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Commentary: Functional mitral regurgitation: The 2 sides of 1 coin

Thierry Bove, MD, PhD

Functional mitral regurgitation (FMR) is a pathophysiological entity in which a morphologically normal mitral valve (MV) is dysfunctional secondary to geometrical distortion of related cavities and/or structures. Although well recognized in primary left ventricular diseases such as ischemic or dilated cardiomyopathy, FMR by primary left atrial dilation, as in longstanding atrial fibrillation or heart failure with preserved ejection fraction, came recently into attention.

Hirji and colleagues¹ investigated the outcome after surgical therapy of significant MR by comparing patients with atrial and ventricular FMR. They found a clear survival benefit for atrial FMR, being, respectively, 90% and 72.2%, compared with 76.4% and 60.3% for ventricular FMR at 5 and 10 years. This difference is not surprising because only patients from the outer boundaries of the FMR spectrum were included for comparison. For patients with ventricular FMR, patients with depressed left ventricle function (left ventricle ejection fraction $\leq 50\%$) were selected, whereas associated coronary artery disease was strictly excluded in atrial FMR. Consequently, patients with ventricular FMR had more left ventricle dysfunction and dilation, and presented more frequently with heart failure symptoms. In contrast, patients with atrial FMR showed more atrial fibrillation, but also severe tricuspid regurgitation and right ventricle dysfunction. Patients with atrial FMR seemed clinically more disabled, suggested by a greater proportion of patients presenting with New York Heart Association functional class III and IV.

Contrary to the well-known MV-left ventricle interaction, the role of left atrial and mitral annular dynamics in developing FMR has been highlighted in relation to the increasing prevalence of atrial fibrillation and heart failure with preserved ejection fraction in the growing population of elderly

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Within the spectrum of functional mitral regurgitation, differentiation between atrial and ventricular FMR is mandatory for therapeutic and prognostic implications.

patients.^{2,3} Hirji and colleagues¹ raise the concern that discrimination between these apparently opposite FMR entities remained unaddressed in the 2017 American Heart Association/American College of Cardiology guidelines on the management of FMR. But this issue is covered in the upcoming 2020 American Heart Association/American College of Cardiology guidelines.^{4,5} Specifically, early differentiation between FMR etiologies is mandatory to enhance a tailored therapy, certainly if one aims to anticipate on progression of FMR by a direct causal therapeutic intervention. It is obvious that FMR represents a spectral disease, where categorization of patients into either FMR subtype might be obscured through findings in the gray zone, like incidental coronaropathy, paroxysmal atrial fibrillation, and/or intermediate left ventricle function impairment.

The therapeutic implications of this study are less evident because only candidates for surgical therapy presenting with severe FMR were included. This narrows the view on the contribution of medical versus surgical therapy in relation to the degree and subtype of FMR. Whether these patients were finally cured of MR remains difficult to ascertain because MV reoperation was taken as the end point, assuming that reoperation for MR recurrence is offered to a minority of patients. Midterm freedom from reoperation was higher for atrial FMR than for ventricular FMR, although the difference was no longer relevant after adjustment for the competing effect of death. Considering that

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Disclosures: The author reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

Received for publication Dec 29, 2020; revisions received Dec 29, 2020; accepted for publication Dec 29, 2020; available ahead of print Jan 9, 2021.

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J Thorac Cardiovasc Surg 2022;164:1816-7

0022-5223/\$36.00

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<https://doi.org/10.1016/j.jtcvs.2020.12.135>

ventricular FMR is intrinsically a ventricular disease, known to have limited effectiveness of MV annuloplasty, it is expected that a restrictive annuloplasty might be a definitive option in atrial FMR. Nonetheless, the lack of echocardiographic data is a strong limitation of this study in its purpose to answer the question about optimal therapy and/or eventual implications for catheter-based strategies for addressing the FMR spectrum.

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Commentary: Pathoanatomic differences in functional mitral regurgitation—a guide for future interventions?

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Dr Hirji and colleagues present an analysis comparing different etiologies of functional mitral regurgitation (FMR) in this month's *Journal*.¹ They have elected to classify atrial FMR as due to atrial enlargement or heart failure with preserved ejection fraction and ventricular FMR as related to any ventricular dysfunction. Significant baseline differences are notable, reflecting the considerable heterogeneity of FMR patients. The rate of operative mortality was low and not different between the groups. After controlling for differences in demographics and comorbid conditions, ventricular FMR was a predictor of both mid-term mortality (hazard ratio

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Ventricular and atrial functional mitral regurgitation are separate entities with different long-term outcomes, necessitating pathoanatomic definitions to determine optimal interventions on this heterogeneous group of patients.

[HR], 1.8) and a composite of mortality or reoperation (HR, 2.1). Although these are logical divisions, they paint an incomplete picture because they do not account for other morphological features of the heart that determine the trajectory of functional mitral regurgitation. The degree of annular dilation, ventricular dysfunction, and dilation and leaflet tethering all affect patient outcomes. Although underpowered to assess each of these features, it is a missed opportunity and should be a focus of future studies.

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Disclosures: The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

Received for publication Jan 12, 2021; revisions received Jan 12, 2021; accepted for publication Jan 13, 2021; available ahead of print Jan 21, 2021.

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J Thorac Cardiovasc Surg 2022;164:1817-8

0022-5223/\$36.00

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<https://doi.org/10.1016/j.jtcvs.2021.01.054>