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The association of eicosanoids and eicosanoid-related metabolites with pulmonary hypertension

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Shareable abstract (@ERSpublications)
Eicosanoids are bioactive lipids that regulate inflammation. This study found that specific eicosanoid metabolites were associated with pulmonary hypertension, including linoleic acid, prostaglandin, arachidonic acid and epoxide derivatives. https://bit.ly/47Ha6Ni

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Abstract

Background Eicosanoids are bioactive lipids that regulate systemic inflammation and exert vasoactive effects. Specific eicosanoid metabolites have previously been associated with pulmonary hypertension (PH), yet their role remains incompletely understood.

Methods We studied 482 participants with chronic dyspnoea who underwent clinically indicated cardiopulmonary exercise testing (CPET) with invasive haemodynamic monitoring. We performed comprehensive profiling of 888 eicosanoids and eicosanoid-related metabolites using directed non-targeted mass spectrometry, and examined associations with PH (mean pulmonary arterial pressure (mPAP) >20 mmHg), PH subtypes and physiological correlates, including transpulmonary metabolite gradients.

Results Among 482 participants (mean±SD age 56±16 years, 62% women), 200 had rest PH. We found 48 eicosanoids and eicosanoid-related metabolites that were associated with PH. Specifically, prostaglandin (11β-dhk-PGF2α), linoleic acid (12,13-EpOME) and arachidonic acid derivatives (11,12-DiHETrE) were associated with higher odds of PH (false discovery rate $q<0.05$ for all). By contrast, epoxide (8(9)-EpETE), α-linolenic acid (13(*S*)-HOTrE(γ)) and lipokine derivatives (12,13-DiHOME) were associated with lower odds. Among PH-related eicosanoids, 14 showed differential transpulmonary metabolite gradients, with directionality suggesting that metabolites associated with lower odds of PH also displayed pulmonary artery uptake. In individuals with exercise PH, eicosanoid profiles were intermediate between no PH and rest PH, with six metabolites that differed between rest and exercise PH.

Conclusions Our findings highlight the role of specific eicosanoids, including linoleic acid and epoxide derivatives, as potential regulators of inflammation in PH. Of note, physiological correlates, including transpulmonary metabolite gradients, may prioritise future studies focused on eicosanoid-related pathways as important contributors to PH pathogenesis.