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Title: Serum levels of microRNA-125a are decreased in patients with precapillary pulmonary hypertension and correlate inversely with hemodynamics

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Body: Background. MicroRNAs (miRNAs) are small, non-coding RNA fragments associated with gene silencing that have emerged as important mediators of vascular remodelling in pulmonary hypertension (PH). Here we addressed the role of miR-125a as potential biomarker in precapillary pulmonary hypertension. Methods. Peripheral venous blood samples were obtained from 31 patients, who had precapillary PH confirmed by right-heart catheterization (WHO group 1: 25 patients, group 4: 6 patients), and from 23 healthy control subjects. RNA was isolated from sera using miRNeasy kit. miR-125a levels were measured with quantitative PCR method and were median-normalized to c. elegans miRNAs spike-in controls. Results. Normalized ct values of miR-125a were found to be significantly altered in patients with PH as compared to healthy controls (28.91 ± 0.89 vs. 27.77 ± 1.29 , $p < 0.001$) showing reduced levels of miR-125a in PH. In PH patients, levels of circulating miR-125a were inversely correlated with mean pulmonary arterial pressure ($R = -0.33$, $p = 0.08$) and pulmonary vascular resistance ($R = -0.32$, $p = 0.11$), indicating that higher pressures are associated with lower serum levels of miR-125a. No significant differences were found in the miR-125a ct values between different groups of patients with PH (WHO group 1: 28.94 ± 0.88 , group 4: 28.78 ± 1.01 , $p = 0.69$) or between female and male patients. Conclusion. These data identify miR-125a as potential biomarker in precapillary PH. Serum levels of miR-125a might be used as diagnostic tool to predict presence and severity of PH.