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LETTER TO THE EDITOR OPEN ACCESS

From Patient-Specific Hemodynamic Modeling to Clinical Decision-Making in Chronic Thromboembolic Pulmonary Hypertension: Opportunities and Caveats

Gianluca Pagnoni[1] | Aurora Vicenzi[2] | Francesca Coppi[3]

[1]Cardiology Unit of Emergency Department, Guglielmo da Saliceto Hospital, Piacenza, Italy | [2]National Institute for Cardiovascular Research (INRC), Bologna, Italy | [3]Department of Medical and Surgical Sciences for Children and Adults, University of Modena and Reggio Emilia, Modena, Italy

Correspondence: Aurora Vicenzi (aurora.vicenzi@gmail.com)

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Dear Editor

We read with great interest the recent article on patient-specific hemodynamic modeling to estimate microvascular disease burden and predict response to pulmonary endarterectomy (PEA) in chronic thromboembolic pulmonary hypertension (CTEPH) [1]. The integration of multiscale structure-based modeling with routine clinical data addresses the key challenges of quantifying distal microvascular remodeling and anticipating heterogeneous hemodynamic responses after technically successful PEA. The strong correlation between modeled and observed changes in mean pulmonary artery pressure (mPAP), together with the use of CT pulmonary angiography–derived vascular geometry and a continuous remodeling scale, is particularly compelling. In parallel, histopathological data describing heterogeneous endothelial features and angiogenic cues along the pulmonary vascular tree in CTEPH further reinforce the biological plausibility of regionally explicit modeling strategies [2].

Several aspects of the framework nevertheless warrant clarification before wider clinical adoption. First, the identification of underperfused territories relies on contrast-enhanced CT voxel intensity as a surrogate of blood flow, which is sensitive to scan timing, contrast kinetics and cardiac output. Robustness across scanners and protocols, ideally benchmarked against perfusion imaging, will be crucial. In this regard, the demonstration that dual-energy CTPA-derived quantitative perfusion blood volume can discriminate between acute pulmonary embolism and CTEPH, with characteristic whole-lung and lobar perfusion patterns, highlights how automated perfusion metrics might complement both diagnostic work-up and model calibration in thromboembolic pulmonary vascular disease [3]. Second, the assumption that microvascular remodeling occurs only in non-occluded, well-perfused regions may underestimate distal vasculopathy downstream of chronic obstruction; allowing for alternative spatial distributions of remodeling could be especially informative in patients with persistently elevated pulmonary vascular resistance after apparently adequate PEA.

The model also idealizes surgery as complete removal of all effective obstructions and assumes a fixed microvascular remodeling burden before and after PEA. In practice, residual thromboembolic material and other sources of resistance are frequent, and at least some distal changes may regress after successful reperfusion. Exploring scenarios of partial clearance, and refitting the model with post-PEA imaging and hemodynamics, could help distinguish fixed from reversible components of microvasculopathy and improve patient-level prognostication. In this context, quantitative SPECT ventilation/perfusion (V/Q) analysis has shown that the volume percentage of mismatched perfusion defects can predict persistent or recurrent pulmonary hypertension after PEA and add value beyond preoperative mPAP, underscoring the role of complementary, noninvasive risk markers alongside mechanistic simulations [4]. More broadly, evidence from systemic sclerosis, linking vitamin D insufficiency with higher systolic pulmonary arterial pressure, a reduced TAPSE/PAPs ratio and an unfavorable cardiovascular risk profile, supports a more integrated interpretation of pulmonary vascular load and right ventricular-pulmonary arterial coupling that goes beyond the pulmonary circulation alone [5]. In addition, HFpEF-focused work on sex-specific differences in diastolic dysfunction, myocardial stiffness, and comorbidity burden, particularly in women, may be highly relevant when considering long-term right ventricular adaptation and global cardiovascular risk in CTEPH survivors [6].

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Finally, a clearer description of computational time, image quality requirements and the degree of automation would be helpful to teams considering real-world implementation. A streamlined pipeline delivering a small set of robust summary outputs, such as estimated remodeling burden and a predicted post-PEA mPAP range, could realistically be integrated into multidisciplinary CTEPH discussions, in conjunction with quantitative SPECT V/Q analysis, dual-energy CT–based perfusion metrics, detailed endothelial phenotyping and systemic, sex-informed cardiovascular risk stratification. Overall, the proposed modeling framework represents an important step toward mechanistic, patient-specific decision-making in CTEPH. Addressing the issues of imaging dependence, spatial distribution, and reversibility of remodeling, surgical realism and integration with complementary diagnostic tools in larger prospective cohorts will be crucial to determine whether this approach can transition from proof-of-concept to routine use in selecting patients for PEA and individualizing their management.

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The authors have nothing to report.

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Gianluca Pagnoni
Aurora Vicenzi
Francesca Coppi

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