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Viewpoint

When to Refer a Patient With Chronic Thromboembolic Pulmonary Hypertension for Pulmonary Endarterectomy

Tiago Machuca, MD, PhD, and Marc de Perrot, MD, MSc

Toronto Pulmonary Endarterectomy Program, Toronto General Hospital, University of Toronto, Toronto, Ontario, Canada

ABSTRACT

Chronic thromboembolic pulmonary hypertension (CTEPH) is much more frequent than previously estimated, potentially occurring with an incidence of several thousand cases per year in Canada. Refinements in the surgical technique of pulmonary endarterectomy, the development of medical therapy and, more recently, the introduction of balloon pulmonary angioplasty have provided an increasing array of therapeutic options for this disease. CTEPH is related to the presence of chronic thromboembolic disease and the development of a secondary vasculopathy that leads to worsening pulmonary hypertension despite adequate anticoagulation, emphasizing the importance of early diagnosis and appropriate referral to achieve optimal therapeutic results. It is increasingly recognized that patients with CTEPH can present with acute on chronic pulmonary emboli. Recognition of the underlying chronic disease at the time of the acute presentation is important to ensure that these patients are adequately managed and followed with ventilation-perfusion scan and echocardiogram after their initial diagnosis of acute pulmonary emboli. Chronic thromboembolic disease should be suspected in the presence of idiopathic and/or recurrent pulmonary emboli, larger perfusion defects, longer

RÉSUMÉ

L'hypertension pulmonaire thromboembolique chronique (HPTEC) est beaucoup plus fréquente que ce qu'elle avait été estimée antérieurement, et compte possiblement plusieurs milliers de nouveaux cas par année au Canada. L'amélioration de la technique chirurgicale de l'endartériectomie pulmonaire, la mise au point de traitements médicaux et plus récemment l'introduction de l'angioplastie pulmonaire par ballonnet ont offert un nombre croissant d'options pour traiter cette maladie. La HPTEC est liée à la présence de la maladie thromboembolique chronique et au développement d'une vasculopathie secondaire qui mènent à l'aggravation de l'hypertension pulmonaire en dépit d'une anticoagulation adéquate, ce qui montre l'importance du diagnostic précoce et de l'orientation appropriée pour obtenir des résultats thérapeutiques optimaux. Il est de plus en plus reconnu que les patients souffrant d'HPTEC peuvent présenter des embolies pulmonaires aiguës ou chroniques. La détection de la maladie chronique sous-jacente au moment de la phase aiguë est importante pour s'assurer que ces patients soient adéquatement pris en charge et suivis au moyen d'une scintigraphie de perfusion/ventilation et d'un échocardiogramme après leur diagnostic initial d'embolies

Chronic thromboembolic pulmonary hypertension (CTEPH) belongs to category IV in the World Health Organization pulmonary hypertension (PH) classification and is defined by a resting mean pulmonary artery pressure > 25 mm Hg combined with the presence of organized thrombi in the pulmonary arteries despite adequate anticoagulation for at least 3 months. CTEPH was initially considered to be a rare disease occuring in 0.1%-0.5% of patients after acute pulmonary emboli. However, recent studies have shown that the prevalence of CTEPH can be as high as 5% after acute symptomatic pulmonary emboli, suggesting that the incidence could be of several thousand cases per year in Canada.[1]

Over the past decade, with increasing awareness and appropriate evaluation, CTEPH has become the leading cause of precapillary PH.[2] Refinements in surgical technique of pulmonary endarterectomy (PEA), the development of medical therapy and, more recently, the introduction of balloon pulmonary angioplasty have provided an increasing array of therapeutic options for these patients. Hence, early diagnosis and appropriate referral has become increasingly important.

Pathophysiology of CTEPH

The pathophysiology leading to CTEPH is complex. An important concept is that the development of PH in the context of chronic thromboembolic disease is not solely dependent on mechanical obstruction by the thromboembolic material, but is also related to the development of a secondary vasculopathy generated by the inflammatory milieu and the continuous shear stress caused by the persistent thromboembolic material. Hence, the disease typically worsens despite adequate anticoagulation as a consequence of the secondary vasculopathy. Because the secondary vasculopathy might potentially lead to residual PH after PEA, patients with CTEPH should undergo PEA early in the course of the disease to provide optimal results.

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Corresponding author: Dr Marc de Perrot, Toronto Pulmonary Endarterectomy Program, Division of Thoracic Surgery, Toronto General Hospital, 9N-961, Toronto, Ontario M5G 2C4, Canada. Tel.: +1-416-340-5549; fax: +1-416-340-3478.

E-mail: marc.deperrot@uhn.on.ca

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times between symptom onset and diagnosis, a systolic pulmonary artery pressure > 50 mm Hg on echocardiogram and the presence of organized mural thrombi, mosaic parenchymal perfusion, and/or arterial web or bands on the computed tomography scan. Pulmonary endarterectomy is the treatment of choice for CTEPH. The surgery leads to major long-term clinical improvement and is curative in a large proportion of patients with resolution of the pulmonary hypertension.

pulmonaires aiguës. La maladie thromboembolique chronique devrait être suspectée en présence d'embolies pulmonaires idiopathiques ou récurrentes, ou les deux, d'anomalies de perfusion plus importantes, d'intervalles plus longs entre l'apparition des symptômes et le diagnostic, d'une pression artérielle pulmonaire systolique > 50 mm Hg à l'échocardiogramme ainsi qu'en présence de thrombus muraux organisés, de perfusion parenchymateuse en mosaïque et/ou de réseau artériel ou de bandes à la tomodensitométrie. L'endartériectomie pulmonaire est le traitement de choix de l'HPTEC. La chirurgie conduit à une amélioration importante à long terme et est curative chez une forte proportion de patients avec une résolution de l'hypertension pulmonaire.

Clinical Presentation of CTEPH

The clinical presentation of patients with CTEPH can be indolent and the diagnosis often overlooked. A recent prospective multicentre registry including several European centres and Toronto, demonstrated that the median time from clinical presentation to diagnosis was 14 months.[3] Shortness of breath was the main symptom, being present in 99% of the patients. Other complaints included chest and/or upper abdominal pain, fatigue, peripheral edema, or syncopal episodes. It is not rare for patients with CTEPH to be initially investigated for parenchymal lung disease such as pulmonary fibrosis or chronic obstructive pulmonary disease, coronary disease, asthma, allergy, or gastroesophageal disorders. Most of these patients are older than 60 years and thus the presence of mild abnormalities on the pulmonary function tests and/or coronary angiogram are not uncommon and should not preclude further investigations. On rare occasions, patients have also been investigated for mediastinal malignancy or atrial myxoma because of misinterpretation of the chronic thromboembolic disease on imaging before the diagnosis of CTEPH was made.

Ventilation-perfusion (V/Q) scan and echocardiogram are the most important noninvasive investigations to evaluate the possibility of CTEPH. The V/Q scan has a negative predictive value of 98.5% to rule out CTEPH, and spiral computed tomography (CT) scan has a negative predictive value of 79.7% compared with the traditional gold standard pulmonary angiogram.[4] Hence, V/Q scan should be part of the investigations performed for patients with unexplained dyspnea, newly diagnosed PH, and/or with residual exercise limitation or fatigue after an episode of acute pulmonary embolism. Symptomatic patients with unmatched perfusion defect on V/Q scan despite adequate anticoagulation for at least 3 months mandate referral to a specialized centre for further evaluation.

Surprisingly, in a recent study including 791 patients with PH enrolled in a quality enhancement initiative registry, 43% never had a V/Q scan during their evaluation.[5] This observation highlights the importance of adequate education of the medical community to recognize this largely underdiagnosed condition and provide patients with PH a potentially curative therapeutic approach.

The echocardiographic findings can range from mild ventricular dysfunction to severe right ventricular pressure overload. Noteworthy, because echocardiographic findings in symptomatic patients can occasionally be minimal despite the presence of CTEPH, the importance of using V/Q scan for the detection of CTEPH cannot be overemphasized. Exertional dyspnea is due to increased dead space ventilation and limitation of cardiac output in response to increased physiologic demand. Occasionally, patients with chronic thromboembolic disease can have severe limitations on exertion despite the absence of PH at rest and still derive major benefit from surgery with significant improvement in their exercise capacity and quality of life.[6]

The absence of pulmonary emboli on CT pulmonary angiogram does not rule out a diagnosis of CTEPH. The evidence of chronic thromboembolic disease can be subtle on CT and be missed on suboptimal CT or by inexperienced radiologists, or both. Coronal and sagittal reconstruction with thin 1-mm slices are of particular importance to see the chronic thromboembolic disease (Fig. 1). Chronic thromboembolic disease predominates in the lower lobes and is usually more prominent on the right compared with the left side. Hence, the sagittal views are very helpful to adequately display the anatomy of the pulmonary arterial tree in the lower lobes bilaterally.

It is increasingly recognized that patients with CTEPH can present with acute on chronic pulmonary emboli. Recognition of the underlying chronic disease at the time of the acute presentation is important to ensure that these patients are adequately managed and followed after their initial diagnosis of pulmonary emboli. A V/Q scan and an echocardiogram should be performed after 3-6 months of follow-up in these patients. It is well documented that the acute component of the pulmonary emboli resolves within 4-6 weeks in 90% of patients and within 6 months in all patients.[1] Hence, persistent mismatched perfusion defects after 3-6 months of anticoagulation should raise concern about the possibility of CTEPH in patients with ongoing dyspnea and/or fatigue. The dyspnea might initially improve with the start of anticoagulation because of the resolution of the acute component of the pulmonary embolism. However, the chronic component of the disease typically prevents the patients from returning to their functional baseline.

The presence of chronic thromboembolic disease in patients who present with a newly diagnosed pulmonary embolism should be suspected in the presence of idiopathic and/or recurrent pulmonary emboli, larger perfusion defects, and longer times between symptom onset and diagnosis. The presence of a systolic pulmonary artery pressure > 50 mm Hg on echocardiogram is also a risk factor for the presence of