Influence of Patient Age on Procedural Selection in Mitral Valve Surgery

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Background. **Previous studies suggest that mitral valve replacement is comparable to repair in the elderly, and a national trend exists toward tissue valves. However, few direct comparison data are available, and this study evaluated the effects of patient age on risk-adjusted survival after mitral procedures.**

Methods. **From 1986 to 2006, 2,064 patients underwent isolated primary mitral operations (±CABG). Maximal follow-up was 20 years with a median of 5 years. Valve disease etiology was the following: degenerative, 864; ischemic, 450; rheumatic, 416; endocarditis, 98; and "other," 236. Overall, 58% had repair and 39% had concomitant coronary artery bypass grafting. Survival differences were evaluated with a Cox proportional hazards model that included baseline characteristics, valve disease etiology, and choice of repair versus replacement with tissue or mechanical valves.**

Results. **Baseline risk profiles generally were better for mechanical valves, and age was the most significant multivariable predictor of late mortality [hazard ratio = 1.4 per 10-year increment, Wald $\chi^2 = 32.7$, $p < 0.0001$]. As compared with repair, risk-adjusted survival was inferior with either tissue valves [1.8, 27.6, <0.0001] or mechanical valves [1.3, 8.1, 0.0044], and no treatment interaction was observed with age ($p = 0.18$). At no patient age did tissue valves achieve equivalent survival to either repair or mechanical valves.**

Conclusions. **Mitral repair is associated with better survival than valve replacement across the spectrum of patient age. If replacement is required, mechanical valves achieve better outcomes, even in the elderly. These data suggest that tissue valves should be reserved only for patients with absolute contraindications to anticoagulation who are not amenable to repair.**

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Improvements in mitral repair have increased the number of valves amenable to autologous reconstruction, as compared with prosthetic valve replacement [1–22]. Nationally, repair rates for isolated mitral procedures have increased to almost 70% in the most recent National sample [23]. While newer analyses suggest that patients with ischemic or degenerative mitral regurgitation experience better survival after valve repair [24, 25], techniques and applicability of mitral repair, as well as the most effective approach for older patients, are controversial [5, 6, 24–35]. National data indicate that elderly patients more frequently receive tissue mitral valve replacement, and this trend seems to be increasing [23]. Unfortunately, few direct multivariable comparisons are available to document outcomes for mitral repair versus replacement in the elderly, as well as for contemporary bioprosthetic versus mechanical valves. The purpose of this study was to examine the influence of patient age on survival after mitral valve repair, and to compare repair survival with that observed with both mechanical and tissue valves.

Material and Methods

This study was performed with approval from the Duke Institutional Review Board and under a waiver of informed consent, but new late patient contact was not allowed. In the Duke Databank for Cardiovascular Disease, 2,064 consecutive patients with isolated mitral disease who underwent cardiac surgery from January 1, 1986 through December 31, 2006 were reviewed. Patients having concomitant coronary artery bypass grafting (CABG) or electrophysiologic procedures were included, but other major cardiac procedures were excluded (eg, aortic valves, tricuspid valves, postinfarct ventricular septal defects, ventricular aneurysm repair). While patients with previous CABG were included, those with previous mitral replacement were excluded, because they were not candidates for either procedure.

Preoperative baseline and intraoperative characteristics for all patients were recorded prospectively over the entire 20 years, with consistent variables throughout. Late outcome data were collected prospectively on pa-

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tients with significant concomitant coronary disease per Duke Databank protocols. A National Death Index search was conducted through 2006 to acquire mortality results for remaining patients. Patients were divided into two groups; the first was patients having mitral repair (n = 1,188), and the second was patients having prosthetic valve replacement (n = 876) with mechanical valves (n = 680 [78%]; predominantly St. Jude valves [St. Jude Medical, Inc, St. Paul, MN] or tissue valves (n = 196 [22%]; predominantly Carpentier Edwards [Edwards Lifesciences, Irvine, CA] porcine or pericardial bioprostheses). Operative notes of all 2,064 patients were audited to ensure proper categorization. Most repairs had full ring annuloplasty (usually Edwards Physio, Carpentier classic, or Séguin [St Jude Medical] rings) along with appropriate leaflet or chordal procedures. Innumerable different repair combinations were used, depending on surgeon preference, anatomy encountered, and evolution of techniques over time, and 18 different surgeons contributed patients. Partial or total chordal sparing valve replacement was performed frequently, but this variable was not documented well and was not assessed in the analysis. Follow-up for survival was 92% complete and only all-cause mortality was available consistently for analysis.

Baseline characteristics and clinical event rates were described using medians with 25th and 75th percentiles for continuous variables and frequencies and proportions for categoric variables. Descriptive data were compared using the Wilcoxon rank-sum test for continuous and ordinal variables, and a Pearson χ^2 or Fisher's exact test for categoric variables. Three propensity models were created to determine the propensity for repair versus mechanical replacement, repair versus tissue replacement, and mechanical versus tissue replacement [36]. A multivariable Cox proportional hazards regression model was employed with an analysis strategy that adjusted for the impact of baseline characteristics on survival [37]. To develop the risk-adjustment model, a pool of all known clinical covariates that have been shown to be important in previous analyses was developed [25]. Variables proving significant by stepwise univariable-multivariable procedures were included in the final Cox model and also used for risk adjustment. Propensity scores also were included in the Cox model, as were the valve repair-replacement variables of interest. Continuous and ordinal variables were tested for linearity over the log hazard and transformed as necessary. Adjusted survival estimates for each group were calculated by applying their baseline hazard functions, along with parameter estimates, to all patients in the entire cohort and then averaging over all patients at each time point. Statistical analyses were performed using SAS version 8.2 (SAS Institute, Cary, NC), and a p value of 0.05 or less was considered significant.

Results

Baseline characteristics of the entire population are detailed in Table 1. Among the groups, tissue replacement patients were significantly older with less elective surgery. Mechanical replacement patients were younger, and repair patients were more predominantly male, had a higher incidence of concurrent 3-vessel disease and CABG, and lower ejection fractions. Procedural incidence over time is shown in Figure 1.

In an analysis subset 65 years of age or greater (n = 998 [data table available at jsrmd.com/table_elderly.pdf and jsrmd.com/90_day_coefficients.pdf]), baseline characteristics were more similar, but mitral repair patients (n = 563) still had more 3-vessel disease, CABG, nonelective presentation, and lower ejection fractions. Mitral replacement patients (mechanical, n = 293; tissue, n = 142) were more predominantly female. Regardless of age and operative procedure, the most common etiology of mitral valve disease was degenerative followed by ischemic (Table 2). Rheumatic patients comprised 20% of the population and more frequently underwent mitral replacement (88%), while ischemic and degenerative usually had repair.

Raw unadjusted 30-day mortality was 3.5% for mitral repair, 5.9% for mechanical replacement, and 8.2% for tissue replacement. Long-term unadjusted Kaplan-Meier survival was not significantly different between mitral valve repair and mechanical mitral valve replacement (Fig 2), and both groups had significantly better raw survival as compared with tissue valve replacement. This finding was preserved in the unadjusted Kaplan-Meier survival comparison of patients 65 years or greater (Fig 3).

Final Cox model coefficients are shown in Table 2, and after adjusting for differences in baseline characteristics, risk-adjusted survival estimates are displayed in Figure 4. Adjusted curves demonstrated better survival with mitral repair, and even after adjustment for adverse risk profiles, tissue replacement survival was still inferior. No treatment interaction was observed between procedural choice and age in the Cox model analysis ($p = 0.1781$). In other words, the hazard associated with each treatment was the same across all ages.

Another Cox model was generated for patients surviving 90 days after surgery (coefficients at jsrmd.com/90_day_coefficients.pdf) in order to compare relative late mortalities. Conditional adjusted survival estimates demonstrated persistent superiority of repair and mechanical replacement as compared with tissue valve replacement (Fig 5). Finally, adjusted survival probabilities at 10 years versus age at valve implant are shown in Figure 6. Regardless of patient age, mitral repair was associated with better risk-adjusted 10-year survival compared with either mechanical or tissues. At no age did tissue valve replacement achieve equivalent results to either of the other two procedures.

Comment

An important issue in this analysis is the validity of comparing procedures that may not have been equally applicable to all patients or all mitral disease pathologies. This is an appropriate criticism, especially for the years included in this study. However, in the more recent era,