Changes in functional mitral regurgitation after cardiac resynchronization therapy

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This editorial refers to 'Impact of reduction in early- and late-systolic functional mitral regurgitation on reverse remodelling after cardiac resynchronization therapy',† by Y.-J. Liang et al., on page 2359

Functional mitral regurgitation (MR) is a common finding in patients with global left ventricular (LV) dilatation and dysfunction. In these patients, the mitral leaflets are structurally normal and leaflet coaptation failure results from an imbalance between valve closing forces and valve tethering forces. Impaired LV contractility, global LV dysynchrony, and reduced mitral annulus systolic contraction lead to a significant reduction in valve closing forces. In turn, valve tethering forces are increased due to mitral annulus dilatation, LV remodelling, and papillary muscle displacement. Furthermore, MR per se induces additional adverse ventricular remodelling through volume overload, and plays an important role in the progression of the cardiomyopathy.

The presence of significant functional MR also has important prognostic implications, and is associated with a relatively high morbidity and mortality. Surgery is the preferred therapeutic option, but several recent studies demonstrated that cardiac resynchronization therapy (CRT) might also be able to reduce functional MR. Reduction of MR following CRT was shown to be related to various issues. First, the reduction in LV dyssynchrony and the improvement in LV contraction immediately after CRT can significantly increase valve closing forces. Secondly, LV reverse remodelling and changes in mitral apparatus geometry can further reduce MR by reducing mitral leaflet tethering; this effect is observed at mid- and long-term (≥6 months) follow-up after CRT.

Liang et al. have described for the first time the differential effects of CRT on the two components of functional MR: early- and late-systolic MR. Understanding the mechanisms underlying these dynamic changes permits a more sophisticated interpretation of the effect of CRT on the different components of functional MR. In most patients, functional MR shows a unique biphasic pattern, with early- and late-systolic peaks of regurgitant flow and a mid-systolic decrease. These dynamic variations mainly result from the changes in mitral annulus dimension and transmitral pressure during systole (Figure 1). Mitral annulus area, and the tethering effect on the subvalvular apparatus related to LV remodelling, decrease to a minimum during LV contraction in mid-systole and partially improve mitral valve competence. However, both these components increase at end-systole (during left atrial filling and LV isovolumetric relaxation), resulting in the late-systolic peak of regurgitant flow. The ventricular–atrial pressure gradient, which represents the closing forces, shows a slow rise during systole due to LV dysfunction, allowing the tethering forces to prevail at the beginning of the systole and resulting in the early-systolic peak of regurgitant flow. However, the transmural pressure gradient reaches its peak at mid-systole, leading to a more effective leaflet coaptation in this phase of the cardiac cycle.

In the study by Liang et al., a significant effect of CRT was observed on both components, but with a predominant improvement in the early-systolic MR. Therefore, the main effect of CRT at short-term follow-up seems to be the improvement in LV contraction and transmitral pressure, which can reach its systolic peak relatively earlier and therefore reduces the early component of MR. In addition, significant LV reverse remodelling was observed and might explain the reduction in the tethering forces and the consequent improvement also in the late-systolic component of MR.

However, since the echocardiographic follow-up was performed at 3 months after CRT onset, clear differentiation between the effects of CRT on the different components of functional MR is not possible. Ideally, an acute follow-up study (within 48 h after CRT onset) and a late follow-up study (6 months after CRT) would have been performed to understand further the pathophysiology underlying MR improvement and the precise time course of the changes in the two components of functional MR after CRT. An acute echocardiographic evaluation performed within 48 h after the implantation would explore whether the increase in LV contraction alone (increase in LV systolic pressure rise, dP/dt) would lead to a significant decrease in functional MR, with a
predominant reduction in the early-systolic component of the MR. Previous studies\textsuperscript{7,10} in patients undergoing CRT suggested that the acute improvement in the valve closing forces may oppose the increased mitral leaflet tethering forces and facilitate more effective valve closure, especially at early- and mid-systole.

A long-term follow-up echocardiographic evaluation (6 months after CRT) would explore the important interaction between improvement in functional MR and LV reverse remodelling. The LV reverse remodelling process requires time to be completed and its favourable effect on mitral annular dimensions and papillary muscle displacement (with consequent reduction in functional MR) can be detected mainly at a later stage after CRT implantation.\textsuperscript{11} In particular, the changes in LV dimensions and geometry can hypothetically improve both components of functional MR, but the predominant effect would be on the late-systolic peak of regurgitant flow.

Another issue that would have been of interest is the relationship between LV dyssynchrony and reduction in functional MR. Measures of LV dyssynchrony were not included in the study by Liang et al.\textsuperscript{12} although several earlier studies suggested that the presence of baseline LV dyssynchrony involving the posterior papillary muscle resulted in an uncoordinated contraction of the papillary muscles with a deformation of the mitral subvalvular apparatus; subsequent resynchronization after CRT was associated with an immediate improvement in functional MR. Furthermore, long-term (6 month) follow-up studies showed that baseline global LV dyssynchrony (in particular when the lateral wall was the latest activated segment) was associated with significant LV reverse remodelling after CRT\textsuperscript{16} and that a further improvement in functional MR was related to the reduction in LV end-systolic volume and mitral annular size.\textsuperscript{8} It would have been of interest to evaluate how the presence of dyssynchrony and resynchronization after CRT would have influenced the early and late components of the MR.

In conclusion, significant improvement in MR has been reported after CRT. Results from the study by Liang et al.\textsuperscript{12} highlighted the existence of different components of MR, and the findings contribute to an improved understanding of changes in functional MR after CRT.

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References


