

# Too much of a good thing in ischemic mitral: lessons for surgeons and cardiologists

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## Keywords

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The newly proposed concept of proportionate and disproportionate ischemic mitral regurgitation (IMR) relies on the geometrical relationship of the mitral valve-left ventricular unit (MV-LV) and has been used to explain the outcomes of percutaneous mitral repair.

Interestingly, the echocardiographical and clinical observations at the basis of this revolutionary concept, are actually substantiated by some more “basic” surgical research on the outcomes of different types of surgical interventions. Evidences on the geometrical alteration of the mitral MV-LV unit before and after annuloplasty prompted the surgical community to a more holistic approach in the treatment of IMR including both the valve and the subvalvular apparatus. Clearly, some “surgical” concepts are widely applicable to percutaneous mitral intervention and might complement and expand the idea of the proportionality between MR and LV dilation. The most important predictor of prognosis after IMR treatment is the residual capacity of the LV to positively remodel. Selecting interventions able to modify the ventricular environment predisposing towards reverse remodeling is paramount. This is possible by a careful selection of the patients and with a “proportionated” action on the valve and/or subvalvular apparatus.

Ischemic mitral regurgitation (IMR), is considered an acquired dysfunction of the mitral valve (MV), secondary to a myocardial infarction (MI). A set of complex geometric alterations directly affecting the profile and function of the valvular and subvalvular apparatus are initiated by left ventricular (LV) distortion and post-infarction remodeling. In particular, annular dilatation, leaflet tethering with impaired coaptation, and papillary muscle (PM) displacement along posterior, apical or lateral vectors have been claimed to play a role in IMR

[1–7].

In a recent novel conceptualization of IMR pathology by Grayburn *et al.* [8, 9], a renovated attention has been given to the “MV-LV unit” and their functional relationships. The concept of a proportionate or disproportionate MR compared to the dimension of LV has been introduced to explain the prognosis of IMR and the surprising differences in the results of the MITRA-FR and COAPT studies. In cases of severely dilated LV, EROA values around 0.2 can be considered as proportionate and consensual to the degree of LV dilation. In other words, the severity of MR is a direct consequence of LV adverse remodeling and dilation and such EROA values remain within the expected levels. In these patients whose MR severity is proportionate to the degree of LV dilation interventions directed towards the MV are not expected to be successful as not addressing the primary pathology. Strategies ameliorating LV remodeling (i.e., medical therapy) might be more promising in these cases, as shown by the MITRA-FR trial. Conversely, a disproportionately large degree of MR in comparison to the degree of LV dilatation points at a reparable defect of the MV and a primary valve intervention could lead to better outcomes [8, 9].

Interestingly, these concepts have been widely investigated in the surgical literature on IMR and many of the clinical reflections proposed are actually substantiated by more basic studies investigating outcomes of surgical interventions. Several geometrical laws have been applied across the literature to explain the sometimes-disappointing results of restrictive mitral annuloplasty (RMA). These speculations leveraged on the need for a more holistic approach including both the MV and LV with subvalvular apparatus in the treatment of MR [10–17]. Consequently, interest has been fueled in subvalvular apparatus surgery, such as papillary muscle approximation (PMA) [1–3, 18] and papillary muscle sling [19], which share the rationale of reducing LV geometrical stress and valve tethering imparted by an asymmetrically dilating LV.

A great deal of work has been lavished on the identification of the appropriate degree of annular restriction to be imparted by mitral annuloplasty given the reported risk of stenosis, SAM and recurrent MR in the case of an overcorrection or excessive undersizing [18, 20–22]. From the biomechanical perspective, the forces on the fibrous skeleton of the heart exerted by annular undersizing would contrast with the displacement vectors relative to the LV dilation expected in these patients. The consequent imbalance of internal forces within the ventricle pushes the system towards a more unstable mechanical equilibrium [13, 15, 23, 24], eventually leading to MR recurrence.

The stress on the MV after surgery can be geometrically considered as the difference between pre-operative and post-operative mitral annulus diameter, divided by LVEDD. This parameter, namely Mitral Annulus Stress Index (MASI), was introduced to describe a measurable clinical correlate of the geometrical alteration of the MV-LV unit after annuloplasty. MASI was shown to predict MR recurrence after repair [11, 23]. MASI expresses and simplifies the contrast among the conflicting geometrical vectors belonging to the undersized annulus on the one side and to the progressively dilating LV on the other. This concept prompted the surgical community to address not only the valve but also the subvalvular apparatus by reducing the interpapillary distance as attenuation of the effects of LV dilation/remodelling appeared necessary to avoid failure of repair [14, 18, 19, 25, 26].

Under this light the MASI closely resembles and complements the concept enunciated by Grayburn *et al.* [9]. A highly dilated LV determines lack of coaptation and because the “*primum movens*” of the pathology relies in the LV itself, any degree of action on the MV will not be able to influence the poor long-term outcomes. The mechanical action of restricting the annulus or clipping the leaflets will not reconstitute a suitable coaptation length to guarantee future valve competence without an additional intervention reversing LV remodeling. Furthermore, the greater the restriction on the mitral annulus in the context of a dilating LV (i.e., high MASI), the higher the mechanical stress on the MV-LV unit with further negative reflections on long-term outcomes. Extrapolating from Grayburn’s data, an index conceptually similar to MASI could be calculated as EROA/LVEDV ratio. Plotting this variable, a cut-off of 1.6 could inform MR severity and indication for intervention.

Braun *et al.* [27] reported that for LVEDD >65 mm and LVESD >55 mm restrictive annuloplasty alone was unable to induce LV reverse remodeling, demanding for a subvalvular or ventricular adjunct procedures. These cutoff values were also predictors for late mortality (5-year survival in LVEDD <65 mm 80% vs 49% in LVEDD >65 mm). In a randomized study on PMA versus RMA alone for IMR, a significant reduction in LVDD was demonstrated in the PMA group at 5 years (LVEDD was  $56.5 \pm 5.7$  mm with PMA versus  $60.6 \pm 4.6$  mm with RMA  $p < 0.001$ ), indicating a long-term beneficial LV remodeling when subvalvular techniques are adopted.

Kim *et al.* [28] demonstrated the importance of interpapillary muscle distance (IPMD) as affecting leaflet tethering and mitral tenting volume and determining IMR severity in patients with LV dysfunction. Roshanali *et al.* [29] suggested that a preoperative interpapillary distance  $\geq 20$  mm was a reliable predictor of late MR after annuloplasty.

More recently, Kalra *et al.* [30] investigated the temporal changes in interpapillary muscle dynamics in IMR. The loss of lateral shortening in IPMD consequent to a regional myocardial ischemia determines tethering of the leaflet edges and impairs their systolic closure, resulting in mitral regurgitation. This occurred even in small ventricles [4, 5, 30–33], somewhat anticipating the concept and effects of disproportionate IMR advocated by Grayburn *et al.* [9]. Importantly, Shudo *et al.* [25] in a study comparing a type of subvalvular intervention, namely PM imbrication (PMI), with RMA alone showed that the latter was unable to induce a significant reduction in IPMD postoperatively and was consequently associated to increased tenting height. Conversely, a significant correlation between the postoperative decrease in tenting height and the postoperative improvement in interpapillary muscle distance was found as result of PMI [23, 25, 32].

It appears that the most important predictor of prognosis in IMR is the residual capacity of the LV to positively remodel and IPMD could be considered a measure of such remodeling [5]. If IMR long-term treatment relies on LV adaptive abilities, selecting interventions able to modify the ventricular environment predisposing towards reverse remodeling is paramount [5].

This is possible by a careful selection of the patients, as elegantly demonstrated by Grayburn *et al.* [9], and with a “proportionated” action on the valve and/or the subvalvular apparatus, considering the MV-LV in its entirety. Unfortunately, in the context of percutaneous mitral intervention is difficult to establish the degree of annular restriction exerted by the mitral clip and its impact on LV geometry. However, the lesson learned from interventional cardiology adds a clinical reflection on what was simply considered as product of geometrical calculations by surgeons and can better elucidate the indications and the selection of patients and type of intervention to be performed [16, 24, 31].

## Author contributions

FN, CS and CM conceptualized, drafted and approved this manuscript.

## Ethics approval and consent to participate

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## Conflict of interest

The authors declare no conflict of interest.

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