

Prognostic impact of neurohormonal inhibition in pulmonary arterial hypertension

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Background: Experimental evidence points towards a hyperactivity of the sympathetic nervous system and renin-angiotensin-aldosterone system in the pathobiology of pulmonary arterial hypertension (PAH), raising the hypothesis that blockade of neurohormonal axis may have favorable effects in this context.

Purpose: To assess the use and prognostic impact of neurohormonal inhibitors (NEUi) in a single centre cohort of subjects with PAH.

Methods: We analysed retrospectively collected data from our register of right heart catheterizations (RHC) performed consecutively from January 1st 2005 until October 31st 2018. We selected patients with PAH and complete information about demographics, biochemical data and drug therapy at the time of RHC. Patients on beta-blocker, angiotensin-converting enzyme inhibitor (ACEi), angiotensin receptor blocker (ARB) or mineralocorticoid receptor antagonist (MRA) at the time of RHC were classified as NEUi users. Comparisons between NEUi recipients and non-recipients were drawn by chi-square or t-test, as appropriate. Death from any cause was assessed by Kaplan-Meier analysis.

Results: Complete data were available for 57 PAH patients. Mean pulmonary artery pressure, pulmonary artery wedge pressure, diastolic pressure gradient, pulmonary vascular resistance and cardiac index were 45.0 ± 14.9 mmHg, 10.9 ± 3.5 mmHg, 16.0 ± 10.2 mmHg, 8.8 ± 5.1 Wood units

and 2.5 ± 0.8 l/min/m² respectively. Twenty-seven subjects (47.4%) were taking at least one NEUi when RHC was performed: 12 (21.1%) were on beta-blocker, 15 (26.3%) on ACEi/ARB and 6 (10.5%) on MRA. NEUi users were significantly older (67.6 ± 11.9 vs. 58.3 ± 15.2 years, $p=0.039$), had a higher body mass index (25.9 ± 4.4 vs. 23.6 ± 3.5 , $p=0.029$), more frequently systemic arterial hypertension (74.1% vs. 40.0% , $p=0.020$), smoking habit (51.9% vs. 20.0% , $p=0.025$) and lower estimated glomerular filtration rate (58.7 ± 22.7 vs. 73.7 ± 24.7 ml/min/1.73 m², $p=0.022$) than non-users. Moreover, 5 NEUi users (18.5%), but no NEUi non-users, had a history of coronary artery disease. Hemodynamic parameters were similar in NEUi recipients and non-recipients ($p=NS$). Seven patients (25.9%) died in the NEUi users group vs. 17 (56.7%) in the non-users one ($p=0.038$). Kaplan-Meier analysis confirmed that subjects not taking NEUi were more likely to die over the course of follow-up (Log-Rank $p=0.020$) (Figure 1).

Conclusions: Our data identify a subset of atypical PAH patients, with pre-capillary pulmonary hypertension and a comorbidity profile for left heart disease (LHD), in whom NEUi have shown to improve survival. A prognostic benefit of NEUi, due to their effects on cardiovascular comorbidities in this kind of patients, has been speculated. Future prospective studies are needed to identify the most appropriate treatment strategies for atypical forms of PAH, with subtle and probably covert LHD.

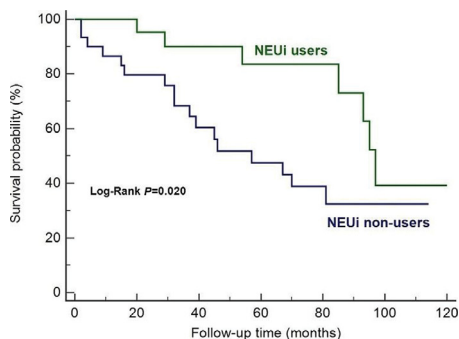


Figure 1. Kaplan-Meier survival curves