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EDITORIAL FOCUS

Stress, Exercise and Cardiovascular Disease

Pulsatile load during exercise: a missing piece in the functional assessment of idiopathic pulmonary arterial hypertension

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In this journal, Hamada et al. (1) elegantly analyze in their study the resistive and pulsatile components of right ventricular (RV) afterload at rest and during exercise, which we read with great interest. The authors demonstrate that in idiopathic pulmonary arterial hypertension (IPAH), exercise induces a disproportionate reduction in pulmonary arterial compliance (PAC) with minimal change in pulmonary vascular resistance (PVR), leading to a significant decrease in right catheterization (RC) time. This pattern, absent in healthy controls, suggests a marked amplification of the pulsatile load faced by the RV during exertion (1).

These findings reinforce the concept that functional limitation in IPAH cannot be explained solely by resistive load. A reduction in RC time reflects a diminished ability to buffer pressure pulsatility, resulting in greater oscillatory power transmission to the pulmonary microcirculation and increased RV workload. This hemodynamic "signature" should encourage the integration of pulsatile metrics, measured invasively or via validated noninvasive surrogates, into IPAH functional assessment protocols. Consistently, recent exercise-wave intensity analysis dates demonstrate phenotype-specific RV-pulmonary vascular impairments in pulmonary hypertension, supporting the feasibility and clinical interpretability of pulsatile metrics during exertion (2). Moreover, ventriculo-arterial coupling can remain preserved, and thus be unsuitable as an early marker of RV dysfunction, in chronic pulmonary regurgitation models, underscoring the context-dependent interpretation of coupling metrics (3).

From a clinical perspective, monitoring RC time during standardized exercise protocols may help identify patients at risk of RV-pulmonary artery uncoupling despite apparently stable resting PVR. This approach could refine stratification for targeted therapy escalation or individualized rehabilitation programs. Moreover, the combined evaluation of oxygenation indices during exercise alongside pulsatile load could reveal distinct pathophysiological phenotypes: patients limited primarily by gas exchange impairment versus those limited by RV pulsatile stress.

Recent data indicate that even in healthy subjects, vascular adaptations to exercise depend on intensity and exhibit significant sex differences, involving both endothelial function and vascular compliance (4). Evidence from the heart failure with preserved ejection fraction (HFpEF) field shows that sex-specific differences in diastolic function, ventricular remodeling, and ventricular-arterial interaction can influence the hemodynamic response to stress and therapeutic options (5). It has also been demonstrated that pulmonary arterial impedance, including its pulsatile component, can be selectively modulated by pharmacological interventions such as nitric oxide inhalation, with different responses between normal subjects and pulmonary hypertension models (6). Additional observations suggest that in Sjögren's syndrome, concomitant interstitial lung disease may be associated with increased risk of pulmonary hypertension and early signs of RV impairment, even in the absence of overt pulmonary hypertension (7). Furthermore, in systemic sclerosis, vitamin D insufficiency has been associated with higher systolic pulmonary arterial pressure and a lower tricuspid annular plane systolic excursion (TAPSE)/systolic pulmonary artery pressure (sPAP) ratio, indicating early RV-pulmonary arterial dysfunction and reinforcing the need for integrated cardiopulmonary surveillance in autoimmune comorbidities (8). Notably, in systemic sclerosis complicated by pulmonary hypertension, a reduced TAPSE/sPAP ratio independently predicts cardiovascular events and mortality, reinforcing the clinical utility of RV-pulmonary arterial coupling metrics in autoimmune-associated pulmonary hypertension (PH) (9). Experimental work further shows that in a rat model of IPAH, RV functional remodeling is strongly influenced by biological sex, with differences in adaptive capacity and response to hemodynamic stress (10). These findings collectively reinforce the need to integrate pulsatile load metrics with sex-specific considerations in clinical protocols.

At the research level, the reported study paves the way for interventional trials aimed not only at reducing PVR but also at preserving or restoring PAC under stress. Agents that improve proximal pulmonary artery stiffness or endothelial function, as well as strategies to optimize heart-lung interaction during exercise, could be evaluated using RC time dynamics and impedance analysis as combined endpoints.

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In conclusion, the evidence suggests that pulsatile load dynamics during exercise represent a critical, yet often overlooked, determinant of functional capacity in IPAH. Integrating these measurements into routine evaluation, alongside vascular factors, sex-related differences, targeted interventions on the pulsatile component, and systemic comorbidities such as Sjögren's syndrome, may bring us closer to truly personalized management, selecting therapies that protect the RV in both the static and dynamic domains of afterload.

DISCLAIMERS

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DISCLOSURES

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AUTHOR CONTRIBUTIONS

A.V. drafted manuscript; F.C. edited and revised manuscript; G.P. approved final version of manuscript.

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