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Commentary: Can indications for asymptomatic mitral regurgitation derive from ratatouille or should we stew on it?

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Chronic mitral regurgitation (MR) is associated with progressive left ventricular (LV) volume loading, yet these patients may remain asymptomatic for many years without displaying any decrease in LV ejection fraction.¹ It has been postulated that chronic severe MR may be associated with ventricular dysfunction that is not manifested as reduced ejection fraction.^{1,2} Furthermore, it has been observed that patients with preserved LV function who undergo mitral repair frequently have postoperative LV dysfunction.¹ An interesting article by Corporan and colleagues³ describes an experimental rat model of MR, achieved by surgically perforating the anterior mitral leaflet. Over a period of 40 weeks, they observed that ventricular dilatation,

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In rat models of mitral regurgitation, myocardial remodeling may precede a fall in ejection fraction.

impaired LV contractility, transcriptomic changes, myocardial remodeling, and oxidative stress pathways activation preceded a fall in LV ejection fraction. This appeared to be biological evidence to support the concept that ventricular dysfunction and adverse remodeling predates the fall in ejection fraction in patients with severe MR. Yet, this diverse mixture of transcriptomic changes, myocardial remodeling, and ventricular dilatation observed in rats is much like a thick ratatouille, the pieces of which are very difficult to separate and even harder to make sense of. Based on the findings in the rat model, it is difficult to make any clinical inferences for surgical management of asymptomatic patients with severe mitral insufficiency.

Given the concern of potential LV dysfunction despite preserved ejection fraction, the most recent American Heart Association guidelines recommend mitral repair in asymptomatic individuals with preserved ejection fraction if the probability of repair is >95% and the risk of mortality <1%.⁴ Are we able to achieve these lofty ambitions? It is a fascinating fact that a recent report on 2259 patients from New York State hospitals who underwent mitral

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surgery for severe asymptomatic MR with preserved ejection fraction demonstrated that only 63% of patients received a mitral repair.⁵ Even amongst surgeons with the highest volume (ie, >47 mitral surgeries per year) the repair rate only reached 92%.⁵ Furthermore, in a propensity matched analysis, patients who underwent mitral replacement had a significantly higher mortality at 4 years (12.1% vs 3.5%; $P < .001$). A mortality rate of 12% at 4 years in patients without heart failure and with preserved LV function is startling.⁵ Even in the most experienced hands, a repair rate of >95% appears to be difficult to achieve. Although excellent results with complex mitral valve repair have been reported,⁶ it would still be not easy to recommend mitral valve repair in all asymptomatic patients with severe mitral insufficiency. Or would it?

The current, thought-provoking study by Corporan and colleagues² is timely and very important because it suggests that, at least in rats, irreversible myocardial remodeling may occur before a significant fall in ventricular ejection

fraction. This appears to be a highly valuable observation for all of us to consider.

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Commentary: The mitral matrix

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Well-standardized mitral repair techniques have provided predictable and durable results for patients with degenerative mitral regurgitation,¹ yet the timing of surgical intervention in asymptomatic patients continues to be debated. Current guidelines² focus on left ventricular size and ejection fraction whereas some investigators suggest the use of more subtle markers such as left atrial volume index,³ myocardial strain,⁴ and circulating peptides⁵ in asymptomatic patients. Although watchful waiting with close surveillance has shown to be safe, fears arise that myocardial

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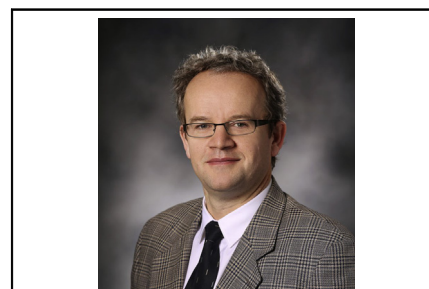
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CENTRAL MESSAGE

Left ventricular transcriptomic and geometric changes may preclude fall in ejection fraction in chronic severe primary mitral regurgitation.

damage may be occurring even in the setting of preserved ventricular function.

Based on the experimental data presented by Corporan and colleagues⁶ in this issue of the *Journal*, these fears may not be unfounded. The investigators from Emory