PLATELET-ACTIVATING FACTOR ACETYLHYDROLASE (PAF-AH): A PREDICTOR OF ADVERSE EVENT IN CTEPH PATIENTS?

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OBJECTIVE Inflammation has been suggested to play a role in the pathogenesis of CTEPH. We have recently shown that CTEPH patients have elevated circulating C-reactive protein (CRP). PAF-AH, a plasmatic enzyme also termed lipoprotein-associated phospholipase A2, is capable of inactivating platelet-activating factor (PAF), a potent lipid inflammatory mediator and vasoconstrictor, and its analogs. When overexpressed in rodents, PAF-AH displayed anti-inflammatory properties and reduced atherogenesis. A recent meta-analysis has identified high circulating PAF-AH levels as an independent predictive risk factor for cardiovascular events. Our aim was to investigate whether PAF-AH could predict outcome in CTEPH patients.

METHODS In a prospective study, we have investigated consecutive operable and non-operable CTEPH patients. Circulating PAF-AH activity has been measured in CTEPH patients (n=115) at the time of diagnosis (date of right heart catheterization) and compared to a control group of healthy subjects (n=115).

RESULTS Circulating PAF-AH activity was lower in CTEPH patients compared to controls (37, 95% CI: 33-41 *vs.* 54, 95% CI: 50-60 $nmol.mL^{-1}.min$; p<0.0001). In CTEPH patients, non-survivors displayed a higher PAF-AH activity compared to survivors (47, 95% CI: 38-58 *vs.* 35, 95% CI: 32-39; p=0.02). PAF-AH activity is correlated to pulmonary vascular resistance (PVR; r=0.21, p=0.02) and to LDL-cholesterol (r=0.22, p=0.01). Operable and non-operable CTEPH patients had similar plasma PAF-AH activity (36, 95% CI: 32-41 *vs.* 38, 95% CI: 33-44). In non-operable CTEPH patients, i) PAF-AH activity was higher in non-survivors compared to survivors (52, 95% CI: 40-68 *vs.* 33, 95% CI: 29-38, p=0.005); ii) PAF-AH activity<50 $nmol.mL^{-1}.min$ indicated a better survival (p=0.02); iii) PAF-AH activity correlated to PVR (r=0.36, p=0.006), to NYHA functional class (r=0.30, p=0.02) and inversely to 6-MWD (r=-0.43, p=0.001). In operable patients, i) PAF-AH activity was similar in patients who normalized their mPAP and those with persistent PH (mPAP>25 mmHg) after PEA (41, 95% CI: 32-52 *vs.* 37, 95% CI: 31-44); ii) PAF-AH activity inversely correlated with mPAP (r=-0.31, p<0.05) and PVR (r=-0.37, p=0.02) in patients with persistent PH.

CONCLUSIONS Our results suggest that PAF-AH could display a prognostic role both in operable and non-operable CTEPH patients.