

# The Future Role of Minimally Invasive Techniques in Surgery on The Mitral Valve

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Normal mitral valve function depends on the complex and delicate interactions of the various components of the valve. Dysfunction of the valve can arise from a variety of factors, resulting in mitral regurgitation. Mitral regurgitation (MR) occurs when the mitral valve allows reversal of blood flow from the left ventricle (LV) to the left atrium. Treatment for mitral regurgitation depends on severity of the condition, the presence or absence of symptoms, and etiology of the condition. Of the half million Americans diagnosed every year with mitral valve disease, only about 18,000 of them undergo mitral valve surgery, annually.<sup>1</sup> Mitral valve surgery via median sternotomy (open-heart surgery) is a successful method of correcting mitral regurgitation and, until recently, it was the only method available to mitral regurgitation. New technologies with lower risks of postoperative morbidity and mortality seek to bring mitral valve repair to patients who are not surgical candidates, but who would benefit from valve repair.



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## **Etiologies and degrees of mitral regurgitation in the general population**

Mitral valve prolapse is the most common cause of mitral regurgitation (20 – 70% of surgical cases). Other significant causes of mitral regurgitation are ischemic heart disease (13 – 30% of surgical cases), rheumatic heart disease (3 – 40%), and endocarditis (10 – 12%).<sup>1</sup>

Mitral regurgitation occurs in varying severities within the general population. The severity of MR is determined using pre-defined angiographic and echocardiographic parameters. The Strong Heart Study examined 3486 American Indian participants to determine the prevalence and correlates of MR in a large population. This study showed MR is related to increased age, increased

hypertension, and decreased kidney function. Mild (1+) MR was present in 19.2% of participants. Moderate (2+) MR was present in 1.6% of participants. Moderately severe (3+) MR was present in 0.3% of participants. Severe (4+) MR was present in 0.2% of participants. Overall, prevalence of MR increases progressively by decade of age. The older the population, the higher the percentage that will have mitral regurgitation, in any severity. In participants <55 years old, 18% had at least mild (1+) MR. In participants 55-64 years old, 20% had at least mild MR. In participants 65 – 74 years old, 27% had at least mild MR. In participants over 75 years old, 29% had at least mild MR. Two other independent studies report similar frequency of MR. Reid and others reports 10.9% (93% of which was mild) in over 4,000 subjects 23 – 35 years old.<sup>2</sup> The Fram-

ingham Study reports a 19% prevalence of MR in 2,881 subjects 44–64 years old. Importantly, these studies show a correlation between presence and severity of MR and renal and vascular dysfunction, and an increased presence and severity of MR in an aging population.<sup>3</sup>

According to the American Heart Association's 2003 Statistics Update, mortality from mitral valve disorders is 10,365, annually.<sup>4</sup> The U.S. Census Bureau estimates the population of the U.S. at roughly 285 million.<sup>5</sup> Therefore, the Strong and Framingham studies indicate that over 54 million people in the U.S. may have at least mild mitral regurgitation.

### methods of diagnosis for determining severity of mitral regurgitation

There are several methods clinicians use to evaluate mitral regurgitation. Determination of the severity of mitral regurgitation by physical examination (auscultation of a heart murmur) is difficult and unreliable. Angiography can be used to visualize the amount of contrast in the left atrium and thereby determine severity of MR, but it is an invasive procedure. However, transthoracic echocardiography is well suited to quantification of regurgitation, and it is a non-invasive technique.

There are pre-defined criteria for grading mitral regurgitation based on angiographic findings. Trace amounts of contrast seen in the left atrium, but insufficient to outline the left atrium indicates mild (1+) regurgitation. Contrast opacifying in the entire left atrium, but less than that of the left ventricle, clearing quickly within 2-3 beats indicates moderate (2+) regurgitation. Contrast opacifying the left atrium and left ventricle equally indicates moderately severe (3+) regurgitation. Finally, contrast opacifying the left atrium more than that of the left ventricle with progression to the pulmonary veins indicates severe (4+) regurgitation.

Similarly, there are also criteria for grading MR in echocardiography. In mild MR, the signal is located in the proximal third of the left atrium near the mitral valve. In moderate MR, the signal is mid cavity; while in severe MR, the signal reaches the posterior third of the left atrium and the pulmonary veins. Transesophageal echocardiography (TEE) may be required if further detailed anatomic information is needed. TEE views correlate better with angiographic grading than transthoracic views.<sup>6</sup>

Color-flow Doppler echocardiography demonstrates duration and direction of the regurgitant flow. The size and extent of the color-flow Doppler signal into the left atrium provides the basis for grading of MR as mild, moderate, or severe. Assessment of the regurgitant color flow

## Three-dimensional echocardiography is optimal for assessing MR resulting from ischemia or dilated cardiomyopathy

jet in several views is the most common method. The parasternal long axis view may provide the best images of mitral valve prolapse, while the parasternal short axis view is better for depicting papillary muscle anatomy and leaflet cleft. Other approaches include calculation of regurgitant flow using standardized methods, calculation of regurgitant orifice size and volume using valve surface area, and measurement of the vena contracta using color flow imaging. Although they require more extensive technical skills and additional time for analysis and interpretation, in quantitative assessment (particularly in moderate cases of MR) these methods are superior to visual examination of the color

regurgitant jet, alone.<sup>7</sup>

Echocardiography is instrumental in deciding not only the cause and severity of MR, but also appropriateness and timing of surgical intervention. Echocardiographic diagnosis of MR resulting from flail leaflet can be done by measuring eccentricity of the flail leaflet using the angle of the mitral regurgitant jet. Prompt diagnosis is crucial for early surgical intervention and improved outcome. Three-dimensional echocardiography is optimal for assessing MR resulting from ischemia or dilated cardiomyopathy. Echocardiography is important in determining timing of surgery and prognosis in ischemic mitral regurgitation, as it assesses left ventricular chamber size and systolic function, left atrial size, and presence of pulmonary hypertension.<sup>8</sup> Ideally, these parameters are considered so that mitral valve repair is done before chronic volume overload causes permanent damage to the left ventricle. Echocardiography can be used to predict the success of a mitral valve repair by determining the thickness and redundancy of valve leaflets, chordal rupture, and the extent of leaflet prolapse. Serial echocardiography is important in managing asymptomatic mitral regurgitation, as it can be used to track left ventricular systolic function by more than ejection fraction, alone (which can be misleading and may not accurately reflect the presence or severity of contractile dysfunction). Deterioration of LV systolic function signals the need for operative intervention<sup>7</sup>, and echocardiography is useful in monitoring this important factor.

### Treatment options

Operation on the mitral valve subjects the patient to short-term risks of surgery and prolonged exposure to the possible complications of a prosthetic valve. Mitral valve surgery is clearly beneficial in improving long-term survival rate.<sup>9</sup> Unfortunately, mitral valve surgery carries with it substantial operative risks, especially in patients with more severe

mitral regurgitation as the result of ischemic disease, dilated cardiomyopathy, and pulmonary and renal comorbidities, and those undergoing re-operation. The STS database shows that operative mortality for a 1st repair is 2%, and for redo repair is four times that.<sup>10</sup>

## **Surgical treatment to eliminate MR prevents further loss of LV function and improves quality of life and survival rate**

Timing of surgery for patients with mitral regurgitation can be difficult, especially in the setting of myocardial infarction (MI) or poor left ventricular function. When acute MR occurs after MI, unless rapidly treated, it is associated with high morbidity and mortality. The SAVE study has shown that any degree of MR diagnosed after MI is a predictor of late cardiovascular mortality. In the study of 727 patients suffering from acute MI, the 19.4% who had MR (mostly mild) had a 3.5 year cardiovascular mortality of 29%, compared to only 12% in the subjects without MR.<sup>11</sup> Delaying surgery too long can result in increased operative mortality and poorer postoperative left ventricular function. Optimal timing for valve surgery should be based on history, physical examination, and noninvasive testing.

Patients with mitral regurgitation who also have advanced age, poor renal function, very low left ventricular ejection fraction (LV EF), history of open-heart operation, or history of myocardial infarction are poor candidates for surgery. For these patients, medical management is often the initial and only treatment strategy. ACE inhibitors and diuretics are the mainstay of medical therapy for patients with MR. By

decreasing the systemic blood pressure, ACE inhibitors decrease the amount of work placed on the heart. The regurgitant fraction also decreases because of the lower systemic blood pressure. Diuretic agents promote excretion of water and electrolytes by the kidneys, and are used to treat heart failure of hepatic, renal, or pulmonary disease when sodium and water retention have resulted in edema. For inpatient management of MR, inotropic agents are effective medications when cardiac function is slightly decreased or compromised by the amount of MR. Positive inotropic agents increase the force of contraction of the myocardium and are used to treat acute and chronic CHF. Some agents also may increase or decrease the heart rate, provide vasodilatation, or improve myocardial relaxation. These additional properties influence the choice of drug for specific circumstances.<sup>6</sup> Medical treatment options for mitral regurgitation can improve hemodynamics in the short term, but the impact of medical therapy on long-term clinical outcomes in the treatment of chronic MR is unknown. In any case, medical therapy does not actually eliminate the cause of the mitral regurgitation.

Surgical treatment to eliminate MR prevents further loss of LV function and improves quality of life and survival rate. If mitral valve surgery could be performed without risk, it could be recommended for all patients with MR.

New minimally invasive techniques designed to repair the mitral valve without open-heart operation are in development, and may prove instrumental in treating mitral regurgitation refractory to medical treatment or in patients that are inoperable. Alfieri developed an edge-to-edge mitral repair technique by which leaflets are fastened together by a central suture, producing a double orifice mitral valve. This technique has proven effective for multiple etiologies of MR in an open-heart approach.<sup>10</sup> Evalve has developed a catheter-based



technology based on the Alfieri technique. In this procedure, a catheter holding a fastening device is threaded from the groin area through the femoral vein to the heart, and after positioning over the mid section of the valve, advanced through the mitral valve, past the leaflets. The implant is closed, forming two openings in the valve, one on either side. The entire procedure is monitored with an echocardiogram. The implant can be adjusted and repositioned until leakage is minimized, and once the implant is securely attached, the delivery catheter is removed.<sup>12</sup> Currently, the procedure takes more than four hours to complete. Researchers participating in the current FDA-approved investigation hope to narrow that window down to a few hours.<sup>13</sup>

A new heart-valve implantation technology, developed by Percutaneous Valve Technologies (PVT), is currently in clin-

ical trials. The PVT device combines balloon-expandable stent technology with a bioprosthetic valve. The device deploys the stent across the old valve, holding it permanently open, and allows replacement of the old valve with a new one. Removal of the failing valve is not

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required. The procedure is for use in correcting aortic stenosis, but it has implications for use in other valve positions, as well, including treatment of mitral stenosis, aortic regurgitation and venous insufficiency.<sup>14</sup>

In February 2002, Edwards Lifesciences Corporation acquired a percutaneous

mitral valve repair program from Jomed N.V. (a European-based firm) and began research and development on a new non-surgical approach to mitral valve repair via the coronary sinus. This program focuses on developing a delivery system for a catheter-based support device in the coronary sinus. Products associated with this program could be ready for clinical trials in Europe in 2004. Edwards predicts that sales of catheter-based valve repair products in 2010 could approximate today's sales of the entire complement of surgical heart valve products.<sup>15</sup>

There are, presently, many companies and researchers pioneering innovative methods for non-surgical, catheter-based heart valve repair. Percutaneous balloon valvuloplasty for pulmonic, mitral, and aortic stenosis has recently been used with good results. In 2000, Philipp Boenhoeffer reported percutaneous prosthetic valve insertion in a right ventricle to pulmonary artery prosthetic valve conduit with valve dysfunction. A pediatric heart group in Europe has used a percutaneous stent approach in the pulmonary position for 14 patients. Additionally, European clinical trials are expected to begin, evaluating percutaneous mitral annular reshap-

ing (PMAR). PMAR is a technology produced by Mitralife, which uses a device (C-Cure) that is placed via catheter into the coronary sinus. Perioperative and mid-term coronary sinus rupture and thrombosis are a major concern with PMAR, but the easy access and speed of the procedure for patients with appropriate anatomy make it very attractive, and worth further investigation.<sup>16</sup>

### Conclusion

The prevalence of mitral valve disease in the general population warrants serious consideration. While open-heart surgery for mitral valve repair or replacement is a viable option for approximately 18,000 people each year, it carries with it complex risks. For a variety of reasons, the vast majority of patients with mitral regurgitation are not surgical candidates. Many of these patients have severe heart failure and their only treatment option is transplantation. It stands to reason, then, that a minimally invasive approach to correct or minimize mitral regurgitation would be of great benefit to patients as a way to postpone or avoid open-heart surgery.

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