



## Editorial

## Chronic Thromboembolic Pulmonary Hypertension: Experience Improves Outcomes<sup>☆</sup>



### Hipertensión pulmonar tromboembólica crónica: la experiencia mejora los resultados

David Jiménez,<sup>a,\*</sup> José Luis Zamorano<sup>b</sup>

<sup>a</sup> Servicio de Neumología, Hospital Ramón y Cajal, IRYCIS, Universidad de Alcalá de Henares, Alcalá de Henares, Madrid, Spain

<sup>b</sup> Servicio de Cardiología, Hospital Ramón y Cajal, IRYCIS, Universidad de Alcalá de Henares, Alcalá de Henares, Madrid, Spain

Pulmonary thromboembolism (PTE) is a common cause of morbidity and mortality.<sup>1</sup> Approximately 20% of patients with PTE die before diagnosis or on the first day after confirmation of the disease; of those who survive longer than one day, up to 11% die within the first 3 months of treatment. The most feared long-term complication is chronic thromboembolic pulmonary hypertension (CTEPH), affecting 1%–4% of patients who survive the thrombotic event.<sup>2</sup> CTEPH is triggered by the incomplete resolution of one or several clots that obstruct the pulmonary vascular bed. The resulting increase in vascular resistance, when associated with pulmonary microvascular disease, leads to disease progression. Small vessel changes explain the progressive nature of CTEPH, even in the absence of recurrent thrombotic events.

Median survival in untreated patients with mean pulmonary arterial pressure >30 mmHg is less than 2 years.<sup>3</sup> However, there have been major advances in the treatment of CTEPH in recent years, reflected in a significant improvement in life expectancy. Clinical practice guidelines, based on indirect evidence, recommend that all patients receive long-term anticoagulation.<sup>4</sup> Although no controlled clinical trials have been published on the efficacy and safety of pulmonary endarterectomy (PE), this technique is the treatment of choice in patients with CTEPH.<sup>5</sup> In 2014, riociguat was approved for use in inoperable patients with functional class II–III, and in those with recurrent or persistent disease after PE.

The management of CTEPH requires highly specialized levels of care, so current clinical guidelines recommend referral of patients to specialized units. In 2008, the authors of the document “Standards of care in pulmonary hypertension” gave the following reasons for this recommendation: (1) the low prevalence of the disease; (2) its poor prognosis; (3) the experience required for performing complex diagnostic techniques and therapeutic procedures; (4) the cost of pharmacological treatment; and (5) the need

for a minimum number of patients for participation in multicenter therapeutic clinical trials.<sup>6</sup>

Some studies suggest that the number of endarterectomies performed in a center and the mortality rate of patients with CTEPH are inversely related,<sup>7</sup> but there are few data available on the effect of specialized management on the prognosis of CTEPH, so the experience of an internationally recognized group in the diagnosis, treatment and follow-up of these patients is very welcome. Coronel et al.<sup>8</sup> present results from the medical and surgical treatment of patients with CTEPH seen in their center during a period of over 12 years. The authors enrolled 80 patients, of whom 40% received surgical treatment and 60% medical treatment. The patients who underwent PE showed significantly greater improvement in the 6-min walk test and pulmonary hemodynamics compared to those who received medical treatment. Survival of the PE group in the last 6 years of the study was significantly greater than that of the group who underwent the procedure in the previous 6 years. There was no difference in survival between the patients who received medical treatment and those who underwent PE. In the group who underwent PE in the last 6 years, and the group of patients who survived the first 100 days post-surgery, survival was greater than in the medical intervention group.

A detailed analysis of the results partially dampens the initial enthusiasm generated by the first reading. Although hemodynamic benefits were greater in the patients who underwent PE, patients who received medical treatment were older, and their pretreatment 6-min walk results were poorer. Moreover, the follow-up hemodynamic study was only performed in about half the patients who received medical treatment, suggesting a possible selection bias. Exclusion of patients who died in the post-operative period from the survival analysis is hard to justify, and the mortality analysis of surgical patients in the two time periods of the study should also have been conducted on the medically treated patients.

Perhaps the most interesting aspect of this study lies the questions it raises: Should an inferior vena cava filter be placed in patients before PE? Does a positive vasodilator response justify the use of calcium antagonists in CTEPH patients? Is there a learning curve for the medical treatment of these patients? Could the effect of medical treatment and surgical treatment be comparable, at least

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\* Corresponding author.

E-mail address: [djc.69.98@yahoo.com](mailto:djc.69.98@yahoo.com) (D. Jiménez).

in selected patients? Are the clinical results of centers with more experience better than those of centers with less experience? To answer these questions, multidisciplinary reference units acting as a focal point for experience, where evidence can be rigorously evaluated and controlled clinical trials with sufficient patient numbers can be performed, are absolutely necessary.

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