

## Pathophysiologic risk stratification of chronic heart failure: coexisting left atrial and right ventricular damage and the role of pulmonary circulation

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**Funding Acknowledgements:** Type of funding sources: None.

**Background:** in heart failure with reduced ejection fraction (HFrEF) the chronic increase of filling pressures progressively involves left atrium (LA), pulmonary circulation (PC) and right ventricle (RV), leading to worse outcome.

**Purpose:** we investigated the prognostic impact of either isolate LA impairment, RV dysfunction combined with pulmonary hypertension, or both, in HFrEF, using basic and advanced echocardiography.

**Methods:** 106 outpatients with HFrEF were enrolled. Exclusion criteria were primary lung disease, non-sinus rhythm, previous cardiac surgery, poor acoustic window. Clinical examination and basic echocardiography were performed. Speckle tracking analysis was used to measure peak atrial longitudinal strain (PALS) and a new marker of interaction between RV and PC: absolute free wall RV longitudinal strain(fwRVLS)/systolic pulmonary artery pressure(sPAP). Patients were followed for all-cause or cardiovascular death and heart failure (HF) hospitalization.

**Results:** of 84 eligible patients [mean age: 60.1 ± 11.5; 82% male, mean left ventricular ejection fraction (LV EF) 28 ± 5%], 48 reached the combined endpoint. Population was divided into 3 groups: Group 1 [PALS≥15 and fwRVLS/sPAP ≤ 0.5]; Group 2 [PALS ≤ 15 and fwRVLS/sPAP ≤ 0.5 or PALS≥15 and fwRVLS/sPAP≥0.5]; Group 3 [PALS ≤ 15 and fwRVLS/sPAP≥0.5]. Mean follow-up was 3.5 ± 0.3years. The increasing severity groups were associated with higher LA volume index (LAVI), New York Heart Association (NYHA) class, mitral regurgitation (MR) and tricuspid regurgitation (TR) grades, lower LV EF, LV global longitudinal strain (GLS), PALS, tricuspid annular plane systolic excursion (TAPSE), sPAP, fwRVLS and global RVLS(p < 0.0001). Reduced PALS and fwRVLS/sPAP were independent predictors of NYHA > 2 at univariate and multivariate analysis adjusted for age, sex, LV EF, and of any events with adjusted Cox models (Table 1). Kaplan-Meier curves showed a clear divergence between the groups for the prediction of the combined endpoint (Fig.1), cardiovascular death and HF hospitalization.

**Conclusions:** the combination of LA and RV damage could represent the transition point to end-stage HF, with considerably worse prognosis. Its assessment with PALS and fwRVLS/sPAP could help risk stratification of HFrEF patients in order to provide early treatment.

Table 1

	Unadjusted hazard ratio [95% CI]	Adjusted for GLS hazard ratio [95% CI]	Adjusted for GLS, LAVi, TR, RVFAC hazard ratio [95% CI]
Group 3 vs 1	10.61 [4.16-27.06], p < 0.0001	10.24 [3.49-30.02], p < 0.0001	9.54 [2.95-30.92], p = 0.0002
Group 3 vs 2	3.90 [1.92-7.93], p = 0.0002	3.82 [1.74-8.36], p = 0.0008	3.78 [1.66-8.61], p = 0.002
Group 2 vs 1	2.72 [1.03-7.20], p = 0.04	2.69 [0.99-7.25], p = 0.05	2.53 [0.84-7.58], p = 0.1

CI, confidence interval; EF, ejection fraction; GLS, global longitudinal strain; LAVI, left atrial volume index; MR, mitral regurgitation, TR, tricuspid regurgitation

Abstract Figure. Fig.1

