GUIDELINE PERSPECTIVE

Authors' Perspective on the International Society for Heart and Lung Transplantation Consensus Statement on Risk Stratification in Pulmonary Arterial Hypertension

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1. BACKGROUND

Pulmonary arterial hypertension (PAH) is a rare, progressive disorder characterized by vascular remodeling and increased pulmonary vascular resistance, ultimately leading to right heart failure and premature death.[1] Given the serious and life-limiting nature of the disease, accurate risk stratification is essential to guide therapeutic decision-making, identify patients at increased risk for clinical deterioration or mortality, and inform prognostic discussions.[2,3] The current European Society of Cardiology/European Respiratory Society (ESC/ERS) guidelines,[1] the 7th World Symposium of Pulmonary Hypertension,[4] and US consensus all recommend risk stratification-based treatment recommendations.[5] Different registries have derived and validated variety of risk stratification tools;[6–12] however, the use of risk stratification tools in real world practice have remained suboptimal.[13] With the mission of improving the understanding and utilization of risk stratification tools in the real world practice, a group of disease state experts worked together for over 2 years to develop this detailed document. In this International Society for Heart and Lung Transplantation consensus statement on risk stratification in PAH, you will find the most updated evidence behind the development of these tools and the rationale for their use in clinical practice. This document presents a thorough review of the current literature and available data, critically evaluating both individual risk factors and their integration within contemporary multivariable risk assessment tools. Its objective is to provide clinicians with a practical framework for the application of risk stratification systems in routine clinical practice along with future directions, thereby promoting evidence-based management and supporting efforts to improve patient outcomes.

2. TOP TAKEAWAYS

1. Clinicians should employ validated risk-stratification tools at both baseline and follow-up visits, integrating quantitative scores with clinical gestalt to guide management decisions.
2. Imaging of the right ventricle (RV), particularly with low-cost modalities like echocardiography, provides prognostic information that can further refine currently available risk assessment tools. These echocardiography parameters must be validated in large prospective studies and registries before being implanted in risk stratification.
3. While traditional hemodynamic parameters carry prognostic value, hemodynamic indices that reflect RV function and RV coupling to the pulmonary circulation may be better markers of prognosis and response to therapy. These indices require further multicenter validation studies.
4. Clinicians using the COMPERA tools should follow the 2022 ESC/ERS guidelines, with the possibility of further refining this model by using hemodynamic parameters. Clinicians using the REVEAL risk tools may use the REVEAL 2.0 calculator for baseline assessment and either REVEAL 2.0 or REVEAL Lite 2 depending on parameters measured for follow up evaluations.
5. Several areas warrant further investigation. First, there is a need to develop and validate pediatric-specific PH risk models that account for age variability as well as the physiological changes associated with growth and development. Second, future studies should explore the integration of genetic, genomic, and transcriptomic data into risk

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stratification frameworks to enhance their predictive power. Finally, validating risk models in prospective studies could pave the way for their use as surrogate endpoints in clinical trials, potentially reducing trial costs, shortening placebo exposure, and accelerating the approval of new and effective therapies.

3. CONCLUSION

This consensus statement on risk stratification in PAH integrates emerging evidence, contemporary clinical practice, and advancements in imaging, hemodynamics, and biomarker discovery since prior frameworks were established. By synthesizing data from observational studies, clinical registries, and expert consensus, these recommendations provide a structured approach to support evidence-based management, standardize risk assessment, and enhance individualized care strategies for patients with PAH. Nonetheless, significant gaps in knowledge persist, particularly regarding the optimal integration of genetic, proteomic, and pediatric-specific risk factors into contemporary models. The consensus emphasizes that risk assessment should complement, rather than replace, clinical judgment, and underscores the necessity for ongoing validation of emerging tools across diverse populations. Additionally, it highlights the importance of multidisciplinary collaboration, patient-centered care models, and systematic efforts to refine and expand the evidence base. As research in PAH continues to evolve, sustained partnerships among clinicians, researchers, industry stakeholders, and professional societies will be essential to advance the science of risk stratification and to improve outcomes for individuals living with this complex and life-threatening disease.

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