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Letter to the Editor

# Pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension incidence in Latvia in 2018

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Pulmonary hypertension (PH) is a heterogeneous group of disorders that can be classified according to clinical, hemodynamic and pathological findings and the prognosis of each group differs substantially [1]. Pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension (CTEPH) are distinct types of pre-capillary PH, defined by mean pulmonary arterial pressure (mPAP) > 20 mmHg, pulmonary arterial wedge pressure (PAWP) ≤15 mmHg and PVR ≥ 3 Wood units [2].

The reported incidence of CTEPH is approximately 4 per 1 million adults, however true incidence and prevalence of CTEPH is still largely unknown due to the lack of specific symptoms and the diagnostic complexity of the disease [3,4]. The incidence of PAH in the developed countries is 1.1–7.6 per million adults each year [5–7].

This is a prospective, observational, study of the Latvian nationwide PH registry. A total of 21 consecutive adult patients (≥18 years old) with newly diagnosed PAH or CTEPH were enrolled between January 1 and December 31 of 2018. The diagnostic criteria were in accordance with latest 6th World Symposium on Pulmonary Hypertension Task Force [2]. 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), was done to confirm the diagnosis of PH for all patients. Patient baseline characteristics are shown in Table 1.

A total of 14 PAH patients and 7 CTEPH patients were enrolled by the end of study period. Patient numbers by PAH subtype were as follows: idiopathic PAH - 10 (71.4%); PAH associated with connective tissue disease - 3 (21.4%) and 1 (7.1%) patient with PAH associated with congenital heart disease. Mean age at diagnosis of PAH and CTEPH was 65.6 ± 15.4 and 64.1 ± 19.0 years, respectively. Mean body mass index was 29.3 ± 8.6 and 25.5 ± 2.1 kg/m$^2$, respectively. Out of 7 CTEPH patients, 3 were female (42.9%), whereas in PAH group all of the patients were female. Hemodynamic parameter values in both study groups revealed severe PH, as indicated by high RAP, mPAP, PVR and low CO and CI. The decreased mean six-minute walk test distance and predominance of New York Heart Association class III and IV in both groups suggest an already advanced disease.

Of all PAH and CTEPH patients who received PH specific medical therapy after confirmation of diagnosis, 12 (57.1%) patients received monotherapy (phosphodiesterase type-5 inhibitors (PDE5i) – 83.3% and entothelin receptor antagonists (ERA) – 16.7%) and 8 (38.1%) initial combination therapy (PDE5i + ERA).

Pulmonary endarterectomy, which is the treatment of choice for CTEPH, was done for 2 patients (28.6%). One of the patients was hospitalized due to acute right heart failure, and after a prompt evaluation for operability by a multidisciplinary CTEPH team, PEA was successfully performed in Riga by visiting PEA expert surgeon from Vienna General Hospital. The other patient, after initial combination therapy with PDE5i and ERA, was referred to Vienna General Hospital for PEA. Lack of experience, limited number of patients in smaller countries and the complexity of the procedure limit availability of PEA in Latvia, where a successful international collaboration has always played a major role in management of CTEPH patients.

All CTEPH patients received anticoagulation – 4 patients recieved warfarin (57.1%) and 3 patients (42.9%) recieved rivaroxaban, although no data exist on the efficacy and safety of therapy with non-vitamin K antagonist oral anticoagulants [1]. At the end of the study two of the patients in CTEPH group were deceased.

In 2018, the number of inhabitants in Latvia was 1.93 million (of them 1.56 million being ≥18 years old) (http://data.csb.gov.lv, website accessed 31 March 2019), the calculated PAH incidence in 2018 was 7.2 per million inhabitants (MI) and 9.0 per million adult inhabitants (MAI), and CTEPH incidence - 3.6 per MI and 4.5 per MAI.

In comparison to data from 2017 National Latvian PAH and CTEPH cohorts [8], the incidence of PAH and CTEPH has decreased significantly. Furthermore CTEPH incidence has dropped from previously reported 5.1 cases per MI in Latvia in time period 2007–2016 [9]. Decrease in incidence was also observed in PAH group – 13.7 cases per MI in period of 2007–2016, 9. 2 per MI in 2017 [9].

This study once again underlines the need for registries in each country or region of the world due to contrasting incidence of different PH clinical groups [10]. Better screening and characterization of patients with PH in well-designed registries, taking into account local specificities, could improve recognition of CTEPH and PAH and provide useful information to health authorities [10].

In conclusion, the benefit of collaboration between European PH registries and expert centers will lead to earlier diagnosis of PH and improve accessibility to specific treatment.

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**Table 1**
Baseline characteristics of Latvian PAH and CTEPH patients. Values are shown as frequencies and proportions (%) or mean ± standard deviation.

| Parameter | PAH | CTEPH |
|---|---|---|
| Number of patients | 14 | 7 |
| Age, years | 65.6 ± 15.4 | 64.1 ± 19.0 |
| Females | 14 (100%) | 3 (42.9%) |
| BMI, kg/m2 | 29.3 ± 8.6 | 25.5 ± 2.1 |
| 6MWD, m | 265.2 ± 147.8 | 171.0 ± 142.1 |
| NYHA class I-II/III/IV, % | 21.4/35.7/42.9 | 0/57.1/42.9 |
| RAP, mmHg | 9.1 ± 5.0 | 7.1 ± 4.9 |
| RVSP, mmHg | 74.2 ± 26.1 | 67.6 ± 21.5 |
| mPAP, mmHg | 48.7 ± 12.6 | 38.0 ± 11.7 |
| PAWP, mmHg | 10.7 ± 4.6 | 7.7 ± 3.2 |
| PVR, Wood units | 10.7 ± 4.2 | 8.0 ± 6.5 |
| CO, l/min | 4.0 ± 1.4 | 3.8 ± 1.3 |
| CI, l/min/m2 | 2.4 ± 0.9 | 1.9 ± 0.7 |
| BNP, pg/ml | 528.8 ± 334.6 | 577.5 ± 411.2 |
| Tiffeneau-Pinelli index, % | 72.8 ± 9.2 | 70.4 ± 4.9 |

CI- cardiac index; CO- cardiac output; BMI- body mass index; BNP- B-type Natriuretic Peptide; mPAP- mean pulmonary artery pressure; NYHA- New York Heart Association; PAWP- pulmonary artery wedge pressure; PVR- pulmonary vascular resistance; RAP- right atrial pressure; RVSP- right ventricle systolic pressure; 6MWD- 6-min walking distance.

## Declarations of interest

None.

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