Revista Portuguesa de Cardiologia 44 (2025) 9–11

Portuguese Society of CARDIOLOGY

Revista Portuguesa de
Cardiologia
Portuguese Journal of Cardiology
www.revportcardiol.org

EDITORIAL COMMENT

Non-invasive estimation of left ventricular filling pressures: In the absence of an ''Holy Grail'', a multiparametric integrative approach may be the key

Avaliacão não invasiva das pressões de enchimento ventricular esquerdas: na ausência de um *Holy Grail*, a chave *estará numa* avaliação integrada e multiparamétrica

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Available online 17 November 2024

Heart failure (HF) is a major public health problem accounting for significant worldwide morbidity and mortality. Pulmonary congestion, which occurs as a consequence of elevated left ventricular filling pressure (LVFP), plays a major role in the pathogenesis, presentation, and prognosis of heart failure (HF); it is an important therapeutic target. It is important to state that LVFP refers to the left ventricular (LV) pressures during diastole. In the absence of mitral inflow obstruction, mean left atrial pressure (LAP) and mean pulmonary capillary wedge pressure (PCWP) are surrogates of LVFP.

In patients with HF, the rise in LV filling pressure usually occurs before the signs of overt clinical pulmonary congestion. This could provide an approach for early titrating of medications and optimization of volume status, based upon filling pressures in ambulatory patients with the aim of preventing hospitalization.

Although clinical symptoms and signs may be useful to assess pulmonary congestion and manage volume status in individual patients, they have limited sensitivity and specificity, especially in the early phases. This leads to diagnostic uncertainty and hampers therapeutic decision-making based solely on clinical evaluation.

Invasive cardiac catheterization is the gold standard for assessment of LVFP, but it cannot nor should not be performed in the vast majority of HF patients.

In response to the frequent hospitalizations caused by HF decompensation, remote hemodynamic monitoring has emerged as one of the potential strategies to reduce HF hospitalizations. The CardioMEMS HF System provides pulmonary artery (PA) hemodynamic data and enables the estimation of the cardiac output (CO) and can be used for the monitoring and management of HF patients. The temporal changes in PA pressure and CO may help the physicians to adjust or modify the treatment, ideally before the worsening of symptoms.

The MONITOR HF trial[1] was an open-label randomized trial using invasive telemonitoring with the CardioMEMS HF System in patients with moderate-to-severe HF treated according to contemporary guidelines. Hemodynamic monitoring substantially improved quality of life and reduced HF hospitalisations. This was a promising result, despite the relatively small number of patients included (n=348) and the open-label nature of the study.

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https://doi.org/10.1016/j.repc.2024.11.001

Also, in a meta-analysis of randomised controlled trials of implantable hemodynamic monitoring (IHM)-guided care,[2] in patients with HF across all ejection fractions, IHM-guided care reduced total HF hospitalisations and worsening events. This benefit was consistent in patients with HF and reduced ejection fraction but not consistent in HF with preserved ejection fraction.

The 2021 ESC HF guidelines[3] give a class II B indication for monitoring of pulmonary artery pressure using a wireless hemodynamic monitoring system in symptomatic patients with HF to improve clinical outcomes.

Nevertheless it is not practical, feasible or cost-effective to extend remote invasive monitoring to the growing number of patients with HF of multiple causes.

Accordingly, there is a continuing search for non-invasive markers of elevated LVFP.

Echocardiography is commonly performed as a first-line test for patients with suspected or known HF and non-invasive estimation of diastolic function and estimation of LVFP is an integral part of the routine evaluation of these patients.

There are specific EACVI/ASE recommendations on how to apply echocardiography to evaluate diastolic dysfunction and estimate LV filling pressures.[4] The key variables for this assessment in patients with depressed LVEF and/or in patients with preserved LVEF, but concomitant myocardial disease, include mitral inflow velocities, E/e′ ratio, peak velocity of TR jet and LA maximum volume. The mortality risk associated with Doppler-estimated LV filling pressure in various clinical settings has long been recognized,[5] but is has to be acknowledged that each parameter has limitations and may provide inconsistent results. In addition, their association with invasive LV filling pressures varies across studies.

In a retrospective study of patients with significantly depressed LVEF who underwent angiography with invasive LVFP measurement and echo-Doppler assessment of diastolic function,[6] it was demonstrated that no single echo-Doppler variable had high accuracy for predicting LVFP $\geq$15 mmHg. However, the current ASE-EAE algorithm using multiple variables predicted LVFP with a relatively good accuracy, underscoring the need for a multiparametric approach for the assessment of LVFP.

Age, heart rate, blood pressure and LV volumes/wall thickness, LVEF, presence and severity of mitral valve disease, as well as rhythm disorders can make this evaluation even more challenging. Additional parameters like diastolic stress testing using a supine bike or treadmill or the assessment of LA systolic strain may also be useful in providing additional information when using the guideline-recommended parameters to estimate LVFP. Importantly, the LVFP echo evaluation should always be interpreted in a wider context that includes clinical status and the two dimensional (2D)/3D data and other Doppler parameters.

Cardiac MRI may also play a role in the assessment of LVFP. In a paper published by Grafton-Clarke et al., raised CMR-derived LVFP was strongly associated with symptoms and signs of HF and independently associated with subsequent HF hospitalization and MACE.[7]

Myocardial strain analysis by speckle-tracking echocardiography was developed as an angle-independent method for the evaluation of myocardial function in a wide variety of clinical contexts enabling the assessment of longitudinal, circumferential, and radial myocardial strain. Left ventricular global longitudinal strain (LVGLS) may be one of the most sensitive markers for detecting early changes in patients with cardiac disease; and impaired GLS has been identified as a significant predictor of adverse cardiovascular events in patients with HF, across all the ranges of LVEF.[8]

Lower absolute value for GLS denotes more impaired LV global longitudinal systolic function, especially in patients with HFpEF. This could be related to higher LVFP. However, there is wide scatter of data so the relation cannot be used for estimation of LV filling pressures.

Hayashi et al. proposed an index of mitral E velocity ratio to GLS (E/GLS), which was strongly associated with invasive LV mean diastolic pressure.[9] These findings encourage further research in the relationship between invasive hemodynamic parameters and myocardial deformation measures.

In the study published by Albuquerque et al. in the current issue of the Portuguese Cardiology Journal,[10] the authors present an interesting correlation between LVGLS and remote invasive hemodynamic PA and CO values in patients with HF with reduced LVEF (HFreEF) in an ambulatory setting. Despite the small number of patients included in this study, these results encourage the continuous search for novel markers of increased LVFP and the inclusion of LVGLS data in all echo studies of HF patients.

Where do we go from here?

The assessment of LVFP is of fundamental importance to the management of HF patients. Invasive cardiac catheterization remains the gold standard for this assessment, but it will not be practical nor possible to submit the majority of symptomatic patients to invasive serial studies.

Remote hemodynamic monitoring is a potential strategy to reduce HF hospitalizations and can be useful in carefully selected patients, but it is not feasible nor cost-effective to use it in the whole HF population. In the daily management of HF patients we will have to continue to use non-invasive methods to estimate LVFP.

The 2016 European Association of Cardiac Imaging/American Society of Echography algorithms have been important investigational tools, providing reasonable correlations in several patient populations and should be used routinely. They do, however, need to be applied with caution in individual patients. Individual measurements will have at most a moderate association with filling pressures and are insufficient for use in isolation. An integrative approach, with compound non-invasive parameters and including clinical data, must be used in each patient.

Conflicts of interest

The author has no conflicts of interest to declare.

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