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Getting expertise in pulmonary thromboendarterectomy: we always need to move forward!

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Chronic thromboembolic pulmonary hypertension (CTEPH) is one of the major causes of pulmonary hypertension (PH), being classified as group 4 PH by the 6th World Symposium of Pulmonary Hypertension.[1] It is one of the chronic complications of acute pulmonary embolism (PE), together with chronic thromboembolic pulmonary disease.[2] About 75% of patients with CTEPH have a documented history of PE.[1]

Chronic thromboembolic pulmonary disease and CTEPH have similar symptoms and imaging findings and differ by the presence of PH at rest in CTEPH patients. CTEPH is currently defined by the presence of a mean pulmonary arterial pressure (mPAP) > 20 mmHg with pulmonary arterial wedge pressure ≤ 15 mmHg and pulmonary vascular resistance (PVR) ≥ 3 Wood units, at least one mismatched perfusion defect on lung scans, and findings of fibrotic thrombi on multidetector CT pulmonary angiography, magnetic resonance imaging, or conventional pulmonary cineangiography (ring-like stenoses, webs, and/or pouch or tapered lesions) after at least three months of effective anticoagulation. Pathology depicts organized thrombi and abnormal vascular remodeling due to defective angiogenesis, impaired fibrinolysis, and endothelial dysfunction.[1,2] Large and peripheral pulmonary arteries are involved, and the magnitude of the latter impacts on the clinical decision regarding the indication and the results of pulmonary endarterectomy (PEA).

The incidence of CTEPH after PE is uncertain and probably underdiagnosed, ranging from 0.4% to 8.8% (pooled incidence of 3.4%; 95% CI, 2.1-4.4%). Prevalence ranges from 0.4% to 9.1%.[3] Survival is poor, with an estimated 5-year survival of 30% when mPAP is above 40 mmHg and of 10% if it is above 50 mmHg.[4]

CTEPH is the only potentially curable cause of PH. PEA is the gold standard therapy and consists of removal of organized thrombotic lesions from the proximal vessels, that is, main, lobar, and segmental arteries (Figure 1). Refinements of the techniques and the growing expertise of surgical teams have allowed reaching more distal lesions, resulting in better short- and long-term outcomes.[5] Other options are medical therapy and percutaneous balloon pulmonary angioplasty (BPA). Riociguat is the sole drug approved for non-operable CTEPH or for patients with persistent/recurrent CTEPH after PEA.[6]

BPA has been incorporated in the arsenal for the management of CTEPH and was initially indicated for non-operable patients; however, as experience with the technique has increased in specialized centers, it has become part of a multimodal CTEPH management, together with PEA and medical therapy as complementary tools.[2,7]

A cohort study evaluated post-PEA hemodynamics and found that residual mPAP ≥ 30 mmHg correlated with initiation of pulmonary vasodilators, and residual mPAP ≥ 38 mmHg and PVR ≥ 425 dyn ··s^{-1}·· cm^{-5} correlated with poorer long-term survival.[8] Currently, the hemodynamic definition of post-PEA PH has been disputed after the new PH criteria recommended by the abovementioned symposium.[1,2]

The results of a European CTEPH Registry[9] revealed a 1-year, 2-year, and 3-year survival of 93% (95% CI, 90-95%), 91% (95% CI, 87-93%), and 89% (95% CI, 86-92%), respectively, in operated patients (n = 404/679) and of 88% (95% CI, 83-91%), 79% (95% CI, 74-83%), and 70% (95% CI, 64-76), respectively, in non-operated patients (n = 275/679), highlighting the central role of PEA. Mortality in operated and non-operated patients was associated with New York Heart Association (NYHA) class IV (hazard ratio [HR] = 4.16 [95% CI, 1.49-11.62]; p = 0.0065 vs. HR = 4.76 [95% CI, 1.76-12.88]; p = 0.0021); increased right atrial pressure (HR = 1.34 [95% CI, 0.95-1.90]; p = 0.0992 vs. HR = 1.50 [95% CI, 1.20-1.88]; p = 0.0004); and history of cancer (HR = 3.02 [95% CI, 1.36-6.69]; p = 0.0065 vs. HR = 2.15 [95% CI, 1.18-3.94]; p = 0.0129).[9]

Other authors have reported 1-month, 1-year, and 3-year survival rates of 97.2%, 93.1%, and 92.5%, respectively, after PEA.[10] They found significant improvement in NYHA class and in six-minute walk distance, as well as a reduction in PVR from 773 ± 353 dyn ··s^{-1}·· cm^{-5} to 307 ± 221 dyn ··s^{-1}·· cm^{-5} ($p < 0.001$) after the procedure.[10]

In this issue of the *Jornal Brasileiro de Pneumologia*, Scudeller et al.[11] present a retrospective analysis of their PEA results in the largest PEA referral center in South America over a 10-year period. They compared three sequential periods of time along with improvements in clinical, anesthetic, and surgical management of the patients: group 1 (January 2007-December 2012), group 2 (January 2013-March 2015) and group 3 (April 2015-May 2016). Previous PE was confirmed in 80% of the sample, and there were no differences in clinical or hemodynamic parameters among the groups, suggesting that the results might have derived from the technical improvement itself, even if we consider the retrospective design of the study. The 2-year survival probability after surgery for groups 1, 2, and 3, respectively, was 70%,

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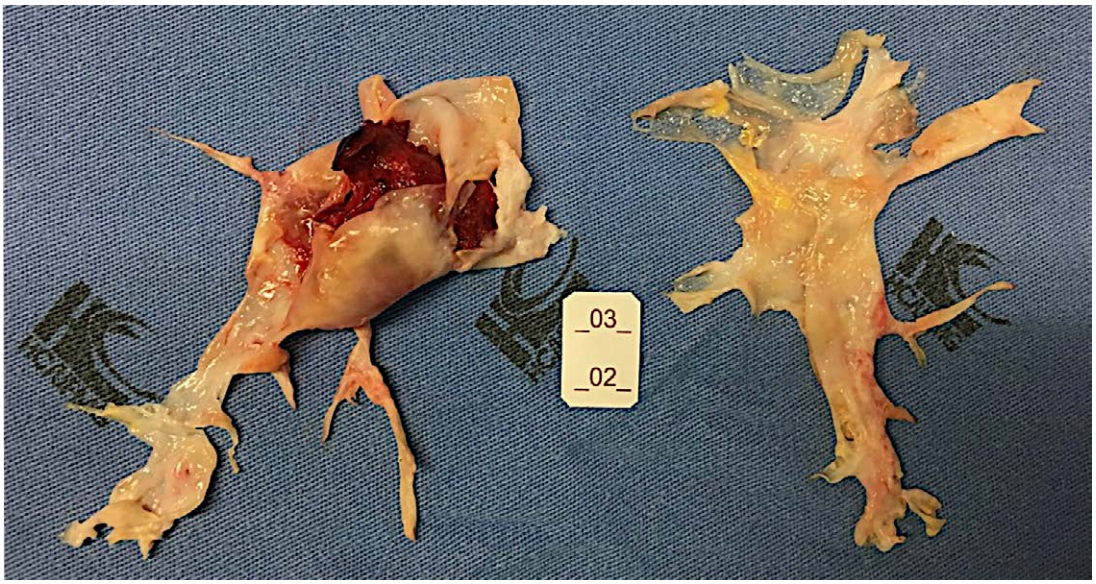

Figure 1. Bilateral pulmonary arterial thrombotic lesions removed by pulmonary thromboendarterectomy. Image kindly provided by the Clinical and Surgical Team of the *Hospital das Clínicas* of the Federal University of Minas Gerais.

77%, and 88% (p = 0.501), somewhat smaller than that reported in a previous study,[9] but there was a reduction in early post-operative complications in group 3 (10.3%) vs. groups 1 and 2 (34.2% and 31.4%, respectively; p = 0.035).

The authors examined variables potentially associated with surgical and infectious complications, as well as with in-hospital mortality. In the multivariate analysis, being in group 3 was associated with fewer surgical complications (OR = 0.221 [95% CI, 0.052-0.939]; p = 0.034 for the comparison of groups 1 and 3). In addition, high pulmonary artery systolic pressure was associated with more surgical complications (OR = 1.031 [95% CI, 1.007-1.056]; p = 0.012), and preoperative NYHA classes III-IV were associated with more infectious complications than were preoperative NYHA classes I-II (OR = 3.538 [95% CI, 1.107-11.309]; p = 0.033). Older age (OR = 1.06 [95% CI, 1.02-1.10; p = 0.047) and higher PVR (OR = 1.00 [95% CI, 1.00-1.01]; p = 0.024) were associated with higher in-hospital mortality. Mortality was 6.2 and 4.1 times more likely to occur in patients ≥ 60 years of age and in those with PVR ≥ 860 dyn ··s^{-1}·· cm^{-5}, respectively. During the follow-up period, 75.0%, 61.5%, and 63.1% of the patients in groups 1, 2, and 3, respectively, were classified as NYHA I at 3-6 months after PEA, and 58.5% of the patients who underwent right heart catheterization developed residual PH.[11] Although hemodynamic definition of residual PH was not reported, the result is higher than was that found in a large recent meta-analysis (25%).[12]

PEA is the gold standard therapy for the treatment of CTEPH, improving outcomes such as clinical and survival rates. Of utmost importance is the continuous improvement in the surgical and anesthetic techniques, as well as in the post-operative care, as has been shown by Scudeller et al.[11] Medical therapy and BPA currently play an important role in the multimodal therapy of CTEPH, which may improve the results and prognosis of these patients even further.

AUTHOR CONTRIBUTIONS

All of the authors equally contributed to the writing and reviewing of the document.

CONFLICT OF INTEREST

None declared.

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