The non-ischaemic dynamics of ischaemic mitral regurgitation: solving the paradox

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This editorial refers to 'Long-term outcome of patients with heart failure and dynamic functional mitral regurgitation'1 by P. Lancellotti et al., on page 1528

A 65-year-old patient with a history of myocardial infarction and known occlusions of the right and distal left anterior descending coronary arteries is admitted to the emergency room for acute pulmonary oedema. Blood pressure is 160/90 mmHg and heart rate is 98 beats/min. An electrocardiogram shows sinus rhythm, Q-waves in the inferior leads, and V1–3 with equivocal ST-segment changes in the chest leads. Troponin is borderline. An echocardiogram shows reduced global left ventricular (LV) contraction with an estimated ejection fraction (EF) of 30–35%, akinesis of the inferior and posterior segments as well as the apex, mitral valve tethering with severe mitral regurgitation (MR), and an estimated systolic pulmonary artery pressure of 50 mmHg. The patient quickly improves on intravenous diuretics and nitrate infusion. A repeat echocardiographic study shows virtually unchanged LV volumes and EF (possibly a mild reduction in cavity size), but a significant decrease in the degree of MR (now mild-to-moderate) and systolic pulmonary artery pressure (now 35 mmHg). A diagnosis of pulmonary oedema secondary to transient ischaemic MR is made and a SPECT thallium scan is performed. The radioisotope study demonstrates extensive and irreversible lack of uptake in the inferoposterior LV wall segments and the apex, with no evidence of myocardial ischaemia. Welcome to the clinical paradox of ischaemic MR!

A paradox is an argument that apparently derives self-contradictory conclusions by valid deduction from acceptable premises.1 Solving paradoxes by recognition of unstated assumptions has often led to progress in science and philosophy. In the present case, the hidden assumption, decades-old, is the equation of dynamic functional MR with transient (reversible) ischaemia. In a series of important studies in patients with ischaemic heart disease and systolic LV dysfunction, Lancellotti and Pierard’s group has helped reveal this hidden assumption. They have elegantly demonstrated the presence of dynamic functional MR during exercise in the absence of transient ischaemic wall-motion abnormalities;2,3 they have shown that acute pulmonary oedema in these patients is associated with dynamic changes in MR and a concomitant increase in pulmonary vascular pressure;4 and they have documented that dynamic increases in effective regurgitant orifice (ERO) area during exercise predict increased short-term mortality.3 The present paper verifies the clinical significance of these findings by extending the observation period to up to 4 years.5

At the root of the hidden equation of dynamic and transient ischaemic changes lies an unfortunate nuance of terminology. 'Ischaemic MR' is convenient shorthand for MR caused by changes in ventricular structure and function, ultimately—but not necessarily directly—related to the effects of ischaemia. In the vast majority of cases, ischaemic MR is essentially post-infarction MR, caused by progressive LV remodelling rather than reversible ischaemia. Rarely does the latter in itself cause significant MR in an otherwise normal ventricle, yet the concept of transient ischaemic MR has intrigued many who associate 'reversible' with 'ischaemia', a concept perpetuated by the frequent finding of significant treatable coronary lesions in these patients along with zones of ischaemic myocardium identified by imaging techniques, even if unrelated to the clinical problem. We need to expand our concept of 'dynamic', 'reversible', and 'transient' to the dynamic behaviour of non-ischaemic myocardium affected by global and regional remodelling as well. As the mitral valve is anchored to the ventricular myocardium through the papillary muscles, variations in LV shape or volume caused by changes in loading conditions will directly affect the tethering forces that oppose valve closure.6–9 Effective leaflet coaptation is further impaired as a result of the diminished closing force exerted by the dysfunctioning ventricle on the restrained mitral leaflets.6–9 The balance of forces acting on the mitral valve—tethering forces vs. closing forces—explains the variations of ERO within one cardiac cycle8,9 and its dynamic response to exercise-induced changes in loading conditions and ventriculoarterial coupling in patients with chronic ventricular dysfunction and heart failure.2,10 Ischaemia can certainly shift this balance and worsen MR,11 but it is by no means a prerequisite for the dynamic character of functional MR. The authors point out
that although patients with definite evidence of exercise-induced myocardial ischaemia were not included, the techniques used for stress echocardiographic assessment of wall-motion abnormality may have been less sensitive for detecting ischaemia, particularly with pre-existing infarctions; nevertheless, pathophysiologically important degrees of induced ischaemia should in principle be detectable.

If dynamic MR is associated with increased mortality, should patients with mild MR at rest and a significant exercise-induced increase in regurgitant severity be referred for surgery? The observed association between dynamic increases in MR and elevations in pulmonary vascular pressure does suggest that dynamically increasing MR may indeed be causally related to adverse outcome. In contrast, the dynamically stretched ERO may simply be a marker of greater myocardial damage, greater dilatation in response to exercise, and, in turn, a higher propensity for progressive remodelling with risk of ventricular arrhythmia and sudden death. As is typical of pathophysiological processes, which more often follow vicious cycles than straight pathways, dynamic ERO is probably both a cause for progressive LV remodelling and the result of it. Whether this vicious cycle can be interrupted by mitral valve surgery or percutaneous approaches needs to be seen. One recent non-randomized study in patients with LV dysfunction who underwent mitral valve repair for ischaemic MR did not show a survival benefit conveyed by surgery, but this is not really surprising considering that current repair techniques, which do not address the principal problem of papillary muscle displacement, do not prevent recurrence of 3+ and 4+ MR within 6 months following surgery in up to 30% of all patients. Our limitations in treating ischaemic MR successfully should not mislead us into discarding its role in the pathogenesis of acute and chronic heart failure. For the time being, the hypothesis that repeated episodes of volume overload caused by dynamic MR may contribute to long-term mortality in patients with chronic heart failure is a tenable one.

References


