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Comprehensive Review

Interventional Imaging Roadmap to Successful Balloon Pulmonary Angioplasty for Chronic Thromboembolic Pulmonary Hypertension

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ABSTRACT

Balloon pulmonary angioplasty (BPA) is an evolving treatment modality for patients with chronic thromboembolic pulmonary hypertension (CTEPH) who are not candidates for pulmonary endarterectomy. Although several imaging modalities currently exist for evaluating CTEPH, their individual use, specifically in the clinical practice of BPA, has not been well described. In this article, we provide a preprocedural, intraprocedural, and postprocedural interventional imaging roadmap for safe and effective BPA performance in routine clinical practice. Preprocedural assessment includes transthoracic echocardiography for right ventricular assessment, ventilation/perfusion scan to identify pulmonary segments with the highest degree of hypoperfusion, cross-sectional chest imaging excluding alternative causes of mismatched defects and providing anatomic and perfusion imaging concurrently, and nonselective invasive pulmonary angiography for risk stratification of individual lesion subtypes. Intraprocedural assessment includes subselective segmental angiography (SSA) for delineating segmental and subsegmental branch anatomy, lesion identification, and vessel sizing. Intravascular ultrasound and optical coherence tomography serve as adjunctive intraprocedural tools for more accurate vessel sizing and lesion characterization when SSA alone is insufficient. Postprocedural considerations include chest radiography to monitor for immediate postprocedure complications and echocardiography for the interval assessment of the right ventricle on longer-term follow-up.

Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) is an infrequent but highly morbid complication of acute pulmonary embolism.[1,2] Surgical pulmonary endarterectomy (PEA) is the preferred treatment for CTEPH, although it is limited to suitable operative candidates with accessible disease in the main, lobar, or proximal segmental branches of the pulmonary arteries.[3,4] Registry data suggest that up to 40% of all patients with CTEPH do not have surgically accessible disease.[5] To address this subgroup of patients, balloon pulmonary angioplasty (BPA) is a percutaneous procedure performed over multiple sessions to revascularize pulmonary artery branches. Increasing experience suggests that BPA is a promising therapeutic option in patients with CTEPH who are not candidates for PEA.[3]

Imaging is vital for preprocedural planning, intraprocedural guidance, and postprocedural follow-up. Although several different imaging modalities currently exist for patients with CTEPH, limited guidance is available on how they should be used in a coordinated fashion to engender safe and effective BPA.[6] In this article, we aim to summarize the current role and specific application of various imaging modalities in patients undergoing BPA. More specifically, this article provides an interventional imaging roadmap for preprocedural, intraprocedural, and postprocedural management of patients undergoing BPA.

Abbreviations: BPA, balloon pulmonary angioplasty; CTEPH, chronic thromboembolic pulmonary hypertension; CTPA, computed tomography pulmonary angiogram; DECT, dual-energy computed tomography; IPA, invasive pulmonary angiography; PEA, pulmonary endarterectomy; SPECT, single-photon emission computed tomography; SSA, subselective segmental angiography; V/Q, ventilation/perfusion.

Keywords: balloon pulmonary angioplasty, interventional imaging, chronic thromboembolic pulmonary hypertension, pulmonary artery angioplasty.

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Preprocedural planning

Echocardiography

Transthoracic echocardiogram (TTE) is one of the primary tests performed in those with signs and symptoms of pulmonary hypertension.[7] TTE provides a qualitative and quantitative assessment of cardiac chamber size and function. Markers that suggest significant pulmonary hypertension (PH) include right atrial and right ventricular (RV) enlargement, increased RV wall thickness, increased RV systolic pressure, and decreased RV systolic function (RVSF). RVSF can be evaluated via parameters including tricuspid annular plane systolic excursion and fractional area change. Tricuspid annular plane systolic excursion under 16 mm and fractional area change of <35% indicates impaired RVSF. Regional assessment of RV function includes tissue doppler-derived and 2-dimensional (2D) strain.[8] Compared with 2D echocardiography, 3-dimensional echocardiography more accurately assesses RV volumes and ejection fraction but requires advanced equipment and image postprocessing.[9]

Ventilation/perfusion scan

A ventilation/perfusion (V/Q) scan is a nuclear medicine test used to investigate ventilation and blood flow distribution throughout the lungs.[10] The imaging for V/Q scanning is performed using single-photon emission computed tomography (SPECT) or with planar imaging. The former is able to generate high-quality 3-dimensional images using multidetector gamma cameras, whereas the later generates 2D images using a dual-headed camera.[11] Matched (concordance between ventilation and perfusion defects), mismatched (defective perfusion with no or limited ventilation), or reverse mismatched (defective ventilation with no or limited perfusion) defects can be assessed.[12]

The V/Q scan remains the initial screening test of choice for ruling out CTEPH, with a sensitivity of >96% and specificity of 90% to 95%. As a screening test, it has been demonstrated to be superior to computed tomography (CT) pulmonary angiography (CTPA), which has a sensitivity of 51% and specificity of 99%.[13,14] Patients with a new diagnosis of PH and those with persistent symptoms for ≥3 months after an acute pulmonary embolism should undergo screening for CTEPH using V/Q scan.[15] The advantages of V/Q scanning include its lower cost, high sensitivity, and avoidance of complications related to the use of intravenous contrast.[6]

Typical findings indicative of a diagnosis of CTEPH on V/Q scan include perfusion defects in segmental distribution without associated ventilatory changes (mismatched defect) within the pulmonary parenchyma.[16,17] Specifically, lobar or segmental level mismatched defects in proximal vessel disease or mottled patchy perfusion defects in the periphery in distal subsegmental disease can be seen.[18] Figure 1 shows the classic appearance of CTEPH on V/Q scan. Table 1 lists various pathologies that can appear as mismatched perfusion defects on V/Q scan. SPECT-CT V/Q scan is a newer form of V/Q imaging shown to be more sensitive and specific compared with standard planar and SPECT V/Q scan. Its advantages include greater accuracy with mapping of perfusion defects and ability to rule out nonembolic etiologies of these defects.[19,20]

The V/Q scan helps with preprocedural planning for BPA by helping identify the lung lobe with the highest degree of hypoperfusion. If corresponding lobes in both lungs have a similar degree of poor perfusion, lobes in the right lung are preferentially selected for the initial BPA sessions because of easier accessibility and potentially greater impact (because of the increased total blood flow distribution of the right lung). These considerations also hold true for inferior lobes versus middle and superior lobes. The V/Q scan can also be utilized to identify areas to target for BPA.

CTPA

CTPA generates thin imaging slices of structures within the thoracic cavity after the administration of intravenous contrast. Although CTPA is considered the first-line imaging modality for assessing acute PE, it is utilized as an adjunctive imaging modality in the assessment of CTEPH.[20] Recent literature, however, shows a growing role for CT due to improved diagnostic accuracy, especially in experienced centers. For instance, a recent meta-analysis showed CT to have a pooled sensitivity of 76% and specificity of 96%.[21] The performance of CT has improved by virtue of technological advancements such as dual-energy CT (DECT) pulmonary angiogram described later in this section.

Imaging findings in patients with CTEPH can vary depending on the degree of PH and vascular obstruction.[22] Acute thrombi are differentiated from chronic thrombi on the basis of the morphology of the thrombus and size of the occluded vessel (Table 2). Chronic thromboembolism manifests as eccentric filling defects forming obtuse angles with the wall (Figure 2), rather than the central location of acute pulmonary embolism. Even if acute thrombi are located eccentrically, they

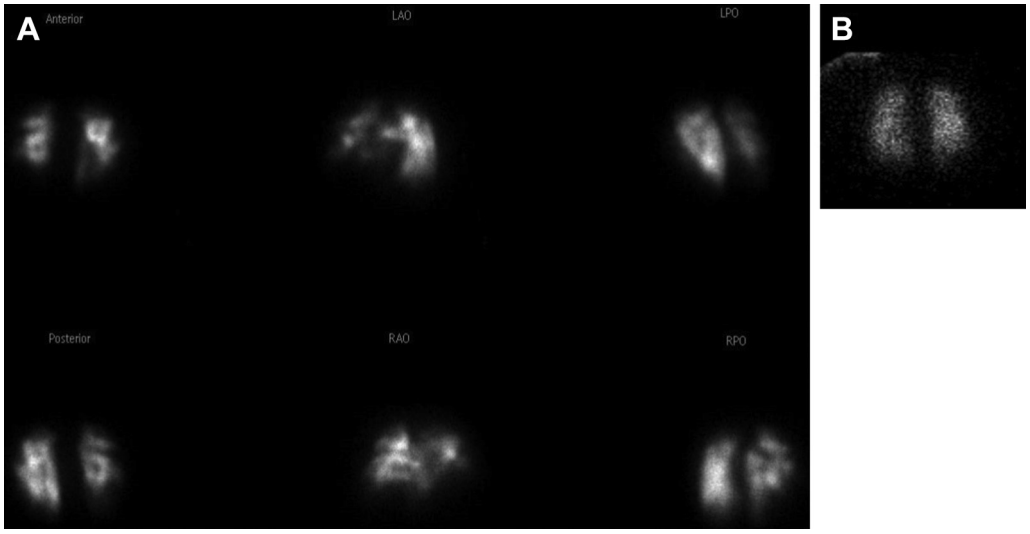


Figure 1. Characteristic appearance of chronic thromboembolic pulmonary hypertension on ventilation/perfusion scan. Ventilation/perfusion scan showing (**A**) Multiple perfusion defects with normal ventilation. (**B**) Mismatched defects.

Table 1. Differential diagnosis of mismatched perfusion defects on ventilation/perfusion scan.

Intrinsic	Extrinsic
PA obstruction	Fibrosing mediastinitis
Thromboembolic (acute and chronic)	Radiation-induced fibrosis
Nonthrombotic (congenital, inflammatory, tumor emboli)	Mass effect by tumor or lymph node enlargement
PV obstruction	
Stenosis from prior catheter ablation	
Thrombosis	
Idiopathic PVOD	

PA, pulmonary artery; PV, pulmonary vein; PVOD, pulmonary veno-occlusive disease.

form acute angles with the wall, allowing for differentiation. Acute emboli tend to distend the occluded vessel, in contrast to retraction and diminished caliber of occluded vessels in CTEPH.[20,23] Other features of chronic thromboembolism include webs or bands (Figure 2), which can be seen at the periphery of vessels and are associated with partial thrombus resolution.[24] Localized stenosis of vessels followed by areas of dilation and calcification can occur because of chronic thrombus organization.[25-27] Other nonspecific findings seen in CTEPH include bronchial artery dilatation, likely as a response to chronically occluded pulmonary arteries, lung scarring from prior infarcts, cylindrical bronchiectasis, and varying lung parenchymal attenuation, which represents differences in geographical tissue perfusion. Attenuated vascular markings can be seen in areas of hypoperfused lung parenchyma, whereas regions of higher parenchymal attenuation correspond to hyperfused tissue secondary to redistribution of blood flow. This varying attenuation pattern has been described as mosaicism and is another nonspecific finding seen in small airway and vessel disease.[20,28] The assessment of vessel size within low attenuation zones and expiratory air trapping can help differentiate small airway disease from CTEPH.[29]

CTPA has been included in European guidelines in the diagnostic algorithm of patients with PH and a mismatched defect on V/Q scan.[30] It can help with the assessment of surgically accessible disease and exclude other obstructing pulmonary arterial lesions such as fibrosing mediastinitis, vasculitis, pulmonary artery sarcomas (Figure 3), and neoplasms.[31] Although CTPA can identify chronic thrombi in the proximal aspects of the pulmonary arterial circulation, it often underestimates or is not able to characterize the distal chronic thrombi (Figure 4), which are typically treated with BPA. More recently, DECT with perfusion imaging has allowed for the assessment of anatomical obstruction and perfusion defects in different lung segments (Figure 4) via iodine perfusion mapping.[32] Differentiation between segments is performed by taking advantage of attenuation differences at different energy levels. Attenuation is dependent on photoelectric absorption which correlates with the composition of different materials and photon energies.[33] Iodine, in part because of its high atomic number, has decreased photoelectric effect with increasing photon energy. DECT takes advantage of the differences in absorption characteristics of different materials to generate maps that highlight perfusion distinctions.[20] Angiographic and perfusion co-relation with concomitant assessment of lung parenchyma is provided. DECT is used in patients undergoing BPA to identify areas of healthy lung parenchyma that are most hypoperfused. This information has the potential for lesion prioritization in BPA interventions to the most hypoperfused areas, thereby minimizing the number of sessions and maximizing the benefit. The limitations of widespread adoption of DECT include artifacts from motion, beam-hardening, which can cause pseudo-defects, lack of standardized protocols for reproducible imaging, and relatively limited availability and expertise.

Table 2. Vascular and parenchymal signs seen on computed tomography pulmonary angiogram in patients with acute and chronic thromboembolic disease.

	Acute thromboembolic disease	Chronic thromboembolic disease
Vascular signs	Vessel expansion; central filling defect forming acute angles with the wall	Abrupt narrowing; eccentric filling defect forming obtuse angles with the wall Webs Bands Focal stenosis Calcification Vessel attenuation Enlargement of bronchial arteries
Parenchymal signs	Pulmonary hemorrhage Pulmonary infarction	Varying "mosaic" attenuation Fibrotic bands Cylindrical bronchiectasis Pleural thickening

Nonselective invasive pulmonary angiography

Nonselective invasive pulmonary angiography (IPA) remains the gold standard for confirming the diagnosis of CTEPH and is usually combined with right heart catheterization with or without exercise testing to provide accurate hemodynamic assessment. The generation of anterior-posterior and lateral images allows for visualization of the pulmonary vasculature and accurate preprocedural localization of chronic vascular changes.[6] Characteristic findings for CTEPH on IPA include pouch defects, intimal irregularities, poststenotic dilatation, abrupt narrowing of pulmonary arteries, or the complete obstruction of larger arteries.[28] The absence of venous return indicates malperfusion of a given vascular territory.[34] The direction of blood flow and perfusion defects can be mapped.[20] Angiographic imaging can be prolonged to record levophase pulmonary vein drainage and thereby exclude pulmonary vein stenosis.[35] Thus, the location, distribution, and characterization of disease can be adequately assessed. The risks of IPA include pulmonary hemorrhage from pulmonary artery perforation and pericardial tamponade from cardiac chamber perforation, although these are quite rare.[36]

The baseline IPA is reviewed before BPA to identify suitable lesion targets. The key is to identify segments with segmental branch origins in which revascularization will provide the most benefit with the lowest predicted risk. The Central Illustration shows how IPA findings are used in combination with other findings from V/Q scan and CTPA for preprocedural BPA target lesion identification. Figure 5 illustrates the generally accepted anatomical definitions of proximal and distal chronic thromboembolic disease on IPA. Surgical inaccessibility is generally defined as disease in the distal segmental and subsegmental branches. However, this definition of surgically inaccessible disease varies from center to center based on surgeon experience. High volume centers have shown successful outcomes even with predominantly distal disease in the pre-BPA era.[37]

All 4 imaging modalities discussed in this section provide complimentary information in several ways. Although TTE, V/Q, CTPA, and IPA are routinely performed in patients undergoing CTEPH evaluation, DECT is still investigational, but we believe that it has ample promise for a major role in these patients, especially in those undergoing BPA (Central Illustration).

Intraprocedural guidance

Subselective segmental angiography

During BPA, subselective segmental angiography (SSA) is performed following selective segmental cannulation.[38] Most segmental pulmonary arteries can be selectively cannulated with coronary guide catheters with adjunctive use of a telescoping guide extension catheter as needed. Table 3 lists suggested guiding catheters used for cannulation. We recommend performing SSA in 2 orthogonal projections at

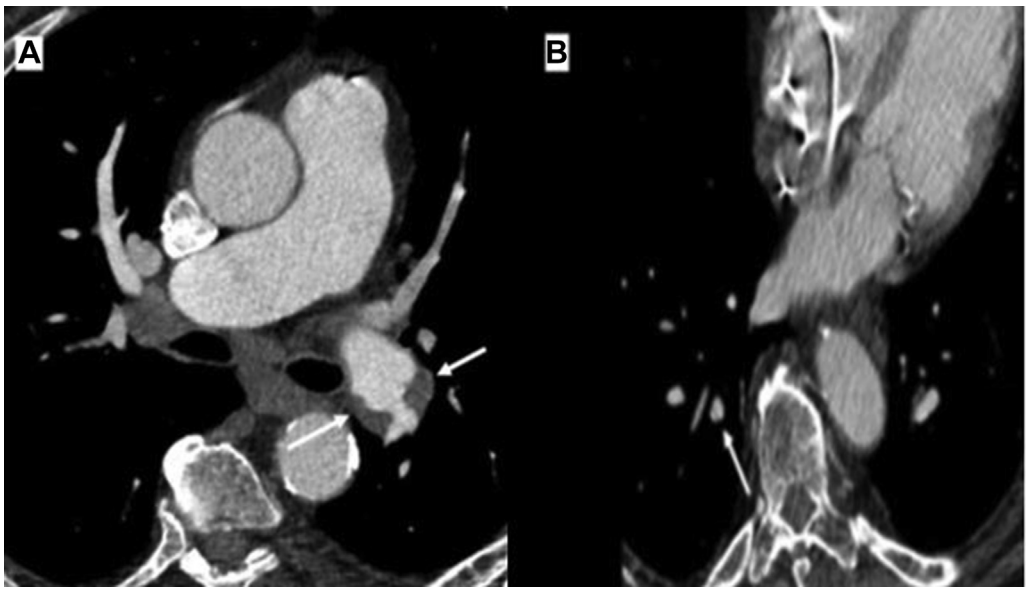


Figure 2. Features of chronic thromboembolic pulmonary hypertension commonly seen on CTPA. Contrast-enhanced axial computed tomographic image (**A**) shows an eccentric filling defect making obtuse angles with the pulmonary arterial wall (arrow), consistent with chronic thromboembolic disease. Another image more caudally (**B**) shows a web-like filling defect in a right lower lobe subsegmental artery (arrow). CTPA, computed tomography pulmonary aniography.

baseline after cannulation for every segment. Orthogonal imaging enhances our understanding of the vessel/branch anatomy and disease type and location. An inspiratory breath hold is recommended for middle and lower lobar segments for optimal vessel visualization. SSA of individual pulmonary artery segments is necessary for delineating subsegmental branch anatomy and for lesion assessment in BPA.[35] Although digital subtraction angiography is necessary for IPA, we do not recommend using digital subtraction angiography for SSA to minimize radiation dose during BPA procedures. SSA can also help identify the rate of perfusion, venous return, and arteriovenous malformations that can occur in CTEPH.

SSA helps further characterize lesions into focal stenosis, band-like lesions, intravascular webbing, pouch lesions, chronic total and subtotal occlusions, diffusely tortuous lesions, arterial wall irregularities, and bronchial collateralization (Figure 6, A-E).[39,40] Previous reports have suggested a direct correlation between certain lesion characteristics and procedural outcomes. BPA has higher success with low complication rates in focal stenosis, band-like lesions, and intravascular webbing. Alternatively, diffusely tortuous lesions, pouch lesions, and chronic total occlusions are associated with lower procedural success rates and a relatively higher rate of vascular injury. The clinical significance of bronchial collateralization is unclear at this time. We believe that this individual per lesion characterization is critical when operators are analyzing risk-benefit profile on a lesion-by-lesion basis intraprocedurally. Ultimately, operator and center experience also plays a considerable role in procedural outcomes, especially in higher-risk lesions.[40]

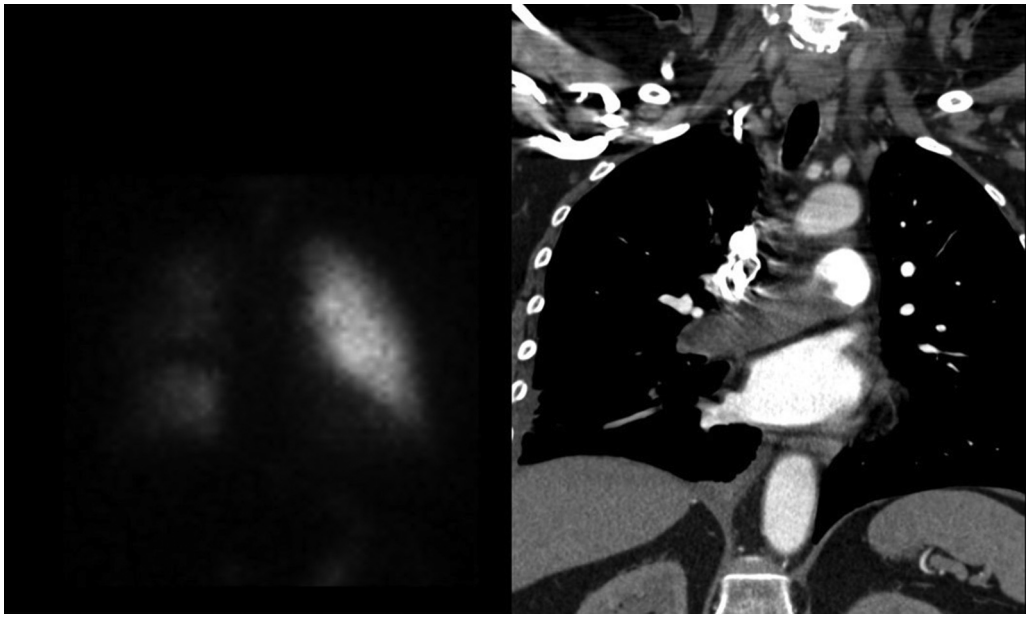


Figure 3. Utility of CT in differentiating pulmonary arterial lesions. Ventilation/perfusion scan with multiple moderately sized perfusion mismatch defects. On coronal contrast-enhanced CT, this corresponded to an occlusive unilateral filling defect in the right pulmonary artery. This defect increased in size on a subsequent CT chest and was proven to be a pulmonary artery sarcoma. CT, computed tomography.

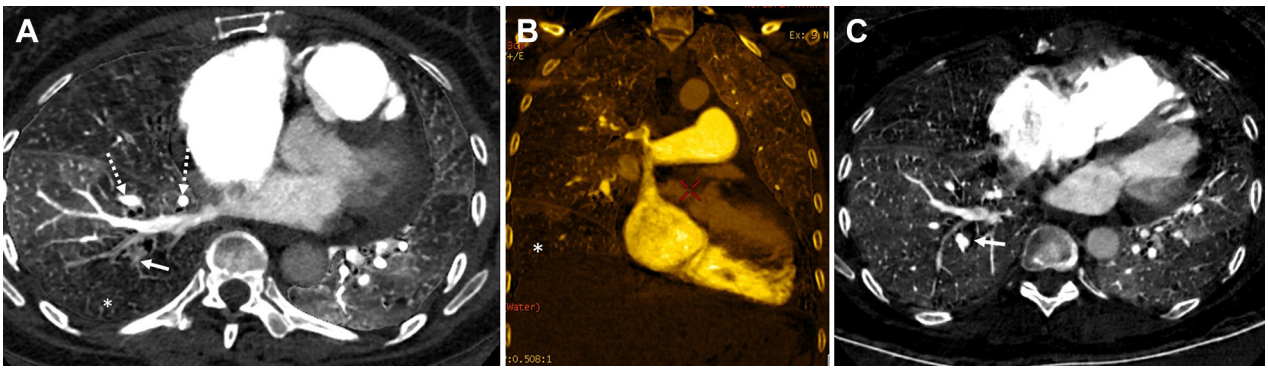


Figure 4. A 70-year-old woman with chronic thromboembolic pulmonary hypertension who underwent BPA. Perfusion maps in the axial (gray scale, **A**) and coronal (color map, **B**) planes are shown before BPA. Note the narrowing of the right lower lobe posterior segmental branch (solid arrow, **A**) compared with the normal appearance of the other right lower lobe segmental branches (dashed arrows, **A**). This corresponds to a perfusion defect (asterisk, **A** and **B**). Additional perfusion defects are also seen bilaterally (darker areas of the lung). After BPA, the revascularized vessel (arrow, **C**) shows improved patency and enhancement with associated improvement in lung parenchymal perfusion. BPA, balloon pulmonary angioplasty.

Adjunctive intraprocedural imaging during BPA session

The absence of brisk venous return in vessels that appear angiographically patent by SSA may result from intravascular webbing that is otherwise not obvious on SSA alone. Adjunctive assessment via intravascular imaging is very useful in such cases. Intravascular ultrasound (IVUS) and optical coherence tomography (OCT) can help identify intravascular webs (Figure 6F). The presence of a pressure drop across these segments is also a sign of significant obstruction. Although established criteria for a significant pressure gradient across these lesions are lacking, we consider an arbitrary cut-off of <0.8 Pd/Pa (Pd: distal pressure, Pa: proximal pressure) as significant (Figure 6, G, H).[41,42] This value has not been shown to correlate with any particular clinical outcomes. We believe that the most useful marker of adequate dilatation is the reestablishment of brisk venous return on SSA.

Intravascular ultrasound and OCT also provide an accurate assessment of vessel size and help with appropriate balloon sizing in cases where SSA alone is insufficient to make that determination. Balloon sizing in BPA is generally very conservative, but IVUS or OCT can be used in selected cases for 1:1 sizing when angiographically undersized balloons are unable to restore brisk venous return.[43] This has been shown to improve hemodynamic outcomes and reduce the risk of complications.[41,44] Another key consideration is the role of sequential dilatation with larger balloons in subsequent sessions. Chronically occluded subsegmental pulmonary arteries may only accommodate a small balloon on initial revascularization, but these vessels subsequently remodel and

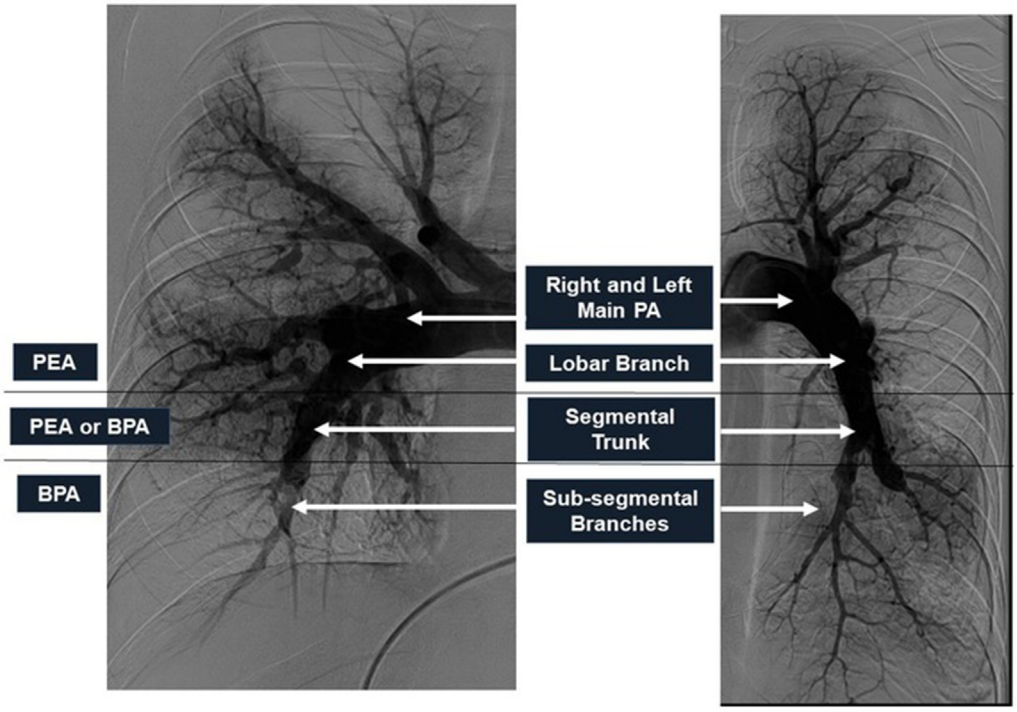


Figure 5. Anatomical definitions of chronic thromboemoblic disease. IPA demonstrating generally accepted pulmonary arterial anatomical definitions and indications for PEA and BPA. BPA, balloon pulmonary angioplasty; IPA, invasive pulmonary angiography; PEA, pulmonary endarterectomy; PA, pulmonary artery.

Table 3. Recommended guiding catheters for subselective cannulation.

Segmental branch	Catheter recommendation
Left apicoposterior trunk (A1-2)	MPA-2 or JR4
Left anterior segment (A3)	JR4
Lingula (A4-5)	JL3.5/4 or Champ 2.5
Left superior segmental (A6)	JR4
Left anterolateral trunk (A7-8-9)	MPA-2 or JR4
Left medial basal (A10)	JR4
Right apical segment (A1)	JR4 or AL3
Right posterior segment (A2)	JR4
Right anterior segment (A3)	JR4
Right middle lobe (A4-5)	JR4
Right lower lobe superior segment	JR4
Right lower lobe anterolateral segmental trunk (A7-8)	JR4
Right lower lobe posteromedial segmental trunk (A9-10)	MPA-2

AL, Amplatz left; JL, Judkins left; JR, Judkins right; MPA, Multipurpose A.

grow to facilitate dilatation with a larger balloon during later treatment sessions. IVUS and OCT are especially useful in such cases. Further work will refine the role of intravascular imaging in BPA beyond balloon sizing and establish pressure gradient cutoffs for significant obstruction in such cases.

Postprocedural considerations

Imaging after BPA is centered around the assessment of immediate postprocedural complications and a follow-up assessment of the right ventricle. We recommend taking a baseline chest radiograph immediately after a BPA session to rule out early reperfusion edema and to establish a baseline that is useful in assessing subsequent delayed reperfusion edema and/or hemoptysis in the first 24 to 48 hours after BPA. A TTE at 3 to 6 months following BPA is also recommended in all patients with baseline RV abnormalities who undergo BPA.[45,46]

A V/Q scan, CTPA, or IPA is not routinely performed following BPA. These studies should be performed in select cases when recurrent disease and/or restenosis is suspected. Future research will help establish the utility of perfusion imaging in the routine follow-up of patients after BPA. A 2D echocardiogram is routinely performed for the assessment of RV size and function.[45,46] Cardiac magnetic resonance imaging and strain imaging echocardiography are more sensitive for RV assessment and may be able to detect RV abnormalities earlier than conventional 2D TTE. At this time, they are only used in selected cases when 2D TTE alone is deemed insufficient for RV characterization and/or findings of RV abnormalities are likely to change management.[47]

Conclusion and future directions

Balloon pulmonary angioplasty has emerged as an effective treatment alternative for patients with CTEPH who are not eligible for PEA. Multimodality imaging plays an integral part in the planning and performance of BPA and is crucial for a successful treatment. Future research is needed to further define the roles of each of the imaging modalities discussed above in such patients.

Declaration of competing interest

Dr Rosenfield holds equity for and serves on the advisory board of Althea Medical; is a consultant for AngioDynamics, Boston Scientific, Contego Medical, Neptune Medical, Penumbra, and Philips; and is a principal investigator or coinvestigator on research grants from the National Institutes of Health and Boston Scientific. Drs Patel, Hyder, Michaud, Moles, Agarwal, Abe, Haft, Visovatti, Cascino, Auger, Mclaughlin, and Aggarwal reported no financial interests.

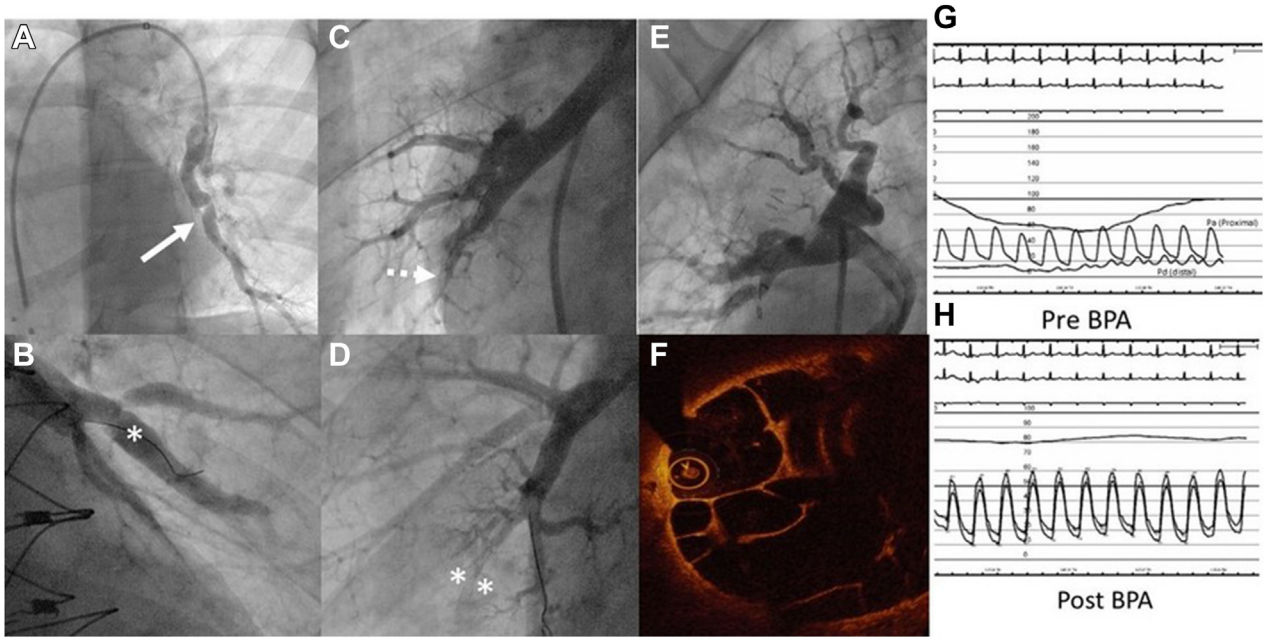
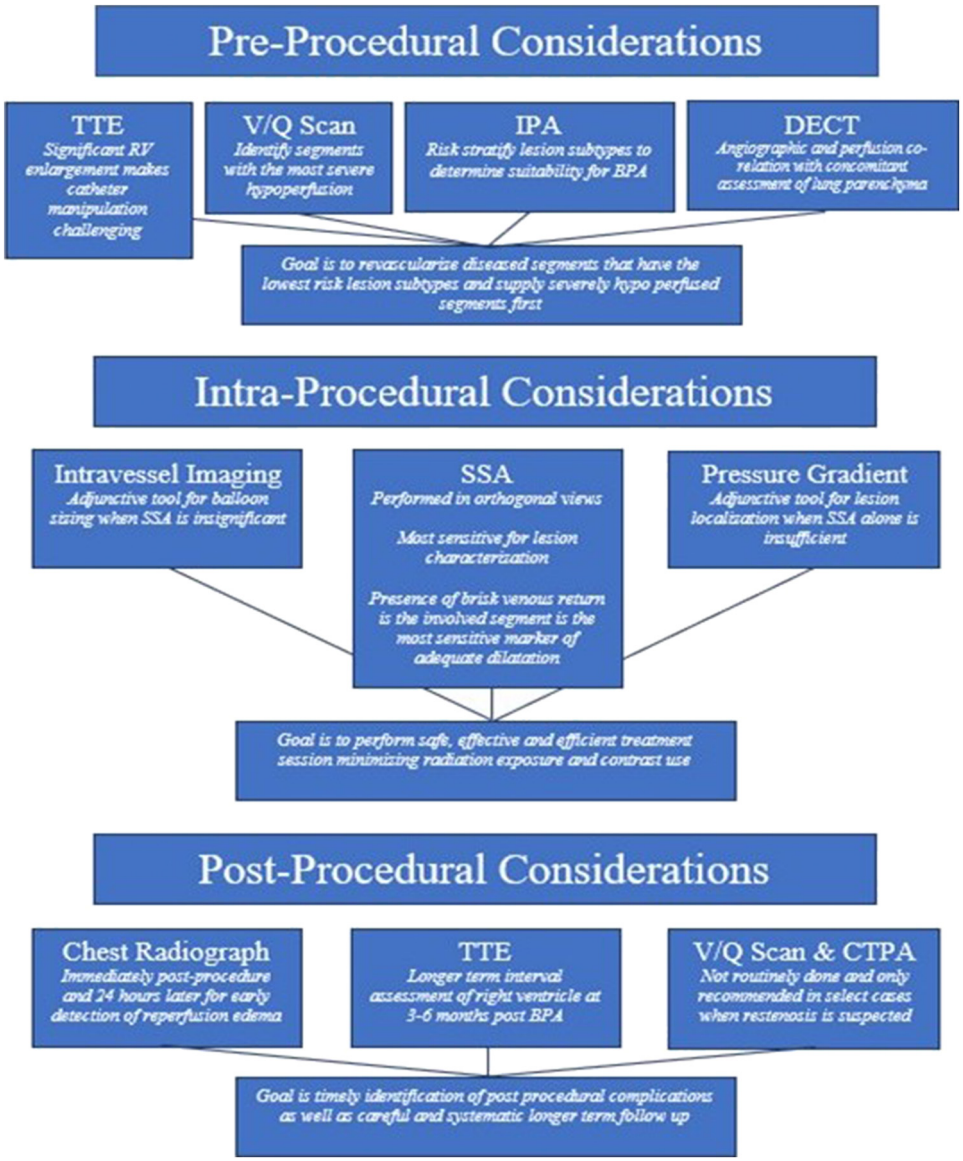


Figure 6. Various lesion abnormalities seen on subselective pulmonary angiography in patients with CTEPH. Subselective pulmonary angiogram appearance of band-like stenosis (solid arrow, **A**), intravascular webbing (asterisk, **B**), subtotal occlusion (dashed arrow, **C**), total occlusion (double asterisk, **D**), tortuous and diseased vessels (**E**), optical coherence tomography image of intravascular webbing (**F**), and pressure gradient measurement during BPA (**G** and **H**). BPA, balloon pulmonary angioplasty; CTEPH, chronic thromboembolic pulmonary hypertension.



Central Illustration. Preprocedural, intraprocedural, and postprocedural considerations of patients undergoing BPA. BPA, balloon pulmonary angioplasty; CTPA, computed tomography pulmonary angiogram; DECT, dual-energy computed tomography; IPA, invasive pulmonary angiography; RV, right ventricular; SSA, subselective segmental angiography; TTE, transthoracic echocardiogram; V/Q, ventilation/perfusion.

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Ethics statement

The research reported in this article adhered to relevant ethical guidelines.

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