Left Ventricular Ejection Fraction in Heart Failure

Josep Lupón¹ and Antoni Bayes-Genis²

1. Heart Institute, Germans Trias i Pujol University Hospital, Badalona, Spain; 2. Department of Medicine, CIBERCV, Autonomous University of Barcelona, Barcelona, Spain.

Disclosures: Antonio Bayes-Genis was supported by grants from CIBER Cardiovascular (CB16/11/00403) and AdvanceCat 2014-2020. The authors have no other relevant conflicts of interest to declare.

Received: 15 October 2018 **Accepted:** 23 October 2018 **Citation:** *European Cardiology Review* 2018;13(2):91–2. **DOI:** <https://doi.org/10.15420/ecr.2018.13.2.GE1>

Correspondence: Antoni Bayes-Genis, Head of Heart Institute, Hospital Universitari Germans Trias i Pujol, Carretera de Canyet s/n 08916, Barcelona, Spain.
E: abayesgenis@gmail.com

The left ventricular ejection fraction (LVEF) – calculated as the stroke volume (end-diastolic volume minus end-systolic volume) divided by the end-diastolic volume – remains the main driver for categorising heart failure (HF) and it is a cornerstone in all randomised clinical trials for patients with HF. Although LVEF has many acknowledged limitations, it remains key for the classification, stratification, management and surveillance of HF during follow-up because it is easy to obtain and non-invasive.¹ LVEF is a pivotal measure for managing HF by HF specialists and general cardiologists, but beyond cardiologists, it is well known and understood by a majority of internists, general practitioners and geriatricians.¹

Traditionally, patients with HF have been divided into those with reduced LVEF (HFrEF) and preserved LVEF (HFpEF). The HFrEF group tends to be younger and has a higher frequency of coronary artery disease (CAD) than the HFpEF group. Conversely, the HFpEF group tends to be older, female, and has a higher frequency of hypertension, obesity, diabetes, metabolic syndrome, AF, anaemia and chronic kidney disease.²

The 2016 European Society of Cardiology guidelines on HF officially adopted the term 'HFmrEF' to introduce a new HF phenotype (LVEF 40–49 %),² which mostly represents an intermediate phenotype between HFrEF and HFpEF. In HFmrEF, CAD prevalence might be similar to that observed in HFrEF.³ However, recent research has emphasised the novel concept that, in many instances, HFmrEF may be a transition phenotype that appears in patients with HFrEF who are recovering or in patients with HFpEF who are declining (most likely less frequent in our series).⁴

It is well known that contemporary HF treatments may achieve an increase or even normalisation of LVEF in a substantial number of patients during the first years of the disease.⁵ However, we lack long-term longitudinal analyses of LVEF trajectories over time.

Recently, Lupón et al. elegantly showed the dynamic changes of LVEF over a 15-year follow-up.⁶ Here, we prospectively examined LVEF trajectories in 1,160 HF patients with LVEFs <50 % that arose from diverse aetiologies. We found that LVEF trajectory variations among HF cases depended on a number of disease modifiers including aetiology, HF duration, sex and baseline LVEF. However, globally, in HF, the LVEF significantly improves at one year, it then plateaus for up to

a decade before slowly declining. This trajectory forms an inverted U-shape, with lower LVEF levels at both ends of the distribution. These data supported the hypothesis that, in most patients, LVEF improvement represented a myocardial remission rather than a true myocardial recovery or a 'myocardial cure'. In the longer-term, our data also indicated that neurohormonal blockade – a key mechanism of contemporary pharmacologic treatment for HF – might simply delay further progression of myocardial damage and deterioration. We also speculate that a neurohormonal blockade might rejuvenate the heart, at least temporarily; however, support for this hypothesis will require further investigation.

The mean age of patients at admission in this study was 64.9 ± 12.3 years; only 21 % were over the age of 75 years. At death, the mean age was 75.0 ± 10.0 years (median 77 years) and 25 % of patients died at ages >82 years. Remarkably, older patients (those ≥ 75 years at baseline) had at least the same degree of LVEF improvement during the first year and a subsequent similar trajectory up to 7 years (unpublished data). Except for a shorter follow-up found in older patients relative to younger patients (4.6 ± 2.6 versus 7.0 ± 4.1 years, respectively $p < 0.001$), driven by a higher mortality rate among older patients (66.3 % versus 40.1 % respectively, $p < 0.001$), no significant differences were found in LVEF trajectories ($p = 0.6$). Baseline LVEF was $31.2 \% \pm 8.4$ in older and $30.1 \% \pm 8.4$ in younger patients ($p = 0.06$), while at 7 years it was $44.0 \% \pm 12.5$ and $42.4 \% \pm 12.3$, respectively ($p = 0.53$). This study also found that a declining LVEF in the preceding period was associated with higher mortality. Indeed, patients who died had lower final LVEFs and worse LVEF dynamics in the immediately preceding periods, compared with survivors.⁶ Whether ageing might impact the LVEF decline remains to be demonstrated. Notwithstanding, mortality as a result of HF progression was similar (27.2 % of deaths) between patients older and those younger than 75 years at study entry.⁶

We must bear in mind that it has been postulated that HF is a disease of accelerated ageing and telomere shortening is an accepted surrogate biomarker of ageing. In a previous study, we found accelerated telomere length attrition in patients with HF (by ~22 % at one year), but we did not observe a relationship between telomere length and LVEF.⁷ Whether accelerated telomere attrition in HF might be partially linked to myocardial ageing and deterioration remains speculative and requires further investigation. ■

1. Lupón J, Bayés-Genís A. Left ventricular ejection fraction in heart failure: a clinician's perspective about a dynamic and imperfect parameter, though still convenient and a cornerstone for patient classification and management. *Eur J Heart Fail* 2018;**20**:433–5. <https://doi.org/10.1002/ejhf.1116>; PMID: 29251402.
2. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur J Heart Fail* 2016;**18**:891–975. <https://doi.org/10.1002/ejhf.592>; PMID: 27207191.
3. Koh AS, Tay WT, Teng TH, et al. A comprehensive population-based characterization of heart failure with mid-range ejection fraction. *Eur J Heart Fail* 2017;**19**:1624–34. <https://doi.org/10.1002/ejhf.945>; PMID: 28948683.
4. Bayes-Genís A, Núñez J, Lupón J. Heart failure with mid-range ejection fraction: a transition phenotype? *Eur J Heart Fail* 2017;**19**:1635–7. <https://doi.org/10.1002/ejhf.977>.
5. Lupón J, Díez-López C, de Antonio M, et al. Recovered heart failure with reduced ejection fraction and outcomes: a prospective study. *Eur J Heart Fail* 2017;**19**:1615–23. <https://doi.org/10.1002/ejhf.824>; PMID: 28387002.
6. Lupón J, Gavidia-Bovadilla G, Ferrer E, et al. Dynamic trajectories of left ventricular ejection fraction in heart failure. *J Am Coll Cardiol* 2018;**72**:591–601. <https://doi.org/10.1016/j.jacc.2018.05.042>; PMID: 30071987.
7. Teubel I, Elchinova E, Roura S, et al. Telomere attrition in heart failure: a flow-FISH longitudinal analysis of circulating monocytes. *J Transl Med* 2018;**16**:35. <https://doi.org/10.1186/s12967-018-1412-z>; PMID: 29463269.