EDITORIAL

Skeletal and cardiac abnormalities in chronic heart failure

In chronic heart failure both heart and skeletal muscle develop profound structural and metabolic changes that may be responsible for further deterioration of clinical status and worsening of symptoms.

In heart failure there is loss of myocardial tissue, incoordinate myocyte contraction, extracellular changes such as fibrosis or cell slippage and changed architecture. Myocardial cells themselves also have abnormal function. Recent studies on single cardiac myocytes isolated from animal models of experimental heart failure and from patients have confirmed earlier results from whole tissue and shown that β adrenoreceptors undergo desensitization which relates to the severity of the disease and not to etiology. This loss of effectiveness to β receptor agonists may explain part of the blunted contractile response of the heart in patients with the heart failure syndrome. The phenomenon of β receptor desensitization is widely accepted to be due to increased levels of the regulatory subunit of the adenylate cyclase (G_i protein). Diastolic function is also impaired. The relaxation of isolated cells is slowed. Data from our group gathered from a large number of patients demonstrates that the lusitropic effect of β-adrenoceptor stimulation is stronger in myocytes from failing human hearts than in cells from non-failing ventricles, suggesting the hypothesis that the lowering of basal cyclic AMP during the development of heart failure has removed a tonic lusitropic influence on contraction and relaxation.

Patients with chronic heart failure develop the symptoms of shortness of breath and fatigue. These symptoms are not directly related to central haemodynamics and there may be many contributory factors. The muscle hypothesis attributes both symptoms to ergo-reflexes arising from skeletal muscle. The structure, metabolism, strength, and fatiguability of skeletal muscle are all abnormal in heart failure. Alteration in the fibre type is difficult to detect in heart failure because of the wide variation in the normal population, although a decrease in type I fibres with a concomitant increase of the percentage of type II has been described. In this issue the analysis of skeletal muscle Myosin Heavy Chain (MHC) subtypes shows an increase of the fast glycolytic MHC2b isoform with a decrease of the slow MHC1. Neonatal myosins have been also detected. Lipid droplets and cores, both features of damaged muscle, are in evidence. Minor changes of the thickness of the basement membrane and the capillaries have been reported. These abnormalities of muscle are not limited to muscles concerned with posture and movement but are also present in the diaphragm. The abnormalities are more prominent in patients with cardiomyopathy. The changes can easily be detected in severe heart failure and are probably a response to the activation of hormonal and cytokine systems. The link between abnormalities of muscle function and symptoms in early or mild heart failure is less certain. A prediction from the muscle hypothesis is that symptoms will not improve unless muscle structure and metabolism is restored toward normal as a consequence of the treatment of heart failure. Favourable changes in skeletal muscle fibres and therefore MHC composition can be attained with training. This may result in patient with heart failure to an improvement of the clinical status with better exercise tolerance. Further studies are needed.

Another field in which possible changes in the skeletal muscle MHC composition could have the potential to improve the clinical outcome of patients with chronic cardiac failure is cardiomyoplasty. Interventions able to induce a shift of the contractile protein pattern toward isoforms that could enable a more vigorous contraction of the latissimus dorsi.

It is widely accepted that in cardiac failure changes occurring in the periphery are at least as important as those happening in the heart, but amongst peripheral organs and tissues, the skeletal muscle seems to deserve special attention.
The working hypothesis, that skeletal muscle is responsible for systemic symptoms and therefore a target for interventions capable of improving survival and quality of life, is an hypothesis which needs testing.

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