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Key Words: chronic thromboembolic pulmonary hypertension, pulmonary endarterectomy, cardiopulmonary exercise test, right heart catheterization, pulmonary hypertension

EDITORIAL COMMENTARY

Understanding pathophysiologic changes occurring in chronic thromboembolic disease

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The pathophysiologic processes involved in the development of chronic pulmonary thromboembolic disease (CTED) from acute pulmonary embolism are poorly understood.^{1,2} In the most simplistic physiologic terms, one or more pulmonary emboli fail to resolve through fibrinolysis, leading to chronic obstruction of the pulmonary vascular bed and resulting in increasing right heart failure. There is substantial evidence, however, that the process may not be quite so simple. First, if simple obstruction were the only issue, pulmonary endarterectomy (PEA) should reliably lead to improvement or resolution of pulmonary hypertension in all cases—in fact, however, this does not occur. Some patients have persistent or residual pulmonary hypertension after PEA, and these patients face higher perioperative mortality as well as worse quality of life after

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Central Message

Measurement and understanding of right ventricular stroke volume response and ventilatory efficiency may be the key in chronic thromboembolic disease.

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surgery.^{2,3} Jamieson and colleagues⁴ noted from their very large experience that patients with postoperative pulmonary vascular resistance greater than $500 \text{ dyne} \cdot \text{s}^{-1} \cdot \text{cm}^{-5}$ had a mortality as high as 30.6%, primarily as a result of residual pulmonary hypertension.⁴ The only preoperative factor

shown to predict poor outcome was pulmonary vascular resistance greater than $1000 \text{ dyne} \cdot \text{s}^{-1} \cdot \text{cm}^{-5}$. If we have improved understanding of the pathophysiology, then better patient selection for PEA, development of better medical therapies to prevent progression to symptomatic disease, and earlier detection of the CTED that leads to chronic thromboembolic pulmonary hypertension all become possible.

In their study in this issue of the *Journal*, van Kan and colleagues⁵ cleverly opted to study an interesting group of patients: patients with symptomatic CTED but with normal pulmonary pressures at rest and exercise-induced pulmonary hypertension. Logically, this patient group, representing potentially early pathophysiologic CTED, could reveal more pathophysiologic information about mechanisms active during the development of chronic thromboembolic pulmonary hypertension than would be seen in patients with more end-stage disease. In fact, van Kan and colleagues⁵ found that there were distinct abnormalities during routine cardiopulmonary exercise testing of pulmonary vascular responses to exercise in patients with CTED. Specifically, a steep mean pulmonary arterial pressure to cardiac output slope was noted, indicating an abnormal right ventricular stroke volume response and a decreased pulmonary vascular compliance. The circulatory responses were also strongly correlated with an increase in dead space ventilation and decreased ventilatory efficiency during exercise. van Kan and colleagues⁵ went on to note that reversal of these findings on cardiopulmonary exercise testing performed 1 year after PEA correlated with improvements in symptoms and in exercise tolerance.

With knowledge of these early pathophysiologic changes in patients with CTED, which could be detected during routine cardiopulmonary exercise testing obtained for exercise-induced dyspnea before the development of late pulmonary arterial hypertension, it may be possible to detect early chronic thromboembolic pulmonary hypertension and therapeutically intervene before the development of advanced disease. From their data, van Kan and colleagues⁵ also suggest that if this is done, surgical mortality may decrease to very low levels simply from early surgical intervention. Limitations of this study, of course, lie in its retrospective design and its small patient numbers. Although definitive conclusions cannot be drawn, these data improve our understanding of CTED and motivate all surgeons to promote prospective trials evaluating these findings and early intervention in a disease that is notoriously difficult to understand and treat.

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