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Global Longitudinal Strain: ready for “prime time” in heart failure characterization

Running title: Need for global longitudinal strain for heart failure patients

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Conflicts of interest:

General Electric Healthcare is providing research facilities to Rennes University Hospital through a contract with Erwan Donal.

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EDITORIAL COMMENT

Recent trials in patients with heart failure with preserved ejection fraction (HFpEF) indicate that heart failure, independently of left ventricular ejection fraction (LVEF), may take advantage of some of these same therapies(1). These trials, together with new information coming from imaging studies, provide support to further discuss the initial concept that HF could be a single syndrome with different phenotypes(2). These phenotypes must be characterized properly. The question is how can we push cardiac imaging, and especially echocardiography, to improve the phenotypic characterization of HF patients.

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In this issue, Brann et al report the results of a retrospective analysis from a cohort of 311 patients with Heart Failure Preserved Ejection Fraction (HFpEF) with a median follow-up of 4.6 years. Every patient had an initial echocardiogram, but also serial examinations. The aim was to evaluate the prognostic role of global longitudinal strain (GLS), but also if GLS could predict a deterioration in ejection fraction (3). The study's inclusion criteria, and the definition of HFpEF, was similar to the one used in the PARAGON trial and therefore it was not surprising that, as mentioned in the supplement, the clinical characteristics of their population was rather similar to other HFpEF trials and recent major registries in Europe and North America(3).

The results provide additional data justifying some enthusiasm in using speckle tracking echocardiography to improve the characterization of the HF population. Several previous studies have shown that GLS is really a need and an additive parameter to LVEF (4). In Brann et al, 59% of the HFpEF population had an abnormal GLS (cut-off of 15.8%) despite a preserved EF (3). An important message, out of the risk of event associated with lowest value of GLS, comes from the 1.9-fold increased risk for LVEF deterioration. It highlights the underlying abnormal contractile function that has been observed in several contexts and promoted largely in the cardio-oncology field for its potential for initiating earlier a therapy that could prevent any further LV-dysfunction(5).

Rather than being considered as separate diseases with a distinct pathophysiology, systolic and preserved LVEF heart failure may be merely different clinical presentations within a phenotypic spectrum of a single disease. Imaging techniques, and especially echocardiography, has been suggested by many as a relevant approach to better characterize the phenotype and the prognosis in the HF-population(6, 7, 8). It is not established in

guidelines but the literature is homogeneous about the added value of GLS in the field of heart failure. Expectations are still existing in the field of cardiac resynchronization therapy for instance(9). The less load dependant myocardial work approach and/or the quantification of the circumferential strain could provide also easily valuable insights and potentially guide for therapy even better than what is recommended for now(8, 9, 10).

On the contrary, and although we use this parameter in everyday clinical practice, the prognostic value of LVEF has not been consistently shown in HF studies. Until now, LV-Global Longitudinal Strain, which directly reflects the motion of the myocardium, is believed to provide a better assessment of myocardial function but guidelines are still conservative. GLS >-16% is considered in the HFA PEFF-score but nowhere yet it is required to report for GLS in the reports about HF-patients(11). Looking at the tremendous contribution of many colleagues in the field of GLS and HF, it is probably relevant to underscore some contributions that reinforced the message of Brann et al(3).

Also, the work published by Brann et al should really be acknowledged(3). It confirms the strong predictive value of GLS to predict clinical events but furthermore, and coming back to concepts suggested by Brutsaert and colleagues(2), can be used to predict future deterioration in LVEF. Their work underscores the cut-off of GLS of -15.8%. It does not have any direct impact on the pharmacological patients' management but one can extrapolate that trials based on GLS could be valuable to reach to a higher level of evidence, and a more individualized way to prescribe drugs such as angiotensin receptor/neprilysin inhibitor (ARNI) or the mineralocorticoid receptors antagonists (MRA), in phenotypes of HF with LVEF > 50%, at the right time and for the right patients.

Comorbid conditions, such as age, DM, obesity, and renal function are largely been advocated for explaining our difficulties to manage HFpEF patients. GLS and imaging characterization of the patients' heart could be used more. It could explain the failure to prescribe some therapies in some phenotypes. The potential benefit of beta-blockers and RAS blockers in patients with the most altered GLS has been reported(12). Based on imaging data, some patients may require more clinical attention, in terms of the optimization of medical therapy, patient consultation, interval for follow-up after discharge, and establishment of future preparation for deterioration. From the viewpoint of real-world practice, the use of LV-GLS in the risk prediction was technically challenging by some but the guidelines, the academic centres should help in completing the challenge. Nowadays, with new software the incorporation of VGLS in clinical practice is highly feasible, easy, and not time consuming. The learning curve is also reported to be short(13). Along with the characterization of the LV, more advantages are expected from the measurement of left atrial and right ventricular longitudinal strain. For example, recently the measurement of LA strain is required for the estimation of the LV filling pressure in addition to the 4 classical diastolic function (14, 15). The heart failure management should then consider seriously the tremendous need of cardiac imaging and echocardiography. It is now well investigated that HFpEF is not HF with preserved systolic function. There are growing evidence supporting the clinical value of LV-GLS and other strains at all stages of HF, in terms of diagnosis, risk stratification and prognostic evaluation, management guidance, and follow-up. Therefore, after the reading of Brann et al manuscript, it is expected that the LV-GLS assessment will be increasingly utilized in clinical practice(3). The time has also come to incorporate GLS in the design of large scale randomized clinical trials to test the role of current and future therapies for patients with heart failure syndrome! GLS is ready for "prime time".

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