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Pulmonary Arterial Hypertension-Related Morbidity Is Prognostic for Mortality

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ABSTRACT

BACKGROUND Registry data suggest that disease progression in pulmonary arterial hypertension (PAH) is indicative of poor prognosis. However, the prognostic relevance of PAH-related morbidity has not been formally evaluated in randomized controlled trials.

OBJECTIVES The purpose of these analyses was to assess the impact of morbidity events on the risk of subsequent mortality using the landmark method and data from the SERAPHIN and GRIPHON studies.

METHODS For each study, the risk of all-cause death up to the end of the study was assessed from the landmark time point (months 3, 6, and 12) according to whether a patient had experienced a primary endpoint morbidity event before the landmark. Each analysis was conducted using data from all patients who were available for survival follow-up at the landmark.

RESULTS In the SERAPHIN study, on the basis of the 3-month landmark time point, patients who experienced a morbidity event before month 3 had an increased risk of death compared with patients who did not (hazard ratio [HR]: 3.39; 95% confidence interval [CI]: 1.94 to 5.92). In the GRIPHON study, on the basis of the 3-month landmark time point, there was also an increased risk with a HR of 4.48; (95% CI: 2.98 to 6.73). Analyses based on 6-month and 12-month landmarks also showed increased risk in patients who experienced morbidity events, albeit with a reduced HR.

CONCLUSIONS These results demonstrate the prognostic relevance of PAH-related morbidity as defined in the SERAPHIN and GRIPHON studies, highlighting the importance of preventing disease progression in patients with PAH and supporting the clinical relevance of SERAPHIN and GRIPHON morbidity events. (Study of Macitentan [ACT-064992] on Morbidity and Mortality in Patients With Symptomatic Pulmonary Arterial Hypertension [SERAPHIN]; NCT00660179; Selexipag [ACT-293987] in Pulmonary Arterial Hypertension [GRIPHON]; NCT01106014) (J Am Coll Cardiol 2018;71:752-63) © 2018 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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Risk assessment plays a key role in the management of progressive diseases such as pulmonary arterial hypertension (PAH) (1). To achieve the best possible outcome for each patient, therapeutic decision making should be driven by the results of regular, multifactorial assessments (2,3). The European Society of Cardiology/European Respiratory Society guidelines recommend classifying patients as low, intermediate, or high risk of death based on a panel of prognostic determinants (2,3). This approach has recently been evaluated by studies from 3 European registries (4–6), which consistently demonstrated that a low-risk profile confers a survival advantage compared with other risk categories. At the same time, these studies showed that deterioration in risk category or individual risk criteria is associated with worse outcomes. A relationship between disease progression and increased risk of death is intuitive and has been observed in clinical practice (7). Moreover, it is supported by a retrospective analysis of data from the REVEAL registry (Registry to Evaluate Early And Long-term PAH Disease Management), which reported that clinical worsening events are prognostic for subsequent mortality (8). However, the prognostic relevance of PAH-related morbidity has not been formally

ABBREVIATIONS AND ACRONYMS

6MWD = 6-min walk distance

CI = confidence interval

ERA = endothelin receptor antagonist

HR = hazard ratio

PAH = pulmonary arterial hypertension

PDE-5i = phosphodiesterase type-5 inhibitor

WHO FC = World Health Organization functional class

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