EDITORIAL COMMENT

Ischemic Mitral Regurgitation and Ventricular Remodeling*

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Over the past several decades, we have learned much about the pathophysiology and therapy for primary mitral regurgitation (MR). The term “primary” is used to indicate that it is an abnormality in the structure of the valve itself that has led to regurgitation. If severe and prolonged, primary MR eventually causes myocardial damage, dysfunction, and death unless the valve is repaired or replaced (1–3).

Much has been learned also of the mechanism of secondary MR, a condition in which the valve itself is normal but abnormalities in left ventricular (LV) volume, function, and shape have led to MR. In both ischemic and dilated cardiomyopathy, shifts in papillary muscle position result in tenting of the mitral valve at closure so that the leaflets do not co-apt properly, in turn leading to MR (4,5). In addition, ventricular dilation results in annular enlargement, which further compounds valve incompetence (6). Conversion of the LV shape from an ellipsoid to a rounder sphere exacerbates the problem. It is generally held that MR begets MR. That is, as a volume overload is added to the pathophysiologic mix, further increases in annular dimension and worsening of papillary muscle alignment increase the amount of leak, setting up a perpetual cycle. This cycle subsequently has important effects on LV geometry, which are crucial in understanding the pathophysiology of the disease (7). Although MR has often been viewed as an afterload-reducing lesion, the ventricular dilation associated with MR increases the radius term in the Laplace equation (stress = pressure × radius/2 × thickness) (8,9). Thus, the effect of MR on LV geometry is to increase ventricular wall stress despite the unloading effect of the leak itself. Increased load further worsens LV performance, leading to further hemodynamic compromise.

As much as we know of the proper therapy for primary MR, we know very little about the best management for secondary MR. What is clear is that the advent of secondary MR worsens prognosis (10), but it is unclear whether poorer outcome stems from the MR itself or is simply a marker for worsening LV function and heart failure.

In acute primary MR, vasodilators are effective in increasing forward flow by reducing aortic impedance. However, little is known about their long-term usage. Conversely, in secondary MR virtually all patients have LV dysfunction, and many have heart failure. As such, almost all are receiving or should be receiving angiotensin-converting enzyme inhibitors. Whether additional vasodilators would be helpful or harmful is unknown, but it seems unlikely that intense vasodilator therapy would have a substantial impact. Thus, in view of the importance of LV geometry in this disease, it is not surprising that the radius term in the Laplace equation has become the focus of both medical (vasodilators) and mechanical therapies.

It is the Laplacian radius that is uniquely addressed by Guy et al. (11) in this issue of the Journal. These investigators created myocardial infarction in three groups of sheep using a model proven to cause substantial secondary ischemic MR. One group was untreated, one group had received an external wrap before infarction designed to limit post-infarct dilation, and the third group received a preinfarction mitral annuloplasty designed to limit the amount of MR that would eventually develop. In both treated groups, the MR that developed was mild compared with the untreated group. However, the wrap group had significantly less dilation and better LV function that the annuloplasty group. The implication of these data is that it is the infarction and the remodeling that follows it that is the major villain after infarction; thus, the MR might not represent a target for therapy if indeed it is not the major culprit. These data are unique and add substantially to what we know about the significance of post-infarct remodeling and how MR contributes to it. In essence, Guy et al. (11) address the question: Once medical therapy is maximized, should we attack the Laplacian radius by reducing volume overload by mitral valve repair or by attempting to prevent ventricular enlargement using other means, such as external restraint? At least as far as the issue relates to the ovine model used in their study, the answer appears clear. Both the wrap and the annuloplasty limited MR, but it was the wrap that provided the better outcome.

How do these data translate to our practice for patients with secondary MR? Do they mean we should abandon mitral repair in patients with secondary MR in favor of external constraint? Do they apply only to ischemic MR or can they be extended to the secondary MR of dilated cardiomyopathy? How close is ovine pathophysiology to that seen in humans? The answers are unfortunately not at all clear. Murkiness is generated by several factors. First, the study was performed temporally opposite to that which

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usually occurs in humans, where the myopathy and ventricular dilatation usually have resulted in severe MR and additional therapy now is required. In the current study, the therapeutic devices were in place before the insult occurred, an event obviously unlikely to occur in our patients. Is the process the same forward as it is in reverse? For now, no one knows, but at least in some selected cases mitral repair has already been demonstrated as being beneficial at least for secondary end points, such as ejection fraction, symptom status, and ventricular volume (12). It should be noted, however, that we have no knowledge yet whether restraint devices would have been as or even more successful in the same patients. Another problem to be addressed is that the annuloplasty group in the current study had a lower ejection fraction than the restraint group despite similar amounts of MR. Did the annuloplasty in some way impede performance that led to worse outcome, or did restraint provide better function? Without an uninfarcted annuloplasty control group and a pure control group, we cannot know for certain.

Guy et al. (1) have performed a real service in the understanding of ischemic MR. Their data clearly demonstrate the importance of post-infarct remodeling in causing both post-infarction MR and LV dysfunction. Their data further emphasize the potential for external restraint devices as a therapy for this problem. However, their studies do not preclude a potential for benefit from mitral valve repair or replacement in selected patients. Indeed, annuloplasty has been of benefit to others at least in terms of LV function. So far, virtually nothing is known about mortality benefits of either therapy on this disease, data that should be forthcoming from randomized trails. In the future, it is likely that both restraint and valve surgery will be beneficial. The identification of which patients will benefit from which therapies has yet to be defined.

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REFERENCES


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