from reference 7.)

for inoperable or recurrent CTEPH is riociguat, a soluble guanylate cyclase stimulator that increases cyclic guanosine monophosphate (GMP) production (a vasodilator) in pulmonary artery smooth muscle cells (61).

Multidisciplinary Assessment of CTEPH Imaging Findings

Management of CTEPH requires a multidisciplinary approach including pulmonologists, cardiothoracic surgeons, cardiologists, and radiologists (Fig 11). This allows a multifaceted review of imaging findings, hemodynamics, and the patient history to confirm or exclude the diagnosis of CTEPH and make subsequent treatment decisions. In addition to potential cases of CTEPH, CTEPD cases without pulmonary hypertension are also discussed, as such patients may still be considered for intervention on the basis of symptoms, hemodynamics, and extent of disease.

Operability assessment of the patient with confirmed CTEPH is the first step in management, as PTE offers a surgical cure with low perioperative mortality in experienced surgical centers (1,62). Preoperative evaluation for PTE includes assessment of technical operability and surgical risk stratification.

Technical operability depends on both the anatomic location of disease, as assessed with imaging, as well as the surgeon's skill. The University of California San Diego intraoperative classification of CTEPH includes four levels based on the most central component of the thromboembolism, although the extent visualized intraoperatively may not correlate with imaging findings (63) (Table 2).

Once technical operability is confirmed, assessment of potential hemodynamic and symptomatic improvement follows, with subsequent perioperative risk stratification based on comorbidities and the presence of unfavorable risk factors, including advanced functional class, right heart failure, severely elevated pulmonary vascular resistance greater than 1000 dynes · sec · cm^{-5} (50), and discordance between hemodynamic derangement and thromboembolic burden at imaging, indicating possible coexistence of small-vessel disease (41,64). Significant parenchymal lung disease in the areas to be surgically reperfused is the main contraindication.

If the patient is not an operative candidate or refuses PTE, BPA or medical therapy may be pursued (Figs 10, 11). This approach is also considered in select cases of residual pulmonary hypertension after PTE. Patients undergoing BPA tend to have more segmental or subsegmental disease, and the procedure is generally more successful in ringlike stenoses and web lesions (65). Areas of complete occlusion are difficult to treat, as a guidewire must be placed beyond the thrombus for treatment. Medical therapy is often used in conjunction with BPA, but the ideal multimodality therapeutic approach for these cases is still not established.

Beyond assessing disease burden and anatomic location, CTPA is particularly useful for evaluation of the lung parenchyma and mediastinum. In addition to identifying chronic lung disease that may preclude PTE, incidental identification of coronary artery disease may aid in preoperative risk assessment. Moreover, CTPA is essential in evaluation for alternative causes of a perfusion defect (mimics), as described earlier. Case discussions for patients presented at our multidisciplinary conference are shown in Figures 1, 7–10, E6, and E7.

Posttreatment Findings and Complications

Normal Postoperative Imaging Findings in CTEPH

The first postoperative imaging examination is chest radiography, at which mild perihilar opacities—due to mild pulmonary edema—are expected. Transthoracic echocardiography is routinely performed, ideally demonstrating improved right ventricular contractility and systolic pressures, with right heart chamber size usually decreasing. Patients are taken off pulmonary hypertension medications on the 1st postoperative day. At our institution, V/Q scanning is also routinely performed postoperatively and will ideally demonstrate resolution of most of the preoperative perfusion defects, although a normal V/Q study is rarely encountered after surgery.

New areas of hypoperfusion are often seen at V/Q scanning owing to steal phenomenon (Fig E6F), which entails redistribution of blood flow from previously nonobstructed arteries to lung regions reperfused with PTE. An immediate postoperative V/Q study provides a postoperative baseline examination that can be used to monitor for subsequent improvements or new thromboembolism at follow-up V/Q scanning performed 6 months later. CTPA and DSPA usually demonstrate preserved patency of vessels at sites of decreased perfusion. This redistributed perfusion tends to improve during the 1st year after surgery (66).

Table 2: University of California San Diego Intraoperative Classification of CTEPH

Level	Most Proximal Location of Disease
1	Central pulmonary arteries
2	Lobar branches
3	Segmental branches
4	Subsegmental branches

Source.—Reference 63.
Note.—Please note that levels are given for both the left and right sides.

If CTPA is performed postoperatively, resolution of macroscopic thrombus should be seen, although some regions of residual distal thrombosis or even rethrombosis are not uncommon. In many instances, the right heart will decrease in size but remain hypertrophied. The main pulmonary artery may show an immediate slight decrease in size, but this often takes time to remodel. As with V/Q scanning, dual-energy CT will show areas of improved perfusion in treated areas. However, the change in thromboembolic burden as visualized at CTPA does not necessarily correlate with the presence of residual pulmonary hypertension, suggesting that microvascular rather than macroscopic obstruction may allow better prediction of residual pulmonary hypertension (67).

Imaging of Complications after PTE

Complications of PTE in the perioperative period include hypoxemia due to V/Q mismatch or reperfusion pulmonary edema, hemorrhage, pericardial effusion or hemopericardium, infection, and death. The perioperative mortality rate for PTE varies substantially, depending on center expertise, but currently is about 2%–7% (40,68). Results from an international registry demonstrated infection in 19% of patients, persistent pulmonary hypertension in 17%, neurologic complications in 11%, bleeding in 10%, reperfusion edema in 10%, and pericardial effusion in 8% (68).

As with other cardiothoracic surgeries, postoperative hypoxemia is common, but it is exacerbated by unique vascular changes after PTE that worsen V/Q matching. Reperfusion edema is a high-permeability edema that occurs in reperfused lung, typically within 48 hours after surgery. Reported rates vary from 10% to 60%, depending on the definition used, with severe preoperative pulmonary hypertension being an identified risk factor (68,69). Key radiographic findings are asymmetric parenchymal opacities that correspond to areas of treated disease (Fig 12). It may be difficult to definitively distinguish reperfusion edema from aspiration or pneumonia with imaging, but rapid resolution is more suggestive of edema. Septal thickening is variably present.

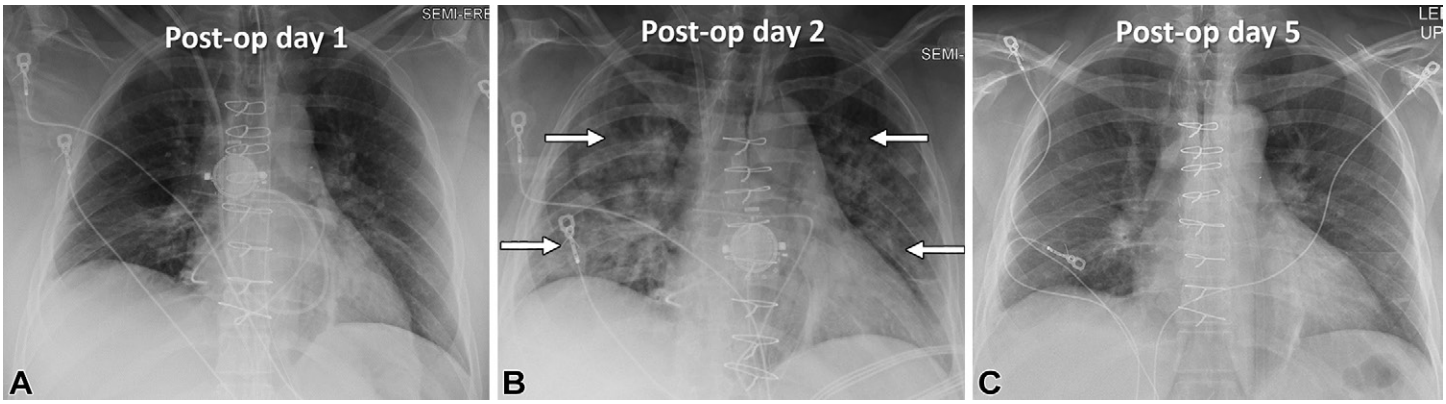


Figure 12. Reperfusion edema in a 36-year-old woman with CTEPH after PTE. **(A)** Chest radiograph 1 day after PTE shows mild bilateral perihilar opacity, likely reflecting mild pulmonary edema and potentially related to reperfusion edema or fluid overload. **(B)** Chest radiograph 1 day later shows markedly increased perihilar opacity (arrows), which is asymmetrically greater on the right and corresponded to the asymmetric distribution of thromboembolic disease in this patient. This is more suggestive of reperfusion edema, although alternative causes such as hemorrhage or infection would be difficult to entirely distinguish. **(C)** Chest radiograph on day 5 shows that the perihilar opacities have essentially resolved. The rapid resolution is compatible with reperfusion edema.

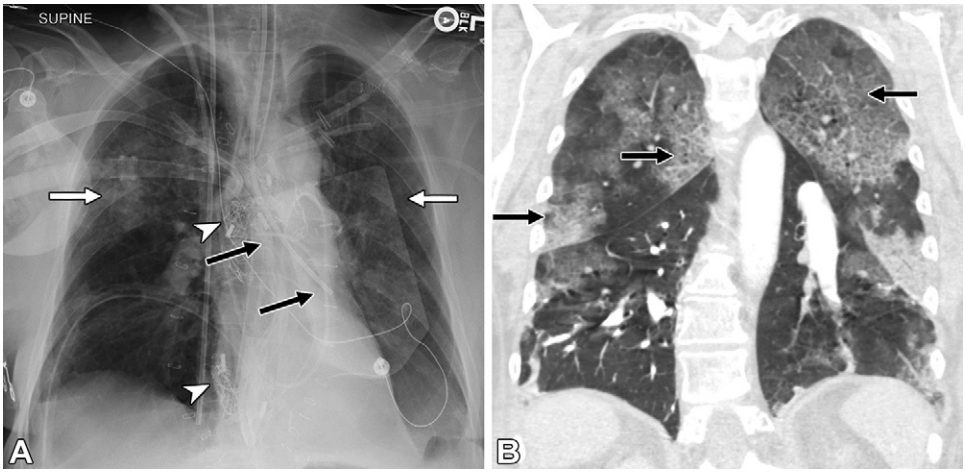


Figure 13. Hemorrhage in a 68-year-old woman after PTE for CTEPH complicated by intraoperative hemorrhage. **(A)** Chest radiograph shows an open chest with surgical packing material (arrowheads). A catheter (black arrows) extends down the left main-stem bronchus, which represents an endobronchial blocker that is used to reduce hemorrhage and hemoptysis. This can be mistaken for a misplaced enteric tube. Bilateral parenchymal opacities (white arrows) in this context are suggestive of hemorrhage. **(B)** Coronal CT image 5 days later shows ground-glass opacity and septal thickening, resulting in a crazy paving appearance (arrows), also compatible with hemorrhage.

Airway hemorrhage can be a severe complication and may be the result of pulmonary artery trauma, severe reperfusion injury, or hypertrophied systemic-to-pulmonary collateral arteries. Like other causes of pulmonary hemorrhage, post-PTE hemorrhage may have a hazy ground-glass appearance with ill-defined margins at CT. Concurrent interlobular and intralobular septal thickening, creating a crazy paving pattern, is also common (Fig 13). At chest radiography, focal hemorrhage cannot be clearly distinguished from reperfusion edema, infection, or aspiration. However, hemoptysis or a decrease in hematocrit level should raise its possibility.

Perfusion steal phenomenon is common after PTE and describes redirection of perfusion from previously normal vessels to endarterectomized arteries (69). It has been proposed that small vessels with more proximal obstruction are shielded from downstream microvascular changes (smooth muscle hypertrophy and intimal proliferation), resulting in lower resistance and preferential flow after endarterectomy (66). These regional changes in resistance can result in redirection of blood flow from healthy lung to abnormal lung, resulting in impaired gas exchange and V/Q mismatch. In the setting of atelectasis or reperfusion edema, hypoxemia can be profound and out of proportion to the opacities seen at imaging.

As mentioned earlier, rethrombosis may occur in the peri- and postoperative periods, even in the setting of adequate anticoagulation. The intimectomy performed during PTE increases this risk, since a primary function of the intima is to create a nonthrombogenic surface. In addition, steal phenomenon can lead to reduced flow in previously perfused areas and thrombosis due to stasis. In the immediate postoperative period, segmental pulmonary arteries should be clear of both acute and chronic thrombus, and the presence of "persistent" or acute-appearing thrombus at imaging is more consistent with rethrombosis rather than a new embolic event (Fig 14). In the late postoperative period, it may be impossible to differentiate between rethrombosis and new embolic events if early postoperative images are not available for comparison.

Pericardial effusion after PTE is common, occurring in 27% of patients. While most cases are clinically inconsequential, nearly 5% of patients develop a moderate to large pericardial effusion requiring intervention (70). Hemopericardium occurs in approximately 2% of post-PTE patients

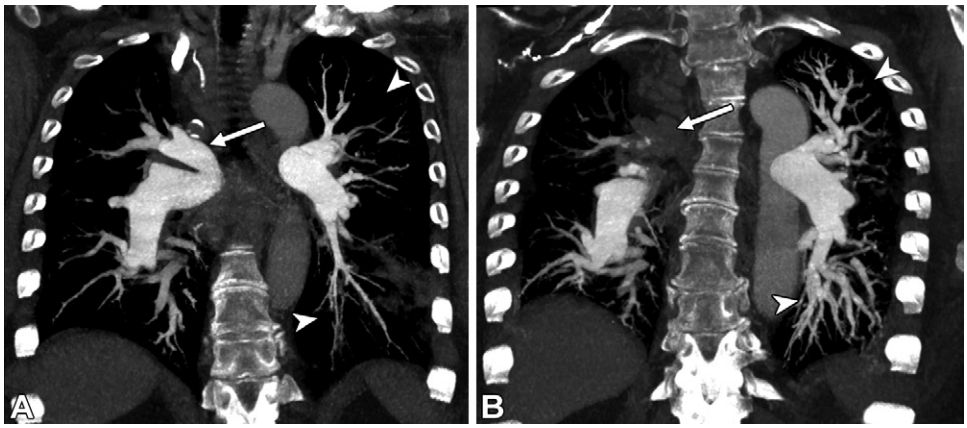


Figure 14. Rethrombosis in a 55-year-old man with CTEPH. **(A)** Coronal oblique MIP CTPA image before surgery shows diminutive vessels throughout the left lung (arrowheads) secondary to CTEPH. Note that the right upper lobe truncus anterior is patent (arrow). After PTE, the patient underwent repeat V/Q scanning, which showed improved left lung perfusion but new right upper lobe defects. **(B)** Coronal MIP CTPA image after PTE shows a dramatic increase in the caliber of left-sided pulmonary arteries (arrowheads) due to surgery. However, there is new thrombus in the right upper lobe (arrow). This was thought to be secondary to a steal phenomenon, where preferential flow through the newly revascularized territories leads to decreased flow in previously preserved regions and subsequent thrombosis due to slow flow. This is not related to new embolic disease.

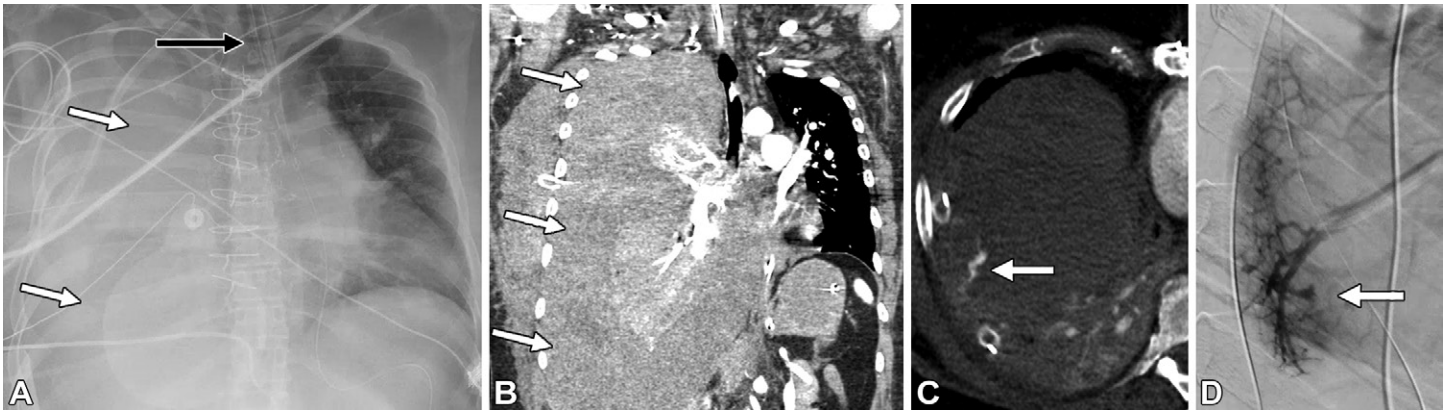


Figure 15. Pulmonary artery injury in a 57-year-old woman with CTEPH after BPA. **(A)** Chest radiograph 9 hours after BPA shows complete opacification of the right hemithorax (white arrows) with tracheal deviation to the left (black arrow), consistent with a large right pleural effusion concerning for hemothorax. **(B)** Coronal CT image 13 hours after BPA shows a large right hemothorax (arrows). A source was not definitively identified, and the patient was taken to the operating room, where a right lower lobe parenchymal injury was identified. Despite this, the patient developed recurrent hemothorax. **(C)** Axial delayed phase image from repeat CT angiography shows active extravasation (arrow) from a subsegmental branch of the anterior basal right lower lobe pulmonary artery. **(D)** Catheter pulmonary angiogram shows active extravasation (arrow) from the subsegmental vessels, which were subsequently embolized.

(71) (Fig E8). A rapidly accumulating pericardial effusion or hemopericardium with evidence of mass effect on the cardiac chambers should raise concern for tamponade.

Imaging of Complications after BPA

As noted earlier, BPA is a treatment option for selected patients who are inoperable or with residual pulmonary hypertension after PTE. Complications that arise during BPA include vascular injury (wire perforation, balloon overdilation, high-pressure contrast material injection) with or without hemoptysis and vascular dissection. The vascular injury observed during BPA differs from the reperfusion lung injury experienced after PTE. Direct pulmonary blood vessel injury results in pulmonary hemorrhage and hemoptysis. Only rarely do BPA patients experience reperfusion lung injury similar to the high-permeability edema after PTE.

With procedural refinements, complication rates for BPA have decreased dramatically over the past 20 years. Most BPA centers now report an approximately 10% risk of complications per procedure and procedure-associated mortality under 2% (72), although severe pulmonary artery injury requiring mechanical ventilator support and use of extracorporeal membrane oxygenation (ECMO) can still occur (Fig 15).

Although some of the bleeding complications are clinically evident or seen during the procedure with DSPA, chest radiography or CT angiography may be helpful to assess the extent and location of the bleeding as well as its evolution over time.

Conclusion

Patient evaluation for possible CTEPH should ideally be performed at specialized referral centers by a multidisciplinary

team. Although radiologists may miss imaging findings of CTEPH at CTPA, sensitivity can be improved through awareness of the imaging characteristics of CTEPH. Multiple pulmonary vascular pathologic conditions can mimic CTEPH, but imaging usually allows reliable distinction. CTPA is indispensable in evaluation of patients with CTEPH by allowing assessment of disease burden and high-risk cardiopulmonary findings. Imaging is also crucial for identifying postprocedure complications of CTEPH treatment, most of which stem from infection, reperfusion edema or injury, or hemorrhage. Thus, radiologists play a central role in the care of patients with CTEPH.

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