

## Preface

# Optimizing and Extending the Risk-Adapted Management of Acute Pulmonary Embolism beyond the Acute Phase: Progress in Pulmonary Embolism Research

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Semin Thromb Hemost 2023;49:783–784.

As we step into 2024, the field of pulmonary embolism (PE) research stands at a unique juncture. Traditional interest concerning venous thromboembolism risk factors and medical therapies is being complemented by unprecedented attention to the potential impact of novel therapies, the study of pathophysiological interplays between PE and comorbidities, and research pointing toward the burden of disease beyond the period of acute care, including health-related quality of life and functional outcomes.

Despite all this progress, in 2023, PE still remains a potentially lethal condition. New therapeutic interventions have burst onto the scene. However, with every innovation, new questions arise. How certain are we that they actually work and help patients live longer, better, or both? How do we integrate these advancements into existing clinical practice? While anticoagulant and fibrinolysis have been traditional treatments, a variety of new interventions have emerged, though they often are not incorporated in main guidelines due to a limited number of robust studies. Dr. Fulton and coauthors stress the need for a standardized treatment approach, emphasizing the importance of early risk assessment and multidisciplinary teams such as a Pulmonary Embolism Response Team, also in light of the growing expertise in mechanical circulatory support systems and progressively increasing spectrum of treatment modalities.<sup>1</sup> In the same topic, Dr. Bejjani and colleagues

discuss right ventricular failure as a critical issue in PE and as the key tool to refine risk assessment for consideration of treatments.<sup>2</sup> This review highlights the impact of PE on right ventricular dysfunction, guiding early risk assessment, acute treatment, and long-term care.

It was our collective endeavor to provide readers with a holistic understanding, combining traditional clinical guidance with cutting-edge insights on the cross-talks between PE and other highly prevalent respiratory diseases. Chronic obstructive pulmonary disease (COPD) is a severe respiratory condition that ranks among the top five global causes of death, with exacerbations occasionally leading to hospitalizations. Dr. Bertolotti and colleagues therefore reviewed the interrelationship between COPD and venous thromboembolism notably PE, highlighting that COPD acts as an important risk factor for venous thrombosis and can at the same time influence the presentation and prognosis of patients with acute PE.<sup>3</sup> The review also presents recent findings from major studies illustrating the prevalence of PE in patients with exacerbated COPD, a condition that may mimic other acute respiratory conditions, including PE, and reflects on the knowledge gaps. In a similar vein, coronavirus disease 2019 (COVID-19) triggers a state characterized by lung inflammation favoring (local) clot formation, which can exacerbate respiratory issues, be easily misdiagnosed, and ultimately prolong hospitalizations and worsen prognosis. In the review

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**Issue Theme** Optimizing and  
Extending the Risk-Adapted  
Management of Acute Pulmonary  
Embolism beyond the Acute  
Phase; Guest Editors: Stefano  
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Thieme Medical Publishers, Inc.,  
333 Seventh Avenue, 18th Floor,  
New York, NY 10001, USA

DOI <https://doi.org/10.1055/s-0043-1775978>.  
ISSN 0094-6176.

from Dr. Ortega-Paz and colleagues, the distinctions between COVID-19-related PE and conventional PE are explored, addressing its origins, significance, and the evolving strategies for prevention, including insights from antithrombotic therapy studies.<sup>4</sup> To a similar extent, Drs. Pengo and Denas review another immune-mediated condition that represents an *unicum* in terms of diagnosis and medical management of patients with venous thromboembolism: antiphospholipid syndrome.<sup>5</sup> In light of recent evidence from phase 3 trials, they emphasize clinically oriented aspects covering diagnostic and therapeutic dilemmas. These include the difficulties in formulating a clear diagnosis, the relative risk of complication across subgroups of patients with antiphospholipid antibodies, and the recommended treatments. A complex differential diagnosis with overlap with inflammation and infection also characterizes septic PE, the clinical entity discussed by Drs. Valerio and Baddour.<sup>6</sup> With clinics and pathophysiology only partially overlapping classic thrombotic PE, septic PE is progressively gaining clinical relevance because of increasing evidence on its poor prognosis and the proposition that the rapidly changing epidemiology of its risk factors—as diverse as injection drug use, cardiac implantable electronic devices, and thrombophlebitis from soft tissue infections—may lead to an escalation of cases seen by physicians worldwide over the next years.

Finally, the concept that acute PE can have lasting repercussions well beyond the initial event may be obvious but has been only recently received extensive attention for investigation. Many survivors may experience residual symptoms and cardiac impairment (i.e., post-PE syndrome). Very few of those may ultimately be diagnosed with chronic thromboembolic pulmonary hypertension, a rare but severe complication arising from residual (chronic) thrombotic obstructions. These conditions often require medical surveillance and multidimensional care to address both physical and psychological sequelae. Dr. Luijten and colleagues highlight that PE survivors can experience a broad spectrum of symptoms and functional discomforts, even after proper anticoagulation.<sup>7</sup> This review discusses not only the components of post-PE syndrome, but also the importance of its diagnosis and management, the role of patient-reported outcomes, and the potential benefits of cardiopulmonary rehabilitation. The impact on patient quality of life comes as a direct consequence of PE-related complications as well as comorbidities, which often represent per se a risk factor for the development of thrombosis. While the link between venous thrombosis and impaired quality of life has been explored, there is limited research on incorporating quality-of-life assessments into clinical practice, and the review by Dr. Tavoly and colleagues illustrated potential approaches based on existing literature.<sup>8</sup>

The past few years have been transformative for PE research. We recognize that we are in a crucial phase as

the disease management undergoes innovative shifts. We hope the readers will share our excitement for the picked trending topics summarized by leading experts.

#### Conflict of Interest

S.B. reports no conflicts of interest. F.A.K. reports grants from Bayer, grants from Bristol-Myers Squibb, grants from The Netherlands Organization for Health Research and Development, grants from Actelion, grants from the Dutch Heart foundation, and grants from the Dutch Thrombosis association, outside the submitted work. B.B. is supported by a Career Development Award from the American Heart Association and VIVA Physicians (#938814). B.B. was supported by the Scott Schoen and Nancy Adams IGNITE Award and is supported by the Mary Ann Tynan Research Scientist award from the Mary Horrigan Connors Center for Women's Health and Gender Biology at Brigham and Women's Hospital, and the Heart and Vascular Center Junior Faculty Award from Brigham and Women's Hospital. B.B. reports that he is a consulting expert, on behalf of the plaintiff, for litigation related to two specific brand models of inferior vena cava filters. B.B. has not been involved in the litigation in 2022 or 2023 nor has he received any compensation in 2022 or 2023. B.B. reports that he is a member of the Medical Advisory Board for North American Thrombosis Forum and serves in the Data Safety and Monitoring Board of the NAIL-IT trial funded by the National Heart, Lung, and Blood Institute, and Translational Sciences.

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