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EDITORIAL

Chronic Thromboembolic Pulmonary Hypertension: A Worldwide View of How Far We Have Come

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Chronic thromboembolic pulmonary hypertension (CTEPH) is classified as group 4 based on the World Health Organization (WHO) classification [1]. The diagnosis of CTEPH is predicated upon the presence of pulmonary hypertension (PH), defined via right heart catheterization as a mean pulmonary artery pressure $\geq$25 mm Hg at rest, in association with persistent pulmonary perfusion defects, despite therapeutic anticoagulation [2]. In CTEPH patients, after an episode or more of pulmonary embolism (PE), there is incomplete resolution of emboli that obstruct or narrow elastic pulmonary arteries. In addition, a progressive distal small vessel vasculopathy develops overtime [3]. The combination of large vessel obstruction and microvascular disease accounts for the elevated pulmonary pressures, and dictate the treatment approach: surgical removal of fibrotic thrombi, the preferred approach versus medical therapy [4].

The reported incidence of CTEPH after PE is variable, but it is unquestionable that CTEPH is an under-recognized disease. If one applies a conservative rate of 1–3 % after PE [4] to the estimated half a million PE survivors in the United States, one ends with around 5000–15,000 new CTEPH cases every year, a number that clearly is not being taken care of by CTEPH centers. This underscores the importance of a heightened awareness, especially for patients with persistent cardiopulmonary symptoms 3–6 months after an episode of acute PE, and for patients with known PH. The ventilation perfusion (VQ) scan remains the screening test of choice due to its high sensitivity [5] and straightforward interpretation. One or more segmental or larger perfusion defects should trigger further work for CTEPH, including pulmonary angiography via computed tomography (CT), and conventional digital subtraction angiography. While CT pulmonary angiography has become the test of choice for the diagnosis of acute PE, CT findings of chronic thromboembolism are frequently more difficult to be ascertained, and require considerable levels of experience and expertise.

Once the CTEPH diagnosis is established, operability assessment by an experienced CTEPH center is recommended [6], as pulmonary endarterectomy (also called pulmonary thromboendarterectomy or PTE) [7] is the only treatment that offers the potential for cure. A majority of patients, approximately 2/3 in the international CTEPH registry [8], are deemed operable. The operation and postoperative care are highly complex and should be performed only in centers with experienced CTEPH teams. When the surgery is not indicated, as determined by an expert center, and for those with PH after surgery, targeted PH therapy is known to be effective [9, 10].

As noted, the diagnosis and treatment of CTEPH present significant challenges, which can certainly be magnified in health care environments with fewer resources. In this issue of *Lung*, Al-Naamani et al. report on the experience of a CTEPH cohort registry (REPHPISSSTE registry) in two medical centers in Mexico [11]. Out of the 45 patients who were evaluated for operability (whether retrospectively by chart review or prospectively), a total of 29 patients (64 %) were deemed operable. Because of the lack of insurance coverage (primary reason) and the lack of the healthcare infrastructure needed to care for these complex patients, only one patient (2 % of the total cohort) had a pulmonary

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endarterectomy, and this patient was the only patient in this cohort who actually had a pulmonary angiogram. All patients were anticoagulated, with increasing use of rivaroxaban in the contemporary cohort. Seventy-two percent of the patients were prescribed pulmonary arterial hypertension (PAH) specific medications, of which sildenafil (70 % of the cohort) and bosentan (10 % of the cohort) were the two most commonly prescribed medications. Inferior vena cava filters were infrequently (16 %) used.

Even within the resource-rich countries, CTEPH management is not uniform as exemplified by the wide range of CTEPH patients' proportions undergoing surgery across countries, ranging from 12 to 61 % [8]. With a median follow up of 20 months, the mortality rate in the Mexican registry reported by Al-Naamani et al. [11] was 28 %, which is consistent with the outcomes reported in other registries in developed countries that are enriched with more resources. Examination of the survival curve for the cohort diagnosed via right heart catheterization discloses a 2-year survival of about 80 %, consistent with the survival rate reported in the international (European countries and Canada) registry for non-operated patients, but more than 10 % lower compared to operated patients [12]. As 67 % of the Mexican patients were deemed operable, it is evident that surgical therapy will improve outcomes should it become available.

Other parts of the world, including India [13], China [14, 15], and Russia [16], have reported improved outcomes after pulmonary endarterectomy, and surgical techniques and expertise are improving. On the other hand, in Japan for example, balloon pulmonary angioplasty (BPA) as a treatment for CTEPH is emerging [17] at least in part due to lack of surgical expertise in and/or availability of pulmonary endarterectomy, cultural reasons, and the available expertise in percutaneous interventional therapies. Some European countries are slowly gaining expertise in this procedure [18], as a select number of high risk frail CTEPH patients may benefit from this non-curative (at times with palliative intent) procedure, i.e., BPA, without the relatively higher risk of pulmonary endarterectomy [4]. Although experience with both pulmonary endarterectomy and BPA is increasing in the developed world and CTEPH centers are increasing in number rapidly, expertise in these procedures is still relatively limited (both geographically and in skill levels), and patients have to travel long distances to reach an experienced center. Many of the emerging CTEPH centers in the last few years have not reported their outcomes yet. In most of the developing world, these procedures are not even an option locally, except for the select few who have the resources to travel abroad for healthcare services.

We commend Dr. Al-Naamani's group on exploring the impact of CTEPH in Mexico, and highlighting the discrepancy between the care in Mexico and the more developed world. Tailoring evaluation and management of diseases, CTEPH in this case, is highly dependent on the local resources (both financial and expertise) available, and this obviously has a direct correlation with outcomes, and would impact the referral process to more experienced centers.

Compliance with Ethical Standards

Conflict of Interest None.

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