Comments on "The management of Heart Failure with preserved ejection fraction"

by Andrew Coats and Louise Shewan

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In their pertinent commentary Professor Coats and Dr Shewan highlight the problems that have bedevilled the field of the condition variously labelled as heart failure with a normal or 'preserved' ejection fraction or previously diastolic heart failure. As the authors conclude many of the problems are of our own (the heart failure community) making. There are several substantial conceptual issues to be resolved:

1. The use of the LV ejection fraction for diagnosing and dividing patients with heart failure is flawed.[1] EF is a poor measurement of ventricular function or mechanics, fails to correlate with functional capacity, and is more a reflection of volume and shape changes. A ventricle with reduced LV systolic function can have an increased EF if there is LV wall hypertrophy and reduction of cavity size[2]. The presumption that systolic function was normal in those with a normal LVEF led to the notion that the mechanical disorder resided in diastole and therefore drugs that might increase relaxation rate or reduced stiffness were considered to be necessary. More recent work has shown widespread abnormalities of systolic function affecting longitudinal function particularly but also twist, torsion, synchrony, radial and circumferential function which all lead to reduced recoil, suction and reduced early diastolic filling[3,4]. Thus the disordered diastolic filling begins in systole and the widespread abnormalities of ventricular mechanics will need to be addressed if overall ventricular function is to be improved.

2. The use of the word "preserved" in the labelling of these patients is irrational and misleading.[5] The definition of preserved (OED) is "maintain (something) in its original or existing state". What evidence is there that the EF is unchanging, especially as there are usually no measurements taken before the onset of symptoms? In fact the opposite appears to be the case. Recent work by Dunlay et al has shown that in HFNEF patients on average EF decreased by 5.8% over 5 years ($P<0.001$) with greater declines in older individuals, and 39% of HFNEF patients had an EF<50% after 5 years i.e. they had developed HFREF[6]. Therefore there is frequently progression of disease with increasing LV remodeling, and dilatation associated with falling EF. The rate at which this occurs depends in part on the aetiology: it appears that myocardial infarction is a potent stimulus to remodeling whereas the process is slower in the older often female patient with hypertension and or diabetes. However, treatment should be directed towards preventing this progression of remodeling. It may be that the standard therapy for HFrEF, which appears to be effective in the remodeled ventricle, may be beneficial in this context and supports the notion that Coats and Shewan put forward that these treatments probably should be used despite the lack of mortality data.

3. Reduced early diastolic filing will require an increased atrial contribution to maintain normal filling. Thus, LA function becomes more important especially on exercise.[7] The beginning of LA failure may herald the onset of symptoms. Little attention has been paid to LA function or how to improve it or prevent the onset of atrial fibrillation, the final manifestation of atrial failure.[8]

4. Changes in venous tone may be important in determining LV filling pressures and the baroreceptors have an important role in determining how venous volume is distributed by affecting sympathetic outflow to the splanchnic bed.[9] Recent work has shown that LV filling pressures can rise even in normal hearts if baroreceptors are "isolated". Such changes would be interpreted in classical terms as a change in ventricular compliance or impaired diastolic function due to a "stiff" ventricle although no such thing has occurred. It is well established that the onset of symptoms due to heart failure often occurs without any changes in fluid volume and changes in venous tone may very important but rarely are taken into account.[10] These concepts underline the importance of studying the intact heart in an intact circulation not isolated preparations, muscle strips or isolated myocytes.[11]

5. HFNEF is likely to be a multifactorial condition with several causes and complex abnormalities of ventricular mechanics affecting both systole and diastole probably mainly due to changes in ventricular matrix or fibrosis, coupled with atrial dysfunction, vascular stiffening including the venous system, autonomic dysfunction affecting heart rate response to exercise (chronotropic incompetence), blood pressure and venous tone. Expecting a "lusitropic" drug or any single medication to cure all these is fanciful.

Thus, basing the diagnosis of heart failure on the LV ejection fraction alone has resulted in excluding a large proportion of heart failure patients from treatment trials. Furthermore, the concept that heart failure is binary, systolic or diastolic, or that there are separate distinct forms of heart failure is clearly fallacious. It would be best just to diagnose the condition as "heart failure" and then determine the main causes, functional abnormalities and tailor the therapy to the individual patient appropriately (this also applies to those with traditional "systolic heart failure" or HFrEF such as the use of cardiac resynchronisation therapy which is clearly not appropriate for all such patients). This way we may begin to develop proper therapy for each individual HF patient.

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