Acute pulmonary embolism (PE) may be a precursor to chronic thromboembolic pulmonary hypertension (CTEPH)\(^1\)

As many as 1 out of 25 previously treated PE patients (>3 months of anticoagulation) may develop CTEPH\(^2,3^*\)

*Based on a study with 223 patients in which 3.8% were diagnosed with CTEPH within 2 years of their first episode of pulmonary embolism with or without prior deep-vein thrombosis (95% CI, 1.1 to 6.5). CTEPH did not develop after 2 years in any of the 132 remaining patients with more than 2 years of follow up.\(^3\)
CTEPH* is a form of PH that may occur after a pulmonary embolism (PE)†

*Chronic thromboembolic pulmonary hypertension

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**CLASSIFICATION**

<table>
<thead>
<tr>
<th>WHO GROUP 1</th>
<th>WHO GROUP 2</th>
<th>WHO GROUP 3</th>
<th>WHO GROUP 4</th>
<th>WHO GROUP 5</th>
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<tr>
<td>Pulmonary arterial hypertension</td>
<td>Pulmonary hypertension due to left heart disease</td>
<td>Pulmonary hypertension due to lung disease and/or hypoxia</td>
<td>Chronic thromboembolic pulmonary hypertension (CTEPH)</td>
<td>Pulmonary hypertension with unclear multifactorial mechanisms</td>
</tr>
</tbody>
</table>

Chronic thromboembolic pulmonary hypertension, or CTEPH, is a form of pulmonary hypertension (PH), designated by the World Health Organization as Group 4 PH.4

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**PATHOPHYSIOLOGY**

CTEPH is a product of a single PE or recurrent PE that creates endothelialized residua that obstruct or substantially narrow pulmonary arteries.1

- Obstruction and narrowing of the pulmonary arteries drive pulmonary arterial pressure (PAP) to abnormal levels and increase pulmonary vascular resistance (PVR).†
- Absence or depletion of endogenous vasodilators like nitric oxide may contribute to endothelial dysfunction in CTEPH.†

The hemodynamic definition of CTEPH is mean PAP >25 mm Hg, with pulmonary capillary wedge pressure (PCWP) ≤15 mm Hg. These levels must be observed in the presence of multiple chronic/organized, occlusive thrombi/emboli in the pulmonary arteries after at least 3 months of effective anticoagulation.5

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**INCIDENCE**

Data from multiple observational studies suggest that as many as 0.57% to 3.8% of patients may go on to develop CTEPH within 2 years after a first acute PE.7 Applying even the lower end of that range to the estimated 600,000 cases of acute PE per year in the US suggests the actual number of CTEPH cases that develop each year may be substantially greater than diagnosed cases suggest.2,3*

Each year, there are between about 500 and 2,500 incident cases of CTEPH in the US.2

The true incidence of CTEPH may be underestimated because postembolism observational studies do not include patients who have no history of venous thromboembolism.7

- As many as 25% to 30% of patients who have CTEPH may never have had an overt PE or a history suggestive of PE.8,9
- Furthermore, as many as 45% to 55% of CTEPH patients may present with no history of deep vein thrombosis.8,9

* Pengo et al conducted a prospective, observational, long-term, follow-up study to evaluate the incidence of symptomatic CTEPH in patients with an acute episode of PE but without prior venous thromboembolism. 314 patients who had an acute PE were evaluated.7

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**SIGNS AND SYMPTOMS**

The symptoms of CTEPH are nonspecific and include:2,10

- Dyspnea on exertion
- Fatigue, weakness
- Chest pain
- Syncope
- Lower extremity edema
- Hemoptysis

As many as 1 in 25 survivors of acute PE (>3 months of anticoagulation) may go on to develop CTEPH within 2 years.10

* Based on a study with 223 patients in which 3.8% were diagnosed with CTEPH within 2 years of their first episode of pulmonary embolism with or without prior deep-vein thrombosis (95% CI, 1.1 to 6.5). CTEPH did not develop after 2 years in any of the 132 remaining patients with more than 2 years of follow up.1

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INFORMATION. ANSWERS. SUPPORT.
It has been estimated that there are as many as 600,000 acute PEs in the US each year.2

- About 95% of acute pulmonary emboli originate from thrombi in the leg or pelvic veins11
- Symptoms of acute PE include dyspnea, pleuritic pain, and cough11

Sudden death owing to right ventricular failure occurs in as many as one-quarter of patients who experience an acute PE.11,12

**ACUTE PE IMAGING**

Computed tomographic pulmonary angiography (CTPA) is highly specific for acute PE and has become the standard diagnostic test for it.11

- When a good-quality CTPA is negative for acute PE, the diagnosis can basically be ruled out.11
- In contrast, the ventilation/perfusion, or V/Q, scan is typically not diagnostic for acute PE.11

**CHRONIC THROMBOEMBOLI**

Sometimes, patients may survive acute PE but do not have sufficient resolution to restore normal lung hemodynamics.4

This incomplete thromboembolic resolution results in residua that obstruct or narrow major pulmonary arteries.4

Over time, developing small vessel vasculopathy can lead to right ventricular afterload, progression of PH, and CTEPH.4

Unlike for acute PE, CTPA is not a reliable diagnostic test for chronic thromboemboli because it is difficult to differentiate chronic from acute PE on CTPA.14

Instead, the V/Q scan is the preferred and recommended screening test for CTEPH.14
It’s not PH without a right heart catheterization and it’s not PAH without a V/Q scan

V/Q SCAN

The V/Q scan has many attributes that contribute to its utility as a screening tool for CTEPH.14

- **Easy to read**—suspected perfusion defects, regardless of origin, are readily recognizable
- **Requires less radiation** exposure than CTPA
- **Avoids complications** from administration of IV contrast
- **Offers lower likelihood of incidental findings**

*Retrospective review of V/Q scans and CTPA results performed on 227 patients with PH referred to Hammersmith Hospital, London, between 2000 and 2005. The final diagnosis of CTEPH or non-CTEPH was obtained from the Hammersmith Hospital Pulmonary Hypertension Service case records.

The V/Q scan with multiple pronounced perfusion deficits, characteristic of CTEPH

Diagnosing CTEPH and Surgical Assessment after unresolved PE

An abnormal V/Q scan showing perfusion defects is not enough on its own to diagnose CTEPH.14

Echocardiography, which can help detect the presence of PH, usually offers the first indication that a patient has CTEPH. When a patient with a history of PE presents with PH, with or without right ventricular dysfunction, CTEPH should be considered.14

To confirm CTEPH, right heart catheterization (RHC) must be performed to assess hemodynamics, and selective pulmonary angiography is typically used to confirm presence of CTEPH lesions.16

**Suspect**
- Echocardiogram
- V/Q scan

**Confirm**
- Right heart catheterization
- Pulmonary angiogram (or CTPA, MRA)

**Assess Risk**
- Hemodynamics
- Comorbidities
- Surgeon/CTEPH team experience

*Underutilization of V/Q scans in screening PH invites potential misdiagnosis of PAH.14"
Pulmonary thromboendarterectomy (PTE) – assess the potential for a cure

OPERABILITY ASSESSMENT

If one experienced CTEPH team determines that a patient has inoperable disease, a corroborating opinion from a second experienced CTEPH team should be secured, if possible.14

All CTEPH patients must be assessed for operability by an experienced CTEPH team.14

The experienced CTEPH team that would plan, perform, and follow up the patient’s surgery must assess the patient’s risk, including quality of and accessibility of lesions, hemodynamic assessment, and consideration of comorbidities and patient characteristics.14

The last, and perhaps most important, step in diagnosing CTEPH is operability assessment for potentially curative pulmonary thromboendarterectomy surgery.14

• CTPA and magnetic resonance angiography can contribute complementary information on the lesions, their surroundings, and their accessibility.14

SURGICAL TREATMENT

PTE (also known as pulmonary endarterectomy [PEA]) is the treatment of choice for surgical candidates with CTEPH because it is the only potentially curative treatment.8,14,21

Patients who have operable CTEPH should be referred for surgery without delay.14

PTE surgery is a complex bilateral procedure, which requires median sternotomy, cardiopulmonary bypass, deep hypothermia, and periods of circulatory arrest.8

• Since the technique’s advent in 1970, survival rates from PTE surgery have steadily improved. Indeed, recent analyses report that in-hospital mortality rates at experienced PTE centers can be less than 5%.22,23

PTE surgery allows for the removal of central obstructing lesions, resulting in improvement and often normalization of pulmonary hemodynamics.10

• About two-thirds of patients have normal hemodynamics following PTE14

Mortality data post-PTE at a single experienced center4,22

<table>
<thead>
<tr>
<th>Timeline</th>
<th>N</th>
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<tbody>
<tr>
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<tr>
<td>1994-1998</td>
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<tr>
<td>1998-2002</td>
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<td>1000</td>
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<tr>
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<tr>
<td>Last consecutive patients up to 12/2010</td>
<td>260</td>
<td>0%</td>
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Anticoagulation therapy alone is not sufficient to treat the pulmonary hypertension component of CTEPH.6*

Potentially curative surgery is the recommended treatment.14

*Based on a study with 223 patients in which 3.8% were diagnosed with CTEPH within 2 years of their first episode of pulmonary embolism with or without prior deep-vein thrombosis (95% CI, 1.1 to 6.5); CTEPH did not develop after 2 years in any of the 132 remaining patients with more than 2 years of follow up. 3
References


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