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LETTER TO THE EDITOR

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Response to letter to the editor "noninvasive determinants of pulmonary hypertension in interstitial lung disease"

From the Authors:

We thank Parikh et al. for their interest in our published work describing noninvasive determinants of pulmonary hypertension in interstitial lung disease (PH-ILD).[1] Using submaximum exercise testing in a cohort of patients with known PH-ILD, we describe gas exchange derangements such as delta end-tidal carbon dioxide ($ETCO_2$) and gas-exchange derived pulmonary vascular capacitance (GX_{CAP}) as predictive of PH-ILD. Furthermore, we use Classification and Regression Tree (CART) analysis to show that the combination of GX_{CAP} with either estimated right ventricular systolic pressure (eRVSP) or FVC/DLCO ratio distinguishes between PH-ILD and non-PH-ILD with high probability.

Parikh et al. raises concerns that GX_{CAP} is not a specific marker of precapillary PH and may be confounded by the presence of heart failure with preserved ejection fraction (HFpEF). While echocardiographic parameters such as left atrial volume index and ratios of mitral inflow velocities are useful adjuncts in this assessment, right heart catheterization remains the reference standard in distinguishing between pre- and postcapillary PH.[2] Supporting the exclusion of HFpEF from our cohort is a PAWP of 9 ± 2 mmHg and an average BMI of 28 kg/m^2, the latter lower compared to the average BMI reported in HFpEF studies.[3] In addition, a BMI <30 kg/m^2 and the low prevalence of atrial fibrillation, both of which constitute the two most significant risk factors for HFpEF,[4] makes the prevalence of HFpEF within the studied PH-ILD cohort less likely.[5]

Regarding the query of whether HFpEF may cause a reduction in GX_{CAP}, our prior work has shown a reduction of GX_{CAP} in combined pre- and postcapillary PH (Cpc-PH) but not with isolated postcapillary PH.[6] This further supports our use of this exercise variable in screening for precapillary PH within ILD patients. Parikh et al. are correct in pointing out differences in cutoffs for GX_{CAP} for Cpc-PH and PH-ILD. We believe this difference is due to the differences in pathophysiology between these disease states. The lower GX_{CAP} in Cpc-PH compared to PH-ILD is explained by the additive effects of increased pulsatile and resistive afterload on the pulmonary arterial compliance.[7–9]

Finally, we agree that individual variables such as eRVSP are a poor screening tool for PH-ILD, which we discussed in our study.[1] Our CART analysis supports this notion by demonstrating that the *combination* of variables such as an elevated eRVSP with a reduced GX_{CAP} greatly improves the probability of diagnosing PH-ILD when compared to individual variables *alone*. We agree that the FVC/DLCO ratio helps improve the accuracy of detecting PH-ILD in multicomponent scoring tools. In our study, recognizing the limits of eRVSP in setting of ILD, the incorporation of FVC/DLCO ratio of >1.7 along with reduced GX_{CAP} helps detect the presence of PH-ILD with high probability.

We recognize that in-office submaximum exercise testing is not readily available and scoring systems using clinical history, physical exam findings, cardiac biomarkers, and chest imaging offer some limited diagnostic clarity in diagnosing PH-ILD.[10] Further studies are required to validate the routine use of submaximum exercise variables in the detection of PH-ILD.

CONFLICT OF INTEREST STATEMENT

Guarantor: Phillip Joseph. Other authors declare no conflict of interest.

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