What should be the focus in the management of patients with heart failure? The importance of peripheral vision

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All of us working with patients suffering from heart failure have seen the phenomenon often. However, there are patients with severe left ventricular dysfunction and dilatation on echo who are feeling well and maintaining active, productive lives. Amazing we think, how do they do it?

The paper by Harrington et al. in this issue confirms our suspicions and is welcome news[1]. Matched symptomatic and asymptomatic patients with similar degrees of left ventricular dysfunction and duration of illness differ importantly with regard to exercise capacity and the extent of peripheral changes characteristic of chronic heart failure. Surprisingly, although the asymptomatic patients had a mean ejection fraction of 16.5% and a mean left ventricular end-diastolic dimension of 72 mm, there were no important differences in the periphery between the asymptomatic patients and matched normal subjects. It is important to note that although the asymptomatic patients in this group did not suffer from exercise intolerance and were classified in NYHA class I, they were all treated with ACE inhibitors and a mean of 80 mg of furosemide, i.e. the reported findings concern treated patients with severe left ventricular dysfunction and large diastolic volumes. This fact most likely explains the discrepancy between these findings and earlier reports of exercise performance in untreated patients[2].

The Harrington paper comes from the Royal Brompton and Harefield NHS Trust, London, U.K., a centre experienced in the field, and the methodology is state of the art. It is worthwhile reading and contains much useful, clearly explained exercise physiology. Asymptomatic patients had a slightly lower peak VO₂ and total exercise time than controls, but maintained almost normal muscle strength and cross-sectional area, endurance and fatigue time, respiratory muscle strength and peak leg blood flow. Especially notable was the well preserved chronotropic competence in asymptomatic patients. The figures and tables quantify the comparisons clearly.

Certainly, this paper does not provide all the answers. We remain curious as to the neurohumoral status of the symptomatic and asymptomatic patients. Although all patients were treated with ACE inhibitors, none were using a beta-blocking agent or aldosterone antagonist. What was the degree of activation of the adrenergic nervous system and natriuretic peptide system? Were there differences in endothelin concentrations or perhaps more importantly, extent of cytokine activation? Obviously, central cardiac mechanisms may also be operative. As the authors state, preserved peak cardiac output could well be due to maintenance of an adequate heart rate response and superior venricular contractility in the asymptomatic group. Reliable measurements of contractility during exercise are difficult. However, substantial differences are unlikely in the presence of similar ejection fractions, end-diastolic dimensions, LVEDP and dP/dt at rest. Similarly, differences in the mechanics of pump function (exercise-induced diastolic dysfunction and mitral insufficiency) could contribute to symptoms in patients with severe left ventricular dilatation and systolic dysfunction.

Now, why is this good news? Simply because peripheral function is easier to improve than myocardial function. Common sense would suggest that asymptomatic patients have preserved their exercise tolerance because they remain physically active. Extensive literature uniformly documents that various training protocols have been shown to improve not only exercise performance but also to reverse the skeletal muscle atrophy and fatigue with attenuated vasodilator capacity that characterizes symptomatic patients[3]. The suggested mechanisms explaining improvement following training are multifactorial. Improvements in regional blood flow, capillary density, muscle bioenergetics, autonomic tone and neurohumoral status have been documented[4].

This paper provides important evidence to support a hypothesis that deserves testing. A proper prospective evaluation of exercise training on morbidity and mortality in a broad group of symptomatic patients is the next step. Such an international effort is in the planning stages and currently recruiting centres[5]. EXIST (Exercise Intervention in Stable Heart Failure Trial) is being led by Andrew Coats and Marcus Flather from the Royal Brompton and Harefield NHS Trust and the National Heart
and Lung Institute. Considerable clinical research collaboration is needed to identify the population most likely to respond favourably to a training programme in order to permit efficient resource utilization. The results of the Harrington paper suggest that the greatest benefit would be observed in deconditioned, well-motivated patients with symptomatic heart failure. This potential treatment deserves to be explored further. Our traditional focus on pharmacological intervention and central haemodynamics is clearly too narrow.

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References

The Brugada syndrome: diagnostic criteria and cellular mechanisms

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Sudden cardiac death occurring in individuals with structurally normal hearts accounts for an estimated 3% to 9% of out-of-hospital cases of ventricular fibrillation[1]. Many of these cases, such as those with the recently highlighted Brugada syndrome, are thought to be due to a primary electrical disease. A syndrome characterized by ST segment elevation in right precordial leads (V₁ to V₃) unrelated to ischaemia, electrolyte disturbances or obvious structural heart disease, displaying a right bundle branch block QRS morphology, was reported as early as 1953, but first described as a distinct clinical entity associated with a high risk of sudden cardiac death by Pedro and Josep Brugada in 1992[2] (see[3–5] for review). The characteristics of the Brugada syndrome are similar, in many cases nearly identical, to those reported by Nademanee and co-workers[6] in patients with sudden unexpected death syndrome. Tragically, sudden death from the Brugada syndrome is often the first symptom of the disease, particularly in the Southeast Asian population.

The Brugada syndrome is most frequently diagnosed in males (8:1 ratio of males:females) of Asian origin. The syndrome is familial, displaying an autosomal dominant mode of transmission with incomplete penetrance. Arrhythmic events are observed at an average age of approximately 40, but have been reported over a very wide range of ages (2 to 77 years)[7]. Although structural heart disease is ruled out by echocardiography and/or magnetic resonance imaging in all cases diagnosed as Brugada syndrome, postmortem examination has revealed some fatty infiltration into the deep subepicardium in isolated cases. Although the typical ECG pattern and a high risk of sudden arrhythmic death have been reported for a segment of the patient population with structural heart disease in the setting of arrhythmogenic right ventricular cardiomyopathy endemic to the Veneto region of Italy[8], the clinical presentation in the vast majority of arrhythmogenic right ventricular cardiomyopathy patients bears little resemblance to that of the Brugada syndrome. Moreover, arrhythmogenic right ventricular cardiomyopathy does not appear to be linked to the same chromosomal loci as the Brugada syndrome.

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