Ischemic Mitral Regurgitation and Its Related Risk After Myocardial Infarction

Tushar V. Salukhe, BSc, MRCP; Michael Y. Henein, MD, MSc, PhD; Richard Sutton, DSc(Med)

In this issue of Circulation, Bursi et al report that ischemic mitral regurgitation is a more common finding after myocardial infarction (MI) than was previously thought and is an independent predictor of heart failure and death among 30-day infarct survivors. Seldom is mitral regurgitation actively investigated, and investigation is often only prompted by clinical examination. The data Bursi et al report support findings from the 1970s, which suggested that clinical examination is not sensitive in the detection and assessment of mitral regurgitation. The authors conclude that Doppler echocardiographic assessment of mitral regurgitation should be actively sought and included in post-MI risk stratification.

Ischemic Mitral Regurgitation and Prognosis After MI

Early invasive studies demonstrated an association between mitral regurgitation and increased 1-year mortality. Tcheng et al reported a mitral regurgitation prevalence of 17% in 255 patients. One-year mortality rates showed a graded association with the degree of mitral regurgitation: 11%, 22%, and 52% in patients with no regurgitation, angiographic grade 1 to 2 regurgitation, and grade 3 to 4 regurgitation, respectively. When clinical confounders were adjusted for by multivariate analysis, only grade 3 to 4 mitral regurgitation carried a significantly increased 1-year mortality risk. A similarly designed study reported a post-MI mitral regurgitation prevalence of 13% and showed that mitral regurgitation predicted cause-specific cardiovascular mortality. The larger SAVE (Survival and Ventricular Enlargement) study of 727 patients reported that even mild (grade 1 to 2) ischemic mitral regurgitation was an independent predictor of cause-specific post-MI cardiovascular mortality.

Echocardiographic studies of ischemic mitral regurgitation also have confirmed the prognostic significance of even mild mitral regurgitation. One-year mortality rates of 4.8%, 12.4%, and 24% were observed among 417 patients assessed within 48 hours of MI with absent, mild, and moderate to severe mitral regurgitation, respectively. Multivariate analysis revealed that even mild mitral regurgitation was independently associated with a significantly increased risk of death at 1 year (adjusted relative risk 2.31). Five-year survival in another study of 303 patients with recent MI showed that total and cardiac mortality was significantly greater in patients with mitral regurgitation than those without. Furthermore, the mortality risk was directly related to the degree of regurgitation as defined by the effective regurgitant orifice area and the regurgitant volume.

These studies contributed significantly to underlining the prognostic importance of assessing ischemic mitral regurgitation in the setting of MI; however, the wide prevalence ranges and variation in the assessment and categorization of mitral regurgitation reflect the large selection bias to which most of these studies were prone. For example, neither patients who are referred for cardiac catheterization after MI nor those who agree to consent for trials would necessarily reflect the average patient with MI in the community.

Bursi et al present a valuable community-based study of a large number of patients that confirms many previous observations. Their study describes the prevalence of mitral regurgitation in a regionally defined MI incidence cohort and its association with heart failure and all-cause mortality. Mitral regurgitation was present in a remarkable 50% of 773 patients who underwent Doppler echocardiographic examination within 30 days of MI. After a mean follow-up of 4.7 years, a graded positive association was observed between the severity of mitral regurgitation and heart failure or death. In addition, they found a graded association of severity of mitral regurgitation and prevalence of other risk factors with pejorative prognostic significance, including older age, hypertension, diabetes, higher Killip class, left ventricular ejection fraction (LVEF), and E wave deceleration time. When the authors made risk adjustments for age, sex, Killip class, and ejection fraction, moderate to severe mitral regurgitation was associated with a significantly increased risk of death among 30-day survivors and with incidence of heart failure.

The value of this study is in its community-based nature, its large number of patients, and its standardized surveillance methods for detecting incident cases of MI. These attributes make it less susceptible to selection biases and more applicable to real-life populations of patients with MI than have been previous studies.

Ischemic Mitral Regurgitation and Left Ventricular Function

Ischemic mitral regurgitation results from geometric changes in left ventricular shape. Regional remodeling after MI displaces papillary muscles and causes tethering of the mitral...
valve leaflets, which results in incomplete leaflet coaptation. Malcoaptation is aggravated further by dilatation of the mitral valve annulus; hence mitral regurgitation ensues. This mechanism is somewhat verified by the observation that mitral leaflet tethering causing tenting of leaflets toward the apex increases during exercise stress.8 Exercise- or stress-induced geometric ventricular change increases regurgitant orifice area and volume and may result in dyspnea; it also is associated with a history of acute pulmonary edema.8 Ischemic mitral regurgitation cannot develop in the setting of regional wall motion abnormalities alone because conformational change of left ventricular shape is necessary for the development of functional mitral regurgitation. The severity of regurgitation is related more to the extent of left ventricular geometric change than it is to the severity of left ventricular disease and systolic dysfunction.9 Regurgitation severity often is described in terms of jet area, effective regurgitant orifice area, or vena contracta diameter, all of which primarily reflect regurgitant volumes. An often-underused measure of functional mitral regurgitation is its duration with respect to the cycle length.

Coronary artery disease and MI together constitute a major cause of intraventricular activation delay and asynchrony, which may or may not manifest as bundle-branch block on the surface ECG. Asynchrony is known for its direct effect on the duration of mitral regurgitation. Prolonged functional mitral regurgitation can abbreviate left ventricular filling,10 thus further compromising stroke volume and cardiac output. Such patterns of ischemic ventricular dysfunction may regress after revascularization when ventricles become more synchronous, and resistant cases may respond to resynchronization therapy. Activation delay usually causes a delay in the onset of segmental contraction of the left ventricle, which in the presence of a regurgitant orifice can prolong the duration of mitral regurgitation with respect to the cardiac cycle length. Activation delay often is manifest on the surface ECG as a broad QRS complex, which itself is a known independent predictor of mortality. The inclusion of QRS duration in multivariate analysis therefore would be particularly useful in assessing the role of mitral regurgitation as an independent predictor of death.

To date, LVEF remains the most established and commonly used estimator of risk after MI. LVEF is, however, prone to gross overestimation of true systolic function in the presence of significant mitral regurgitation; thus, its quantification should be interpreted with caution, regardless of how it is measured when mitral regurgitation is present.

Management of Ischemic Mitral Regurgitation and Stratifying Risk
Rarely does a single test determine the treatment strategy for a patient. Likewise, planning management and assessment of risk after MI cannot be based on one measurement alone. When mitral regurgitation is trivial or mild, it will have little if any impact on treatment. When ischemic mitral regurgitation is moderate or severe, a patient’s symptom profile and ventricular and atrial dimensions will still have the greatest influence on management strategy. In asymptomatic patients with near-normal cavity dimensions, moderate to severe mitral regurgitation would simply necessitate closer follow-up.

Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers have been the mainstay of treatment for symptomatic left ventricular systolic disease. Both have been shown to reduce ventricular volumes in medium- and long-term follow-up. Theoretically, the effects of vasodilators on left ventricular volumes and the remodeling process should reduce the regurgitant orifice area, yet no trials to date have shown clinical benefit in patients with ischemic mitral regurgitation from vasodilator treatment. β-Blocker therapy has been shown to reduce regurgitant volumes in patients with heart failure and ischemic mitral regurgitation.11

Surgical treatment for ischemic mitral regurgitation generally combines mitral valvuloplasty or replacement with coronary artery bypass grafting. In such patients, operative mortality is generally better after surgical repair rather than replacement of the mitral valve. With either technique, the surgical risk for ischemic mitral valve dysfunction is greater than that for nonischemic mitral valve disease; hence, patients with severe ischemic mitral regurgitation should be considered candidates for mitral surgery only if they are to undergo coronary bypass grafting.

Mitral regurgitation does not appear among the currently accepted eligibility criteria for cardiac resynchronization therapy. Prolonged mitral regurgitation that extends beyond aortic valve closure to impede the early phase of left ventricular filling can represent abnormal ventricular activation, which may be amenable to resynchronization therapy. Biventricular pacing in such patients can reduce the duration and volume of functional mitral regurgitation, improve left ventricular filling, and increase stroke volume.12,13

The assessment of mitral regurgitation may even prove valuable when deciding on candidacy for defibrillator implantation in an MI survivor. Predictors of death in patients with a recent MI have been of particular interest since the publication of MADIT II (Multicenter Automated Defibrillator Implantation Trial II),14 which demonstrated a clear survival advantage from defibrillator implantation in patients with MI and LVEF <30%. Although US policymakers have recognized the validity of the MADIT II results, cost-effectiveness concerns initially restricted support for defibrillator implantation to only those with QRS duration >120 ms, thus cutting the number of eligible patients by two thirds. Only recently has coverage been extended, aided in part by preliminary results of SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial), to include all patients with previous MI and LVEF of ≤30%.15

Cardiologists have since been diligently seeking readily definable patient characteristics that even more clearly define the risk of death than LVEF alone. Current evidence would not support defibrillator implantation in a notional patient with a previous MI and an LVEF of 40%. If this patient had severe mitral regurgitation or a QRS duration of 170 ms, then his or her risk of death may be similar to that of a patient with an LVEF of <30% with no mitral regurgitation and normal activation who would benefit from defibrillator implantation. Like LVEF, QRS duration and mitral regurgitation are
independently associated with an increased risk of all-cause death, of which half of the cases are potentially avertable with a defibrillator. Therefore, defibrillator implantation may theoretically be of benefit in a number or permutations and combinations of risk factors. It is likely that future decisions about whether to implant a defibrillator in a patient with or without a history of MI will not hinge on a single parameter but on a collective risk score based on a number of investigations. In this regard, the study of Bursi et al highlights the emerging role of mitral regurgitation, which may usurp the importance of LVEF for risk assessment in up to half of all patients with MI. Their data advocate the investigation of mitral regurgitation in all post-MI patients as part of routine risk assessment and management planning, particularly because clinical examination is a relatively poor indicator of its presence or severity.

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References

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