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ORIGINAL RESEARCH

SURGERY

Population-Based Analysis of Late Outcomes of Mitral Valve Repair for Degenerative Mitral Valve Regurgitation

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ABSTRACT

BACKGROUND Population-based analyses may reduce uncertainty related to referral bias and/or incomplete follow-up.

OBJECTIVES This study analyzed long-term mortality and durability of mitral valve repair in a geographically defined population with clinical and echocardiographic follow-up.

METHODS We used the Rochester Epidemiology Project to identify 153 Olmsted County patients who underwent mitral valve repair for degenerative regurgitation from 1993 to 2018. Survival was compared to a gender- and age-matched U.S. population using the Kaplan-Meier method. Cumulative incidence and repeat operation rates were estimated, accounting for the completing risk of death.

RESULTS The median age of the cohort was 61 years (IQR: 53-73 years), 112 patients (73%) were men, and the left ventricular ejection fraction was 65% (IQR: 60%-69%). Triangular resection of the P2 scallop combined with a 63 mm posterior band annuloplasty was performed in 108 (71%) patients. The median clinical follow-up was 13.8 years (IQR: 11.5-16.2 years), while echocardiography follow-up was available in 152 (99%) patients at 6.6 years (IQR: 1.3-12.8 years). The probability of developing severe mitral regurgitation was 4% (IQR: 3%-7%) in 9 years. Cumulative incidence of repeat mitral valve operation was 8% ($n = 10$) at 20 years. The probability of developing severe tricuspid regurgitation was 5% (IQR: 4%-8%) in 10 years, but no subsequent tricuspid valve operation was performed. Survival following mitral valve repair was superior to an age- and sex-matched control population ($P < 0.001$).

CONCLUSIONS Mitral valve repair for degenerative disease is durable with exceedingly low repeat operation and mortality up to 20 years of follow-up. There was also a low rate of subsequent development of significant tricuspid valve regurgitation. (JACC Adv. 2024;3:101398) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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ABBREVIATIONS AND ACRONYMS

MR = mitral valve regurgitation

REP = Rochester Epidemiology Project

TR = tricuspid valve regurgitation

It is generally accepted that mitral valve repair is the preferred surgical approach for patients with degenerative severe mitral regurgitation.[1-3] Early correction of severe mitral regurgitation improves survival and may diminish late heart failure risk.[1-3] An increasing number of asymptomatic patients are undergoing mitral valve repair to prevent poor outcomes related to heart failure and low ejection fraction.[4,5] Hence, it is important that the valve repair remain durable for many years.

Most long-term studies on mitral valve repair have evaluated patient survival with variable attention to durability of the procedure.[6-8] A previous study from our institute demonstrated that the repeat operation rate following mitral valve repair was approximately 0.5% to 1% per year. But this overlooks the important outcome of nonoperated recurrent severe mitral regurgitation and its clinical implications.[9] This study analyzed the long-term outcomes of mitral valve repair in terms of mortality, morbidity, durability, and need for reoperation using the Rochester Epidemiology Project (REP) to achieve the complete objective assessment of mitral valve and patient outcomes.

METHODS

The Institutional Review Boards at the Mayo Clinic and REP each approved this study (IRB 17-010238 in December 14, 2017). As it is a low-risk study, the boards waived the need for written consent. According to Minnesota state law, patients who denied authorization for their data to be used for research were excluded from the study.

We used the REP and identified 153 Olmsted County patients operated with mitral valve repair from 1993 to 2018. No patients were excluded. The study's primary endpoint was mortality. Secondary endpoints included morbidity, repair durability, repeat operation, and postoperative atrial fibrillation.

REP is a unique record linkage system that has more than half a century of medical records linked in the United States.[10] REP provides record linkage for inpatient and outpatient health care providers and residency status to residents of Olmsted County, Minnesota, USA.[11] As REP has linked and archived the medical records of almost all residents of Olmsted County for more than 50 years with near-complete follow-up in scientific studies.[10]

One can argue that REP studies are based on isolated locoregional areas and can be a source of referral bias, but Hasan et al[12] from our institution concluded that usually local and regional patients presented with more comorbidities compared with the national referral group, and early outcomes were similar. Hence, REP provides a unique opportunity to study mitral valve regurgitation (MR) because it has a single echocardiographic laboratory, centralizing diagnoses facilities, large samples of patients with single-valve heart disorders, and health care providers linked through the REP.

SURGICAL APPROACH. Our group used a general standard approach to repair MR for degenerative valve disease. This included triangular resection of the prolapsing posterior segment and suture repair of the involved portion of the leaflet supplemented by a standard length (63-mm) flexible posterior band annuloplasty.[13] We defined a complex repair as one that involved intervention on the anterior leaflet of the mitral valve.

STATISTICAL ANALYSIS. Statistical analyses were carried out in SAS statistical software (version 9.4M6) and R statistical language (version 3.6.2). An alpha of 0.05 was used to determine statistical significance.

Categorical variables were expressed as number (percentage) and compared with Fisher's exact test, while continuous variables are reported as median (IQR) and assessed for differences with Kruskal-Wallis test.

The Kaplan-Meier method was used to estimate overall survival, and we compared it to the expected survival for a gender- and age-matched U.S. population. Cause-specific mortality rates were estimated with cumulative incidence and further repeat operation rates were estimated with cumulative incidence accounting for the completing risk of death.

Longitudinal trends in postoperative MR, tricuspid valve regurgitation (TR), and atrial fibrillation were estimated using all available measures over the follow-up period. Mitral regurgitation was analyzed with proportional odds logistic regression, and time was modeled using a logarithmic transformation. Tricuspid regurgitation was analyzed with proportional odds logistic regression, and time was modeled using a linear transformation. The expedience probabilities of regurgitation (ie, probability of being at or above each possible level of severity; eg, regurgitation grades classified as trivial or worse, mild or worse, moderate or worse, and severe) are reported. Atrial fibrillation was analyzed with a logistic regression model, and time was modeled as a logarithmic transformed restricted cubic spline function with 7 degrees of freedom. The atrial fibrillation model was adjusted for age, as older age is known to have an increased probability of atrial fibrillation. All

TABLE 1 Patient Baseline Characteristics (N = 153)

Age (y)	61 (53-73)
BMI (kg/m^2)	26 (24-28)
Creatinine (mg/dL)	1.0 (0.9-1.2)
Ejection fraction (%)	65 (60-69)
Female	41 (27)
Diabetes	5 (3)
Dialysis	0 (0)
Hypertension	61 (40)
Infectious endocarditis	8 (5)
Treated	7
Active	1
Chronic lung disease, severe	2 (1)
Immunosuppression	4 (3)
Peripheral vascular disease	5 (3)
Cerebrovascular disease	10 (7)
Cardiogenic shock	0 (0)
Previous pacemaker	0 (0)
Previous coronary artery bypass graft	6 (4)
Previous valve procedure	0 (0)
Atrial fibrillation	8 (5)
NYHA functional class	
I	50 (33)
II	55 (36)
III	45 (29)
IV	3 (2)
Resuscitation	0 (0)
Coronary artery disease	25 (16)
Number of diseased vessels	
None	128 (84)
1	17 (11)
2	1 (1)
3	7 (5)
Left main coronary artery stenosis >50%	0 (0)
Aortic valve stenosis	3 (2)
Mitral valve stenosis	0 (0)
Aortic valve insufficiency	
None	86 (56)
Trivial	40 (26)
Mild	23 (15)
Moderate	4 (3)
Mitral valve insufficiency	
Moderate	4 (3)
Severe	149 (97)
Tricuspid valve insufficiency	
None	37 (24)
Trivial	46 (30)
Mild	57 (37)
Moderate	13 (9)
Status	
Elective	149 (97)
Urgent	3 (2)
Emergent	1 (1)
Intra-aortic balloon pump, preoperative	2 (1)

Values are median (IQR) or n (%).
BMI = body mass index.

models were corrected for multiple observations per subject by utilizing the Huber-White standard errors.

RESULTS

Baseline patient characteristics included median age of 61 years (IQR: 53-73 years), male in 112 patients (73%), atrial fibrillation in 8 (5%), and ejection fraction of 65% (IQR: 60%-69%). Most patients were NYHA functional class I-II (n = 105, 69%) (Table 1).

We categorized mitral valve repair into 3 types: standard repair, isolated partial posterior band annuloplasty, or complex repair. A standard repair of triangular resection of the P2 scallop combined with a 63 mm partial posterior band annuloplasty was performed in 108 (71%) patients. Isolated partial posterior band annuloplasty was performed in 12 patients (8%). A complex repair was performed in 13 patients (22%). We compared the 3 types of valve repair in terms of baseline characteristics (Table 2).

The index mitral valve repair included closure of patent foramen ovale in 27 (17.6%) patients, closure of ostium of the left atrial appendage in 13 (8.5%), resection of vegetation in 3 (2%), and an Alfieri stitch in 2 (1.3%) (Table 3). In 1 patient, the ascending aorta was replaced due to intraoperative aortic dissection. The 63 mm band was used in 151 patients; ring exceptions included 1 patient who received an AnnuloFlex ring and 1 who received a complete ring annuloplasty.

Median aortic cross clamp time was 37 minutes (IQR: 27-53 minutes) and median cardiopulmonary bypass time was 50 minutes (IQR: 38-74 minutes). Intraoperative transesophageal echocardiography was done in all patients with a single exception in a patient for whom we could not place the echocardiography probe. A subsequent double sampling curve was done in that patient. Post-bypass transthoracic echocardiography showed no MR in 54 (35%) patients and trivial regurgitation in 86 (56%) patients (Table 3). Discharge postoperative MR was graded none-trivial in all patients. Complications were seen in 53 (35%) patients, including atrial fibrillation in 43 (28%) patients, and 2 patients developed neurological complications (Table 4).

Follow-up was complete in all patients at a median of 13.8 years (IQR: 11.5-16.2 years). Overall survival was 98% at 5 years, 85% at 10 years, and 68% at 15 years (Figure 1). The incidence of cardiac cause mortality was 0% (95% CI: 0%-0%), 3% (95% CI: 1%-8%), and 6% (95% CI: 3%-14%) at 5, 10, and 15 years postoperative, respectively.

TABLE 2 Patient Baseline Characteristics Stratified by Repair Type (N = 153)

	Repair Type			
	Standard Repair (n = 108)	Isolated Annuloplasty (n = 12)	Complex Repair (n = 33)	*P* Value
Age (y)	62 (55-73)	64 (47-77)	60 (49-72)	0.795[a]
BMI (kg/m^2)	26 (24-29)	25 (23-26)	24 (22-27)	0.025[a]
Creatinine (mg/dL)	1.0 (0.9-1.2)	1.0 (0.9-1.1)	1.0 (0.9-1.2)	0.652[a]
Ejection fraction (%)	65 (62-70)	61 (60-65)	64 (58-67)	0.029[a]
Female	23 (21)	6 (50)	12 (36)	0.036[b]
Diabetes	3 (3)	1 (8)	1 (3)	0.394[b]
Dialysis	0 (0)	0 (0)	0 (0)	
Hypertension	40 (37)	5 (42)	16 (49)	0.479[b]
Infectious endocarditis	5 (5)	0 (0)	3 (9)	0.451[b]
Treated	4	0	3	
Active	1	0	0	
Chronic lung disease, severe	1 (1)	0 (0)	1 (3)	0.389[b]
Immunosuppression	4 (4)	0 (0)	0 (0)	0.693[b]
Peripheral vascular disease	4 (4)	0 (0)	1 (3)	1.000[b]
Cerebrovascular disease	5 (5)	1 (8)	4 (12)	0.223[b]
Cardiogenic shock	0 (0)	0 (0)	0 (0)	
Previous pacemaker	0 (0)	0 (0)	0 (0)	
Previous coronary artery bypass graft	4 (4)	1 (8)	1 (3)	0.597[b]
Previous valve procedure	0 (0)	0 (0)	0 (0)	
Atrial fibrillation	6 (6)	1 (8)	1 (3)	0.688[b]
NYHA functional class				0.714[b]
I	34 (32)	6 (50)	10 (30)	
II	39 (36)	2 (17)	14 (42)	
III	32 (30)	4 (33)	9 (27)	
IV	3 (3)	0 (0)	0 (0)	
Resuscitation	0 (0)	0 (0)	0 (0)	
Coronary artery disease	19 (18)	3 (25)	3 (9)	0.336[b]
Number of diseased vessels				0.406[b]
0	89 (82)	9 (75)	30 (91)	
1	14 (13)	2 (17)	1 (3)	
2	1 (1)	0 (0)	0 (0)	
3	4 (4)	1 (8)	2 (6)	
Left main coronary artery stenosis >50%	0 (0)	0 (0)	0 (0)	
Aortic valve stenosis	2 (2)	1 (8)	0 (0)	0.325[b]
Mitral valve stenosis	0 (0)	0 (0)	0 (0)	
Aortic valve insufficiency				0.543[b]
None	61 (57)	7 (58)	18 (55)	
Trivial	31 (29)	2 (17)	7 (21)	
Mild	14 (13)	2 (17)	7 (21)	
Moderate	2 (2)	1 (8)	1 (3)	
Mitral valve insufficiency				0.094[b]
Moderate	1 (1)	1 (8)	2 (6)	
Severe	107 (99)	11 (92)	31 (94)	
Tricuspid valve insufficiency				0.817[b]
None	27 (25)	2 (17)	8 (24)	
Trivial	34 (32)	3 (25)	9 (27)	
Mild	40 (37)	5 (42)	12 (36)	
Moderate	7 (7)	2 (17)	4 (12)	
Status				1.000[b]
Elective	104 (96)	12 (100)	33 (100)	
Urgent	3 (3)	0 (0)	0 (0)	
Emergent	1 (1)	0 (0)	0 (0)	
Intra-aortic balloon pump, preoperative	2 (2)	0 (0)	0 (0)	1.000[b]

Values are median (IQR) or n (%). [a]Kruskal-Wallis *P* value. [b]Fisher exact *P* value.

TABLE 3 Operative Characteristics (N = 153)

Repair type	
Standard repair	108 (71)
Annuloplasty only	12 (8)
Complex repair	33 (22)
Other cardiac operation	41 (27)
Closure of PFO	27 (18)
Left atrial appendage ligation	13 (9)
Alfieri stitch	2 (1)
Excision of vegetation	3 (2)
Replacement of ascending aorta	1 (1)
Annuloplasty device	
63-mm band	151 (94)
Use of 34-mm band	1 (3)
Ring annuloplasty	1 (3)
Nonsternotomy approaches	
Right thoracotomy approach	2
Robotic	10
Completion intraoperative grade of mitral valve regurgitation	
None	54 (35)
Trivial	86 (56)
Mild	13 (9)
Cardiopulmonary bypass time (min)	50 (38-74)
Cross-clamp time (min)	37 (27-53)

Values are n (%), n, or median (IQR).
PFO = patent foramen ovale.

Median echocardiography follow-up was 6.6 years (IQR: 1.3-12.8 years). At 9-year follow-up, the estimated probability of severe MR was 4%[3-7] and of atrial fibrillation was 30% (IQR: 21%-40%) with median time to last electrocardiogram of 8.4 years. The probability of developing severe TR was 5%[4-8] in 10 years. No subsequent tricuspid valve operation was performed.

Repeat mitral valve operation was performed in 10 patients. Cumulative incidence of repeat mitral valve operation was 8.0% at 20-year follow-up (**Figure 2**). Two patients received mitral valve replacement at 1 and 10 years after the index operation. Operative findings included ring dehiscence and complex systolic anterior motion of mitral leaflet associated with mitral regurgitation, respectively. Eight patients underwent re-repair of the mitral valve. There were 2 patients who developed left ventricular outflow tract obstruction from systolic anterior motion of the anterior mitral valve leaflet during the index operation; both patients underwent segmental leaflet resection and posterior annuloplasty. Late repeat operation was done in 6 patients. One patient with leaflet perforation underwent repeat operation 6 years after the index operation; the valve was re-repaired with cleft closure and repeat posterior annuloplasty. The remaining 5 patients underwent

TABLE 4 Procedure-Related Complications (N = 153)

Any complication	53 (35)
Atrial fibrillation	43 (28)
Operative	6 (4)
Infection	4 (3)
Neurologic	2 (1)
Pulmonary	2 (1)
Renal	0 (0)
Vascular	1 (1)

Values are n (%).

repeat operation at 1, 6, 9, 12, and 16 years after the index operation; all the patients presented with chordal rupture, and all valves were repaired using neochords.

DISCUSSION

In this study, we found excellent long-term outcomes following mitral valve repair in a geographically isolated patient population (**Central Illustration**). The majority of patients were male (73%) with preserved ejection fraction (mean 65%) and belonged to NYHA functional class I-II (69%). Most patients received triangular resection of the P2 scallop combined with a 63 mm partial posterior band annuloplasty (71%). All patients had complete follow-up at a median of 13.8 years (IQR: 11.5-16.2 years). Overall survival was 98% at 5 years, 85% at 10 years, 68% at 15 years, and reoperation-free survival was 94% at 5 years, 76% at 10 years, and 60% at 15 years, respectively. The estimated probability of severe MR was 4% [3-7] at 9-year follow-up after mitral valve repair.

Many retrospective studies available in the literature have shown that mitral valve repair is better in terms of survival and outcomes as compared to mitral valve replacement.[6-9,14] But the durability of mitral valve repair and long-term outcomes have not been based on objective functional evaluation of the repaired valve. In this study, we used the REP to achieve complete clinical and echocardiography evaluation follow-up after mitral valve repair in a geographically isolated population. A recent long-term study with follow-up for more than 2 decades has not only encouraging outcomes but also limitations related to objective assessment of mitral valve due to different cardiologists and echocardiography laboratories.[9] To overcome the heterogeneity of the objective mitral valve evaluation, we chose the REP to give us a homogeneous echocardiographic laboratory with centralizing diagnoses and health care providers linked through REP.[10,11]

Most of the studies mainly mentioned the need for reoperation after mitral valve repair including the landmark study by Braunberger et al[15] on 20-year follow-up based on Carpentier's technique. Better outcomes can be achieved with high-volume centers of

FIGURE 1 Kaplan-Meier Survival Curve With Expected Survival Using Age- and Gender-Matched U.S. Population

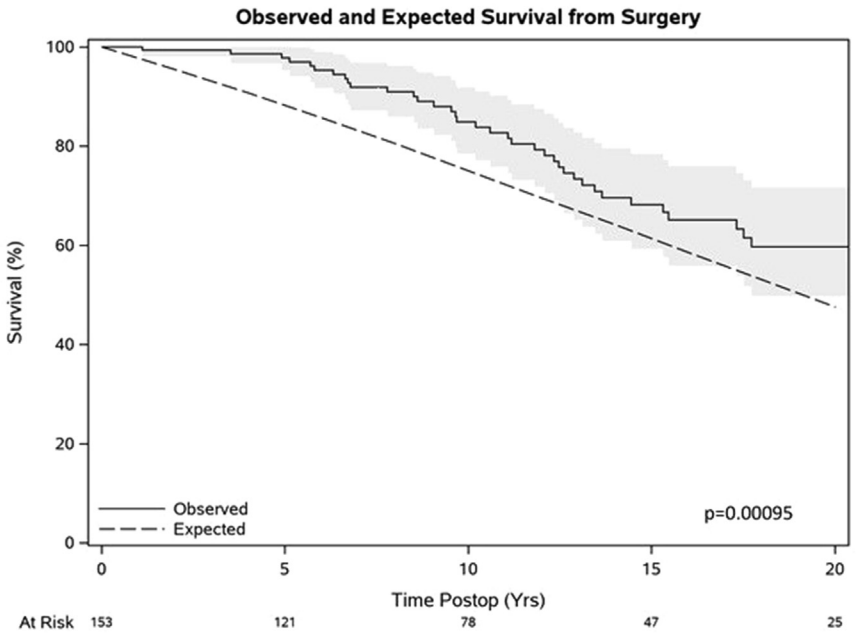
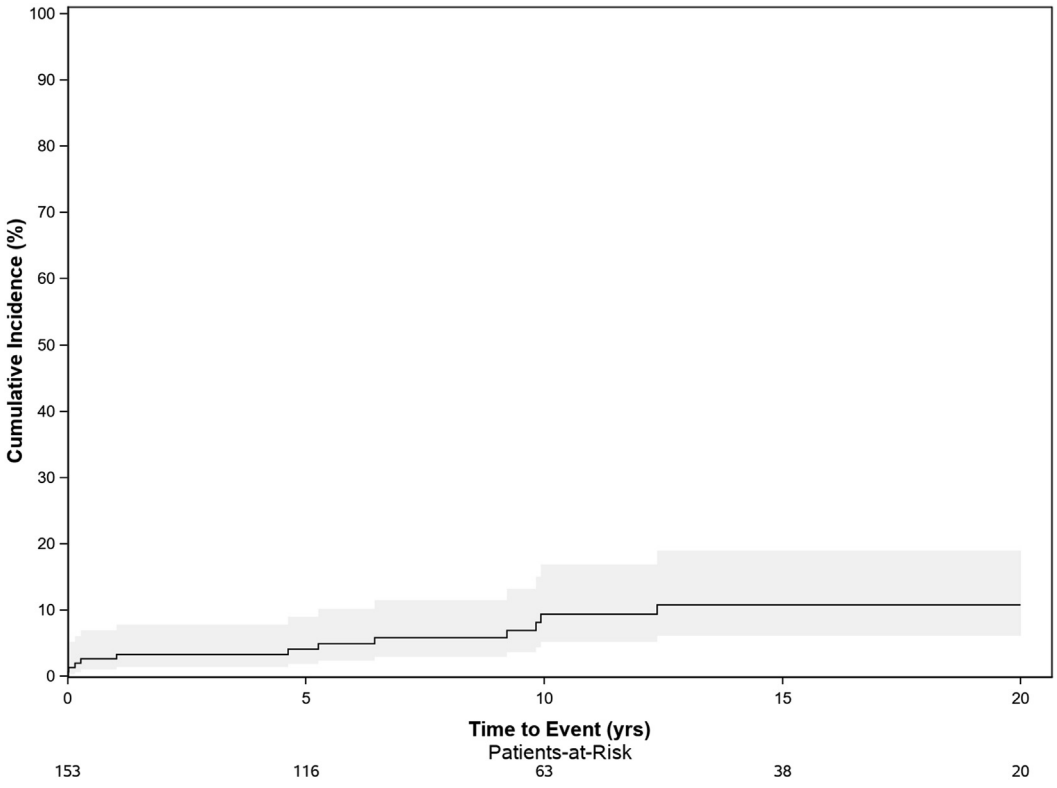


FIGURE 2 Cumulative Incidence of Repeat Mitral Valve Operation Adjusting for Death



excellence.[4] Our mitral valve repeat operation rate is also comparable with the long-term outcomes of 4.6% reported by David et al.[16] We chose to re-repair 8 out of 10 patients who needed reoperation, which is comparative to our institution experience with re-repair of the valve and good outcomes.[17] Our study estimated the probability of a patient having severe MR after mitral valve repair was 4% [3-7] at 9-year follow-up. Importantly, postdischarge echocardiography was available in 152 (99%) patients at a median of 6.6 years (IQR: 1.3-12.8 years). In a comparable study with 20-year follow-up from David et al, the probability of developing moderate or severe MR was 12.5%.[16] And in another long-term study, Javadikasgari et al[18] estimated severe MR in 6.2% of propensity-matched patients.

We also studied the issue of atrial fibrillation after mitral valve repair. New-onset atrial fibrillation after mitral valve repair has been reported in 28% to 32% of patients in recent studies.[16,18] In our study, we found that the probability of experiencing atrial fibrillation postoperatively was 30% (IQR: 21%-40%) in 9 years of follow-up with median time to last electrocardiogram of 8.4 years. We feel that this is comparable with the available literature. But our assumption is that our median age at operation was 61 years, which makes our population more prone to develop age-related sporadic atrial fibrillation.

We have also evaluated the probability of developing severe TR after mitral valve repair. The probability of developing severe TR was 5% [4-8] in 10 years, which is comparative to David et al,[16] who reported the probability of developing severe TR was 9%.[6-13] We had 57 (37.3%) patients with mild tricuspid regurgitation and 13 (8.5%) patients with moderate TR at the time of index mitral valve repair. They did not undergo any surgical intervention during the index mitral valve repair, and neither subsequent tricuspid valve operation was performed for recurrence or progression of regurgitation in our cohort. Our current paradigm is that of addressing at least moderate regurgitation or significant annular enlargement at the time of mitral valve repair in accordance with 2020 American College of Cardiology/American Heart Association guidelines.[19] We expect this will help in preventing future tricuspid regurgitation in patients with degenerative valve disease who are operated on for mitral valve repair.

CENTRAL ILLUSTRATION **Durability of Mitral Valve Repair for Degenerative Mitral Regurgitation**

Key Question

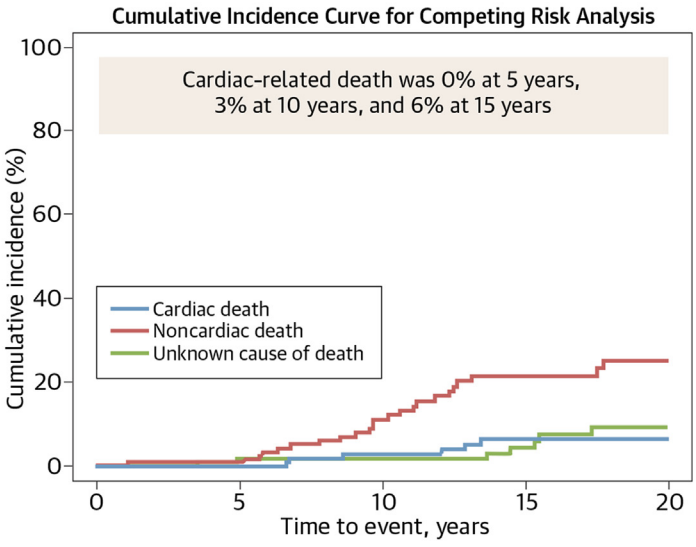
What is the durability of mitral valve repair after surgery?

Key Finding

- Probability of developing severe mitral valve regurgitation was 4% (IQR: 3%-7%) in 9 years.
- Cumulative incidence of repeat mitral valve operation was 8% (n = 10) at 20 years.

Conclusion

Mitral valve repair is very durable with low reoperation rates at up to 20 years of follow-up.



Time	Cardiac death	Noncardiac death	Unknown cause of death
5 years (95% CI)	0 (0.00-0.00)	0.01 (0.00-0.05)	0.02 (0.00-0.06)
10 years (95% CI)	0.03 (0.01-0.08)	0.11 (0.06-0.19)	0.02 (0.00-0.06)
15 years (95% CI)	0.06 (0.03-0.14)	0.21 (0.14-0.31)	0.04 (0.02-0.11)

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In this study, overall survival was 98% at 5 years, 85% at 10 years, and 68% at 15 years. This is comparable to the long-term survival of 62% after repair in 20 years in the propensity-matched model reported by Javadikasgari et al.[18] Our patient survival matches or is slightly better than expected in general population (Figure 1). The incidence of cardiac cause mortality was 0% (95% CI: 0%-0%), 3% (95% CI: 1%-8%), and 6% (95% CI: 3%-14%) at 5, 10, and 15 years postoperative, respectively, which is comparable with David et al, where cardiac cause mortality was >5% in 20 years.[16]

STUDY LIMITATIONS. This is a retrospective, single-center study. Although it has a limited number of patients, it has the benefit of complete follow-up.

CONCLUSIONS

Mitral valve repair for degenerative disease is durable with exceedingly low reoperation rate up to 20 years of follow-up and great long-term survival matching those of general population. There was also a low rate of subsequent development of significant TR.

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The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Population-based analyses may reduce uncertainty related to referral bias and/or incomplete follow-up related to mitral valve repair. Most long-term studies have evaluated clinical outcomes of mitral valve repair, but with limited objective assessment of mitral valve function.

TRANSLATIONAL OUTLOOK: This study analyzed long-term mortality and durability outcomes following mitral valve repair by using geographically defined population with detailed and up-to-date clinical and echocardiographic follow-up. We identified that MV repair for degenerative disease is durable with an exceedingly low reoperation rate up to 20 years of follow-up. The great long-term survival matches those of the general population. There was a low rate of subsequent development of significant TR. This is a retrospective, single-center study. Although it has a limited number of patients, it has complete follow-up.

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