PULMONARY HYPERTENSION ASSOCIATION OF CANADA

L'ASSOCIATION D'HYPERTENSION PULMONAIRE DU CANADA

Diagnosis of Chronic Thromboembolic Pulmonary Hypertension:

Patient Summary of the Canadian Thoracic Society Clinical Practice Guidelines

Background

Pulmonary hypertension (PH):

PH is a serious disease in which the blood pressure in the pulmonary arteries is increased, which leads to strain on the right side of the heart, especially the right ventricle (RV). Patients with PH typically experience shortness of breath, exercise limitation and fatigue. Development of RV failure is suggested by symptoms of swelling in feet or ankles, lightheadedness, fainting, and chest pain or discomfort.

Some signs of PH can be seen with ultrasound of the heart (echocardiogram). Confirmation of PH is done by a procedure called right heart catheterization (RHC) in which a catheter is inserted through the neck or groin into the pulmonary arteries to measure the blood pressure directly.

PH is classified by the World Health Organization (WHO) into five groups (Table 1).

Table 1 – Updated World Health Organization (WHO) clinical classification of PH

Group 1	**Pulmonary arterial hypertension (PAH)** eg: Idiopathic PAH, hereditary PAH, PAH associated with scleroderma, cirrhosis, etc, pulmonary veno-occlusive disease (PVOD)
Group 2	**PH associated with diseases of the left side of the heart** eg: Left-sided heart failure, mitral or aortic valve disease
Group 3	**PH associated with diseases of the lungs and/or hypoxia (low oxygen)** eg: Chronic obstructive pulmonary disease (COPD), pulmonary fibrosis / interstitial lung disease (ILD), sleep apnea
Group 4	**PH due to obstruction (blockage) of the pulmonary arteries** eg: Chronic thromboembolic pulmonary hypertension (CTEPH)
Group 5	**PH due to miscellaneous causes** eg: Sickle-cell disease, sarcoidosis, chronic kidney failure

Chronic Thromboembolic Pulmonary Hypertension (CTEPH):

CTEPH is an important and common cause of group 4 PH and is found in some patients after suffering an acute pulmonary embolus (PE; blood clot in the lung). CTEPH can develop after large or recurrent PE which leads to scar formation along the inside lining of the pulmonary arteries.

Diagnosis of CTEPH in a timely fashion is key to preventing severe RV failure and to improving patient quality of life and survival. Available treatment options include pulmonary endarterectomy (PEA, formerly known as PTE) - a surgery that removes the clot and scar tissue from inside the pulmonary arteries; balloon pulmonary angioplasty (BPA), which uses a balloon to open the pulmonary arteries that have been narrowed by the scarring; and medications to treat PH.

The best treatment for most patients with CTEPH is PEA if they are surgical candidates. Many patients with CTEPH can be cured with PEA. Clinical benefits of surgery include reduced shortness of breath, improved exercise tolerance, and improved survival. Some patients with CTEPH are not cured of their PH with surgery but may still experience significant improvements in quality of life and survival. For those who are not candidates for PEA, PH medications or BPA can also improve quality of life and survival.

Canadian Thoracic Society (CTS) CTEPH Diagnosis Clinical Practice Guidelines

This Guideline was developed for use by health care providers who care for individuals who may have CTEPH. It was published in 2019 by Helmersen D, et al. and is published in the C*anadian Journal of Respiratory, Critical Care, and Sleep Medicine* (2019;3(4):177-198). It focusses on providing clinical recommendations based on the most current and best scientific evidence. We have adapted this document for patients to allow them to better understand the recommendations made in the CTEPH Guidelines.

This guideline was developed by a committee of physicians with expertise in the diagnosis and management of CTEPH, consisting of respirologists, a cardiologist, a radiologist, and a thoracic CTEPH surgeon, and includes both Canadian and International experts. The committee searched the global medical literature to review all English and French-language research publications on CTEPH Diagnosis in adults. The research quality and evidence strength were assessed based on an accepted GRADE system.

The committee considered all scientific evidence, the specific health benefits for individual patients, potential risks and burdens on patients and cost to the healthcare system in developing recommendations in these guidelines. Additionally, the committee summarized available information about patient's perspectives on CTEPH diagnosis including their beliefs, expectations, and goals for health and life.

Target patient population:

This Guideline specifically applies to 2 groups of individuals: (i) patients diagnosed with PH without a clear cause, who may have had a previous undiagnosed PE; and (ii) patients who have already been diagnosed with PE who may be at risk for developing CTEPH.

Screening for CTEPH

Patients that suffer PE are treated with blood thinners to allow the body to break down existing clots and prevent future clot development. There is a small chance (2-4%) however, that the clots develop into scars and damage the pulmonary arteries, resulting in CTEPH. It has been suggested that all patients with PE should be regularly assessed (screened) to see if they have developed CTEPH. Two methods can be used to screen (assess) for CTEPH, including echocardiography to detect PH, and through radiologic imaging of the lungs to look for blockages of the pulmonary arteries due to clot and scar tissue. In previous studies, screening did not increase the diagnosis of CTEPH.

Recommendation: In patients who suffer acute PE, the committee recommends **not** to perform routine testing for CTEPH, including echo or radiologic testing (V/Q scan, CTPA). (Grade 1C: Strong recommendation; Low Quality of Evidence)

The committee recognized the clear but small risk of patients developing CTEPH after acute PE. However, the committee did not recommend routine testing for CTEPH in all patients with PE because this extensive testing would only benefit a few patients, would be an unnecessary burden on most patients who would never develop CTEPH, and would be too costly for the healthcare system.

Other considerations:

Although testing all patients for CTEPH after acute PE is not recommended, the committee emphasized that some patients with acute PE may be at higher risk of developing CTEPH than the average patient. These patients should be followed more closely for signs of symptoms of CTEPH including regular clinical assessment for symptoms, and selective testing.
Patients at a higher risk of CTEPH may include:

1. Patients with persistent or worsening symptoms 3-6 months after PE, including shortness of breath, lightheadedness, chest pain, exercise / activity limitation.
2. Patients with more than 1 episode of PE (recurrent PE).
3. Patients with other medical conditions such as higher BMI, varicose veins or hypothyroidism which are known risk factors for CTEPH

Areas for future research:

Future research should focus on identifying patients at higher risk of developing CTEPH after an acute PE and define how these patients should be assessed.

Future Directions:

The CTS has proposed to review and update this clinical practice guideline every 3-5 years or possibly sooner, depending on new research information.

Diagnosing CTEPH

CTEPH is categorized as WHO group 4 PH (Table 1) and is **defined by 2 features**:

1. A mean pulmonary artery pressure (PAP) of 25 mmHg or higher, and pulmonary vascular resistance (PVR) of 3 Wood units or more; and
2. Chronic clot and scar in the pulmonary arteries despite at least 3 months of uninterrupted anticoagulation.

Diagnosing CTEPH is important for several reasons:

1. CTEPH is one of the more common causes of PH, affecting 2-4% of all patients who suffer from a PE.
2. In patients who have PH without a clear cause, it is important to assess for possible CTEPH even if they never had any symptoms of PE. Acute PE is easily missed but can still cause PH, especially in patients who also have lung and heart diseases.
3. If CTEPH is not diagnosed and/or treated appropriately, it will progress with time which results in poor quality of life and is typically life threatening within a few years.
4. Several effective treatment options are available for patients with CTEPH, including surgical PEA, BPA and PH medications.

SECTION 1 – Patients already diagnosed with PH:

Initial Testing for Possible CTEPH

In patients with PH without clear cause it is important to evaluate for CTEPH as it is a common and important cause of PH with several effective treatments.

Evidence of current or previous PE is usually detected using 2 radiologic imaging tests:

1. Nuclear ventilation/perfusion (V/Q) scan

   A V/Q scan assesses whether air flow and pulmonary artery blood flow into the lungs is normally matched; a scan that shows normal air flow but abnormal (mismatched) blood flow suggests the possible presence of PE and obstruction of pulmonary arteries.

2. CT Pulmonary Angiogram (CTPA)

   This is a special type of CT scan where contrast dye is injected through an arm vein to highlight the inside of pulmonary arteries. An abnormal CTPA can show blockages of pulmonary arteries due to clots and/or scar tissue.

Recommendation: Patients diagnosed with PH without a clear cause should undergo nuclear ventilation/perfusion (V/Q) lung scan to assess for possible CTEPH. (GRADE: 1C; Strong Recommendation; Low Quality of Evidence).

Special notes:

1. There are 2 methods for nuclear V/Q scan (Planar and SPECT), both of which are acceptable tests to assess CTEPH.
2. A normal V/Q lung scan confirms that the patient does not have CTEPH.
3. An abnormal V/Q lung scan suggests possible CTEPH; these patients should undergo further investigation for diagnosis.
4. CTPA is not recommended to screen for CTEPH, as a normal CTPA does not completely exclude CTEPH.

Other considerations:

1. Some PH patients may not need to be tested for CTEPH. For example, patients diagnosed with PH clearly due to other causes, including PH due to left heart disease (WHO group 2), or PH due to lung disease (WHO group 3).
2. Patients with suspected CTEPH should be further assessed by radiologic testing to confirm a diagnosis of CTEPH (see Section 2 – Confirming a Diagnosis of CTEPH) and referred to an expert PH centre (listed at www.phacanada.ca/PHcentres).

In patients diagnosed with PH without a clear cause, an abnormal nuclear V/Q scan suggests possible CTEPH; these patients should undergo further investigation to diagnose CTEPH.

Recommendation: The committee recommends CTPA to confirm a diagnosis of CTEPH and assess the extent and location of clot/scar. (GRADE 1B: Strong recommendation; Moderate Quality of Evidence)

Special notes:

1. CTPA provides important information on the amount and extent of chronic PE to decide on the best treatment approach for each patient, for example PEA surgery vs BPA vs medical PH treatment.
2. A "normal" CTPA may not completely exclude the possibility of CTEPH.
3. A positive CTPA should prompt referral to an expert PH centre (listed at www.phacanada.ca/PHcentres).

Other considerations:

1. The accuracy of CTPA for diagnosing CTEPH relies on the technical aspects of the imaging test and the radiologist's expertise in identifying signs of chronic PE. Most imaging can underestimate the extent of disease.
2. CTPA may appear "normal" (negative) in some CTEPH patients who have small amounts of scar tissue in the pulmonary arteries – a negative CTPA does not rule out CTEPH.
3. In patients who are highly suspected to have CTEPH, a "normal" (negative) or inconclusive CTPA may be inaccurate. These patients should be referred to an expert PH center for further testing.
4. Magnetic resonance pulmonary angiography (MRPA) can confirm a diagnosis of CTEPH. However, MRPA is not widely available, is expensive, and there is a lack of radiologic expertise in MRPA interpretation to diagnose CTEPH. Therefore, MRPA is not currently recommended to diagnose CTEPH. The committee recognized that in some patients who may have a serious allergy to contrast dye, MRPA could be an appropriate alternative to CTPA or pulmonary angiography.

Areas for future research

The committee recommends further research into MRPA and new generations of CT

scanners to see how these new radiologic technologies could improve CTEPH diagnosis compared to current CTPA. Research is also needed to assess which radiologic techniques are best at finding clots in smaller pulmonary arteries.

ABBREVIATIONS

BPA Balloon pulmonary angioplasty

CT Computed tomography

CTEPH Chronic thromboembolic pulmonary hypertension

CTPA Computed tomography pulmonary angiogram

CTS Canadian Thoracic Society

Mean PAP mean Pulmonary Arterial Pressure

MRPA Magnetic Resonance pulmonary angiography

PAH Pulmonary arterial hypertension

PAP Pulmonary arterial pressure

PE Pulmonary embolism or emboli

PEA Pulmonary endarterectomy

PH Pulmonary hypertension

PVOD Pulmonary veno-occlusive disease

PVR Pulmonary vascular resistance

RHC Right heart catheterization

RVSP Right ventricular systolic pressure

V/Q Ventilation/perfusion

WHO World Health Organization

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