Pharmacological stress echocardiography for exercise independent assessment of anti-ischaemic therapy

See page 242 for the article to which this Editorial refers

Stress echocardiography has completed its life cycle by moving from the status of a promising innovation used by a few enthusiastic supporters amid general scepticism, up to the rank of an established technology accepted by virtually the whole cardiological community. However, many practical aspects remain to be clarified regarding the two most used pharmacological stress echocardiography drugs, dipyridamole and dobutamine\[I1. The study by Dodi et al. in this issue addresses the effect of non-beta-blocker antianginal therapy on dobutamine stress echocardiography results\[21. To put these data in perspective, we will briefly address the pathophysiological concept of the 'exercise simulating agent', and we will review the available data on the use of pharmacological stress echocardiography for medical therapy assessment.

Exercise simulating agents: scientific fact or fancy definition?

Among pharmacological stresses, a currently used differentiation exists between 'exercise simulating agents', such as dobutamine or arbutamine, and vasodilator stressors, such as dipyridamole or adenosine. The pathophysiological mechanisms of each stress have been extensively discussed elsewhere\[11. Here, it is important to emphasize that none of the pharmacological stresses is exercise simulating, if this meant to imply the possibility of supplying the complex information that exercise offers, not only on coronary flow reserve, but also on cardiac reserve and cardiovascular efficiency. Both coronary reserve and cardiovascular efficiency are co-determinants of exercise tolerance and therefore of the quality of life in the individual patient. No pharmacological stress can mimic the complex haemodynamic, neural and hormonal adaptations triggered by exercise, or offer information on cardiovascular efficiency\[31.

Exercise explores the entire physiological chain supporting external work: physiological motivation, the central and peripheral nervous system, lungs, the myocardium, the coronary circulation, blood peripheral circulation, skeletal muscle, up to cell respiration and mitochondrial oxygen utilization. Of this chain, pharmacological stresses only test the 'coronary' ring.

On the other hand, all stresses are 'exercise simulating' since their mechanism of action is the exaggeration of a biochemical and haemodynamic mechanism that operates during exercise: e.g. adrenergic stimulation with increased myocardial oxygen consumption of dobutamine and arbutamine, or the stimulation of adenosine receptors with absolute reduction of perfusion in subendocardial layers, as occurs with dipyridamole. In addition, the mechanical pattern of stress-induced increase in function is totally different with exercise and dobutamine — which is, from the mechanical point of view, a 'pacing-simulating agent' affecting regional wall function — and induces left ventricular cavity changes similar to those produced by atrial pacing rather than dynamic exercise\[41. Last but not least, from a less physiological but more pragmatic viewpoint, all stresses are to be considered 'exercise-simulating' since they induce ischaemia with similar frequency, in the same region, and to a comparable extent as exercise. They also titrate the positive response but the equivalent of the ischaemic workload is the drug dose necessary to elicit ischaemia\[11.

Pharmacological stress echocardiography test for medical therapy assessment

Physical and pharmacological stress tests are frequently used to assess medical therapy efficacy. Lattanzi et al. have convincingly shown that this goal can be achieved with dipyridamole stress echocardiography\[51. Antianginal therapy with nitrates, beta-blockers and calcium antagonists, alone or in various combinations, decreased the sensitivity of dipyridamole echocardiography.

These effects parallel the influence of drug therapy on the results of exercise testing. In particu-
there was a significant correlation between therapy-induced variations in dipyridamole time (i.e. the time from onset of exercise to 0.1 mV of ST segment depression) in the 38 patients with positivity of both tests off treatment[5]. Recently, these findings have been reproduced using beta-blocker therapy alone. Ferrara et al[6] have also documented that the anti-ischaemic effect of beta-blockade is largely independent of the effect on heart rate and is probably linked to a direct 'anti-steal' effect of beta-blockade. These data should be contrasted with those obtained with dobutamine stress. Beta-blocker therapy reduces the sensitivity of dobutamine stress echocardiography[7] much less than dobutamine stress perfusion. However, this does not reflect a physiological anti-ischaemic action of beta-blockade, but rather a rightward shift in receptor stimulation. As shown by Fioretti et al., atropine coadministration restores an acceptable sensitivity to dobutamine stress[8]. The present paper by Dodi et al. moves along this line, providing useful information to the clinical cardiologist. In contrast to what happens with dipyridamole stress, calcium antagonists and nitrates do not significantly lower the sensitivity of dobutamine-atropine, and mild changes induced by these drugs are not mirrored by changes in exercise testing.

Conclusion
For exercise-independent assessment of therapy efficacy, data support the use of dipyridamole rather than dobutamine stress echocardiography.

For primary diagnosis of coronary artery disease, dobutamine sensitivity is less affected by medical therapy than dipyridamole stress echocardiography. No test is 'exercise simulating', although fancy marketing definitions are frequently and inappropriately bandied about in scientific debates.

References

Growth hormone in the treatment of heart failure: a new tool for the future?

See page 340 for the article to which this Editorial refers

Severe impairment of left ventricular pump function leads to the clinical syndrome of heart failure. Initial myocardial damage induces a process of remodelling, which is a combination of dilatation and compensatory, but mainly inadequate, hypertrophy of the left ventricle. Dilatation of the cardiac cavity increases wall stress, which accelerates cardiac remodelling in a vicious circle of cardiovascular deterioration[1]. Until recently, clinicians approached heart failure as a disturbance of haemodynamic regulation. Reduction of preload (diuretics, nitrates, ACE inhibitors) and afterload (ACE inhibitors, hydralazine) would reduce wall stress and thereby prevent further progression of cardiac dysfunction.

Since the 1980s, many details on the role of the neurohumoral system and on the pathophysiology of heart failure have been revealed. Neurohumoral