Left ventricular dyssynchrony and functional mitral regurgitation: two dynamic conditions

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This editorial refers to ‘Effect of dynamic myocardial dyssynchrony on mitral regurgitation during supine bicycle exercise stress echocardiography in patients with idiopathic dilated cardiomyopathy and “narrow” QRS’ by A. D’Andrea et al., on page 1004

A 30-year-old-man was admitted to the hospital in NYHA class IV without any medical treatment. The coronary arteries were normal. Left ventricular (LV) ejection fraction (EF) was 30%, mean capillary wedge pressure was 38 mmHg. The QRS duration was 120 ms. Myocardial biopsy revealed signs of idiopathic cardiomyopathy without inflammatory infiltration. The patient was treated by lisinopril, carvedilol, and spironolactone and progressively improved. One month later, a Doppler echocardiogram revealed important LV dilatation and reduced EF of 21%. Severe mitral regurgitation (MR) was observed: the effective regurgitant orifice (ERO) was 30 mm². Significant LV dyssynchrony was found: the difference between time to peak systolic velocities of septal and lateral segments was 170 ms and the standard deviation of time to peak systolic velocity of 12 LV segments was 98 ms. Surprisingly, cardiopulmonary exercise testing showed a normal VE/VCO₂ slope and peak VO₂ was 28 mL/kg/min. How can we explain the discrepancy between severe LV dysfunction and preserved exercise capacity? Exercise Doppler echocardiography was performed. An important decrease was observed during exercise in both the degree of functional MR (ERO = 10 mm²) and of LV dyssynchrony (septal to lateral delay = 20 ms).

This case illustrates the dynamic characteristics of both functional MR and LV dyssynchrony. During exercise, MR may vary substantially with loading conditions that modulate mitral valve geometry, thus tethering forces. The strongest determinant of dynamic MR is indeed exercise-induced changes in valvular deformation, as measured by the systolic tenting area. Another mechanism of functional MR is abnormal mitral valve closing force. The abnormal coapting force may result from reduced contractility, abnormal ventricular–arterial coupling, or LV dyssynchrony.

Dynamic MR may thus be related to intermittent changes in LV synchrony during exercise. In a series of 35 patients with chronic ischaemic LV dysfunction and at least mild functional MR, important changes in LV dyssynchrony during exercise were found in most patients, in the absence of exercise-induced ischaemia. Exercise improved LV synchronicity in 15 patients and increased LV dyssynchrony in 16 patients. Exercise-induced changes in LV dyssynchrony strongly correlated with those in secondary MR and in forward stroke volume. These observations were confirmed in a series of 65 heart failure patients compared with 50 matched healthy control subjects. The origin of heart failure was non-ischaemic in half of the population; a wide QRS complex (≥120 ms) was present in two-thirds of the patients. Several parameters of LV dyssynchrony were measured at rest and during exercise. Exercise-induced alterations in LV synchrony were also found to be associated with the changes in stroke volume and the severity of MR. Of the patients exhibiting >20% changes in LV synchrony during exercise, 80% presented with ischaemic cardiomyopathy.

D’Andrea et al. describe a series of 60 patients with idiopathic dilated cardiomyopathy and QRS interval <120 ms who were submitted to supine bicycle exercise Doppler echocardiography and cardiopulmonary exercise testing. Cardiac synchronicity was measured at rest and during exercise; the standard deviation of time intervals between the onset of the QRS complex and the peak myocardial systolic velocity of 12 LV segments (six at basal level and six at mid level) was calculated. The ERO was obtained at rest and exercise by the proximal flow convergence technique. Dynamic LV dyssynchrony unmasked by exercise was found in more than 50% of the patients. Increased LV dyssynchrony during exercise was independently associated with increased functional MR, reduced exercise capacity, and lower LV stroke volume at peak test.

This study strengthens the concept of dynamic dysynchrony. Further investigations are necessary to clarify its mechanisms and its clinical implications. An obvious possible mechanism of an increase in LV dyssynchrony is segmental tardokinesis resulting from exercise-induced ischaemia. All patients studied by D’Andrea et al. had angiographically normal coronary arteries. In the study by Lafitte et al., no patient experienced chest pain or developed ST-segment depression during exercise. As changes in the parameters of dyssynchrony during exercise were more frequent in patients with ischaemic cardiomyopathy, the
authors hypothesized that subclinical ischaemia could have occurred, leading to segmental prolongation of electromechanical activation. All patients studied by Lancellotti et al.\textsuperscript{3} underwent simultaneous exercise Doppler echocardiography and technetium-99m sestamibi single photon emission computed tomography. Only three of 35 patients with ischaemic cardiomyopathy developed ischaemia according to a $\geq 10\%$ in hyperperfusion index severity. Ischaemia was limited to only one of the 16 LV segments. Thus, it seems likely that ischaemia is not a major determinant of exercise-induced increase in LV dysynchrony. It would be interesting to test the hypothesis that changes in dysynchrony during exercise relate to changes in synchronicity between the two papillary muscles.\textsuperscript{6} The use of more reliable techniques—such as cardiac magnetic resonance imaging—to identify ischaemia in LV segments partly affected by necrosis could also be relevant. The dynamically increased ERO and dysynchrony may potentially be a marker of greater amount of fibrotic tissue in idiopathic cardiomyopathy and more extensive coronary artery disease in ischaemic LV dysfunction, but this remains to be studied.

The close relation between exercise-induced changes in dysynchrony and secondary MR is not surprising: there are in line with acute changes in MR observed with the induction and interruption of cardiac resynchronization therapy. Biventricular pacing acutely reduces MR severity at rest and its dynamic component during exercise well before the occurrence of a significant LV inverse remodelling.\textsuperscript{7,8} In addition, the interruption of biventricular pacing is associated with an acute increase in MR.\textsuperscript{9}

Some clinical implications of dynamic functional MR have been recently demonstrated. In the setting of chronic systolic LV dysfunction, exercise-induced increase in MR can be associated with dyspnoea or acute pulmonary oedema.\textsuperscript{10,11} Dynamic MR is also a determinant of rapid QRS widening, and predicts short-term mortality and long-term mortality and hospitalization for cardiac decompensation.\textsuperscript{12–14} Exercise-induced MR has incremental prognostic value for cardiac death over an exercise echocardiogram that does not incorporate information on MR.\textsuperscript{15} Because of the link between dynamic MR and dynamic LV dysynchrony, it can be hypothesized that exercise-induced increase in dysynchrony can be associated with a worse outcome and that conversely exercise-induced normalization of LV dysynchrony can predict a better outcome and/or be one of the possible explanations of why a patient is not clinically improved by biventricular pacing.

How should patients with dynamic MR and/or dynamic LV dysynchrony be treated? The hypothesis that cardiac resynchronization therapy is a useful option when both conditions coexist should be tested. If this hypothesis is confirmed, the criteria for selecting candidates for biventricular pacing could include dynamic changes in dysynchrony during exercise.

Conflict of interest: none declared.

References