Editorial

Appearances can deceive: even brave hearts can fail

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This editorial refers to “Differences between patients with a preserved and a depressed left ventricular function: a report from the EuroHeart Failure Survey” by M.J. Lenzen et al. on page 1214.

The enigma faces us every day and we still do not know how to define or manage it. Patients develop the typical signs and symptoms of heart failure although they apparently have "normal" left ventricular systolic function. The syndrome occurs both acutely and chronically and is responsible for approximately half of the heart failure epidemic. The terminology is the subject of debate. There is consensus that patients with "diastolic heart failure" or "heart failure with preserved left ventricular function" tend to be older and more frequently female with a history of hypertension. The rates of other common co-morbidities appear to be similar. Prognosis is generally as poor as in patients with systolic dysfunction.

Given the paucity of studies assessing the incidence and prevalence of this common condition, the paper "Differences between patients with a preserved and a depressed left ventricular function: a report from the EuroHeart Failure Survey" by Lenzen et al., published in this issue, is a welcome contribution. The report compares the demographic differences between patients with reduced ejection fractions and patients with preserved left ventricular function based on data from the EuroHeart Failure Survey. The reported data helps us to understand some of the similarities and differences between the patient characteristics of these two groups.

The red herring may be our traditional dependence on the time-honoured concept of the ejection fraction, and the relatively arbitrary thresholds for "normal" that lie somewhere between 35% and 45%. Although the concept of the ejection fraction is intuitively attractive, the focus on contractility is mechanistically flawed in its simplicity. Haemodynamics are more complex than measurement of contractility and the impairment of left ventricular filling may be as important as impairment of left ventricular emptying. Various methods exist for assessing ejection fraction with considerable inter-observer variation. There is agreement on how it should be expressed (percent) and clinicians know how to interpret the number. No such agreement or simple measure exists for assessing diastolic function. The trend is to describe the problem as clinical heart failure with preserved LV function, which is an admission that we do not yet adequately understand the pathophysiology.

Two reviews of the literature have recently been published that demonstrate that much of the controversy stems from inadequate epidemiological data. Divergent definitions make comparisons of observational studies difficult and major inconsistencies are evident in case definition, demographics, cardiovascular and non-cardiovascular co-morbidities, and causal mechanisms.

Abnormal left ventricular relaxation and increased left ventricular chamber stiffness with a shift in the diastolic pressure–volume relationship has been demonstrated in symptomatic patients with heart failure and normal ejection fraction and this has shed some light on the controversy. There are abnormalities in diastolic function in these patients and the term "diastolic dysfunction" may not be a misnomer after all. Patients with heart failure and "normal" ejection fractions have abnormally high end-diastolic pressures and low end-diastolic volumes leading to dyspnoea and exercise intolerance. Despite increased filling pressure, the cardiac output does not increase.

The current EuroHeart Failure Survey report describes the 6806 patients from 24 countries that were included in the Survey with evaluation of LV function by echocardiography. To be eligible for inclusion in the Survey, patients had to satisfy several clinical criteria compatible with a hospital admission diagnosis of heart failure or requirement of treatment with a loop diuretic. The patients were divided into two groups; patients with left ventricular systolic dysfunction (LVSD) and patients with preserved left ventricular function (PLVF). LVSD was defined as an ejection fraction <40%. The results demonstrate that the patients with PLVF were older, more often women and likely to have hypertension and atrial fibrillation. PLVF patients also received less cardiovascular medication. Overall morbidity and mortality was...
high in both groups although LVSD was shown to be a strong independent predictor for mortality in multivariate analysis in this cohort.

In patients hospitalised for heart failure, the EuroHeart Failure Survey provided an opportunity to collect data demonstrating the extent to which the presence or absence of LVSD influenced management and outcomes. There were certain methodological limitations to this subanalysis of the Survey. A relatively soft assessment of left ventricular function was used. Patients were considered to have PLVF if the ejection fraction >40% or if normal or mildly depressed systolic left ventricular function by echocardiography was found. In contrast, patients were considered to have LVSD if the EF was <40% or moderate to severe left ventricular systolic function, or left ventricular dilatation was observed. More rigorous methodology had been preferable, using the conventional echo indices of diastolic function that routinely assess LV filling and atrial flow in patients with symptomatic heart failure and PLVF.

In the EuroHeart Failure Survey, 10,701 patients with a discharge diagnosis including heart failure were assessed. Only 6806 of these patients had measurements of LV function. It is unlikely that the 3895 patients without LV function data had identical demographic characteristics. This creates a potential selection bias that might impact on the findings. Additionally, hospitals participated on a voluntary basis so that the Survey does not reflect a representative sample. Although 115 hospitals from 24 ESC member countries contributed data, many of these were academic centres or hospitals affiliated to these centres. Do these data truly reflect the management and outcomes of patients with these conditions seen in everyday clinical practice across Europe? Not perfectly, but the comparison of the demographics of patients with LVSD and PLVF should be valid.

There was a substantial difference in the proportion of patients managed in cardiology departments, with considerably more patients with LVSD going to cardiology and similarly more patients with PLVF going to general internal medicine. This would also influence the determination of aetiology, detection of valvular dysfunction, co-morbidity, pharmacological management, and invasive investigation. These limitations are detailed in the discussion as potentially important confounding factors and the authors interpret the results with appropriate conservatism.

Clinicians must not conclude that the findings demonstrate that patients with PLVF benefit from the same pharmacological treatment as patients with left ventricular systolic dysfunction. The authors emphasise that the “impact of the various cardiovascular medication was made in a context of an observational study not of a randomised trial”. However, the final sentence “a comparison of the effect of pharmacologic treatment did not reveal an interaction of the treatment effect on mortality between LVSD and PLVF” must be interpreted with caution due to the important methodological limitations. Novel therapeutic targets theoretically emerge. Along with typical systemic neurohumoral activation and vascular dysfunction, hypertrophy and an increased fibrillar collagen content in the extracellular matrix is characteristic of the stiff left ventricle. Interventions that inhibit the rate of collagen turnover, such as aldosterone and angiotensin II antagonists might be efficacious.

These are early days in this controversy. Major questions remain such as, what are the clinical implications of these findings in everyday practice? What is the message to the physician responsible for the care of patients with suspected heart failure? Do we always need to evaluate LV function? If so, does this impact on the indication for diagnostic procedures and pharmacological management? At least we no longer doubt the existence of heart failure with preserved systolic function. The next initiative must be a broad strategic co-operation. EuroHeart Failure Survey II in acute heart failure is a step in the right direction. More brave hearts can be preserved.

References