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Letter to the Editor

Growing number of incident pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension patients in Latvia: a shifting epidemiological landscape? Data from a national pulmonary hypertension registry

Pulmonary hypertension (PH) is a complex, progressing and debilitating pulmonary vascular disease associated with poor prognosis. Pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension (CTEPH) are two distinct subtypes of PH with different pathophysiologic mechanisms and treatment strategies [1].

Both PAH and CTEPH are rare diseases with a reported incidence and prevalence of 0.9–13.7 and 7–52 cases per million inhabitants (MI), respectively, for PAH [2–5] and 0.3–5.7 and 3–19 cases per MI, respectively, for CTEPH [4,6–8]. However, the true incidence and prevalence could be higher, especially for CTEPH- according to recent systematic analysis, the calculated crude full incidence (i.e. diagnosed and undiagnosed) of CTEPH in the USA and Europe ranged from 30 to 50 cases per MI, suggesting that CTEPH is still largely underdiagnosed [9].

Since the creation of National Institutes of Health (NIH) registry more than three decades ago, patient registries have provided important insights into the evolving epidemiology of PH.

This is a prospective, observational, single-center study of the Latvian PH registry. A total of 41 consecutive adult patients (≥18 years old) with newly diagnosed PAH or CTEPH were enrolled between 1 January and 31 December 2017. The diagnostic criteria were in accordance with the current international guidelines [1]. The diagnosis of PAH and CTEPH for all patients was confirmed by right heart catheterization which measured right atrial pressure (RAP), mean pulmonary artery pressure (mPAP), pulmonary artery wedge pressure (PAWP), pulmonary vascular resistance (PVR), cardiac output (CO) and cardiac index (CI). Patient baseline characteristics are summarized in Table 1.

By the end of study time period 18 patients with PAH and 23 patients with CTEPH were included in Latvian PH registry. Mean age at diagnosis for PAH and CTEPH patients was 63.7 ± 18.0 and 71.4 ± 8.2 years, respectively. Mean body mass index was high at 29.2 ± 6.7 and 29.4 ± 7.1 kg/m^2, respectively. Female gender was predominant in both patient groups (83% in PAH and 74% in CTEPH group). Patient hemodynamic parameter analysis in the two study groups showed elevated pressures in the right heart (high RAP, mPAP), increased vascular resistance in the pulmonary tree (high PVR), and decreased cardiac function (low CO, CI), which together with decreased functional capacity (low 6-min walking distance, high proportion of NYHA class III/IV) indicated already progressed disease at the time of diagnosis.

Of the 39 (95%) PAH and CTEPH patients who received PH-specific medical therapy after the diagnosis, 33 (80%) patients received monotherapy (of them, 76% with phosphodiesterase type 5 inhibitors (PDE5i), 24% - endothelin receptor antagonists (ERA)); 6 (15%) patients received initial combination therapy (PDE5i + ERA). A small proportion of patients (5%) did not receive PH-targeted drug therapy. Anticoagulant therapy was used in all CTEPH patients, predominantly warfarin (65% of CTEPH patients). Remaining 35% of patients with CTEPH received non–vitamin K antagonist oral anticoagulants.

Table 1
Baseline characteristics of Latvian PAH and CTEPH patients. Values are shown as frequencies and proportions (%) or mean ± standard deviation. BMI- body mass index; 6MWD- 6-min walking distance; NYHA- New York Heart Association; RAP- right atrial pressure; mPAP- mean pulmonary artery pressure; PAWP- pulmonary artery wedge pressure; PVR- pulmonary vascular resistance; CO– cardiac output; CI- cardiac index.

Parameter	PAH	CTEPH
Number of patients	18	23
Age, years	63.7 ± 18.0	71.4 ± 8.2
Females	15 (83%)	17 (74%)
BMI, kg/m^2	29.2 ± 6.7	29.4 ± 7.1
6MWD, m	268 ± 118	244 ± 159
NYHA class I–II/III/IV, %	5/67/28	35/43/22
RAP, mmHg	7 ± 4	7 ± 5
mPAP, mmHg	43 ± 14	41 ± 8
PAWP, mmHg	9 ± 4	9 ± 6
PVR, dyn·s·cm^{-5}	616 ± 366	621 ± 239
CO, l/min	4.5 ± 1.1	4.1 ± 1.3
CI, l/min/m^2	2.4 ± 0.5	2.2 ± 0.6

No CTEPH patient underwent pulmonary endarterectomy/balloon pulmonary angioplasty as these therapeutic modalities are not available in Latvia.

Given the 1.95 million inhabitants (of them 1.59 million being ≥18 years old) living in Latvia in 2017 (http://data.csb.gov.lv, website accessed 31 August 2018), the calculated PAH incidence in 2017 was 9.2 per MI and 11.3 per million adult inhabitants (MAI), whereas CTEPH incidence in 2017 was 11.8 per MI and 14.5 per MAI.

When comparing the obtained results with earlier Latvian PAH and CTEPH cohorts [2] or contemporary PH registries in Europe [2,4–8,10], there were no prominent differences in the demographic, functional or hemodynamic parameter values between the studies, apart from older age of patients and higher proportion of females in present study (especially in CTEPH patient group). However, the calculated incidence of CTEPH in Latvia has been growing over the past decade and, to our knowledge, it is the highest among reported to this date, although it is still far from estimated crude full incidence mentioned earlier. The incidence of PAH in Latvia has also increased over recent years (Latvian PH registry data). Moreover, for the first time there were more patients diagnosed with CTEPH than PAH in Latvia in 2017, possibly indicating a new trend in the epidemiology of PH.

More work should be continued towards wider collaboration between European PH registries as small patient population is one of the main limitations of the current study. Latvian PH registry has already

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taken the first step in this direction by joining COMPERA registry, therefore contributing to current research about this multifactorial disease.

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