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Rheumatic mitral valve repair or replacement in the valve-in-valve era

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Abstract

Objective: For degenerative mitral disease, repair is superior to replacement; however, the best operative strategy for rheumatic mitral disease remains unclear. We evaluated the association between decision-making in choosing repair versus replacement and outcomes across 2 decades of rheumatic mitral surgery.

Methods: Patients undergoing isolated, first-time rheumatic mitral surgery were identified. Era 1 (1997–2008) and Era 2 (2009–2018) were distinguished by intraoperative assessment of anterior leaflet mobility/calcification (Era 2) in deciding between mitral repair versus replacement. Primary outcome was a composite of death, reoperation, and severe valve dysfunction.

Results: Among 180 patients, age was 59 ± 14 years, and ejection fraction was $58\% \pm 10\%$. A higher proportion in Era 1 ($n = 56$) compared with Era 2 ($n = 124$) had preoperative atrial fibrillation (68% vs 46%; $P = .006$); the groups were otherwise similar. Primary indication was mitral stenosis in 69% (124 out of 180; pure = 35, mixed = 89) and did not differ by era ($P = .67$). During Era 1, 70% (39 out of 56) underwent repair, compared with 33% (41 out of 124) during Era 2 ($P < .001$). Freedom from death, reoperation, or severe valve dysfunction at 5 years was higher in Era 2 ($72\% \pm 9\%$) than Era 1 ($54\% \pm 13\%$; $P = .04$). Five-year survival was higher in Era 2 than Era 1, but did not differ between repair versus replacement. Five-year cumulative incidence of reoperation with death as a competing risk did not differ by era, but was higher after repair than replacement.

Conclusions: Careful assessment of anterior leaflet mobility/calcification to determine mitral repair or replacement was associated with improved outcomes. This decision-making strategy may alter the threshold for rheumatic mitral replacement in the current valve-in-valve era.

Graphical Abstract

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Overall survival after rheumatic mitral surgery by era.

CENTRAL MESSAGE

Anterior leaflet assessment to decide between rheumatic mitral repair or replacement could improve outcomes in the valve-in-valve era.

Keywords

rheumatic heart disease; mitral valve; mitral valve repair; mitral valve replacement

Rheumatic heart disease (RHD) is defined by long-term myocardial damage initiated by either a single severe episode or multiple recurrent episodes of acute rheumatic fever and causes significant morbidity and mortality worldwide.¹ RHD most commonly affects the mitral valve (MV) and manifests as mitral stenosis (MS) and/or mitral regurgitation (MR).² Surgical treatment of rheumatic MV disease is challenging, and the diversity of worldwide RHD populations necessitates a variety of operative approaches that may differ in the United States compared with developing countries.

Whereas degenerative mitral repair for severe MR has been proven superior to replacement,^{3–11} the optimal operative strategy for mitral RHD remains unclear. In developing countries, mitral RHD commonly develops in young patients, predominantly consists of MR rather than MS, and occurs more frequently than in the United States.^{12–16} As a result, these patients may benefit more from MV repair than replacement^{15–17} because MV replacement in pediatric populations confers diminished survival, valve-related complications, and potential valve mismatch.¹⁸ In addition, the predominant MR etiology (rather than MS), relatively early intervention in the RHD timeline, and variation in Carpentier MR types among developing world populations further make these rheumatic MVs more amenable to repair than replacement.^{19,20} The few prior series from the United States and Canada have found rheumatic MV repair to confer improved survival with fewer thromboembolic complications, but higher rate of reoperation.²¹ One analysis

reported that likelihood of reoperation for those surviving >20 years after rheumatic mitral repair approaches 100%.²² However, in contemporary practice, percutaneous valve-in-valve approaches to MV re-intervention have provided a previously unavailable option for treatment that may influence the decision to primarily repair or replace rheumatic MVs.

To highlight the considerations in choosing repair versus replacement for contemporary rheumatic MV surgery in a single US practice, we evaluated the association between decision making and outcomes across 2 decades. We hypothesized that implementing a system assessing anterior leaflet mobility and calcification during the second decade improved decision making and would be associated with improved outcomes for both MV repair and replacement.

PATIENTS AND METHODS

Data

Our data were obtained from the institutional component of the Society of Thoracic Surgeons Adult Cardiac Surgery Database and supplemented through chart review. These data were compiled and supplemented with clinical, echocardiographic, and reoperative data obtained during in-person or telephone follow-up. This study was deemed exempt from review by the University of Michigan Institutional Review Board (No. HUM00148119).

Patient Population

Our study population included adults undergoing first-time rheumatic MV surgery at a single academic center between September 1997 and March 2018 (N =180). Patients undergoing concomitant aortic or aortic valve surgery and those with RHD involving any valve other than the MV were excluded. Those undergoing concomitant coronary artery bypass grafting, antiarrhythmia procedures, and tricuspid repair/replacement were included. This population consisted solely of US-native RHD patients, rather than international referrals.

Patients were divided into Era 1 (1997–2008) and Era 2 (2009–2018). Eras were distinguished by implementation of echocardiographic and intraoperative assessment of anterior leaflet mobility and calcification during the second era in deciding whether to repair or replace, in consideration of future valve-in-valve options.

Rheumatic MV Decision Making

During Era 1 (1997–2008), we attempted universal valve repair, regardless of presentation and disease distribution (repair rate, 70% [n = 39 out of 56]). Era 2 (2009–2018) included an echocardiographic and intraoperative system of assessing the anterior leaflet to guide the decision of repair versus replacement (repair rate, 33% [41 out of 124]). Specifically, the threshold to replace valves with impaired mobility in the body of the anterior leaflet or with calcification was lower during Era 2. Repair was favored for valves with mobile anterior leaflets and at least some amount of translucency. Although the presence and degree of MR alone did not influence our decision to repair or replace, patients with an etiology of pure MR rather than MS tended to be earlier in disease progression, with less leaflet

calcification, more amenable to repair. The division into operative eras before and after 2009 is an approximation of when we modified our approach to rheumatic MV surgery.

The majority (141 out of 180; 78%) of operations were performed by a single surgeon, who also ensured adoption of this system of anterior leaflet assessment throughout the institution. The surgeon performing the majority of these rheumatic mitral repairs utilizes postoperative systemic anticoagulation for 1 month, whereas the other surgeons do not initiate anticoagulation therapy after repair, unless the patient has a concurrent indication.

Operative Techniques

Rheumatic MV repair techniques remained similar throughout the study period. The majority of patients undergoing repair received a Cosgrove-Edwards (Edwards Lifesciences, Irvine, Calif) annuloplasty ring (n = 67 out of 80; 84%). The standard repair technique included an overcommissurotomy extended to the annulus, extensive subvalvular debridement, papillary muscle splitting, lysing of secondary chords, and ring annuloplasty.

Rheumatic MV replacement included a preference toward increasing use of bioprosthetic valves during the second era due to increased consideration for potential reintervention through transcatheter valve-in-valve methods in case of valve failure. For patients undergoing concomitant antiarrhythmia procedure, a biatrial lesion set was performed utilizing both cryo and radiofrequency ablation and left atrial appendage ligation.

Outcomes

Primary outcome was a composite of death, reoperation, or severe valve dysfunction, defined as severe MR and/or severe MS (mean gradient >10 mm Hg) on latest follow-up echocardiogram. Patient deaths were confirmed by 1 of 4 methods: institution electronic health records, Society of Thoracic Surgeons database file, the National Death Index (utilized to confirm deceased but not to confirm alive), or through telephone calls to patients and their primary care physicians and/or cardiologists.

Secondary outcomes included mortality, severe valve dysfunction, MV repair, postoperative length of stay, and mitral-related reoperation. Intraoperative postprocedure mean gradient and residual MR were reported for 176 out of 180 (98%) patients as a categorical variable in MR grades 0 to 3 (none, mild, moderate, and severe). We also report presence of severe MS, grade of MR, and mean gradient at latest long-term echocardiographic follow-up in 143 out of 180 patients (79%).

Reoperation was defined as any subsequent intervention on the MV and was collected through chart review and telephone calls with patients or their other providers. Among the 131 patients alive at time of follow-up, the patient, primary care physician, and/or cardiologist were reached by telephone for 128 patients (98%), whereas institutional and regionally shared electronic medical record data was available for 100% of patients. Follow-up for patients who did not experience an event (death, reoperation, or severe valve dysfunction) was defined by date of surgery to latest clinical encounter and was complete.

Statistical Analysis

Bivariate comparisons utilized paired, 2-tailed t tests and χ^2 testing. Fisher exact test was used to compare categorical variables with frequencies <5 . Time-to-event survival analyses for the composite primary outcome and mortality were performed using the log-rank test and Kaplan-Meier estimates.

Cox proportional hazards modeling was performed to identify predictors of the composite outcome of death, reoperation, or severe valve dysfunction and reported in hazards ratios and 95% confidence intervals. Covariates included in the multivariable Cox model included those with baseline differences between eras on univariate analysis (eg, dyslipidemia and preoperative atrial fibrillation) as well as those suggested to be associated with our composite outcome (repair vs replacement, older age, and increased bypass time), based on prior studies and our own hypotheses. Both global and covariate-specific proportional hazards assumptions were evaluated using Schoenfeld residuals. Finally, we tested the interaction between repair/replacement and operative era within our Cox model. There were no missing observations in any of the Kaplan-Meier, competing risk, or Cox models.

Reoperation was assessed using two separate competing risks regressions to determine the cumulative incidence function of reoperation for each group (Era 1 vs Era 2 and repair vs replacement), with death as a competing risk. Gray's test was used to determine differences in cumulative incidence between groups. Statistical significance was defined as $P < .05$. All data construction and analyses were performed in Stata version 16.0 (StataCorp LLC, College Station, Tex).

RESULTS

Demographic Characteristics

Among 180 patients undergoing isolated rheumatic MV surgery, mean age was 59 ± 14 years (range, 20–85 years), 152 (84%) were women, and ejection fraction was $58\% \pm 10\%$. Approximately two-thirds of patients had New York Heart Association class III or IV heart failure ($n = 85$ out of 123; 69%), more than half had preoperative atrial fibrillation ($n = 95$; 53%) and dyslipidemia ($n = 96$; 53%), and 28% ($n = 50$) had undergone a previous cardiovascular intervention.

In total, 56 (31%) of patients underwent MV surgery during Era 1 and 124 (69%) during Era 2. A higher proportion of patients in Era 1 compared with Era 2 had preoperative atrial fibrillation (68% vs 46%; $P = .006$), whereas a lower proportion had dyslipidemia (20% vs 69%; $P < .001$). Age, sex, history of diabetes, treated endocarditis, liver disease, intravenous drug use, cerebrovascular disease, and prior cardiovascular interventions did not differ between eras. Primary indication for surgery was MS in 69% (124 out of 180) of patients (pure MS in 35, mixed etiology in 89) and pure MR in 56 (31%), with no difference in indications between the 2 eras ($P = .67$) (Table 1).

Surgical Technique

Overall, 44% (80 out of 180) of patients underwent MV repair during the study period, including 70% ($n = 39$) of patients during Era 1 versus 33% ($n = 41$) of patients during Era 2. The most common repair techniques used were subvalvular debridement (69 out of 80; 86%), commissurotomy (64 out of 80; 80%), and chordal splitting (55 out of 80; 69%), whereas the proportion of patients undergoing each technique did not differ between eras (Table 2). All but 1 mitral repair (79 out of 80; 99%) underwent annuloplasty with a median ring size of 26 mm (range, 23–32 mm). Among 100 (56%) patients who underwent replacement, 89 (89%) received a bioprosthetic (median size, 26 mm [range, 23–31 mm]) and 11 (11%) received a mechanical valve (median size, 29 mm [range, 25–31 mm]). One of these patients (out of 100; 1%) underwent initial repair that was converted to replacement in the operating room. Chordal continuity was maintained for every valve replacement through sparing of native chords, Gore-Tex (W. L. Gore and Associates, Newark, Del) chordal replacement, or both (Video 1).

Operative and Postoperative Outcomes

A higher proportion of patients in Era 1 had concomitant coronary artery bypass grafting (21% vs 10%; $P = .049$) and surgical ablation procedures (65% vs 46%; $P = .04$), while rates of concomitant tricuspid valve surgery did not differ between Era 1 and Era 2 (39% vs 37%; $P = .78$). Cardiopulmonary bypass (Era 1: 96 ± 30 vs Era 2: 104 ± 41 min; $P = .19$) and crossclamp (Era 1: 77 ± 30 vs Era 2: 80 ± 30 min; $P = .05$) times did not significantly differ by era, nor did postoperative length of stay. Mean postprocedure gradient was 3.7 ± 1.6 mm Hg and did not differ by era (Era 1: 3.9 ± 1.9 vs Era 2: 3.6 ± 1.4 mm Hg; $P = .35$), whereas 85% of patients (150 out of 176) had no residual MR and the remaining 26 patients had mild residual MR. Overall clinical follow-up was 100% complete at a mean 5.0 ± 3.9 years (range, 0–17.2 years), totaling 907 patient-years. Follow-up was longer in Era 1 (7.0 ± 5.1 years) than Era 2 (4.1 ± 2.8 years). Among those with long-term echocardiographic follow-up, 54% (77 out of 143) had no MR, while the distribution of MR grade and mean gradient did not differ between groups (Table 3).

Primary Outcome

Freedom from death, reoperation, or severe valve dysfunction was higher in Era 2 (5-year: 72% $\pm$ 9%) compared with Era 1 (5-year: 54% $\pm$ 13%) (Figure 1, A) ($P = .04$), but did not differ between patients undergoing repair (5-year: 56% $\pm$ 11%) or replacement (5-year: 76% $\pm$ 10%) (Figure 1, B) ($P = .19$). Operative era was the strongest independent predictor of the composite outcome of death, reoperation, or severe valve dysfunction (hazard ratio, 3.37; 95% confidence interval, 1.40–8.10; $P = .007$). Other predictors included undergoing repair and increased bypass time, whereas the interaction between era and repair was not statistically significant ($P = .09$) (Table 4).

Survival

Four (2%) in-hospital deaths occurred: 2 in each Era ($P = .59$), including 1 operative death during Era 1 (Table 3). Among 49 mortalities, death without additional information was confirmed for 23 (47%), whereas 1 had thoracic hemorrhage requiring placement on

extracorporeal membrane oxygenation, 1 underwent tricuspid valve reoperation complicated by acute aortic dissection, 1 had cervical cancer and acute renal failure, 1 developed sepsis and endocarditis, and the other 22 died from various medical causes. Five-year survival was higher in Era 2 ($88\% \pm 6\%$) compared with Era 1 ($64\% \pm 13\%$; $P = .002$) (Figure 2, A), but did not differ between patients undergoing repair ($78\% \pm 10\%$) or replacement ($81\% \pm 9\%$; $P = .70$) (Figure 2, C). When assessing repair and replacement separately, survival after repair during Era 2 was superior to Era 1 (log-rank $P = .004$), whereas survival after replacement during Era 2 was also higher compared to Era 1 (log-rank $P = .049$) (Figure E1).

Reoperation

A total of 18 (10%) patients underwent MV reoperation during the study period: 8 (14%) in Era 1 and 10 (8%) in Era 2 ($P = .20$), with no difference in the cumulative incidence of reoperation between Era 1 (5-year: 10.7%) and Era 2 (5-year: 10.5%), with death as a competing risk (Gray test $P = .96$) (Figure 2, B). All 18 patients who had a reoperation underwent replacement, including 1 transcatheter valve-in-valve procedure, and mean time to reoperation did not differ between eras (Era 1: 4.7 ± 3.8 years vs Era 2: 3.4 ± 2.2 years; $P = .37$). Characteristics of all 18 reoperations, including mechanisms of valve failure are listed in Table 5. Among the 18 ($n = 3$ primary replacements, $n = 15$ primary repairs), 5 of the repairs and 1 replacement had mild postprocedure residual MR and the remaining 12 patients had no residual MR after their initial operation. Thirty-day mortality after reoperation was 0% (0 out of 18), whereas 5 patients undergoing reoperation ultimately died at 3, 5, 24, 73, and 486 months after reoperation. Fifteen (19%) primary repairs underwent reoperation compared with 3 (3%) reoperations after replacement ($P = .001$). The cumulative incidence of reoperation with death as a competing risk at 5 years was 17.0% after repair and 3.7% after replacement (Gray's test $P = .014$) (Figure 2, D).

DISCUSSION

In this retrospective 2-decade series of rheumatic MV surgery in a US population, guided decision making during the second operative era influenced outcomes. Although only 33% of patients underwent repair during Era 2 compared with 70% in Era 1, estimated survival was superior in the second era, whereas cumulative incidence of reoperation did not differ. In addition, adjusted analysis showed that operative era (Era 1 vs Era 2) was the strongest independent predictor of the composite outcome of death, reoperation, or severe valve dysfunction.

Carpentier and colleagues^{19,20} have reported extensively on rheumatic MV repair with excellent outcomes, but in a different patient population compared with the current American study. The patients operated on by Carpentier and colleagues^{19,20} were primarily of North African descent and significantly younger with mean age in the 20s, faced challenges to lifelong anticoagulation, and predominantly presented with mitral insufficiency.¹⁹ In contrast, the mean age of this contemporary study's patients was 59 years, and 69% (124 out of 180) had a primary indication of MS (pure MS in 35 patients, mixed etiology MS/MR in 89 patients). Furthermore, the series by Carpentier and colleagues^{19,20}

included MR etiology of normal leaflet motion in 7% (type I), leaflet prolapse in 33% (type II), and combined prolapse and restriction in 24%, whereas all patients with MR in the current study had type IIIa characterized by leaflet restriction, as commonly seen in US RHD patients. Additional large series from the developed world have described reasonable outcomes after MV repair for RHD.^{21–23} One major series of Canadian patients reports superior survival after RHD repair compared with replacement, but also increased risk of reoperation,²¹ whereas a US series concluded patients living beyond 20 years after RHD repair approach a 100% likelihood of undergoing reoperation.²² In contrast, a Belgian series of similarly-aged patients reported an excellent $94\% \pm 5\%$ freedom from MV reoperation at 8 years,²³ but did not directly compare outcomes between repair and replacement. Our patients tended to be in the sixth or seventh decade of life (mean age, 59 ± 14 years), whereas series from developing nations are more often in the second, third, or fourth decades.^{13–16}

In contrast to prior series of degenerative and rheumatic MV repair, we did not find a long-term survival advantage for MV repair over replacement, but did find improved overall survival in the second decade of our operative experience, during which significantly more patients underwent MV replacement rather than repair (67% vs 33% ; $P < .001$). Because preoperative patient characteristics (Table 1), operative techniques (Table 2), and operative characteristics (Table 3) were similar between eras, the survival advantage of Era 2 may result from more appropriate decision making, with an avoidance of anterior leaflet body immobility and leaflet calcification in guiding whether to attempt repair.

In addition to anterior leaflet mobility and calcification, other investigators have also used anterior leaflet evaluation techniques in efforts to improve outcomes after rheumatic MV repair. A report from China cited anterior leaflet flexibility as important in assessing repairability, utilizing the bending angle of the anterior leaflet (eg, a surrogate for rigidity/flexibility) to predict repair suitability reasonably well in a Chinese population.²⁴ Indian researchers found anterior leaflet length 26 mm (indexed length, 18 mm/m²) to be associated with successful repair.²⁵ However, many of these assessments were performed in developing nations, in which pure MR and mixed lesions are more common than MS, which is more commonly seen in the older US population. To address patients with insufficient anterior leaflet length due to retraction or shortening, augmentation with a glutaraldehyde-treated, autologous pericardial patch has been utilized in the United States with promising short-term outcomes,^{26–28} but unclear long-term durability. Anterior leaflet augmentation continues to be performed, especially in younger patients who are more susceptible to the adverse effects of bioprosthetic or mechanical valve replacement. Although we have previously utilized patch augmentation, in our current practice we would more likely choose to replace these valves with significant calcium or impaired mobility, especially due to the availability of subsequent transcatheter valve-in-valve options if reoperation is required.

MV replacement for RHD is also routinely performed as the alternative to repair. Like repair, replacement approach and technique have evolved. Historically, bioprosthetic MV replacement has been avoided in younger patients due to the high likelihood of requiring reoperation after valve degeneration, with a recent analysis indicating expected bioprosthetic valve durability of approximately 14 years in patients younger than age 65

years.²⁹ The primary alternative to bioprotheses is mechanical MV replacement, which carries increased risk of thromboembolic complications and bleeding events from lifelong anticoagulation, but lower rate of reoperation and potentially improved survival compared with bioprosthetic valves in younger patients.^{30,31} However, contemporary practice now includes multiple entirely percutaneous, transcatheter, transseptal options for mitral valve-in-valve replacement, with excellent success rates and low rates of residual MR and need for reoperation.^{32–34} These techniques offer results comparable to surgical bioprosthetic replacement and can be performed substantially less invasively across all levels of patient risk. Valve-in-ring procedures have also been performed after failed mitral annuloplasty, but have demonstrated inferior outcomes to valve-in-valve technique,^{32,33} likely due to anatomical challenges inherent in placing a circular valve into a noncircular annuloplasty ring and left ventricular outflow tract obstruction. Within the context of the current valve-in-valve era, our data indicate that many patients (eg, those with stiff, calcified anterior leaflets) may benefit from consideration of replacement over repair. Similar to most valve referral centers, we utilize a preponderance of bioprosthetic rather than mechanical valves, and this percentage went up to 92% bioprosthetic during the second era due to increased awareness of potential valve-in-valve options.

This study has several limitations. First, our analysis is retrospective and performed at a single center. However, our series is among the largest available in the United States and comparing different worldwide populations would be inappropriate due to the heterogeneity of rheumatic populations. Second, although we do report postprocedure and/or long-term echocardiographic follow-up for 100% of patients, we do not have universal long-term echocardiographic follow-up for all patients. In addition, we include long-term clinical follow-up and complete survival data, obtained through multiple methods, including chart review and telephone calls to patients, primary care physicians, and cardiologists. Nonetheless, for most patients we cannot be completely sure of specific medical or nonmedical causes of death. Third, our study period spans 2 decades and due to the sequential study design, follow-up time is longer during Era 1 than Era 2. However, we have attempted to mitigate these differences by performing standard time-to-event analyses, including Kaplan-Meier, competing risks, and Cox modeling. Fourth, medical care has undoubtedly improved over the course of the study which is likely a source of unmeasured confounding. Although we attempted to adjust with multivariable modeling and found operative era to be the strongest independent risk factor for the composite outcome of death, reoperation, or severe valve dysfunction, the interaction between operative era and choice of repair versus replacement within the model was not statistically significant ($P = .09$), suggesting the difference in outcomes between eras could also be due to temporal changes rather than choice of surgical strategy. Nonetheless, we find that the striking decrease in MV repair rate from 70% to 33% from Era 1 to Era 2 among patients with comparable risk profiles, operated on by the same surgeons within a center with a degenerative MV repair rate >99%,³⁵ to be extremely compelling. These findings and implications have been summarized in our visual abstract (Figure 3).

CONCLUSIONS

A strategy of careful assessment of anterior leaflet mobility and calcification to help guide MV repair versus replacement decision making appeared to be associated with improved outcomes among patients with rheumatic heart disease in the United States. This decision-making strategy may lower the threshold for performing appropriate MV replacement in patients with rheumatic heart disease in the current valve-in-valve era.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://aats.blob.core.windows.net/media/19%20AM/Saturday_May4/206BD/206BD/S29%20-%20Global%20challenges%20rheumatic%20valve%20disease/S29_6_webcast_024303023.mp4.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Discussion

Presenter: Dr Alexander A. Brescia

Dr Vinay Badhwar (*Morgantown, WV*). First of all, congratulations, Dr Brescia, for an elegant presentation as a University of Michigan resident. I received the manuscript in advance; thank you. I will attempt to summarize this in the following statement that I would like you to imagine in bold letters. The take-home observations are: calcified

anterior leaflets-bad! and, age-related severely thickened subvalvular apparatus-bad! Is that an appropriate summary?

Dr Alexander A. Brescia (*Ann Arbor, Mich*). Yes sir.

Dr Badhwar. This is really a retrospective analysis, and not really being an intent-to-treat analysis, which is really the appropriate way to discern appropriate decision making. Maybe that's the real message here-that you've made an intention to treat in a separate way and move forward. With that, I'm going to ask you a few quick questions. Number 1, the sample size appears pretty low for a 20-year experience in a really experienced mitral center. Before we conclude that this is the population in Michigan, where rheumatic disease is low, how did you actually identify over a 20-year span in the database, knowing full well that the Society of Thoracic Surgeons database was not fully developed 20 years ago to actually define etiology-so how did you define etiology in this dataset, and did you actually capture all of the patients?

Dr Brescia. Thank you, Dr Badhwar, for your comments and question. We started out casting a very wide net of essentially every rheumatic mitral repair, and that's through the Society of Thoracic Surgeons database, keyword searches, and through paper copies of operative reports that we go over for all of our retrospective analyses. I think the key point that provides a reason for why it's a little lower than you'd expect is that we really wanted to focus on pure mitral rheumatic disease. These aren't patients with aortic rheumatic disease or tricuspid rheumatic disease. If we include all mitral rheumatic repairs, it would be many more, but we wanted to narrow it down to mitral only for the rheumatic disease distribution.

Dr Badhwar. The second question pertains to reoperation. The average ring size in the manuscript was 26. Because this is an article about the 80 patients who had repair and the 14% that failed, how did you define the mechanism of reoperation failure in those 80 patients? Was the mechanism stenosis? Or were there other etiologies?

Dr Brescia. We had a total of 14 reoperations, and 11 of those were in the repair group. It was split pretty evenly into thirds. A third of the failures were due to mitral stenosis, a third were mitral regurgitation, and a third were a mixed etiology. One point about the ring size, which is a great point you brought up, because it does seem pretty small. One lesson that Dr Bolling reiterated to me since a lot of these go back to the 1990s, some of these rings are Stimulus rings (Medtronic, Minneapolis, Minn), which I was taught is actually labeled smaller. A different ring of the same size might be up to a few sizes bigger, so it's not actually a median of a 26 if it is compared with other rings.

Dr Badhwar. You have presented all of these excellent techniques. This was a retrospective snapshot of the entire database. You decided to dichotomize by era. However, if you were to dichotomize by age; that is, the younger patients who had mitral valve repair versus the older patients, what do you think the results would show?

Dr Brescia. That is a great question and a great point. We did take a look at that and the reason it was not presented is that it did not change the overall outcome. Something that we really want to stress is that this is an American rheumatic heart disease population, which is very different than in other parts of the world. Out of our 180 patients, only 41 were aged 50 years or younger. Of those 41, for overall survival, there was no difference whatsoever between repair and replacement. There was still a survival difference by era, just as with the overall analysis.

Dr Badhwar. Last question, based on that last statement: We want to make sure we don't overinterpret the reading of the conclusions here. We know, through the literature, that mitral repair long-term is better than mitral valve replacement, and I think everyone agrees on that. Have you had a chance to look at, or could you look at those who had successful primary mitral valve repair and look at their long-term survival compared with primary replacement?

Dr Brescia. That's a great point and is definitely something we could look at. We agree that a durable, successful mitral repair is the best outcome. The trouble with that now is that it seems like betting on a race when you know the outcome. You could hand-pick all of the successful repairs. I think the point is very well taken that that is our goal.

Abbreviations and Acronyms

CPB	cardiopulmonary bypass
KM	Kaplan-Meier
LOS	length of stay
MR	mitral regurgitation
MS	mitral stenosis
MV	mitral valve
RHD	rheumatic heart disease
TV	tricuspid valve

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PERSPECTIVE

A strategy of careful assessment of anterior leaflet mobility and calcification to help guide decision making was associated with improved outcomes among similar American patients with rheumatic heart disease. Adhering to this decision-making strategy may lower the threshold for performing mitral valve replacement in appropriate patients during the current valve-in-valve era.

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FIGURE 1.

Cumulative freedom from death, reoperation, and severe valve dysfunction at latest follow-up echocardiogram by Kaplan-Meier estimates. A, Era 1 versus Era 2 (log-rank $P = .04$). B, Mitral valve repair versus replacement (log-rank $P = .19$). *CI*, Confidence interval.

FIGURE 2.

Kaplan-Meier overall survival estimates and cumulative incidence of mitral valve reoperation with death as a competing risk after rheumatic mitral valve surgery. A, Overall survival Era 1 versus Era 2 (log-rank $P = .002$). B, Cumulative incidence of reoperation Era 1 versus Era 2 (Gray test $P = .96$). C, Overall survival mitral repair versus replacement (log-rank $P = .70$). D, Cumulative incidence of reoperation mitral repair versus replacement (Gray test $P = .014$). *CI*, Confidence interval; *SHR*, subhazard ratio.

180 patients undergoing isolated, first-time rheumatic mitral surgery (1997-2018) divided into eras by use of intraoperative anterior leaflet assessment to determine repair vs. replacement

FIGURE 3.

Graphical abstract of manuscript methods, results, and implications, including comparison of repair rate, overall survival, and cumulative incidence of reoperation between operative eras. *reop*, Reoperation; *MS*, mitral stenosis; *MR*, mitral regurgitation.

VIDEO 1.

Chordal-sparing rheumatic mitral valve replacement with a 27-mm Carpentier-Edwards Perimount Magna Mitral Ease valve (Edwards Lifesciences, Irvine, Calif). Video available at: [https://www.jtcvs.org/article/S0022-5223\(20\)31090-4/fulltext](https://www.jtcvs.org/article/S0022-5223(20)31090-4/fulltext).

TABLE 1.

Patient characteristics by era

Variable	Total (n = 180)	Era 1 (1997–2008) (n = 56)	Era 2 (2009–2018) (n = 124)	P value
Age (y)	59 ± 14	59 ± 11	60 ± 15	.67
Female sex	152 (84)	48 (86)	104 (84)	.75
Diabetes	38 (21)	13 (23)	25 (20)	.64
Dyslipidemia	96 (53)	11 (20)	85 (69)	<.001
Preoperative ejection fraction (%)	58 ± 10	55 ± 11	59 ± 9	.01
History of endocarditis	9(5)	5(9)	4(3)	.14
Liver disease	3(2)	0(0)	3(2)	.55
Intravenous drug abuse	6(3)	0(0)	6(5)	.18
Cerebrovascular disease	39 (22)	11 (20)	28 (23)	.66
Prior CV intervention	50 (28)	14 (25)	36 (29)	.58
Atrial fibrillation	95 (53)	38 (68)	57 (46)	.006
NYHA functional class [*]				
I	7(6)	1(2)	6(8)	
II	31 (25)	17 (35)	14 (19)	.11
III	71 (58)	24 (50)	47 (63)	
IV	14(11)	6(13)	8(11)	
Surgical indication				
Mitral regurgitation	56 (31)	20 (36)	36 (29)	
Mitral stenosis	35 (19)	10(18)	25 (20)	.67
Mixed etiology	89 (49)	26 (46)	63 (51)	

Values are presented as n (%) or mean ± standard deviation. Bold *P* values indicate statistical significance. CV, Cardiovascular; NYHA, New York Heart Association.

^{*}Total n = 123.

TABLE 2.

Operative techniques by era. More than 1 mitral valve repair technique may have been used per patient

Variable	Total (n = 180)	Era 1 (1997–2008) (n = 56)	Era 2 (2009–2018) (n = 124)	P value
Mitral valve repair	80 (44)	39 (70)	41 (33)	< .001
Subvalvular debridement	69 (86)	36 (92)	33 (80)	.13
Commissurotomy	64 (80)	33 (85)	31 (76)	.31
Chordal splitting	55 (69)	26 (67)	29 (71)	.70
Leaflet/commissure plasty	10 (13)	2 (5)	8 (20)	.09
Decalcification	7 (9)	1 (3)	6 (15)	.11
Resection	5 (6)	3 (8)	2 (5)	.67
Patch augmentation	1 (1)	0	1 (2)	1.00
Additional techniques	4 (5)	1 (3)	3 (7)	.62
Annuloplasty ring size (mm)	26 (23–32)	26 (26–30)	28 (23–32)	.002
Mitral valve replacement	100 (56)	17 (30)	83 (67)	< .001
Bioprosthetic	89 (89)	13 (76)	76 (92)	
Mechanical	11 (11)	4 (24)	7 (8)	.09

Values are presented as n (%), mean ± standard deviation, or median (range). Bold *P* values indicate statistical significance.

TABLE 3.

Operative and postoperative outcomes by era

Variable	Total (n = 180)	Era 1 (1997–2008) (n = 56)	Era 2 (2009–2018) (n = 124)	P value
Concomitant procedures				
CABG	25 (14)	12 (21)	13 (10)	.049
TV repair/replacement	68 (38)	22 (39)	46 (37)	.78
Maze	93 (53)	35 (65)	57 (46)	.04
CPB time (min)	102 ± 38	96 ± 30	104 ± 41	.19
Crossclamp time (min)	77 ± 30	70 ± 22	80 ± 33	.05
MR grade on postprocedure echocardiogram				
None	150 (83)	47 (84)	103 (83)	
Mild	26 (14)	7 (13)	19 (15)	
Moderate	0	0	0	.64
Severe	0	0	0	
Missing	4 (2)	2 (4)	2 (2)	
Postprocedure mitral gradient (mm Hg) *	3.7 ± 1.6	3.9 ± 1.9	3.6 ± 1.4	.35
MR grade at latest echocardiographic follow-up				
None	77 (43)	19 (34)	58 (47)	
Mild	38 (21)	15 (27)	23 (19)	
Moderate	17 (9)	8 (14)	9 (7)	.30
Severe	11 (6)	3 (5)	8 (6)	
Missing	37 (21)	11 (20)	26 (21)	
Mitral gradient at latest follow-up (mm Hg) †	6.8 ± 3.9	6.8 ± 3.7	6.7 ± 4.1	.88
Severe MS [‡] at latest echocardiographic follow-up [§]	19 (13)	8 (18)	11 (11)	.28
Postoperative LOS (d)	8.9 ± 8.6	9.3 ± 12.2	8.8 ± 6.3	.68
In-hospital mortality	4 (2)	2 (4)	2 (2)	.59
Follow-up (y)	5.0 ± 3.9	7.0 ± 5.1	4.1 ± 2.8	<.001

Values are presented as n (%) or mean ± standard deviation. Bold P values indicate statistical significance. CABG, Coronary artery bypass grafting; TV, tricuspid valve; CPB, cardiopulmonary bypass; MR, mitral regurgitation; MS, mitral stenosis; LOS, length of stay.

* n = 169 out of 180; 94%.

† n = 136 out of 180; 76%.

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*Gradient >10 mm Hg.
§n = 143 out of 180; 79%.

TABLE 4.

Cox proportional hazards regression for independent predictors of the composite primary outcome of death, reoperation, or severe valve dysfunction, defined as severe mitral regurgitation or severe mitral stenosis (mean gradient >10 mm Hg) on latest follow-up echocardiogram. The interaction between operative era and mitral repair within the Cox model was not statistically significant ($P = .09$)

Variable	Hazard ratio (95% confidence interval)	<i>P</i> value
Era 1 vs Era 2	3.37 (1.40–8.10)	.007
Mitral repair vs replacement	3.21 (1.46–7.03)	.004
Age per 10 y	1.23 (0.99–1.52)	.07
Cardiopulmonary bypass time per 20 min	1.34 (1.17–1.54)	<.001
Preoperative atrial fibrillation	0.48 (0.28–0.83)	.008
Dyslipidemia	1.05 (0.58–1.92)	.87

Bold *P* values indicate statistical significance.

TABLE 5.

Mechanisms of failure and reoperative details for all valve reoperations (n = 18)

Patient	Era	Initial operation	Postprocedure residual MR	Time to reoperation (y)	Mechanism of failure	Reoperation performed
1	1	Bioprosthetic replacement	None	10.1	Bioprosthetic degeneration and MS	Transcatheter transapical valve-in-valve
2	1	Repair	None	4.4	Unknown	Surgical MVR
3	1	Repair	None	4.7	MR and MS	Surgical MVR
4	1	Repair	None	6.5	MS	Surgical MVR
5	1	Repair	None	0.6	MR and MS	Surgical MVR
6	1	Repair	None	0.8	MR and MS	Surgical MVR
7	1	Repair	None	9.8	Unknown	Surgical MVR
8	1	Repair	None	1.2	Unknown	Surgical MVR
9	2	Repair	Mild	0.9	MS	Surgical MVR
10	2	Bioprosthetic replacement	None	7.9	Early bioprosthetic structural degeneration; LVOT obstruction from prosthetic MV struts	Surgical mechanical MVR
11	2	Repair	Mild	3.8	MR and MS	Surgical mechanical MVR
12	2	Repair	None	0.2	Severe MR, severe MS, and hemolytic anemia	Surgical MVR
13	2	Repair	None	4.7	MR	Surgical MVR
14	2	Repair	None	3.6	MR & MS	Surgical MVR
15	2	Repair	Mild	1.3	MR	Surgical MVR
16	2	Repair	Mild	4.9	MR	Surgical MVR
17	2	Bioprosthetic replacement	Mild	3.2	MR and MS	Surgical mechanical MVR
18	2	Repair	Mild	3.7	MR – Aborted MitraClip prior to surgical reoperation	Surgical MVR

MR, Mitral regurgitation; MS, mitral stenosis; MVR, mitral valve replacement; LVOT, left ventricular outflow tract; MV, mitral valve.