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Altered metabolism in pulmonary hypertension: fuelling the fire or just smoke?

Daisy Duan[1], Chenjuan Gu[2] and Jonathan C. Jun[2]

Affiliations: [1]Division of Endocrinology, Diabetes and Metabolism, Dept of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA. [2]Division of Pulmonary and Critical Care Medicine, Dept of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA.

Correspondence: Jonathan C. Jun, Pulmonary and Critical Care Medicine, Johns Hopkins University School of Medicine, 5501 Hopkins Bayview Circle, Rm 5A50.B, Baltimore, MD 21224, USA. E-mail: jjun2@jhmi.edu

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Glucose and fat metabolism are altered in pulmonary arterial hypertension, but it is not yet clear if these changes are causes or effects of the disease http://bit.ly/3cWyf66

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Pulmonary arterial hypertension (PAH) is characterised by progressive obliteration of the pulmonary vasculature, culminating in right-sided heart failure (HF). In recent years, studies have observed an association between systemic metabolic dysfunction, PAH and right ventricular failure [1]. Patients with PAH have an increased prevalence of obesity [2] and type 2 diabetes [3, 4]. Interestingly, abnormal glucose metabolism is evident even in non-diabetic individuals with PAH [5–7], and serves as an independent predictor of prognosis [8]. Right ventricular function is also associated with metabolic syndrome [9, 10], and myocardial tissue in mouse models of PAH exhibit defects in fatty acid oxidation associated with increased lipid deposition [11]. In addition, peroxisome proliferator-activated receptor-γ (PPARγ), a master regulator of adipogenesis and glucose homeostasis, has been implicated in the pathogenesis of vascular remodelling and subsequent development of PAH [12, 13]. PPARγ is also a downstream target of bone morphogenic protein receptor 2 (BMPR2) [14]. BMPR2 mutations are seen in up to 80% of hereditary PAH, and BMPR2 sporadic mutations occur in idiopathic PAH [15]. A rodent model of inducible BMPR2 overexpression develops insulin resistance preceding features of PAH [16]. Collectively, these observations suggest that impaired glucose metabolism may be a causative factor in PAH. However, most of the clinical data above is derived from cross-sectional studies with very limited metabolic outcomes.