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EDITORIAL

New insights into assessing severity of advanced heart failure through left atrial mechanics

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This editorial refers to 'Left ventricular fibrosis as a main determinant of filling pressures and left atrial function in advanced heart failure', by G.E. Mandoli *et al.*, https://doi.org/10.1093/ehjci/jead340.

Patients with advanced heart failure (HF) face poor outcomes with up to 69% annual mortality or rehospitalization rate.[1] This emphasizes the imperative for meticulous risk stratification and tailored therapeutic interventions employing innovative prognostic indicators. In particular in HF patients eligible for heart transplantation, there is a compelling necessity for recurrent monitoring of haemodynamic parameters, notably left ventricular filling pressures and pulmonary hypertension. Nonetheless, the non-invasive assessment of these parameters poses inherent challenges. The increase of left ventricular (LV) filling pressures may be related to higher myocardial stiffening attributed to myocardial fibrosis.[2] Also the role of left atrial (LA) mechanics in HF is now increasingly recognized. Formerly construed as a predominantly passive component, the LA has now garnered recognition for its pivotal involvement in the progression of HF. Adaptive alterations in both size and function of the LA serve as indispensable markers in advanced HF. Significantly, LA remodelling exerts a direct influence on pulmonary circulation, culminating in consequential ramifications such as pulmonary capillary engagement, pulmonary artery hypertension, and eventual right ventricular failure.[3] Peak atrial longitudinal strain (PALS) accurately reflects LA reservoir function and may outperform traditional measurements (LA volume or LV global longitudinal strain) in predicting all-cause mortality and hospitalization. Moreover, PALS demonstrates a good correlation with LV filling pressures even in severely reduced ejection fraction, highlighting its potential as a robust and independent tool for assessing and managing patients with advanced HF.[4]

The study by Mandoli *et al.*[5] in this issue of the journal by combining echocardiographic data with invasive measures and histopathological examination allows to increase our insight in the relation between LV fibrosis on LV filling pressures and LA function, in patients with advanced HF with reduced ejection fraction (HFrEF). The authors conducted an observational, cross-sectional analysis involving patients with advanced HF who were candidates for heart transplantation. This study enrolled 64 patients, all in sinus rhythm, with a predominant majority (81%) manifesting HFrEF attributed to ischaemic cardiomyopathy, while specifically excluding cases associated with restrictive or infiltrative cardiomyopathies. Each participant underwent a comprehensive echocardiographic evaluation, which included measuring PALS. Additionally, right heart catheterization was performed, and histopathological samples from the explanted hearts were analysed to assess the extent of LV fibrosis. The authors should be congratulated for successfully conducting such a remarkable and intricate study. A noteworthy observation was the remarkably brief time interval of 16 ± 7 days between echocardiography, right heart catheterization, and heart transplantation. This expeditious timeline was realized through the authors' capacity to conduct repeat echocardiographic examinations and right heart catheterizations mere hours before the scheduled heart transplantation, when the initial assessments had taken place more than one month earlier.

The results of the study by Mandoli *et al.* showed a strong inverse correlation between PALS and LV fibrosis severity. Notably, PALS demonstrated a more robust correlation with LV fibrosis compared with traditional measures such as LV ejection fraction and global longitudinal strain. This finding elevates PALS as a more effective marker for identifying severe LV fibrosis (>30%), highlighting its potential utility in clinical assessments.

Another key finding of the present study was the strong inverse correlation between global PALS and pulmonary capillary wedge pressures (PCWP) whereas E/e′ ratio proved to have limited value in identifying most patients with raised PCWP. Notably, among all the analysed echocardiographic parameters, a global PALS < 13% emerged as the strongest predictor of increased PCWP (>18 mmHg), with high sensitivity and specificity.

Therefore, this study by Mandoli *et al.* study deserves commendation for its groundbreaking finding: the inverse correlation between global PALS and both PCWP and LV fibrosis. This pivotal finding supports the potential value of PALS as a non-invasive, echocardiographic parameter for assessing HF severity. Indeed, PALS emerged as the most robust echocardiographic parameter in predicting PCWP of all echocardiographic parameters. By establishing a strong inverse correlation between PALS, PCWP, and LV fibrosis, the authors have given clinicians a widely available, fast, and reliable tool to assess patients in the difficult scenario of advanced HF. The study's findings can significantly impact clinical practice, as the identification of robust, non-invasive parameters like PALS may play a vital role in refining patient stratification. Integrating PALS into clinical evaluations represents a substantial advancement, offering a more knowledgeable approach to managing these complex cases, and thereby enhancing patient care. Additionally, it sets the stage for further research into atrial function and strain analysis, heralding new directions for future investigations.

While this remarkable study marks a significant milestone and the authors deserve commendation, it's essential to mention certain

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limitations. The study's cohort, composed of advanced HFrEF patients undergoing heart transplantation, represents a highly selected group. This may limit the generalizability of the findings to the broader HF population, and in particular to HF patients with preserved LVEF. The study also did not evaluate prognostic implication of PALS in patients on the transplantation waiting list, nor correlate PALS to the outcome after heart transplantation. Also, it would be interesting to know if PALS improves post-transplantation, since the LA of the recipient is generally preserved during transplantation. Another important limitation is the lack of fibrosis data in the LA. This could have provided a more comprehensive understanding of atrial-ventricular interactions in HF.

In conclusion, the study by Mandoli *et al*. is a valuable addition to the existing literature on HF. The authors provide valuable insights into heart failure pathophysiology, demonstrating a strong correlation between reduced global PALS and increased PCWP and LV fibrosis in advanced HF. These findings suggest that global PALS can be a valuable non-invasive marker for patient stratification and could significantly influence therapeutic strategies in advanced HF management.

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Data availability

No new data were generated or analysed in support of this research.

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