



What is Chronic Thromboembolic Pulmonary Hypertension and when to refer to a specialized CTEPH center?

Information for Health Professionals about CTEPH diagnosis and management

TORONTO CTEPH PROGRAM

“To optimize the care of patients with CTEPH in Canada”

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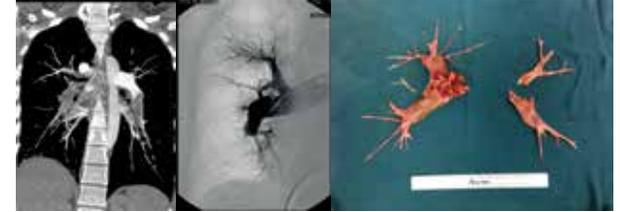
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What is CTEPH?

Chronic thromboembolic pulmonary hypertension (CTEPH) is a form of pulmonary hypertension (PH) caused by recurrent and/or unresolved pulmonary emboli (PE) leading to obstruction of the pulmonary arteries and small vessel vasculopathy (1, 2).

CTEPH represents Group IV pulmonary hypertension (PH) according to the World Health Organization classification.

CTEPH Epidemiology

- Previously considered a rare disease with an estimated prevalence of 0.1-0.5% after acute PE, CTEPH is increasingly recognized to be more widespread across all populations than previously estimated. Recent studies indicate the incidence of CTEPH can be as high as 5 % after acute PE with a potential prevalence of several thousand cases in Canada (2, 3).
- CTEPH remains under diagnosed and under recognized with an average time from the onset of symptoms to diagnosis of 14 months (4).
- The mortality rate among untreated patients with CTEPH can be as high as 80-90% at two to three years with anticoagulation treatment alone (2).

CTEPH Pathophysiology

A significant number of patients with acute pulmonary embolism achieve resolution of obstruction and return to normal hemodynamics while on therapeutic anticoagulation.

A subset of patients with PE develop chronic thromboembolic disease with embolic material adhering to the vascular wall causing the formation of organized, fibrous obstruction within the pulmonary arteries (1). These organized, fibrous clots occlude the vascular lumen and impede the blood flow within the pulmonary vascular tree leading to an increase in pulmonary vascular resistance (PVR) and dead space ventilation despite adequate anticoagulation.

The development of CTEPH is not solely attributed to a mechanical obstruction by thromboembolic material. The second process leading to disease progression is related to the distal vasculopathy created by inflammation and continuous shear stress secondary to persistent thromboembolic material (3). Vascular remodeling (distal vasculopathy) contributes to the increasing PVR and disease progression despite adequate anticoagulation and may potentially lead to some residual PH after successful pulmonary endarterectomy (PEA) surgery (1, 3). Therefore, to achieve optimal results, patients with CTEPH should be referred to centers experienced in CTEPH diagnosis and treatment early in the course of disease.

The development of CTEPH is related to the acute or recurrent PE accompanied by the incomplete resolution of the emboli.

Clinical Manifestations of CTEPH

Patients with CTEPH present with vague and indolent symptoms; therefore, the diagnosis can be overlooked leading to a median time from the clinical presentation to diagnosis of 14 months (3).

Clinical presentation is related to:

- 1) Alveolar dead space ventilation associated with elevated PVR leading to hypoxemia
- 2) Strain on the right ventricle (RV) limiting cardiac output during exercise
- 3) Progressive RV failure manifested as RV wall hypertrophy and RV dilatation

Symptoms

Symptoms include ***exertional dyspnea in all patients.***

Other less frequent symptoms are chest and/or upper abdominal pain/ discomfort, fatigue, syncopal episodes, hemoptysis, and peripheral edema.

The only constant symptom present in all patients is exertional dyspnea.



When to suspect CTEPH?

In addition to the Pulmonary Hypertension program, The Toronto CTEPH program receives a number of referrals directly from cardiologists, respirologists, thrombosis clinics, and family physicians. Therefore, it is important for health care providers in the community to suspect CTEPH in a certain subset of patients and to make a timely referral to a specialized CTEPH center.

Table 1

Suspect chronic thromboembolic disease in patients with a recent diagnosis of acute PE in the presence of one or more of these findings:

- Idiopathic PE
- Large perfusion defects on imaging
- Systolic pulmonary artery pressure (PAsP or RVSP) >50 mmHg on echocardiogram (ECHO)

Signs of CTEPH on the computed tomography pulmonary angiogram (CTPA) at the time of acute PE:

- ⇨ Organized mural thrombi
- ⇨ Arterial webs or bands
- ⇨ Dilated pulmonary arteries
- ⇨ Mosaic parenchymal perfusion pattern

(3, 5)

Table 2

Suspect chronic thromboembolic disease in patients with previous or recurrent PE in the presence of one or more of these findings:

- Idiopathic PE
- Symptomatic patients (ongoing dyspnea, fatigue, exercise limitation) despite 3 months of anticoagulation
- Residual symptoms (patient is not back to their functional prepulmonary embolism baseline) while on anticoagulation
- Systolic pulmonary artery pressure (PAsP or RVSP) > 50 mmHg on echocardiogram (ECHO) at the time of acute PE diagnosis or during follow-up

(3)

When to make a referral to the specialized CTEPH Center?

When CTEPH is suspected, health care providers should follow up by obtaining the most sensitive non-invasive test: *Ventilation/Perfusion (V/Q) nuclear lung scan*.

Symptomatic patient with *unmatched perfusion defects on V/Q scan* despite adequate anticoagulation for at least 3 months mandate referral to specialized CTEPH Center for further diagnostic evaluation and possible treatment

(3)

If V/Q scan is not available and CTEPH is strongly suspected based on the findings from Tables 1 and 2, patients can be referred to the Toronto CTEPH program for further evaluation.



Treatment Options for CTEPH

1. Pulmonary Endarterectomy (PEA)

CTEPH is the only type of PH that is curable with pulmonary endarterectomy surgery as the treatment of choice. At the Toronto CTEPH program, more than 80% of patients diagnosed with CTEPH are surgical candidates and the exclusion of patients for PEA based on distal disease is unusual (3).

PEA surgery results in major clinical benefits by:

- Improving RV strain from high PVR leading to normalization of hemodynamic parameters
- Improving ventilation/perfusion matching and reducing dead space ventilation leading to normalization of oxygenation
- Preventing RV dysfunction and death related to heart failure (1)

After PEA surgery, the vast majority of the patients experience major functional recovery and are able to return to their baseline physical activity level without supplemental oxygen use.

PEA surgery can be performed safely and lead to resolution of the PH when performed at an expert center. At the Toronto CTEPH Program, the largest Canadian PEA center, the procedure can be done safely thanks to the expertise of the surgical and multidisciplinary teams. Considering the safety and success of PEA, patients who are deemed inoperable should receive a re-evaluation of operability by a second experienced CTEPH center according to the fifth Symposium on PH guidelines (6).

Chronic thromboembolic obstruction removed by PEA surgery from a patients' pulmonary arteries



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2. PH-specific Medical Therapy

If the patient is not eligible for surgery, they will be referred to the Pulmonary Hypertension Program for medical therapy assessment. Riociguat®, a member of a new class of medications called soluble guanylate cyclase (sGC) stimulators, is the only medical therapy that has been approved by the Health Canada for management of inoperable CTEPH or persistent or recurrent PH after PEA surgical treatment (7). Despite clinical advances, medical therapy should not be considered a replacement to curative PEA surgery (3).

3. Balloon Pulmonary Angioplasty

Balloon pulmonary angioplasty is a new and experimental procedure that has shown some benefit in patients who are not surgical candidates. This procedure is currently being performed at the Toronto General Hospital.

How to make a referral to the Toronto CTEPH Program?

When making a referral to the Toronto CTEPH Program, please include:

1. A letter of referral
2. Clinical notes
3. Reports of investigations (*V/Q scan, CT thorax, echocardiogram, etc.*)

Please fax referrals to 416-340-3853

Contact Information

Toronto CTEPH Program Division of Thoracic Surgery – 9N927
Toronto General Hospital 200 Elizabeth Street Toronto, ON M5G 2C4

Phone: 416-340-4800 ext. 5274

Pager: 416-714-0840

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More information

Doctors of Thoracic Surgery, the Toronto CTEPH Program website:
<http://www.dotscanada.com/patient-information/clinical-programs/#ChronicThromboembolic>

