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EDITORIAL COMMENT

New insights into chronic thromboembolic pulmonary hypertension

Novas perspetivas sobre hipertensão pulmonar tromboembólica crónica

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Chronic thromboembolic pulmonary hypertension (CTEPH) is a life-threatening condition that occurs as a late complication of acute pulmonary embolism (PE). It is currently accepted that both central pulmonary vascular occlusion caused by unresolved fibrotic clots, and the development of secondary small vessel vasculopathy due to pulmonary vascular remodeling, play a role in the development of the disease.[1,2] The treatment of choice for CTEPH is pulmonary endarterectomy, but this is not suitable for all patients. Other treatment strategies include balloon pulmonary angioplasty and pulmonary hypertension (PH) drugs targeting endothelial cell dysfunction.

The exact incidence of CTEPH is unknown, but in studies that used active surveillance after PE, estimates ranged between 0.1% and 8.8% within two years of a diagnosis of PE.[3] This wide range across studies may be explained by differences in patient selection and, importantly, by the inconsistent use of right heart catheterization (RHC) for definitive diagnosis. Nevertheless, its incidence is considered low, and as such the current European guidelines for the diagnosis and treatment of PE recommend against routine screening for CTEPH after an acute PE episode.[4] The recommended strategy focuses on patients with persistent symptoms or functional limitations three to six months after PE as well as on those with conditions known to predispose to the development of CTEPH. However, clinical symptoms and signs are often hard to identify at early stages, which makes early diagnosis truly challenging, and even in expert centers the median time between symptom onset and diagnosis has been found to exceed one year.[5] Improvement in the diagnosis and treatment of this condition depends mainly on a high level of suspicion, and knowledge of CTEPH incidence and prevalence at a local level, as well as its predictors, are essential to achieve such improvement.

These factors underline the relevance of the study by Pargana et al. presented in this issue of the *Journal*, which aimed to assess the prevalence and predictors of CTEPH two years after a symptomatic high- or intermediate-high risk PE in a national referral center for PH.[6] The main finding of this retrospective single-center cohort study was an overall prevalence of suspected CTEPH by clinical assessment, Doppler echocardiography and V/Q lung scan of 6.2%, and of confirmed CTEPH by RHC of 3.1%. The presence of varicose veins and pulmonary artery systolic pressure higher than 60 mmHg at admission for the index event were identified as

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early predictors of CTEPH. Despite the limitation of a small sample, which resulted in only four patients with definite CTEPH, clearly undermining assessment of the predictors, the study has the merit of addressing this important topic, which is indeed understudied in Portugal.

Recently, this group specializing in PE analyzed the current clinical recommendations for the use of percutaneous catheter-directed therapy (CDT) and proposed a standardized approach for severe forms of acute PE, highlighting the role of pulmonary embolism response teams in this setting.[7] Empirically, the treatment of acute PE should have a critical impact on CTEPH development, although the effect of systemic thrombolysis or CDT on this condition remains questionable. Fortunately, there are promising ongoing randomized trials that may help to answer these questions: the PEITHO-3 study will assess the efficacy and safety of reduced dose thrombolysis in intermediate-high-risk PE,[8] while HI-PEITHO is comparing CDT with parenteral anticoagulation in the same PE risk category.[9] It should be noted that both will have confirmed CTEPH at follow-up as a secondary outcome. Meanwhile, all efforts should be made to optimize early detection and appropriate treatment of CTEPH, in order to improve functional capacity after acute PE and ultimately the patient's quality of life.

Conflicts of interest

The author has no conflicts of interest to declare.

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