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Assessment of physical capacity and function of the cardiovascular system in invasively treated patients with chronic thromboembolic pulmonary hypertension

ABSTRACT

Background. Chronic thromboembolic pulmonary hypertension (CTEPH) is a complication of venous thromboembolism (VTE) resulting from non-dissolving thromboemboli in the pulmonary arteries and one of the possible causes of it is vascular wall dysfunction. However, the exact etiology of this occurence is unknown. Previous observations indicate more frequent atherosclerosis and diseases associated with it in patients with VTE, but so far it has not been investigated whether this also applies to patients with CTEPH. In our study, we assessed the early marker of arterial dysfunction, pulse wave velocity (PWV), in CTEPH patients in comparison with a matched control group (CG) and its changes after invasive treatment of balloon pulmonary angioplasty (BPA). The physical capacity was assessed by a 6-minute walk test (6MWT).

Hypothesis:

1) Patients with CTEPH have increased systemic arterial stiffness. 2) Patients with CTEPH have reduced physical capacity.

3) Invasive treatment can improve physical capacity in the 6-minute walk test and systemic arterial function assessed by pulse wave velocity in patients with CTEPH.

Material and methods. The study group consisted of 26 CTEPH patients (9 males (M) and 17 females (F), aged 69±10 years) and 22 CG patients (10 M, 12 F, aged 67±8 years) matched by age, gender, and concomitant diseases associated with atherosclerosis. Of the 26 patients with CTEPH included in the study, 16 patients (10 M, 6 F aged 70±10 years) were qualified for BPA.

In all cases we performed:

- medical history with the assessment of demographic characteristics, the presence of cardiovascular risk factors, cardiovascular diseases, the familial occurrence of cardiovascular diseases, the co-occurrence of comorbidities, medicines
- clinical examination with measurement of blood pressure, heart rate, body mass index (BMI), oxygen saturation (SaO2)
- laboratory tests (morphology, lipidogram, glomerular filtration rate (eGFR), fasting glucose (mg/dl)
- transthorasic echocardiography (TTE) with evaluation of basic left and right ventricular function parameters using 2.5-3.5 MHz linear probe (Philips iE 33, Andeouver, Massachusetts USA)
- carotid-femoral pulse wave velocity (cfPWV) with the use of Complior SR once in CG and twice (before and after BPA) in CTEPH patients
- 6-minute walk test

In all CTEPH patients included in the study we performed:

- right heart catheterization (RHC) before and after BPA

The protocol was approved by the Warsaw Medical University's Bioethics Committee (KB/170/2014) on August 12, 2014.

Results. (1) Patients with CTEPH had significantly shorter distance in 6MWT (348±136 vs. 599±107, $p<0.0001$) and significantly lower SaO2 (91±7 vs. 98±1, $p=0.002$) compared to the CG. **(2)** Significantly higher cfPWV was found in CTEPH group than in CG (10.3±2.5m/s vs 9±1.3m/s, $p<0.05$) despite higher systolic blood pressure (SBP) and pulse pressure (PP) in CG (120±11mmHg vs. 132±14mmHg, $p=0.002$ and 43±11mmHg vs. 53±12mmHg, $p=0.005$, respectively). **(3)** The cfPWV correlated with age and pulmonary vascular resistance (PVR) in CTEPH patients ($r=0.45$, $p=0.03$ and $r=0.43$, $p=0.03$, respectively) while in CG cfPWV correlated with age and inversely with BMI ($r=0.54$, $p=0.01$ and $r=-0.43$, $p<0.05$, respectively). There was a borderline correlation between cfPWV and pulmonary compliance ($r=0.37$, $p=0.07$). **(4)** Arterial stiffness, defined as cfPWV>10 m/s was found in 11 (42%) patients with CTEPH and 5 (23%) cases with CG. Patients with CTEPH with cfPWV>10 m/s compared to CTEPH patients with cfPWV≤10 m/s were older (74±8yrs vs. 66±10yrs, $p<0.05$), had a decreased SaO2 (89(73-96)% vs. 96(85-98)%, $p<0.01$) and had a tendency to higher PVR

(8.1(3.1-14.0) vs. 5.2(3.1-12.7)HRU, p=0.10). The cfPWV>10m/s was not related to the lower SaO2 in the CG. **(5)** In multivariable analysis SaO2 (OR 0.90; 95% CI: 0.68-0.95, p<0.01) was found to be the only significant predictor of cfPWV>10m/s. **(6)** In patients qualified for BPA, both SBP (122±12mmHg vs. 123±11 mmHg, p=0.89) and DBP (77±11mmHg vs. 79±9 mmHg, p=0.62) and PP (47±10mmHg vs. 53±17mmHg, p=0.20) did not significantly change after BPA. **(7)** Patients with CTEPH achieved significantly longer distance in 6MWT (385 (135-570) vs. 447(180-675)m, p<0.01) after BPA than before BPA. The SaO2 tended to improve(92(80-98)% vs. 94(79-97)%, p=0.39) in these patients. **(8)** The mean pulmonary artery pressure (mPAP 43±10mmHg vs. 33±12mmHg, p<0.0001) and PVR (7.0±3.4HRU vs. 4.2±2,0HRU, p<0.002) declined significantly after BPA, while cardiac index difference (CI 2.7±0.7ml/min/m2 vs. 2.9±0.4ml/min/m2, p=0.23) was not significant. **(9)** The cfPWV value tended to decrease after BPA (10.5±2.8m/s vs. 9.6±1.9m/s, p=0.08) even though SBP did not change. Interestingly, cfPWV was reduced (median reduction 2.9, range: 0.9-3.7 m/s) in all patients with cfPWV>10m/s before BPA. **(10)** The cfPWV after BPA correlated with PVR before BPA (r=0.51, p<0.05) and with the change of CI (r=0.51, p<0.05) and inversely with CI before BPA (r=-0.73, p=0.001) and with the change of PVR (r=-0.53, p=0.03).

Conclusions:

1) Systemic arterial stiffness, as a marker of atherosclerosis assessed by carotid-femoral pulse wave velocity, is increased in patients with chronic thromboembolic pulmonary hypertension compared to the matched controls.

2) Patients with chronic thromboembolic pulmonary hypertension have reduced physical capacity assesed by 6-minute walk test.

3) The elevated carotid-femoral pulse wave velocity is associated with older age, higher pulmonary vascular resistance and lower oxygen saturation in chronic thromboembolic pulmonary hypertension.

4) Systemic arterial stiffness, assesed by carotid-femoral pulse wave velocity decreased after the balloon pulmonary angioplasty in patients with chronic thromboembolic pulmonary hypertension. The final pulse wave velocity is associated with a decline of pulmonary vascular resistance and an increase of cardiac index.

5) The balloon pulmonary angioplasty significantly improves physical capacity assesed by 6-minute walk test in patients with chronic thromboembolic pulmonary hypertension.