

Valve Repair for Degenerative Mitral Regurgitation

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Mitral regurgitation is the most frequent valvular heart disease¹ and is projected to affect more than 6 million US residents by 2030, of whom 4 million will be clinically diagnosed. Mitral regurgitation is functional in two-thirds of cases, with struc-



Related article [page 1957](#)

turally normal valve leaflets and regurgitation due to valve deformation caused by atrial or ventricular remodeling. In the remaining third of cases, it is organic, with a structurally abnormal valve causing the regurgitation. In Western countries, most cases of organic mitral regurgitation are of a degenerative cause, stemming from mitral valve prolapse or flail segments.² Patients affected by moderate or severe mitral regurgitation are generally diagnosed by echocardiography in their late 60s, most often with no or minimal symptoms.³ Despite this benign presentation, degenerative mitral regurgitation causes mortality in excess of that expected for age and sex, with severe complications such as heart failure, atrial fibrillation, pulmonary hypertension, or left ventricular dysfunction.³ Excess mortality also affects patients without these complications, proportionately to the severity of the regurgitation⁴ and to the left atrial enlargement resulting from degenerative mitral regurgitation.⁵ Even patients with degenerative mitral regurgitation of moderate severity incur excess mortality with increasing regurgitation volume.⁴ Considerable progress has been made in quantifying these markers of outcome and in combining them in clinical scores to quantify the risks⁶ and to select patients for treatment. The standard of care is surgical repair, which has better outcomes than valve replacement.⁷ When performed early, ie, before occurrence of symptoms or ventricular dysfunction, life expectancy is restored,⁸ and outcomes are better than watchful waiting.⁹ Hence, degenerative mitral regurgitation is a unique disorder in which timely, appropriate surgical treatment returns most patients to their life-expectancy before the degenerative mitral regurgitation developed.¹⁰ This extraordinary outcome of degenerative mitral regurgitation treatment has led to guidelines recommending early surgery (a class II indication) if surgical reparability is highly probable and projected operative mortality less than 1%.¹¹

In view of such favorable results, almost all patients with degenerative mitral regurgitation should be evaluated for treatment. However, such is not the case. Profound undertreatment affects all patients, even those with degenerative mitral regurgitation, which is most treatable by valve repair.² In this issue of *JAMA*, 2 studies of critical importance are published on approaches to treatment of degenerative mitral regurgitation.

Akowuah and colleagues,¹² in a randomized clinical trial, examined the hypothesis that mitral repair for degenerative mitral regurgitation through minithoracotomy would provide su-

perior outcomes vs standard sternotomy. This UK-conducted trial measured the functional primary end point of the 36-Item Short Form Health Survey (36-SF) physical functioning scale 12 weeks after surgery in a pragmatic trial whereby allocation was expertise-based (surgeons used the approach they have mastered). Secondary end points were quality of life and quality of repair measured by residual mitral regurgitation at 12 weeks and 1 year. There were 330 patients randomized, 309 received surgery, and 294 provided data on the primary end point. The main conclusion was that minithoracotomy repair vs sternotomy repair failed to demonstrate superiority in the 12-week SF-36 physical functioning scale end point, in achieving repair without significant residual mitral regurgitation or in the safety end point, although both approaches provided excellent outcomes.

Makkar and colleagues¹³ examined the transcatheter valvular treatment registry to evaluate the mitral transcatheter edge-to-edge repair safety profile and outcomes in the treatment of degenerative mitral regurgitation. Entering data into the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapies Registry is mandatory for reimbursement; thus, the registry analysis provides insights into national routine practice and outcomes. The authors report on 19 088 patients with moderate or severe degenerative mitral regurgitation treated by transcatheter edge-to-edge repair, median age 82 years, who incurred a low 30-day mortality of 2.7% (vs expected 4.6%). Patients were categorized according to repair success, based on the residual mitral regurgitation and the mean diastolic mitral gradient. Categorization of success, defined as residual mitral regurgitation of moderate or less, was reported in 88.9% of patients. Patients who did not reach this definition of success incurred a doubling of mortality within the first year after the procedure. An alternate definition of mitral repair success—mild or less residual mitral regurgitation and diastolic gradient of 5 mm Hg or less—represented only 52% of treated patients, but these patients had a further decrease by one-third in 1-year mortality. Thus, this national registry demonstrated not only the low risk of transcatheter edge-to-edge repair but also the association of residual mitral regurgitation after the repair with poorer outcomes.

Together, these clinical trials provide valuable information on the management of degenerative mitral regurgitation, but both trials had limitations. The randomized clinical trial of Akowuah and colleagues selected the physical component of the quality-of-life assessment at 12 weeks as the primary end point, but an earlier end point might have shown benefit of the minithoracotomy. This possibility was reflected in data showing transient higher 6-week moderate or vigorous physical activity, better sleep efficiency, and earlier discharge among those who had undergone minithoracotomy.

The registry used by Makkar and colleagues is limited by incomplete data. Echocardiograms at 30 days were missing in an unspecified proportion and replaced by pre-discharge or even postprocedural echocardiograms, which may yield residual mitral regurgitation underestimation. More concerning is the missing 1-year outcome from 24% of patients. Although methodological and statistical approaches are used to mitigate these shortcomings, some results are of uncertain validity due to these data limitations.

Irrespective of these limitations, these 2 studies provide crucial information that must be integrated into patient management. Minithoracotomy mitral repair carried low risk and was highly effective compared with sternotomy. It can thus be applied successfully by surgeons who achieve the necessary expertise. Minithoracotomy may appeal to patients because the procedure is less disfiguring than sternotomy. The early (6-week) benefit, albeit small and transient, is important to patients.

Transcatheter edge-to-edge repair fulfills the promise of being low risk. It is a critical tool for reducing undertreatment and improving outcomes in patients affected by degenerative mitral regurgitation. The rate of transcatheter edge-to-edge repair success, which is crucial for survival improvement,¹⁴ is insufficient in routine practice, barely higher than 50% with the standard definition of mild or less residual mitral regurgitation with a mean gradient of 5 mm Hg or less. In choosing referral to surgical or interventional repair, this low global effective-

ness should raise caution for practitioners. It is also essential that a national effort of quality control be conducted, with preferential access to proficient centers, adequate training of operators, and consistent verification of success by standardized and verifiable imaging.

The association of higher residual mitral regurgitation with poorer clinical outcomes is not exclusively the hallmark of transcatheter edge-to-edge repair for degenerative mitral regurgitation; it is generalized and also observed after surgical repair for degenerative mitral regurgitation¹⁵ or transcatheter edge-to-edge repair for functional mitral regurgitation.¹⁶ Thus, the insistence on high-quality results, measured and verifiable, applies similarly to mitral surgery and transcatheter treatment.

Addressing undertreatment of degenerative mitral regurgitation will require concerted efforts enlightened by the results of the present important studies. Specialized heart teams have an important role in working with patients to identify the best approach to treatment. Future results of ongoing clinical trials (eg, the PRIMARY trial) comparing transcatheter edge-to-edge repair with surgical repair, will allow better definition of the appropriate use of these treatment modalities for each subset of patients. These procedures warrant formal guidance by updated guidelines,¹¹ underscoring the importance of early repair and the goal of achieving correction of degenerative mitral regurgitation as perfectly as possible, to provide patients with the optimal intervention and durable restoration of their life expectancy.

ARTICLE INFORMATION

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