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► **To cite this version:**

Corentin Bourg, K Charlotte Lee, Erwan Donal. Understanding myocardial mechanics in primary mitral regurgitation: A contemporary approach. *International Journal of Cardiology*, 2024, *International Journal of Cardiology*, 401, pp.131882. 10.1016/j.ijcard.2024.131882 . hal-04480638

HAL Id: hal-04480638

<https://hal.science/hal-04480638v1>

Submitted on 29 May 2024

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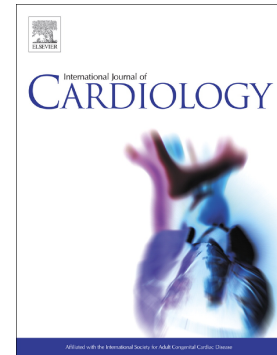


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Journal Pre-proof

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PII: S0167-5273(24)00328-0

DOI: <https://doi.org/10.1016/j.ijcard.2024.131882>

Reference: IJCA 131882

To appear in: *International Journal of Cardiology*

Received date: 14 February 2024

Accepted date: 15 February 2024

Please cite this article as: C. Bourg, K.C. Lee and E. Donal, Understanding myocardial mechanics in primary mitral regurgitation: A contemporary approach, *International Journal of Cardiology* (2024), <https://doi.org/10.1016/j.ijcard.2024.131882>

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EDITORIAL: Understanding Myocardial Mechanics in Primary Mitral Regurgitation: A Contemporary Approach

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In response to: Pastore MC, Vannuccini F, Mandoli GE, Lisi M, Iuliano MA, Santoro A, Niglio FP, Diviggiano EE, Lorenz V, Montesi G, Cavigli L, Focardi M, D'Ascenzi F, Cameli M. Myocardial work and left heart deformation parameters across primary mitral regurgitation severity. *Int J Cardiol.* 2024 Mar 15;399:131772. doi: 10.1016/j.ijcard.2024.131772. Epub 2024 Jan 9. PMID: 38211675.

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Word Count: 878

Exploring Primary Mitral Regurgitation

Mitral regurgitation (MR) is the most prevalent valvular pathology in the United States and the second most prevalent in Europe.^{1,2} Among the two subtypes of MR, primary MR is the most common and results from direct damage to the mitral valve (MV) or its sub-valvular apparatus. In contrast, secondary MR results from abnormal dilation or dysfunction of the left atrium (LA), mitral annulus, or left ventricle (LV).

Regardless of etiology, MR induces volume overload, which affects the LA and subsequently the LV. To compensate for this overload, these chambers augment their preload to increase their contractility in keeping with Frank-Starling mechanisms. However, when these compensatory mechanisms are overwhelmed, the LV undergoes excess dilation, causing myocardial dysfunction and poor outcomes if left untreated.³ Similarly, LA compliance also increases as MR progresses, which further facilitates worsening LV dysfunction.

Ultrasound Evaluation of Mitral Regurgitation

Current ESC guidelines⁴ recommend transthoracic echocardiography as the first-line test for etiologic diagnosis and severity assessment of MR. Using qualitative, semi-quantitative, and quantitative measurements, MR can be classified into four grades (trace, mild, moderate, and severe), which in turn predict patient prognosis. Namely, as effective regurgitant orifice area (EROA) size increases, so does all-cause mortality. In addition, greater LA or LV size and lower LV ejection fraction (LVEF) at baseline are associated with greater mortality, and as such inform therapeutic strategies.^{5,6} Currently, MV replacement or repair is recommended in all patients with severe MR and LVEF <60%, LV end-systolic diameter >40 mm, or LA diameter 60 ml/m², even in asymptomatic patients.

Although not yet included in MR treatment guidelines, LA and LV strain (as derived from speckle-tracking echocardiography) may hold additional prognostic value beyond LVEF.⁷ These novel markers may be particularly relevant in situations where it is difficult to assess MR severity grade, such as in the presence of multiple or eccentric regurgitant jets.

Myocardial Work: Breaking Free from the Load

In recent years, new imaging techniques based on speckle-tracking imaging have emerged, including myocardial work (MW) as proposed by Russell et al's team.⁸ MW is a non-invasive technique that calculates myocardial energetic expenditures using 1) LV global longitudinal strain (GLS) curves from 2D echocardiography, 2) valve opening and closing times from Doppler imaging, and 3) non-invasive arterial blood pressure (as a surrogate for intraventricular pressure). MW can be further subdivided into "constructive" and "wasted" categories, with global constructive work (GCW) being that which contributes to appropriate myocardial actions during systole (i.e. ejection) and diastole (i.e. relaxation). Any work not included in these categories is considered global wasted work (GWW), and the ratio of GCW to GWW can be calculated to determine global work efficiency (GWE).

Compared to traditional echocardiographic parameters such as LVEF and LV GLS, MW has been shown to accurately reflect myocardial oxygen consumption and metabolism, and as

such provides a more accurate assessment of ventricular function. Importantly, MW is also inherently load-independent, as arterial pressure is directly accounted for in MW calculations. The importance of this load-independence cannot be understated, since LVEF and GLS do not possess this benefit. Moreover, loading conditions change constantly in patients with MR and depend on instantaneous fluid status, concomitant valvular disease, arrhythmias, catecholamines, and more.

Previous literature has already established the utility of MW in assessing cardiac function across patients with heart failure, aortic stenosis, obstructive cardiomyopathy, amyloidosis, and lupus, and its clinical utility in other disease phenotypes remains promising.

In the present study, Pastore et al⁹ used MW to characterize LV function across different degrees of MR. Interestingly, they found that GCW was relatively unimpaired with increasing severity of MR, reflecting ventricular adaptation to excess afterload. Conversely, GWW increased and global work efficiency GWE decreased with increasing severity of MR. Notably, there were minimal differences in LVEF (± 3 percentage points) and no differences in LV GLS between the mild, moderate, and severe MR groups, suggesting that GWW and GWE may be more sensitive markers of myocardial damage in the setting of MR.

Clinical Implications

In practice, optimizing the timing of mitral valve interventions remains a key challenge in managing patients with MR. This challenge may be partially mitigated by including myocardial work into clinical calculus, given that myocardial work has enhanced sensitivity for detecting early disease and may allow for the treatment of patients at stages where adverse myocardial remodeling is still reversible. Previously, Galli et al¹⁰ showed that in a retrospective study of patients undergoing transcatheter edge-to-edge repair, GWW was an independent predictor of LV reverse remodeling at one-year post procedure. Although this result suggests possible utility of MW in pre-operative clinical decision making, further studies are needed to prospectively confirm this finding.

Regarding limitations, the main shortcoming of Pastore et al's study is the lack of inclusion of patients with atrial fibrillation (AF), which is highly prevalent among those with MR. The utility of MW parameters in AF and MR warrants thorough evaluation, as AF is both a cause and a consequence of MR.

In conclusion, Pastore et al have shown that the assessment of myocardial work and LA strain in patients with primary MR is of key clinical interest. These parameters should as such be included in routine TTE for patients with primary MR in order to better characterize ventricular function and guide the timing of possible interventions.

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