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EDITORIAL

Heart failure and systolic function: time to leave diagnostics based on ejection fraction?

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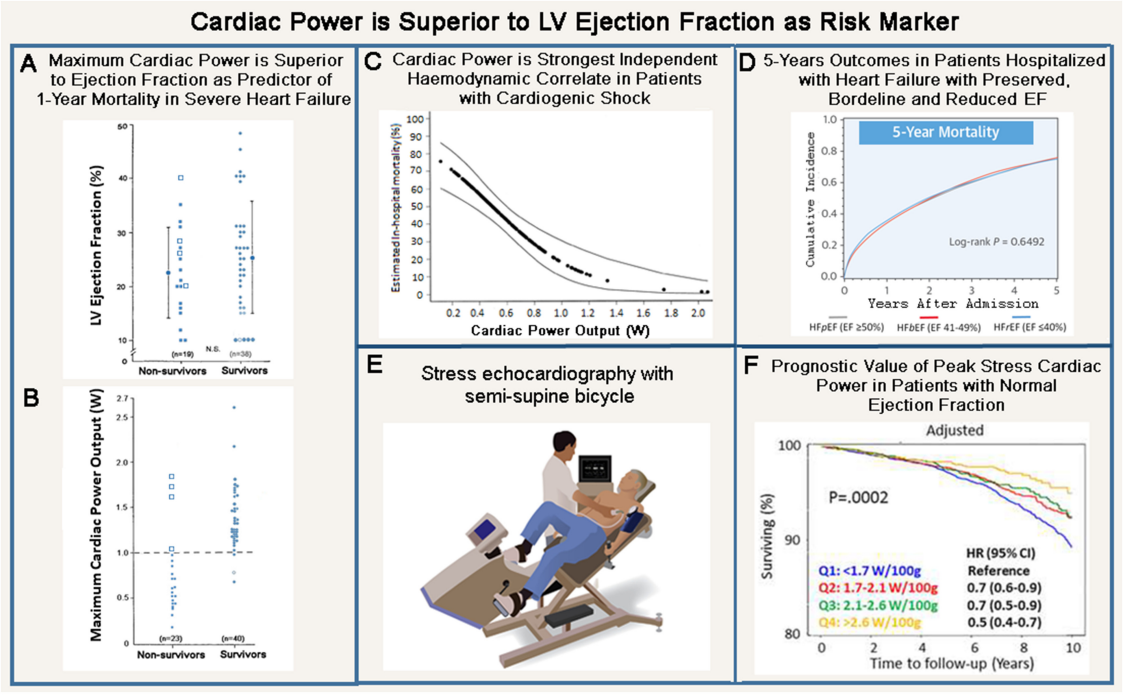

Graphical abstract (*A* and *B*) Prediction of 1-year mortality by LVEF measured during rest (*A*) and by maximum cardiac power during dobutamine stress (*B*) in patients with severe acute or chronic heart failure. Means ± SD. For LVEF, there is considerable overlap, whereas maximum cardiac power differentiates well between survivors and non-survivors. An open circle indicates cardiac transplanted and open squares indicate sudden deaths. Modified from Tan.[8] (*C*) Data from the SHOCK Trial Registry showing that cardiac power was a strong predictor of mortality in cardiogenic shock. Modified from Fincke *et al.*[9] (*D*) Five-year mortality was similar in heart failure patients with preserved, borderline, and reduced ejection fraction. Modified from Shah *et al.*[10] (*E*) Illustration of a patient during stress echocardiography with a semi-supine bicycle. (*F*) Five-year Kaplan–Meier survival curves for mortality stratified by quartiles of peak stress cardiac power/mass. Patients with the lowest cardiac power/mass in quartile 1 had the worst survival followed by quartiles 2 and 3, and was the best in quartile 4. Adjusted for age, sex, peak metabolic equivalents, diabetes mellitus, and diastolic function at baseline. Reproduced from Anand *et al.*[1]

The opinions expressed in this article are not necessarily those of the Editors of the *European Heart Journal* or of the European Society of Cardiology.

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This editorial refers to 'Prognostic value of peak stress cardiac power in patients with normal ejection fraction undergoing exercise stress echocardiography'†, by V. Anand *et al.*, on page 776.

At first glance, left ventricular (LV) function may seem easy to understand, and most physicians are familiar with frequently used parameters such as ejection fraction (EF), stroke volume, and cardiac output. Although well known, these measurements do not necessarily provide a comprehensive measurement of LV function. Additionally, they are often measured during resting conditions where even patients with severe heart disease most often are asymptomatic. Furthermore, about a half of patients with heart failure (HF) have normal EF. In the study by Anand and colleagues in this issue of the *European Heart Journal*,[1] cardiac power and power reserve were investigated as an alternative measure of LV pump function in patients with normal EF.

In physics, power is the amount of energy transferred or converted per unit time, and the unit is Watt, equal to one Joule per second. Power is also a valid measure of cardiac function and is calculated as cardiac index multiplied by aortic pressure. Cardiac power integrates pressure (afterload), flow and heart rate (chronotropy), and expresses the energy transfer from the left ventricle to the aorta. The latter seems especially attractive during exercise and other situations where demands are elevated. In the study of Anand and colleagues, cardiac power was used to quantify LV function during rest and exercise.[1] They retrospectively examined almost 25 000 patients undergoing stress echocardiography, with exertional dyspnoea as the most common indication. All patients had LVEF in the normal range and no right ventricular dysfunction or significant valve disease. They found that the patients in the quartile with highest cardiac power at peak exercise as well as highest cardiac power reserve (the difference between power at rest and peak exercise) showed markedly better survival than those in the lowest quartile. Of note, the findings were consistent after adjusting for age, sex, metabolic equivalents, ischaemia, medication, and comorbidities.

The authors should be acknowledged for the impressive number of included patients, who all underwent stress echocardiography. The finding that cardiac power can improve risk prediction beyond exercise capacity and the presence of ischaemia in patients with normal LVEF clearly indicates added value of a more comprehensive assessment of LV function. Moreover, the findings support the rationale for exercise testing in risk stratification of patients with normal cardiac function at rest. The study, however, is somewhat limited by its retrospective design. Furthermore, there was no measure of cardiovascular mortality, only total mortality. Potentially, underlying non-cardiovascular disorders may have limited exercise performance and may have contributed to total mortality. The study would have been even more interesting if there had been a separate analysis of patients suspected of HF with preserved EF (HFpEF).

With the exception of antihypertensive therapy, there is essentially only symptomatic therapy available for patients with HFpEF. The exception is a few relatively rare phenotypes with specific therapies. The rather non-specific nature of HF symptoms and lack of unified diagnostic criteria for HFpEF are major limitations for clinical trials of medical therapies for HFpEF. A non-invasive method which can quantify LV pump function better than EF would be a major step forward. In this regard, LV global longitudinal strain (GLS), is more sensitive than LVEF for mild systolic dysfunction and is a useful supplementary method. Therefore, when patients with HF symptoms and normal LVEF have reduced GLS (<16%), it is likely that LV dysfunction contributes to their symptoms.

The apparent discrepancy between GLS and EF is explained by EF being related predominantly to LV circumferential shortening, whereas GLS measures longitudinal shortening.[2,3] Since myofibres that account for longitudinal shortening are located mainly in the vulnerable subendocardium, reduction in GLS may precede reduction in LVEF. Furthermore, with concentric hypertrophy, which is common in HFpEF patients, there is typically a small LV cavity and therefore normal or supernormal EF even when stroke volume is reduced. A limitation of GLS, as well as of EF, is the marked afterload dependency. Additionally, reduced GLS is found in only ∼50% of HFpEF cases.[4,5] Therefore, in a large fraction of HFpEF patients, GLS will not provide the information needed.

A few years ago we introduced LV myocardial work using a non-invasive estimate of LV pressure in combination with strain imaging as a measure of LV systolic function.[6] This method also provides a measure of pump efficiency and, as shown recently, is a powerful tool to identify patients who may benefit from CRT.[7] The method, however, has not yet been extensively tested as a general measure of LV systolic function.

Graphical abstract shows data from several studies and illustrates that cardiac power is a strong predictor of mortality in HF patients regardless of LVEF. This suggests that cardiac power could be a more suitable measure of systolic function than LVEF. As suggested by the study of Anand and colleagues, this may require a stress test in order to identify peak power.

What is needed to measure cardiac power is stroke volume and simultaneous mean aortic pressure. The latter is calculated as diastolic pressure plus one-third of pulse pressure. Stroke volume can be measured at the LV outflow tract from Doppler velocities and outflow tract diameter. Since the technical setup is similar to what is used in a standard diastolic stress test, it should be explored whether the two tests combined provide incremental diagnostic information when evaluating patients suspected of HFpEF. If assessment of systolic and diastolic function could be combined, it might strengthen the HFpEF diagnostics. John Tyberg's group recently proposed a novel approach which combines quantification of vascular conductance and the head-capacity curve to assess LV pump performance.[11] This method remains to be tested clinically.

In total, the study of Anand and colleagues offers convincing evidence that comprehensive assessment of LV function including measurements during peak exercise provides incremental prognostic information in patients with apparently normal LV systolic function. There is need for further testing of the cardiac power method in prospective studies before it can potentially replace EF as a measure of LV systolic function.

Conflict of interest: none declared.

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Corrigendum

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Corrigendum to: Edoxaban in AF patients with PCI by acute or chronic coronary syndrome presentation: a pre-specified analysis of the ENTRUST-AF PCI trial

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In the originally published version of this manuscript, the following sentence in the Results section should read: "Among patients assigned to the VKA regimen, triple-antithrombotic therapy was taken for a median of 90.0 days (IQR 30–266) in ACS patients and 34.0 days (IQR 29–161) in CCS patients.". This has now been corrected online.