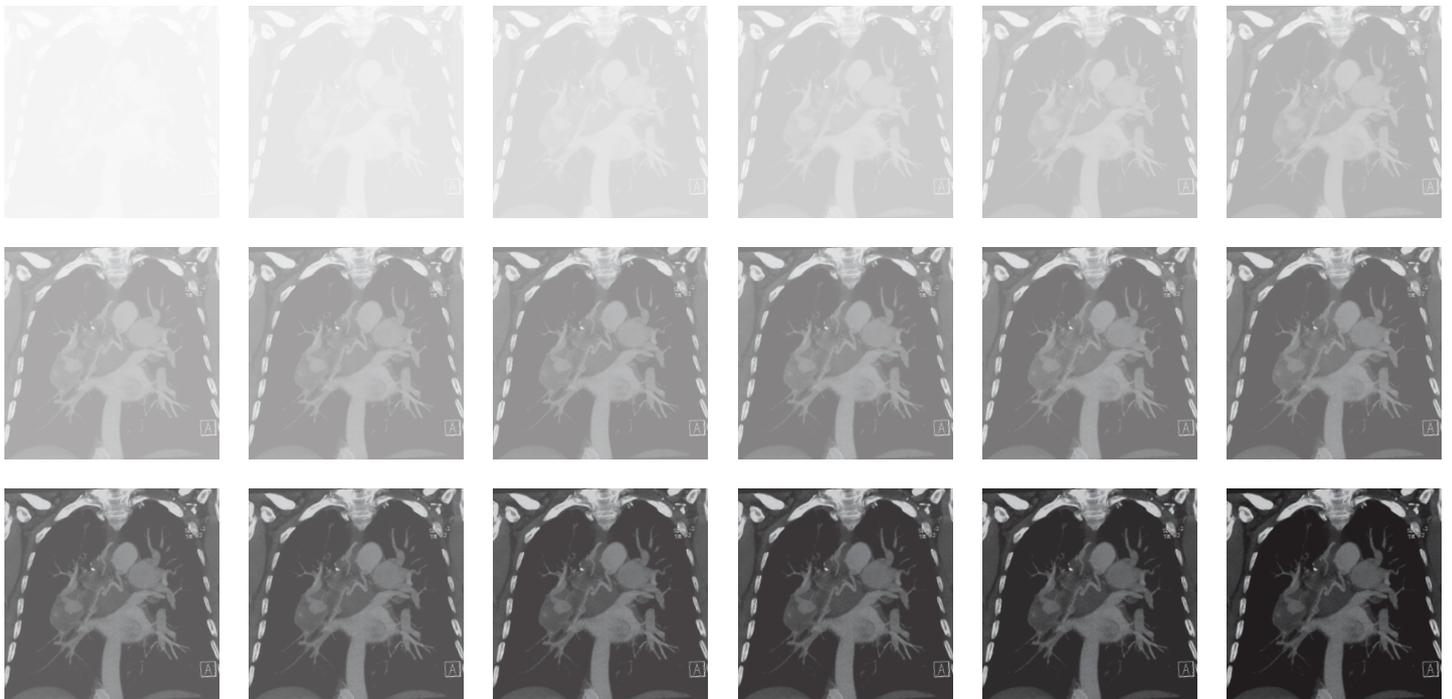


Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

Diagnosis and Differential Diagnoses in CT



CTEPH

Scan for it, for the chance to surgically cure it



Foreword

CT Case Studies provided by courtesy of JF Paul, MD

Chronic thromboembolic pulmonary hypertension (CTEPH) is a type of severe pulmonary hypertension (PH), a rare disease that is associated with significant morbidity and mortality.^{1,2} It is the only type of PH that is potentially curable using a complex surgical procedure called pulmonary endarterectomy (PEA). However, CTEPH is often under-recognized and underdiagnosed because the symptoms are non-specific and often subtle.³

CTEPH is characterized by high pulmonary vascular resistance and organized fibrous material obstructing the pulmonary artery branches.⁴ Acute pulmonary embolism (PE) is the most common cause.⁵ As many as 1 in 25 PE survivors, who have received more than 3 months of anticoagulation, may develop CTEPH within 2 years.⁶ The possibility and seriousness of developing CTEPH subsequent to acute PE should not be underestimated or overlooked.² Early and accurate diagnosis of CTEPH is critical in patients who present with clinical features of PH, or who are at high risk following an acute PE, to avoid missing out on a potential cure.²

This brochure aims to support radiologists and referring physicians to recognize and differentiate CTEPH by supplementing guideline recommendations with illustrative case studies and typical radiological findings using computed tomography (CT). It shows different presentations of CTEPH and other forms of PH to facilitate a correct diagnosis. We have an early opportunity to recognize CTEPH, and therefore play a key role in ensuring a timely and accurate diagnosis.

The brochure also provides information about imaging protocols, post-processing techniques and CT results for CTEPH as well as other types of PH.

More information for general practitioners, pulmonologists, and cardiologists is also available from Bayer.

The 'Referring Physician' brochure provides information on the utility of different imaging modalities including ventilation/perfusion scintigraphy (V/Q), CT, magnetic resonance imaging (MRI) and the right heart catheter (RHC) examination.

JF Paul, MD

About the Author:

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Methods

CT has become the reference standard for acute PE due to its high sensitivity and specificity^{7,8} to detect chronic thromboembolic disease in segmental, lobar, or main pulmonary arteries.^{9,10} However, CT pulmonary angiography (CTPA) may miss disease that is confined to very distal segmental or subsegmental pulmonary arteries. Hence, V/Q is the guideline recommended screening test for CTEPH. It shows 96–100% sensitivity, meaning that a negative (i.e. normal) V/Q essentially rules out the presence of CTEPH.³

Once a CTEPH diagnosis is confirmed, all patients should be evaluated for potentially curative PEA surgery based on RHC and pulmonary angiography (CT and/or conventional) to assess disease severity as well as the site and accessibility of the obstruction.³

The imaging of postembolic fibrotic tissue differs from that of fresh clots. Using CT, a fresh clot is typically seen surrounded by contrast. Chronic material sticks to the pulmonary arterial wall and makes detection more difficult, as arteries look thinner and the contrast stays centrally. Obstructive material may be either thick (typically in proximal obstructive forms) or thin (in distal forms).

- Proximal obstructive forms are easy to detect; however, some differential diagnoses are important to know, for example pulmonary sarcoma or idiopathic pulmonary arterial hypertension (IPAH) with non-obstructive clots due to slow pulmonary flow.
- Distal forms require a rigorous protocol for both CT acquisition and interpretation. With 15 years' experience in a cardiothoracic center, I recommend using a sufficient contrast injection rate and appropriate radiation parameters. Achieving good image quality is crucial to detect subtle anatomical changes in matter. A second acquisition at systemic arterial phase may be useful to evaluate collateral blood supply and analyze whether distal pulmonary arteries are obstructed. In both left and right parasagittal planes, 15 mm thin slab maximum intensity projections (MIP) are appropriate.

References:

1. Fedullo P et al. *Am J Respir Crit Care Med* 2011;183:1605–1613.
2. Mehta S et al. *Can Respir J* 2010;17:301–334.
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The case reports shown in this brochure were obtained at the "Centre Chirurgical Marie Lannelongue", Le Plessis-Robinson, France

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Orientation of anatomy in CT



Perspective: front view



Perspective: left back side view



Perspective: left front side view



Perspective: view from feet towards head, with patient position lying on his/her back

Case 1

Proximal CTEPH

Patient history

A 56-year-old female patient with a history of PE presented with progressive dyspnea. A V/Q scan revealed multiple perfusion defects that were suggestive of CTEPH. An additional pulmonary angiography showed severe PH associated with multiple segmental pulmonary obstructions. A CT scan was performed to confirm the diagnosis of CTEPH and to evaluate presurgical conditions.

Protocol

| Spiral CT acquisition | |
|-----------------------|--|
| Injection | 60 cc of iodinated LOCM 370 mg / mL |
| Rate | 4 cc/s |
| Saline chaser | 40 cc at 4 cc/s |
| Start delay | Care bolus: acquisition starts when 300 HU is obtained in pulmonary artery |
| Second spiral | Immediately after, without reinjection (arterial systemic phase) |
| Collimation | 0.6 mm |
| Parameters | 120 kVp, 180 mAs |
| Reconstructions | Axial, multiplanar reformat, and 15 mm thin-slab MIP reconstructions |

Findings

At pulmonary phase:

The CT scan shows thick endovascular soft tissue images along the pulmonary arteries, with predominant right pulmonary artery involvement (Figure 1). Multiple segmental arteries are obstructed on both sides by endovascular material (Figures 2 and 3). Most obstructions are located at the origin of segmental arteries (Figure 4).

At arterial phase:

Enlarged bronchial arteries are depicted, providing systemic blood flow to pulmonary arteries (Figure 5).

Patient outcome

Successful surgical PEA was performed.

Take-home messages

Proximal forms are more easily accessible during PEA than distal forms.¹

CT is helpful to confirm diagnosis and to diagnose proximal forms, thus determining a patient's suitability for PEA surgery.^{1,2}

References:

1. Jenkins D. Eur Respir Rev 2015;24:263–271.
2. Galiè N et al. Eur Heart J 2016;37:67–119.

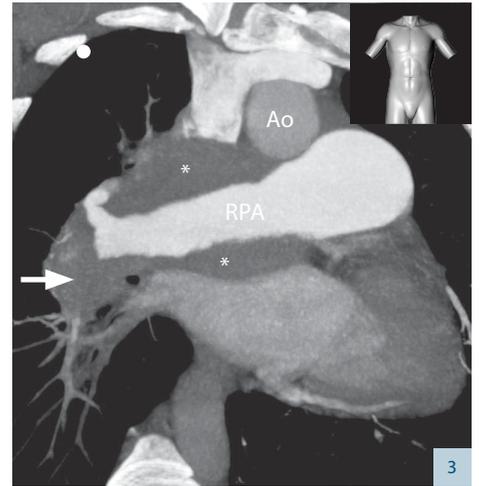
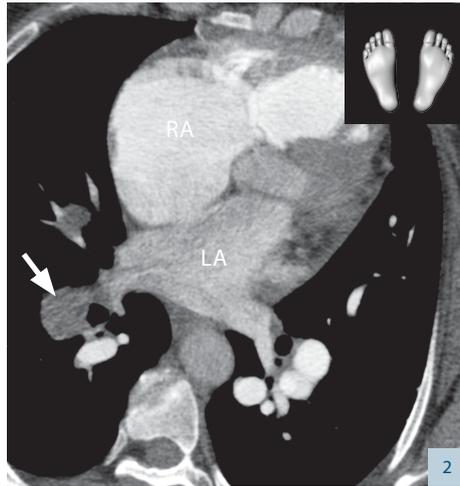
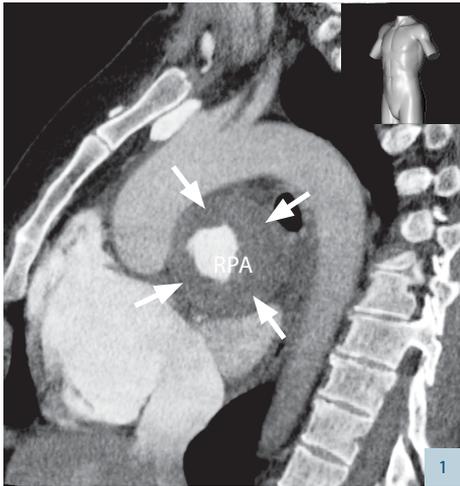


Figure 1. Sagittal view centered on aorta shows very thick tissue along the right pulmonary artery wall (arrows).

Figure 2. Mid-thoracic axial view shows obstruction of both the right lateral and postero-lateral pulmonary arteries (arrow).

Figure 3. Mid-thoracic frontal view confirms both very thick soft tissue along the right pulmonary artery (asterisks) and obstruction of the intermediate pulmonary artery (arrow).

Figure 4. Sagittal view of the left pulmonary artery shows multiple occlusions at the origin of segmental pulmonary arteries (arrows).

Figure 5. Arterial phase: mid-thoracic frontal view shows enlarged bronchial artery originating from aorta artery (arrow), providing blood flow to right pulmonary lower lobe.

Case 2

Segmental CTEPH

Patient history

An 84-year-old female patient presented with dyspnea. She had no previous history of PE. Echocardiography revealed PH. CT was performed to look for an etiology.

Protocol

| Dual-source spiral CT acquisition (single-source mode) | |
|--|--|
| Injection | 60 cc of iodinated LOCM 370 mg / mL |
| Rate | 4 cc/s |
| Saline chaser | 40 cc at 4 cc/s |
| Start delay | Care bolus: acquisition starts when 300 HU is obtained in pulmonary artery |
| Collimation | 0.6 mm |
| Parameters | 120 kVp, 180 mAs |
| Reconstructions | Axial, multiplanar reformat, and 15 mm thin-slab MIP reconstructions |

Findings

CT scans show endovascular material obstructing pulmonary arteries, mainly depicted at the level of segmental arteries (Figures 1–4). On the left side, obstructive material was less abundant and more distal.

Patient outcome

A partial relief of PH was achieved by PEA. Soft tissue specimens were removed mainly from the right pulmonary artery.

Take-home messages

Unlike proximal forms of CTEPH, distal forms, i.e. segmental or subsegmental obstructions, are difficult to diagnose. This is mainly due to the small size of postembolic fibrotic tissue.

The performance of CT should be exercised using a submillimeter collimation. In order to get a low noise level and at the same time gain a high contrast enhancement in the pulmonary arteries, protocol parameters should be selected.

In distal forms of CTEPH, surgical treatment is far more challenging.¹ To remove endovascular fibrotic tissue, the surgeon is dependent on finding a plane for PEA.¹

A thickening of at least 2 mm in the main or lobar arteries on CT serves as an indicator of operability.²

References:

1. Jenkins D. Eur Respir Rev 2015;24:263–271.
2. Paul JF et al. Am J Roentgenol 2007;188(4):1059–62.

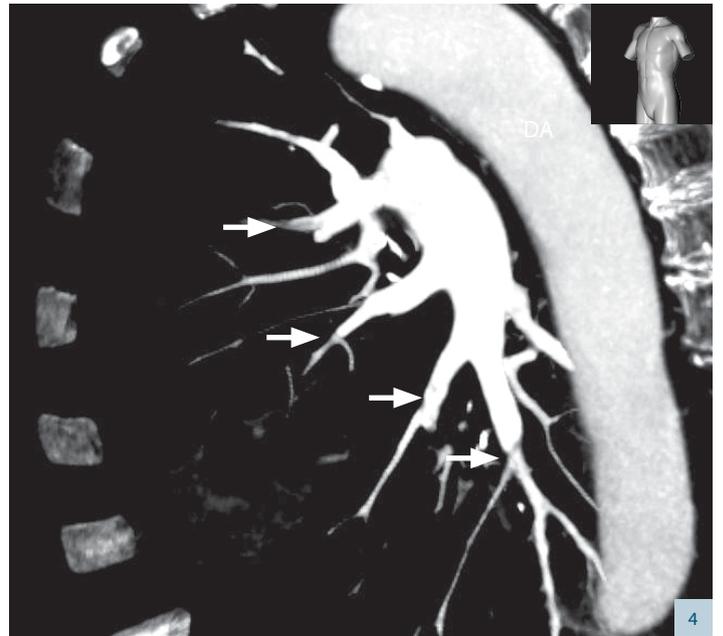
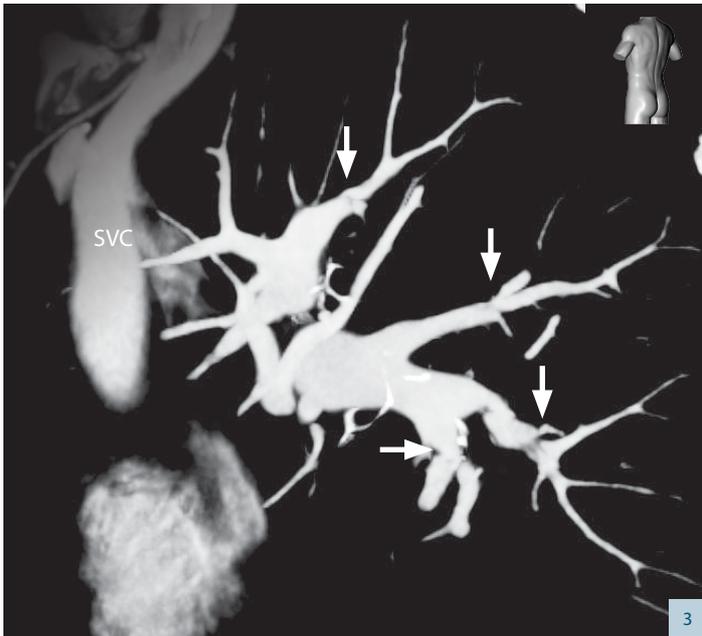
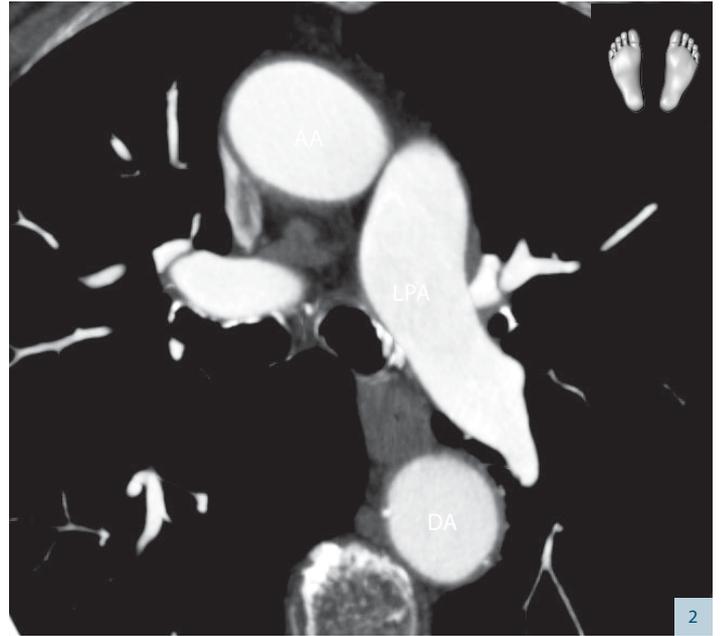
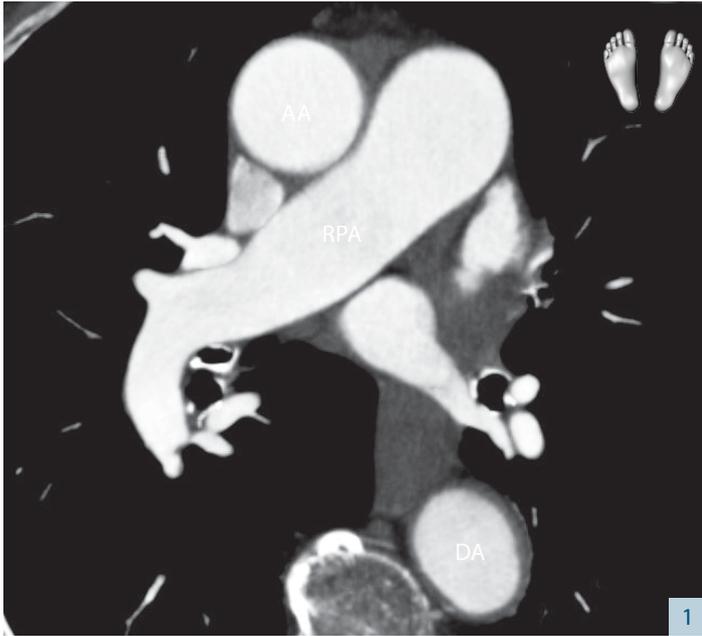


Figure 1. Axial view centered on right pulmonary artery shows normal-size vessel without wall thickening.

Figure 2. Axial view centered on left pulmonary artery shows normal-size vessel without wall thickening.

Figure 3. 15 mm thick parasagittal MIP view of the right pulmonary artery shows multiple web-like soft tissue obstructions (arrows) at the level of segmental arteries.

Figure 4. 15 mm thick parasagittal MIP view of the left pulmonary artery shows multiple web-like soft tissue obstructions (arrows) at the level of both segmental and subsegmental arteries.

Case 3

Subsegmental CTEPH

Patient history

A 25-year-old male patient presented with severe PH. He had a recent medical history of bone sarcoma treated with surgery and chemotherapy via a central catheter. His severe PH developed subsequently. A thrombus was found around the catheter and removed. CT was performed to define eligibility for surgical intervention.

Protocol

| Dual-source CT using single-source spiral mode | |
|--|--|
| Injection | 60 cc of iodinated LOCM 370 mg / mL |
| Rate | 4 cc/s |
| Saline chaser | 40 cc at 4 cc/s |
| Start delay | Care bolus: automatic start at 300 HU in pulmonary artery |
| Collimation | 0.6 mm |
| Parameters | 120 kVp, 180 mAs |
| Reconstructions | Axial, multiplanar reformat, and 15 mm thin-slab MIP reconstructions |

Findings

At pulmonary phase:
CT shows very distal endovascular material obstructing the pulmonary arteries, depicted mainly at the subsegmental level (Figures 1–4).

Patient outcome

Due to the very distal location of the obstructive lesions, the patient was not eligible for surgery and was treated with medical therapy.

Take-home messages

When using standard axial images, subsegmental obstructions as very distal forms of CTEPH are not visible. Therefore, thin slab-MIP images in various planes are recommended.

A definite distinction between a purely distal form of CTEPH and IPAH may be impossible. In both cases surgery is not possible due to high risk – a fact that makes such a distinction less crucial for the patient.

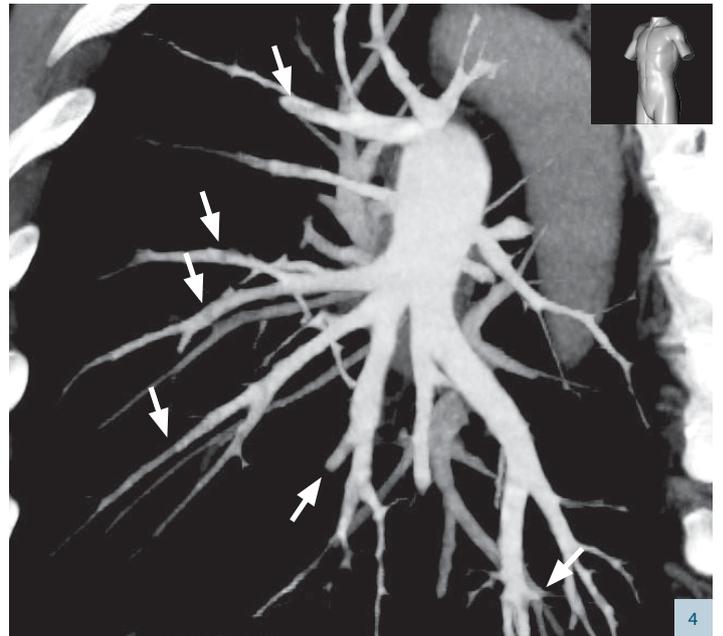
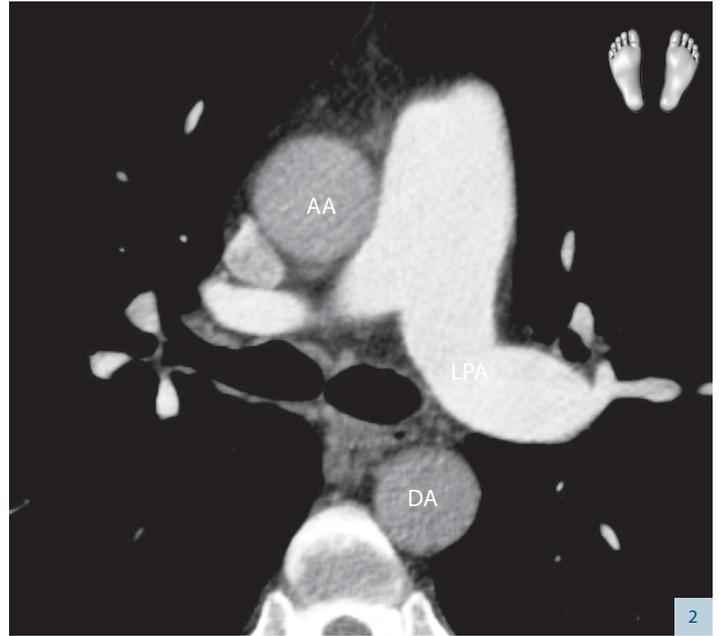
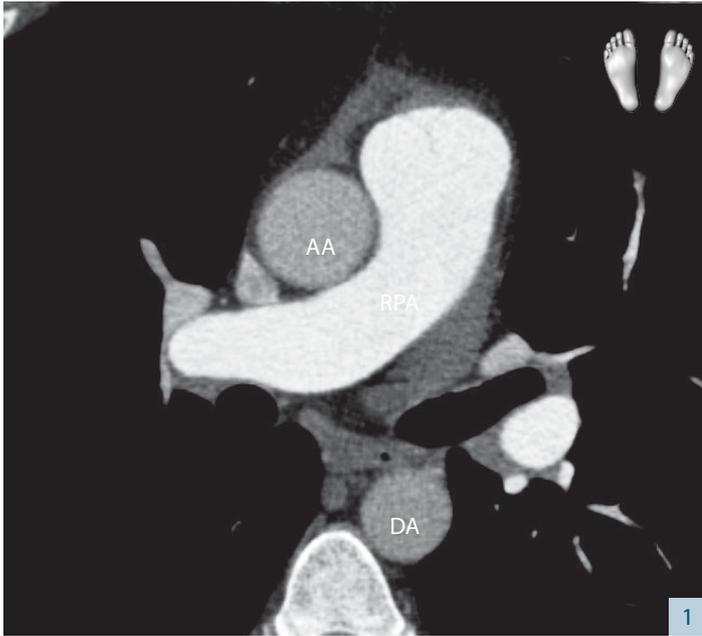


Figure 1. Axial view centered on right pulmonary artery shows normal-size pulmonary vessel without wall thickening.

Figure 2. Axial view centered on left pulmonary artery shows normal-size pulmonary vessel without wall thickening.

Figure 3. 15 mm thick parasagittal MIP view of the right pulmonary artery shows multiple soft tissue obstructions (arrows) mainly at the level of subsegmental arteries.

Figure 4. 15 mm thick parasagittal MIP view of the left pulmonary artery shows multiple very distal obstructions (arrows) at the level subsegmental arteries.

Case 4

Idiopathic pulmonary arterial hypertension with thrombus

Patient history

A 54-year-old female patient was diagnosed with IPAH. As she had a previous history of PE, CT was performed to exclude CTEPH as an alternative diagnosis.

Protocol

| Dual-source CT acquisition in single spiral mode | |
|--|--|
| Injection | 60 cc of iodinated LOCM 370 mg / mL |
| Rate | 4 cc/s |
| Saline chaser | 40 cc at 4 cc/s |
| Start delay | Care bolus: automatic start at 300 HU in pulmonary artery |
| Collimation | 0.6 mm |
| Parameters | 120 kVp, 180 mAs |
| Reconstructions | Axial, multiplanar reformat, and 15 mm thin-slab MIP reconstructions |

Findings

The CT scans show very large arteries with very few endovascular, non-obstructing material (Figures 1–5). A small clot may not necessarily be the cause of PH; however, a thrombus is likely to occur due to slow flow within the pulmonary arteries.

Patient outcome

On CT, there was no evidence of CTEPH, which may provide justification for PAH-targeted medical therapy.

Take-home messages

In CTEPH, endovascular obstructive fibrous lesions are responsible for increased pulmonary vascular resistance (PVR) and PH.¹

As shown in this clinical presentation, a slow flow in the pulmonary vascular bed may be the cause for clot formation in IPAH. In CTEPH, the organized thromboembolic obstruction is the cause of pulmonary hypertension;¹ whereas in pulmonary arterial hypertension (PAH), the clot is a consequence of PH. CT should be used to determine if the clot is obstructive.

A clot due to slow flow within the pulmonary arteries of a patient with IPAH is often found along the right pulmonary artery and may be misleading. Incorrect diagnosis of CTEPH may lead to unsuccessful and risky surgical intervention.

References:

1. Mehta S et al. Can Respir J 2010;17:301–334.

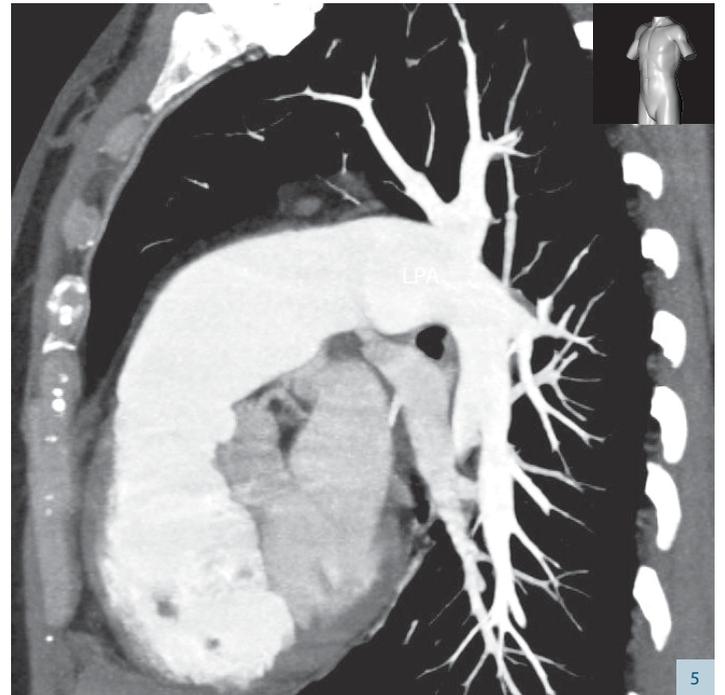
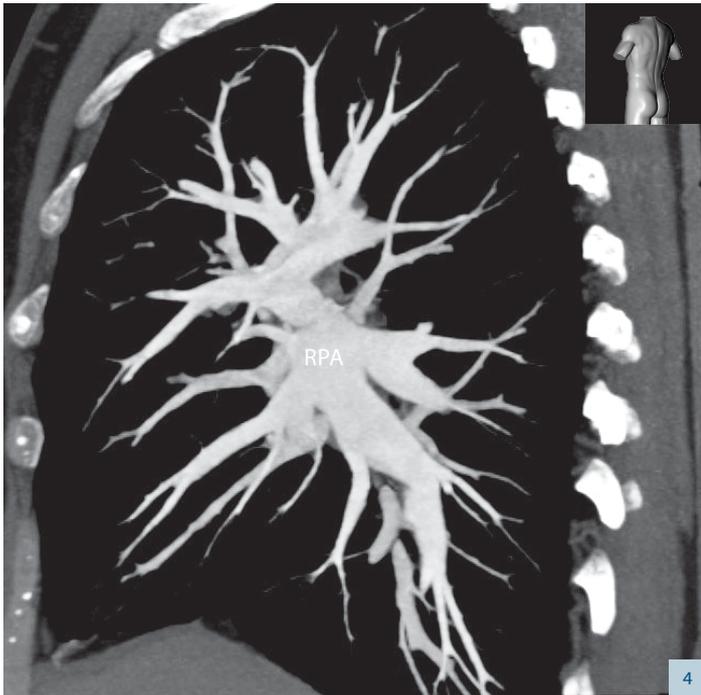
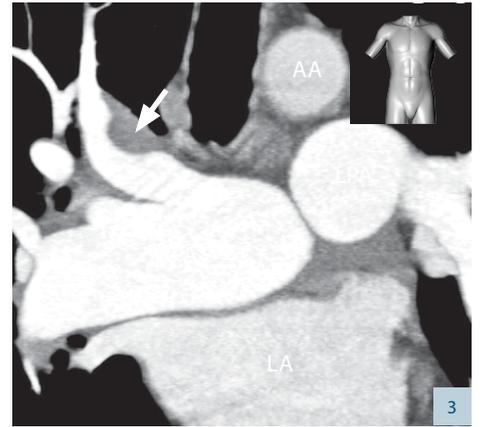
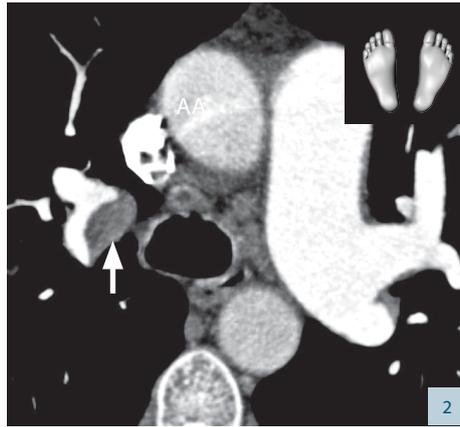
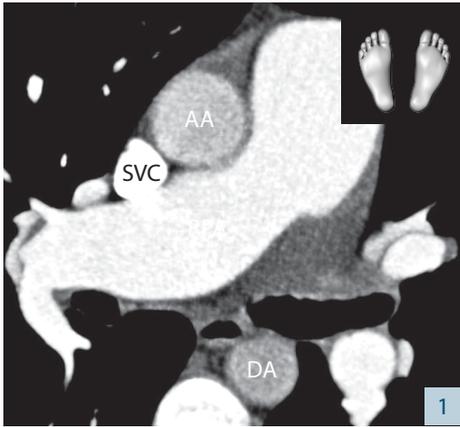


Figure 1. Axial view centered on right pulmonary artery shows enlarged vessel without wall thickening.

Figure 2. Axial view centered on left pulmonary artery shows enlarged vessel without wall thickening. Note endovascular soft tissue within the right upper lobe pulmonary artery (arrow)

Figure 3. 10 mm thick frontal MIP view confirms an isolated and non-obstructive clot of the upper lobe artery (arrow).

Figure 4. 15 mm thick parasagittal MIP view of the right pulmonary artery shows large and regular segmental and subsegmental pulmonary arteries, without any evidence of obstruction.

Figure 5. 15 mm thick parasagittal MIP view of the left pulmonary artery shows large and regular segmental and subsegmental pulmonary artery branches, without any evidence of obstruction.

Case 5

Pulmonary sarcoma

Patient history

A 34-year-old female patient presented with recent dyspnea and fatigue. She had no previous history of deep venous thrombosis (DVT) or PE. A serum blood test showed elevated erythrocyte sedimentation rate (ESR). Echocardiography disclosed PH. A chest CT scan was performed for further evaluation.

Protocol

| Dual-source CT acquisition in single spiral mode | |
|--|--|
| Injection | 60 cc of iodinated LOCM 370 mg/mL |
| Rate | 4 cc/s |
| Saline chaser | 40 cc at 4 cc/s |
| Start delay | Care bolus: automatic start at 300 HU in pulmonary artery |
| Collimation | 0.6 mm |
| Parameters | 100 kVp, 200 mAs |
| Reconstructions | Axial, multiplanar reformat, and 15 mm thin-slab MIP reconstructions |

Findings

The CT scan shows a complete right pulmonary obstruction triggered by expansive tumor-like soft tissue that is highly vascularized (Figures 1–3). The tumoral tissue starts at the level of the pulmonary valve and also involves the origin of the left pulmonary artery (Figure 4).

Patient outcome

The diagnosis was pulmonary sarcoma. Interventions included a surgical resection of the tumor and chemotherapy. One year later, the patient died of pulmonary metastases.

Take-home messages

Pulmonary sarcoma may mimic CTEPH. Valve involvement and highly vascularized endovascular tissue are very suggestive of pulmonary sarcoma. To disclose a vascular enhancement still present in the tumoral tissue, a delayed enhancement CT scan may be advisable.

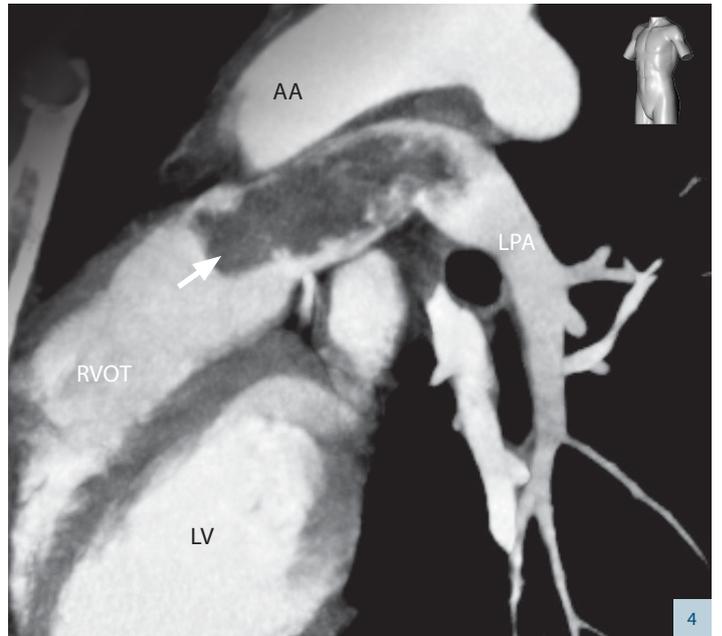
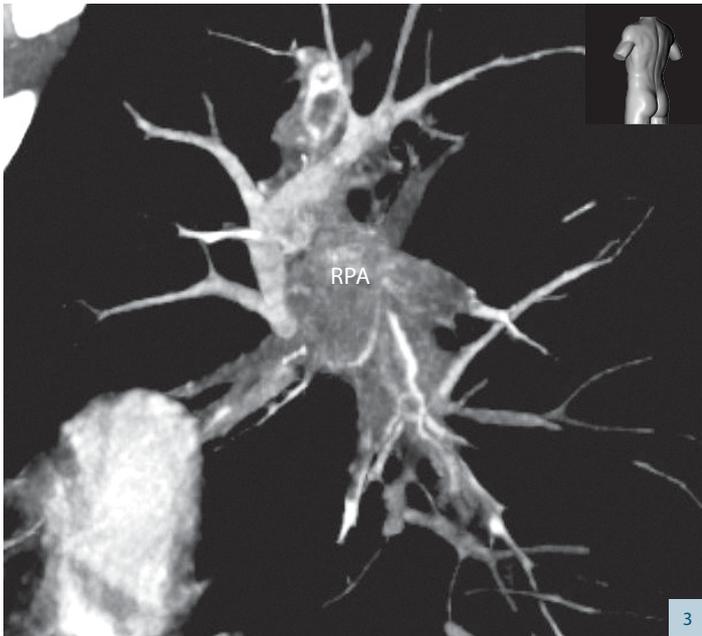
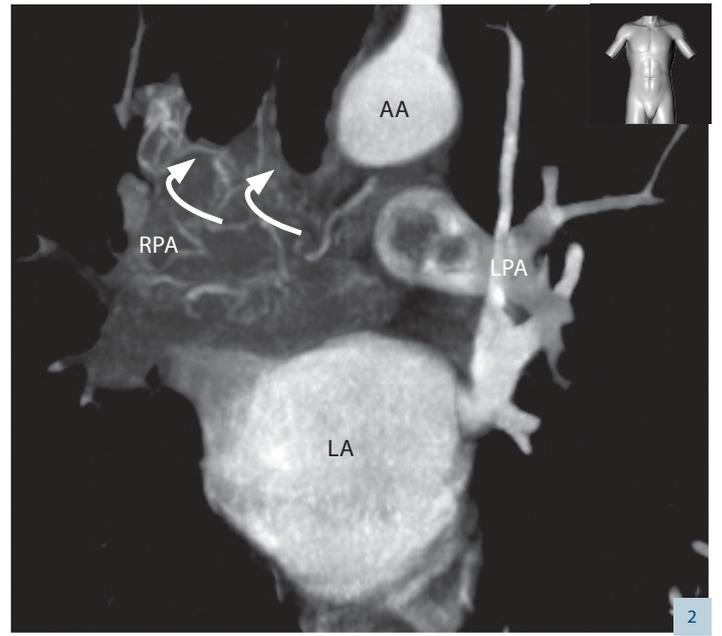
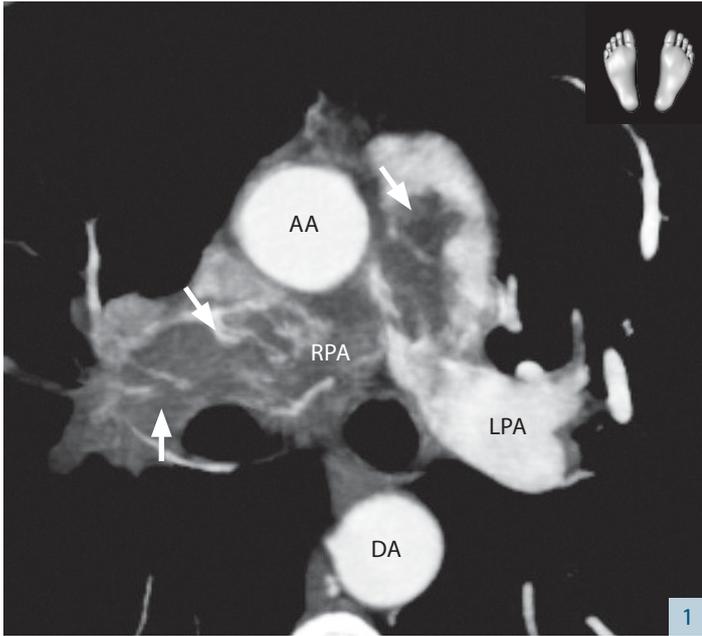


Figure 1. Axial 10 mm thin slab MIP view centered on right pulmonary artery shows enlarged and obstructive soft tissue with full obstruction of right pulmonary artery (arrows). Note that multiple blood vessels are feeding the tumoral tissue.

Figure 2. Frontal 10 mm thin slab MIP view centered on right pulmonary artery shows expansion (paunching) of tissue enlarging right pulmonary artery (curved arrows).

Figure 3. 15 mm thick sagittal MIP view showing obstruction of all segmental branches of the right pulmonary artery.

Figure 4. 15 mm thick parasagittal MIP view of the main and left pulmonary arteries showing pulmonary valve involvement (arrow). Distal left pulmonary artery is normal in size, free of endovascular material.

Case 6

Severe pulmonary hypertension due to atrial septal defect

Patient history

A 67-year-old female patient presented with a worsening dyspnea. She had a previous history of DVT, but no evidence of PE. An echocardiography disclosed an atrial septal defect. In order to totally exclude an association with CTEPH, a CT scan was performed to evaluate both heart chambers as well as pulmonary arteries.

Protocol

| ECG-gated spiral CT acquisition with dual-source CT | |
|---|---|
| Dual Injection | 90 cc of iodinated LOCM 370 mg / mL |
| Rate | 4.5 cc/s |
| Saline chaser | 40 cc at 4.5 cc/s |
| Start delay | Care bolus: automatic start at 300 HU in ascending aorta |
| Collimation | 0.6 mm |
| Parameters | 100 kVp, 700 mAs |
| Reconstructions | Performed at diastolic phase: 75% of the RR interval; 0.75 mm axial, and 15 mm thin-slab MIP reconstructions |

Findings

Cardiac CT scan confirms an atrial septal defect associated with enlargement of right cavities (Figures 1–4). No sign of CTEPH was found.

Patient outcome

The atrial septal defect was successfully closed percutaneously.

Take-home messages

PH may be due to cardiac disease, for example, a left-to-right shunt. Electrocardiography (ECG)-gated cardiac CT may visualize both cardiac abnormalities and pulmonary arteries allowing for comprehensive analysis of the case.

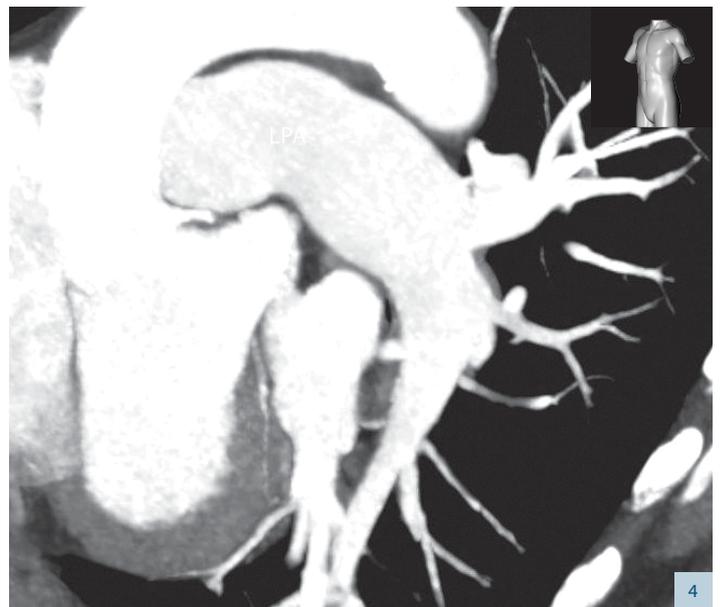
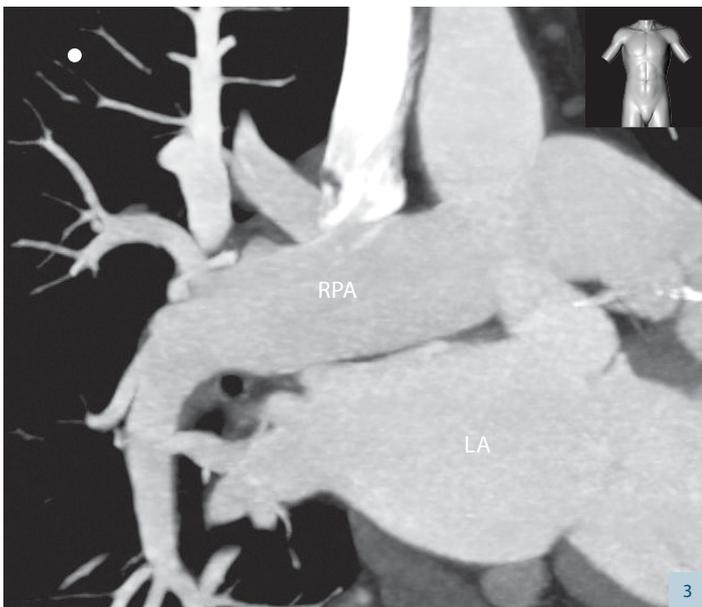
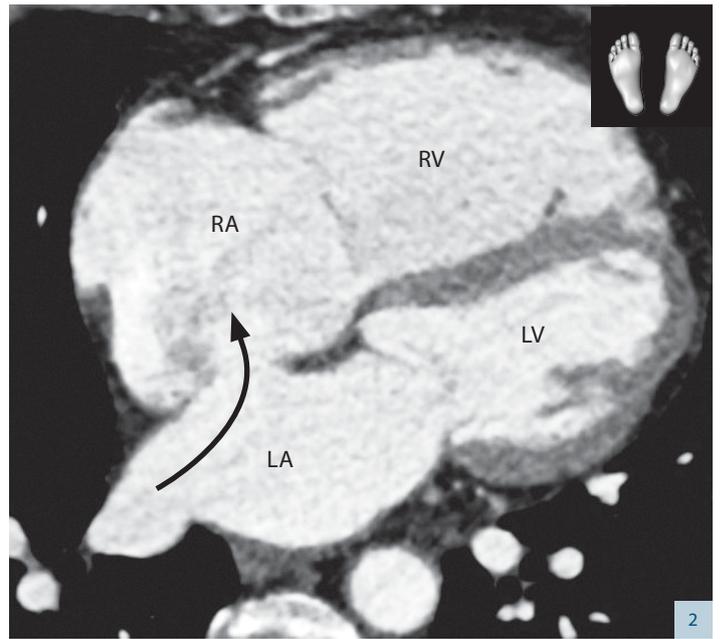
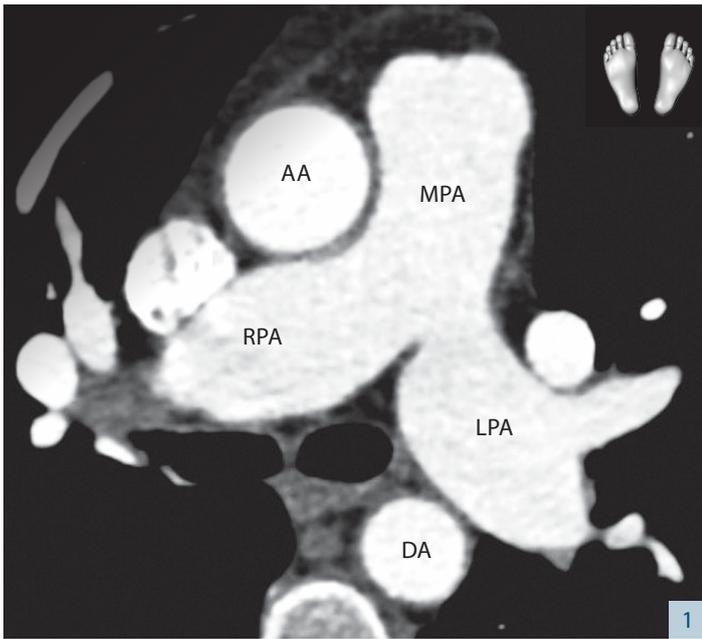


Figure 1. Axial view centered on right pulmonary artery shows enlarged pulmonary vessel without wall thickening.

Figure 2. Axial view centered on heart shows large atrial septal defect (>2 cm²) responsible for left-to-right shunt (curved arrow). Note the substantial enlargement of both right atrium and right ventricle.

Figure 3. 10 mm thick frontal MIP view of the right pulmonary artery shows enlarged right pulmonary artery and branches, which are regular in shape, with absence of endovascular material.

Figure 4. 15 mm thick parasagittal MIP view of the left pulmonary artery shows enlarged left pulmonary artery and branches of regular shape, without vascular narrowing or obstruction.

Case 7

Chest pain in a patient with severe pulmonary hypertension

Patient history

A 53-year-old female patient with a previous history of PH presented with chest pain while exercising. The patient's presentation was suggestive of coronary heart disease.

Protocol

| ECG-gated spiral CT acquisition with dual-source CT | |
|---|--|
| Dual Injection | 65 cc of iodinated LOCM 370 mg / mL |
| Rate | 5 cc/s |
| Saline chaser | 40 cc at 4 cc/s |
| Start delay | Care bolus: automatic start at 300 HU in ascending aorta |
| Collimation | 0.6 mm |
| Parameters | 120 kVp, 500 mAs |
| Reconstructions | Performed at diastolic phase: 75% of the RR interval; 0.75 mm axial, and 15 mm thin-slab MIP reconstructions |

Findings

Cardiac CT shows moderate compression of the left main coronary by the dilated pulmonary artery at rest (Figures 1–4). Left main compression during physical activity was considered to be the most likely cause of symptoms.

Patient outcome

Medical treatment.

Take-home messages

Pulmonary or coronary related symptoms may be difficult to distinguish. ECG-gated CT provides detailed anatomical information of heart, aorta, and pulmonary vessels.

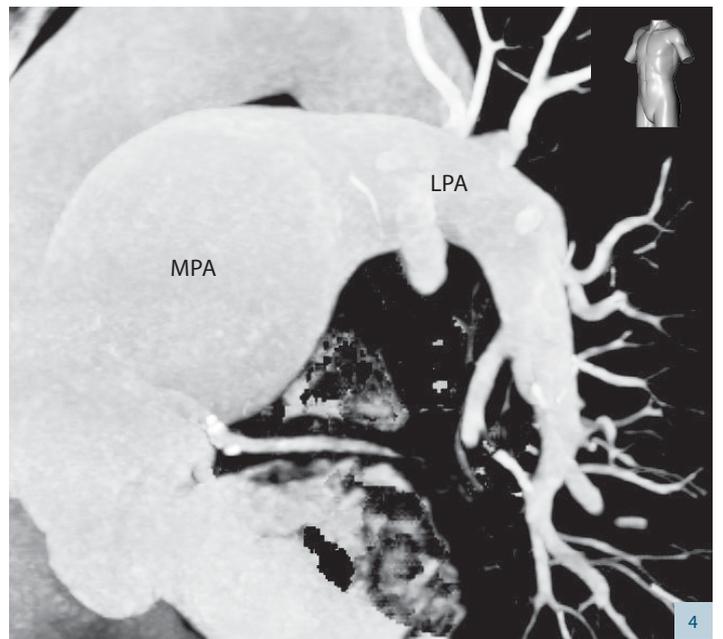
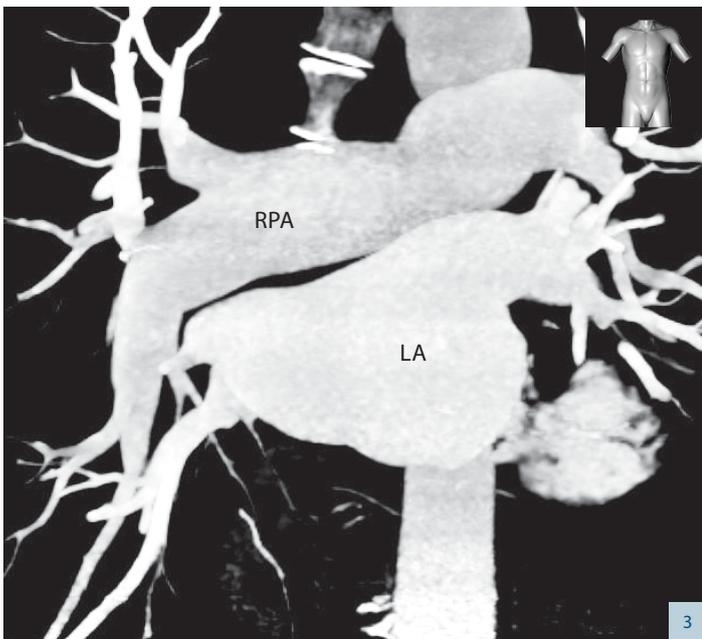
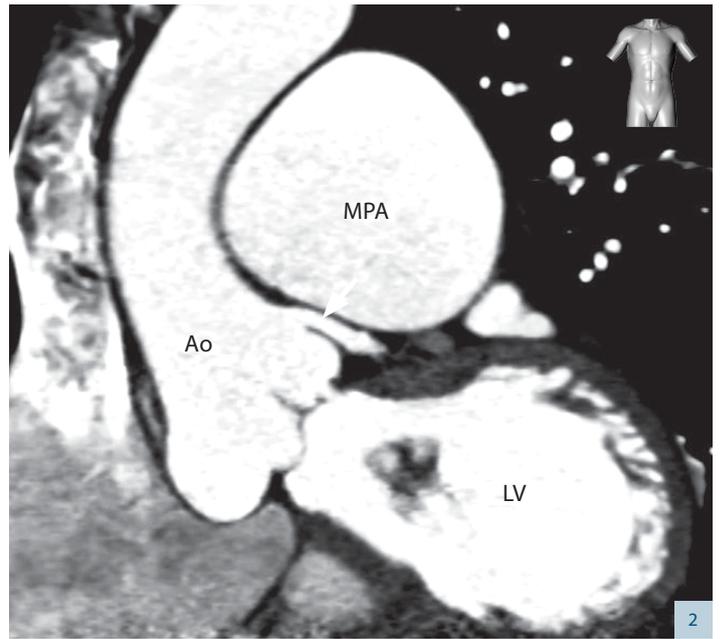
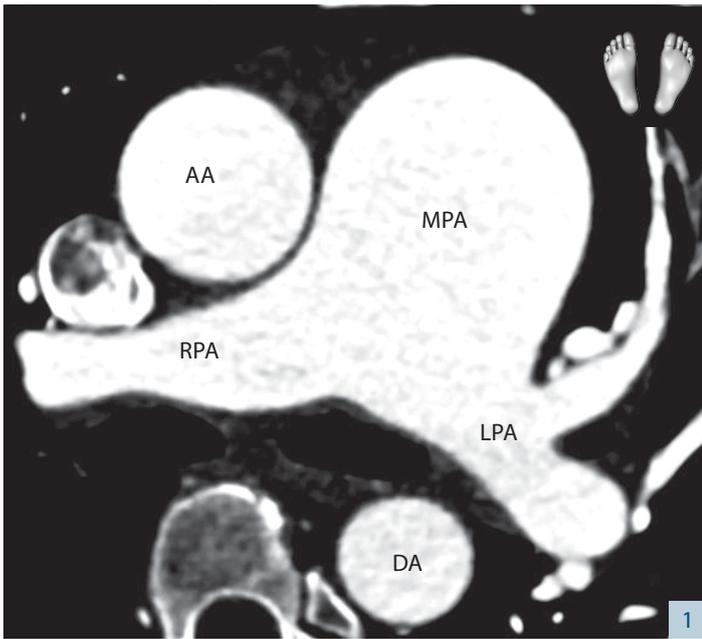


Figure 1. Axial view centered main pulmonary artery shows huge main pulmonary artery with right and left pulmonary arteries of normal size.

Figure 2. Frontal view centered on aortic root shows moderate compression of the left main coronary artery by the aneurysm of the main pulmonary artery.

Figure 3. 10 mm thick frontal MIP view of the right pulmonary artery shows normal right pulmonary artery and branches, without evidence of clot.

Figure 4. 15 mm thick parasagittal MIP view of the left pulmonary artery shows normal left pulmonary artery and aneurysm of the main pulmonary artery.

Case 8

Pulmonary hypertension due to veno-occlusive disease

Patient history

A 52-year-old male patient presented with rapidly worsening dyspnea, accompanied by severe PH. Following a pulmonary surgical biopsy, he was diagnosed with veno-occlusive disease. Prior to lung transplantation, a CT was performed for tumor screening.

Protocol

| Spiral CT acquisition – 64 slice CT | |
|-------------------------------------|--|
| Dual Injection | 90 cc of iodinated LOCM 370 mg / mL |
| Rate | 3 cc/s |
| Saline chaser | no |
| Start delay | 40 s |
| Collimation | 0.6 mm |
| Parameters | 120 kVp, 120 mAs |
| Reconstructions | Axial, multiplanar reformat, reconstructions |

Findings

CT scan shows normal sized pulmonary arteries (Figure 1). No endovascular soft tissue is seen.

Consistent with the diagnosis of a pulmonary venoocclusive disease (PVOD), lymph node enlargement, ground-glass opacities, and septal lines were observed (Figures 2–4, respectively).

Patient outcome

Pulmonary transplantation.

Take-home messages

PVOD is a rare cause of PAH.¹ Ground-glass opacities, septal lines, and lymph nodal enlargement on CT was found to be 100% specific for PVOD in cases of PAH with 66% specificity.¹

References:

1. Galiè N et al. Eur Heart J 2016;37:67–119.

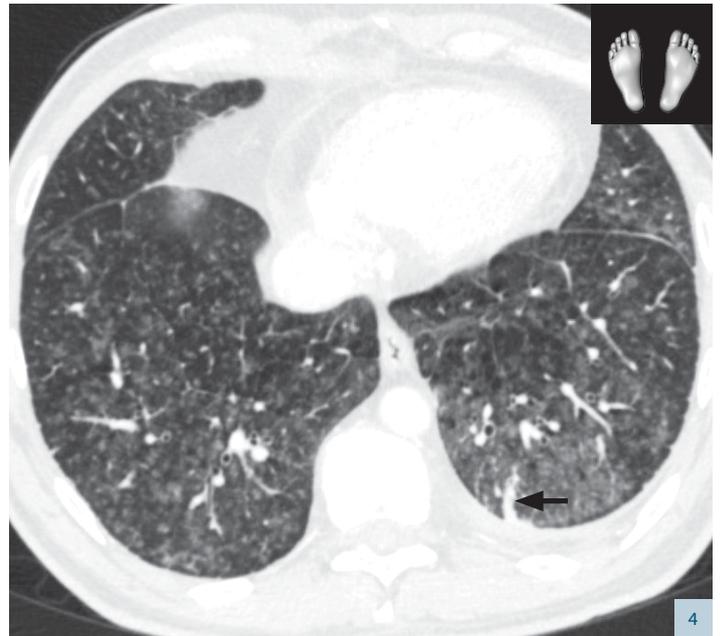
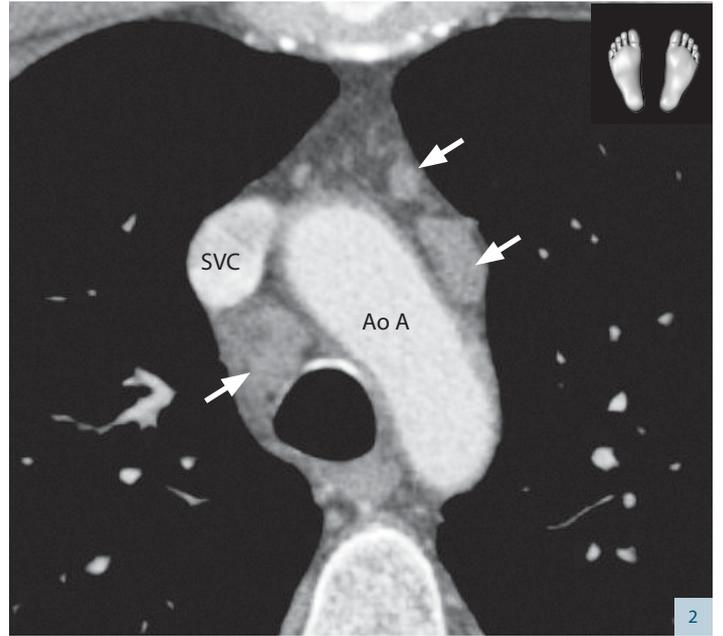
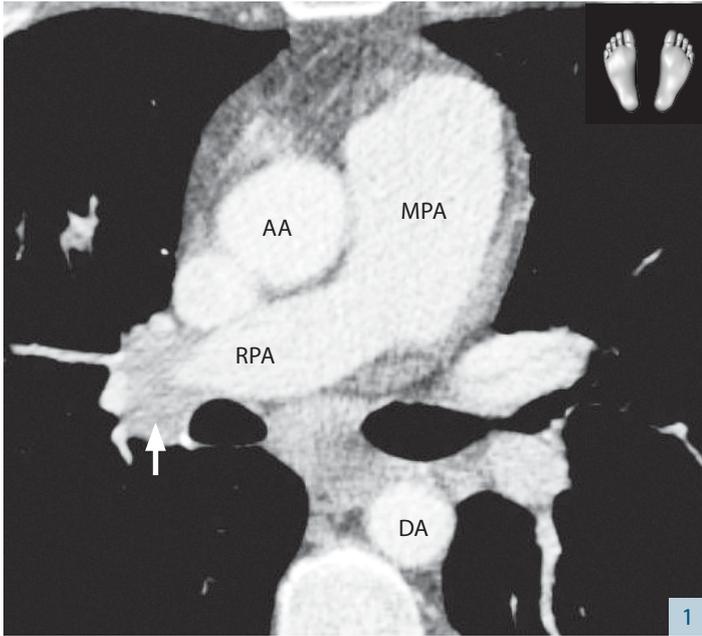


Figure 1. Axial view on right pulmonary artery shows normal-size vessel without any wall thickening. Note enlarged lymph nodes of the right pulmonary hilum (arrow).

Figure 2. Axial view on aortic arch shows additional enlarged mediastinal lymph nodes (arrows).

Figure 3. Mid-thoracic frontal view of the pulmonary parenchyma shows poorly defined nodular opacities of both lungs, with a diffuse and symmetric distribution.

Figure 4. Axial view of the pulmonary parenchyma discloses bilateral ground-glass opacities and a large septal line (arrow).

Abbreviations

| | |
|-------|---|
| CT | computed tomography |
| CTEPH | chronic thromboembolic pulmonary hypertension |
| CTPA | CT pulmonary angiography |
| DVT | deep venous thrombosis |
| ECG | electrocardiography |
| ESR | erythrocyte sedimentation rate |
| HU | Hounsfield units |
| IPAH | idiopathic pulmonary arterial hypertension |
| LOCM | Iopromide |
| MIP | maximum intensity projections |
| MRI | magnetic resonance imaging |
| PAH | pulmonary arterial hypertension |
| PE | pulmonary embolism |
| PEA | pulmonary endarterectomy |
| PH | pulmonary hypertension |
| PVOD | pulmonary veno-occlusive disease |
| PVR | pulmonary vascular resistance |
| RHC | right heart catheterization |
| RR | relative risk |
| s | second |
| V/Q | ventilation/perfusion |



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PP-ADE-ALL-0009-1