Commentary: From the bedside to the laboratory and back

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Central Message

Despite a number of clinical trials and studies, optimal management of IMR remains unclear. This study provides some groundwork to improve our understanding.

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Expansion of our understanding of clinical observations and changes in our clinical practice often derive from large randomized trials, clinical series, and case reports. The occasional investigator will take a clinical question and go to the experimental laboratory in an attempt to understand the mechanism behind the clinical observation. An example is the work of Lillehei and colleagues,[1] who more than half a century ago investigated a clinical observation that preservation of the subvalvular apparatus when replacing the mitral valve had a positive impact on cardiac function, and they tested this in a canine model.

More recently, surgical management of ischemic mitral regurgitation (IMR) has been a point of contention, with recent clinical trials suggesting that repairing or replacing the mitral valve in IMR does not have a significant impact on left ventricular (LV) remodeling. Smith and colleagues[2] reported findings from the Cardiothoracic Surgical Trials Network study on IMR and noted that in the 301 patients with moderate IMR randomized to undergo coronary artery bypass grafting (CABG) alone versus CABG and mitral valve repair, the addition of a mitral repair to CABG did not result in a higher degree of LV reverse remodeling at 1 year. These findings were similar to those of Acker and colleagues[3] in a comparison of repair versus replacement for severe IMR (there was no CABG only arm in this study). The difficulty in interpreting these results was the inability to separate out the effects of ischemic disease from the regurgitant lesion and not being able to control for the severity and chronicity of the mitral regurgitation (MR). A recent "Expert Opinion" in the *Journal* noted that recovery with CABG alone is more likely if there is a substantial portion of myocardium that is viable but hibernating or poorly functioning.[4]

Onohara and colleagues[5] attempt to address some of these issues with an experimental model of MR and myocardial ischemia. The authors were able to create MR or ischemia in a rat model in a reproducible manner. In their study, they find that when MR is present in the setting of ischemia (group I vs II), decreased contractility occurs. Although the authors find this counterintuitive, as noted by McGee,[6] the concept of the mitral valve "pop-off" has been disproven time and again. The authors also found that when controlling for ischemia, MR with or without ischemia led to a larger LV mass and end-diastolic volume (group I vs III). In a sense, the dual lesions led to both systolic and diastolic dysfunction albeit with different time-courses and severity. This study verified in the laboratory what is often seen clinically.

There are some criticisms of this study. Although the MR is created the same way in every animal, the degree varies. This may have contributed to the wide range of values in both mass and volume. Nevertheless, the overall findings are important and supplement the clinical findings of both Smith and colleagues[2] and Acker and colleagues,[3] namely, the suggestion that although late correction of IMR may not have an impact on LV remodeling, early correction may. Obviously, the experimental animals never had their ischemia reversed (and this would have been impressive if the authors had been able to accomplish this). We are left wondering that if ischemia is corrected before the development of or in the early stages of moderate MR, can the LV recover? Or should even mild MR be addressed early on? These are questions that might better be addressed in further experimental models rather than clinical trials.

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