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Title: Impaired peripheral brachial endothelial function in IPAH and CTEPH without cardiovascular risk factors

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Body: Background: Pulmonary hypertension (PH) is associated with dysfunction of pulmonary endothelium. Shearstress dependent peripheral arterial endothelial dysfunction has been found in various cardiovascular diseases and data in PH is limited. The aim of this study was to evaluate peripheral endothelial function in IPAH and CTEPH and the relation to right heart function. Methods: Flow mediated dilation (FMD) of the brachial artery was determined in 26 patients (55.5±15.5y, PAPm: 48.0±13.7mmHg, PVR: 837.6±476.8dyn*s*cm-5) with IPAH or CTEPH and 14 healthy controls. FMD was defined as the maximum change in vessel diameter after reactive hyperemia. Right ventricular function was examined by echocardiography. Results: Patients and controls were similar in terms of peripheral flow conditions and cardiovascular risk factors including Intima-media thickness (IMT) (IMT: 0.57±0.14 vs. 0.59±0.14 mm, p=0.39). Patients with PH demonstrated impaired peripheral endothelial function (FMD absolute change: 0.17±0.15 vs. 0.26±0.14 mm, p=0.008, relative change: 5.32±5.31 vs. 8.12±5.51 %, p=0.01). There were no differences in peripheral endothelial function between IPAH and CTEPH (FMD: 3.39±5.76 vs. 4.12±3.80 %, p=0.69). A correlation with right atrial enddiastolic area (RAAd) was found (r=-0.43, p=0.01). Conclusions: In addition to changes of the pulmonary vascular bed, PH is associated with peripheral arterial endothelial dysfunction in patients with IPAH and CTEPH. An increased RAAd points to chronically increased RV filling pressures and therefore a failing ventricle. The negative correlation with FMD might be regarded as result of impaired hemodynamics rather than a primary endothelial defect.