

Ischemic Mitral Regurgitation After Acute Myocardial Infarction in the Percutaneous Coronary Intervention Era

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Ischemic mitral regurgitation (IMR) is a term used to denote IMR (mitral regurgitation) that occurs secondary to ischemic heart disease. Although transient ischemia can provoke IMR that is reversible with relief of ischemia, the most common form of IMR in clinical practice is associated with chronic ischemic cardiomyopathy. In such patients, global or regional left ventricular (LV) remodeling leads to a combination of leaflet tethering, reduced LV closing force, and annular dilation.^{1,2} LV dyssynchrony may also play a role when there is left bundle branch block. It has been demonstrated in multiple studies that IMR is associated with a poor prognosis in ischemic cardiomyopathy. Importantly, the initiating event that leads to ischemic cardiomyopathy is usually a first myocardial infarction (MI). Lamas et al³ reported that IMR in the setting of acute MI was associated with adverse prognosis SAVE trial (Survival And Ventricular Enlargement). Subsequently, Grigioni et al⁴ reported the effect of IMR on prognosis in the late phase post MI. However, those trials were performed before the routine use of acute percutaneous coronary intervention (PCI) as treatment of acute MI.

See Article by Nishino et al

In this issue of *Circulation: Cardiovascular Imaging*, Nishino et al⁵ report a serial evaluation of the degree of MR in the setting of first-onset acute MI treated with successful PCI, from the first access to the emergency room to 6 to 8 months later. In 546 patients, the prevalence of significant IMR in the acute MI phase was 35%, defined semiquantitatively (vena contracta method). The authors evaluated the changes of IMR severity over time, the predictors of such changes, and the relationship of IMR severity at each stage (acute, early post-PCI, and late post-PCI) to LV dimensions and on early and long-term survival.⁵ They found that IMR severity often changed between the early and chronic phase after primary PCI for acute myocardial infarction, which is consistent with the well-known dynamic nature of functional MR and the potential for revascularization to improve IMR. Interestingly, a predictor of IMR reduction in the early phase was a shorter onset-to-reperfusion time, whereas lower peak creatine kinase-MB level was

found to be a predictor of improvement of IMR after PCI in the chronic phase.⁵ There was a correlation between the reduction of IMR severity and reduction in LV end-diastolic and end-systolic diameters as well as an important increase in LV ejection fraction, both acutely and at long-term. Taken together, these results support the concept that the changes in the magnitude of IMR are related to the degree of LV remodeling, which reflects the amount of myocardium rescued by primary PCI.⁶⁻⁹ The authors excluded patients in whom PCI was not successful; however, having these as a control group might have provided a better understanding of IMR evolution and impact on survival.

Interestingly, in their study, the degree of IMR was not influenced by blood pressure, which is known to strongly influence MR severity. Importantly, this could be an artifact of not using quantification to measure IMR severity in terms of effective regurgitant orifice area and regurgitant volume, as recommended by echocardiographic guidelines.^{10,11} Failure to quantify IMR severity is the major weakness of the present study. This is particularly relevant in light of evidence that lower thresholds for effective regurgitant orifice area and regurgitant volume confer an adverse prognosis in IMR compared with values associated with a severe amount of MR. This has generated controversy as to the definition of severe functional MR and whether there are clinically important differences between lesion severity and prognostic severity.^{10,12}

The authors report that incidence of IMR per culprit coronary vessel was not statistically different. Although clinical experience suggests that IMR is more likely with inferoposterior or lateral MI, the literature has been controversial, perhaps because of unequal distribution of patients included in different studies.¹³ In some trials, patients with MR were more likely to have sustained an anterior MI, but in other investigations, an inferior MI, a posterolateral MI, a combined anterior-inferior, or an MI of indeterminate location were predominant. Moreover, the definition of chronicity after MI varies widely, with cutoffs going from 16 days to 1 month to 6 to 8 months. Although in the long term after MI, scar tissue and LV remodeling with distortion of the mitral valve apparatus play a big role in pathogenesis of IMR, in the acute phase of MI, MR may preexist or result from acute, but potentially reversible, regional LV dilation and loss of contraction.¹ Most studies have shown that functional MR in early MI is associated with a worse prognosis and is an important, independent predictor of cardiovascular mortality. The article by Nishino et al corroborates this data, showing that IMR on arrival and persistent IMR in the chronic phase worsened short-term and long-term prognosis after acute myocardial infarction, respectively.^{1,4,5,8} Although they found that IMR was related to LV volume, data on regional wall motion abnormalities,

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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LV regional dyssynchrony, presence of posterior aneurysm, mitral annular diameter, and global longitudinal strain were not reported, nor did they comment on new left bundle branch block after MI. Cardiac resynchronization therapy (CRT) has been shown, indeed, to reduce the degree of MR in chronic left bundle branch block by inducing LV reverse remodeling and increasing the force of contraction.¹⁴ Because delayed posterolateral wall contraction is characteristic of left bundle branch block, CRT may also reduce discoordinate papillary muscle contraction early post MI, thereby reducing MR. Persistent or recurrent MR after CRT has been shown to portend worsen prognosis, with less reverse remodeling and higher clinical events rate.¹⁵ Unfortunately, there is no evidence regarding the early use of CRT in a post-MI setting. Moreover, more aggressive treatment of ischemic functional MR by surgical or percutaneous repair or replacement has not been proven to be effective at improving prognosis. Current American College of Cardiology/American Heart Association guidelines for the management of valvular heart disease list a Class IIb indication for mitral valve repair in patients with chronic severe secondary MR because of severe LV dysfunction (ejection fraction <30%) who have persistent symptoms despite optimal medical therapy and CRT when indicated. The European guidelines have, instead, a Class IC indication for surgery in patients with severe MR and LV ejection fraction >30% undergoing coronary artery bypass grafting, even though retrospective analyses using propensity score matching showed no survival benefit of adding mitral valve repair to coronary artery bypass grafting.^{16,17} In the STICH trial (Surgical Treatment for Ischemic Heart Failure), survival in the medically treated cohort (with high use of guideline-directed medical therapy) depended strongly on MR grade at baseline, with mortality hazard doubled in patients with moderate to severe MR compared with patients with no MR.¹⁸ In patients with moderate to severe MR, adding mitral valve repair to coronary artery bypass grafting tended to improve survival compared with coronary artery bypass grafting alone or medical therapy alone.¹⁸ However, the decision to repair the valve was not randomized. Therefore, although it is very clear that any degree of IMR confers an adverse prognosis, it remains unclear whether surgical or percutaneous correction of MR shifts a patient from an adverse survival curve to a more favorable one. Results of randomized clinical trials, such as the COAPT trial (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation), will provide an answer to this critical question. Until then, it remains uncertain whether IMR is mainly a marker for worse LV function (and hence survival) or a target for therapy.

Disclosures

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KEY WORDS: Editorials ■ bundle branch block ■ coronary artery disease ■ mitral valve regurgitation ■ myocardial infarction ■ percutaneous coronary intervention

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