Percutaneous Intervention for Mitral Regurgitation

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KEYWORDS

• Mitral regurgitation • Mitral valve • Valve replacement • Heart failure

KEY POINTS

- Percutaneous treatment of mitral regurgitation (MR) is a promising alternative for patients with functional MR (FMR) who are not appropriate for surgery and are not responding to optimal medical therapy and cardiac resynchronization therapy.
- Unlike degenerative MR, where repair therapy is clearly preferred, the optimal approach for FMR has not been defined.
- Challenges for novel mitral repair devices are to demonstrate safety and superior efficacy to medical management in higher risk patients.
- Transcatheter mitral valve replacement is emerging as a feasible therapy, but requires significant additional clinical trials to define its place in treating heart failure related to MR.

Our understanding of mitral regurgitation (MR) as a clinical and pathophysiologic entity has evolved greatly over the last decade. As recently as in the 2006 valvular heart disease guidelines, no explicit distinction was made between degenerative and functional MR (FMR) in terms of broad management principles.[1] Today, we understand the pathogenesis, clinical course, and therapy for degenerative and FMR differ in more detail. Degenerative MR (DMR), involving a structural abnormality of the mitral leaflets, is treated as a disease of the valve itself. Typically, left ventricular (LV) dysfunction in DMR is secondary to the valvular abnormality, with heart failure (HF) as a late manifestation of disease. The presentation for many of these patients is acute HF owing to chordal rupture with acute MR. In contradistinction, FMR represents a disease of the LV with normal mitral leaflet structure and MR as a secondary or bystander abnormality. The discussion of intervention for MR in the context of HF is thus a discussion of FMR.

BACKGROUND

Mitral Regurgitation and Left Ventricular Dysfunction: Prevalence and Outcome

The true incidence of FMR is difficult to ascertain. Different studies have used varied criteria for grading of MR severity based on echocardiography. Nkomo and colleagues[2] conducted a population-based study combining the echocardiographic database from 3 studies that examined young patients in Coronary Artery Revascularisation in Diabetes (CARDIA) trial, middle-aged patients in Atherosclerosis Risk in Communities (ARIC) trial, and older adults in the Cardiovascular Health Study (CHS). The aim of the study was to assess the prevalence, distribution patterns, and consequences of moderate or severe mitral and

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Heart Failure Clin 11 (2015) 243–259
http://dx.doi.org/10.1016/j.hfc.2014.12.004
1551-7136/15/$ – see front matter

aortic valve disease in the general population and in Olmsted County, Minnesota. MR was the most common disease, with an incidence of less than 1% before age 54 years but increasing each decade and reaching greater than 9% after age 75 years. Similar findings were observed in the Olmsted County community with slightly higher incidence. The incidence of valve disease was similar between men and women, and between whites and blacks. Patients with MR had significantly greater LV end-diastolic volume (LVEDV) and left atrial volume. The adjusted mortality risk ratio was 1.36 (95% CI, 1.15–1.62; $P = .0005$) in the population and 1.75 (95% CI, 1.61–1.90; $P<.0001$) in the community. A major limitation of this study is the lack of differentiation between DMR and FMR.

A more recent analysis attempted to determine the prevalence of MR in the US population based on the digital data from the National Institutes of Health, and classified the type of MR according to Carpentier's classification (**Table 1**). This analysis estimated that MR affected more than 2.5 million people in the United States in 2000. The largest group could be classified as having Carpentier type IIIb, with restricted motion owing to LV dysfunction with ischemic or nonischemic etiology. The investigators reported the prevalence of MR owing to ischemic cardiomyopathy at 7500 to 9000 per million, and of MR owing to nonischemic etiology of cardiomyopathy at 16,250 per million.[3]

The prognosis of patients with FMR is poor. Even the slightest degree of FMR can impact the survival of patients with LV dysfunction with or without coronary artery disease.[4] The impact of FMR on survival is irrespective of age, LV ejection fraction (LVEF), sex, mitral filling pattern on echocardiogram, and New York Heart Association (NYHA) functional class.[5] FMR has a 50% composite rate of mortality and HF hospitalization at 3 years, compared with 30% in HF patients without FMR.[6] Not surprisingly, in patients with ischemic FMR, the 5-year total and cardiac mortality rates were increased (62 ± 2% and 50 ± 0%, respectively) compared with those without associated coronary artery disease (39 ± 9% and 30 ± 0%, respectively).[7] Increasing severity of FMR is a strong predictor of mortality or transplantation in patients with an EF of less than 35%[8] and associated with higher mortality rates and HF hospitalizations.[9]

PATHOPHYSIOLOGY

Normal mitral valve function depends on a balance between the closing forces of the LV, that is, LV contraction, and the tethering forces that prevent the valve from prolapsing into the left atrium.[10] The papillary muscles counterbalance the force of LV contraction on the mitral leaflets via chordae tendinae by exerting force parallel and perpendicular to the leaflets that prevents leaflet prolapse. The traditional teaching for the mechanism of FMR is that altered geometry and reduced global or regional contractility, in the presence of "normal" mitral valve leaflets, results in MR. As new data emerge, this picture seems to provide an incomplete description of the mechanism of FMR. For example, this description does not explain as to why vast majority of patients with isolated severe aortic insufficiency (AI) do not have and do not develop FMR.[11] Patients with severe AI have the largest LVEDV and LV end-systolic volume (LVESV), yet the incidence of FMR is relatively

Table 1
Carpentier's classification for mitral regurgitation

	Leaflet Motion	Lesion	Etiology
Type I	Normal	Annular dilation Leaflet tear	Dilated cardiomyopathy Endocarditis
Type II	Excess motion	Elongation owing to rupture of chordae or papillary muscles	Degenerative valve disease (Barlow's disease) Endocarditis Myocardial infarction Trauma
Type IIIa	Limited motion in systole and diastole	Leaflet fibrosis/thickening/calcification Chordal fibrosis/fusion/thickening Commissural fusion	Rheumatic heart disease Carcinoid syndrome Mitral valve apparatus calcification
Type IIIb	Limited motion in systole	Left ventricular dilatation Chordal tethering	Ischemic/nonischemic cardiomyopathy