Real-world outcomes of surgery for native mitral valve endocarditis

Nana Toyoda, MD, PhD,[a] Shinobu Itagaki, MD, MS,[a] Natalia N. Egorova, PhD,[b] Henry Tannous, MD,[a,c] Anelechi C. Anyanwu, MD,[a] Ahmed El-Eshmawi, MD,[a] David H. Adams, MD,[a] and Joanna Chikwe, MD[a,c]

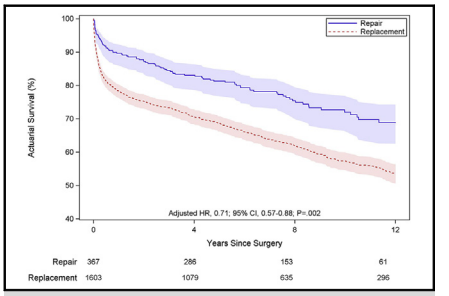
ABSTRACT

Background: Consensus guidelines recommend repair over replacement for the surgical treatment of active native mitral valve infective endocarditis. However, contemporary practice and long-term outcome data are limited.

Methods: Multivariable Cox regression was used to compare outcomes of 1970 patients undergoing isolated primary mitral valve repair (n = 367, 19%) or replacement (n = 1603, 81%) for active infective endocarditis between 1998 and 2010 in New York and California states. The primary outcome was long-term survival. Secondary outcomes were recurrent endocarditis and mitral reoperation. Median follow-up time was 6.6 years (range 0-12), and last follow-up date was December 31, 2015.

Results: Mitral valve repair rates increased from 10.7% to 19.4% over the study period ($P < .001$). Patients undergoing mitral repair were younger (55 ± 15 vs 57 ± 15 years, $P = .005$), less likely to have congestive heart failure (46.3% vs 57.1%, $P < .001$), and less likely to have staphylococcal infections (21.3% vs 32.0%, $P < .001$). Twelve-year survival was 68.8% (95% confidence interval [CI], 62.5%-74.3%) after mitral repair, versus 53.5% (95% CI, 50.6%-56.4%) after replacement (adjusted hazard ratio, 0.71; 95% CI, 0.57-0.88; $P = .002$). Mitral repair was associated with lower rate of recurrent endocarditis at 12 years than replacement (4.7% [95% CI, 2.8%-7.2%] vs 9.5% [95% CI, 8.0-11.1%]; $P = .03$), and similar rate of reoperation (9.1% [95% CI, 6.2%-12.8%] vs 8.6% [95% CI, 7.1%-10.4%]; $P = .12$).

Conclusions: In active endocarditis, mitral valve repair is associated with better survival and lower risk of recurrent infection compared with valve replacement and should be the surgery of choice when feasible. (J Thorac Cardiovasc Surg 2017;154:1906-12)



Improved survival after mitral valve repair versus replacement for active endocarditis.

Central Message

In active endocarditis, mitral valve repair is associated with better survival and lower risk of recurrent infection compared with valve replacement and should be the surgery of choice when feasible.

Perspective

The benefits of mitral repair over replacement for endocarditis are not well established, particularly in terms of recurrence, freedom from reoperation, and survival. This analysis of long-term outcomes of mitral surgery for endocarditis in California and New York State suggests that repair is underused, even though it is associated with better survival and lower recurrence compared with replacement.

See Editorial Commentary page 1913.

See Editorial page 1904.

The benefits of mitral repair over replacement for infective endocarditis are not well established, particularly in terms of recurrent infection, long-term freedom from reoperation, and survival. Based primarily on the results reported in single-center case series, current American and European consensus guidelines recommend mitral valve repair over replacement for the surgical treatment of active mitral

From the Departments of [a]Cardiovascular Surgery, and [b]Population Health Science and Policy, Icahn School of Medicine at Mount Sinai; and [c]Department of Surgery, Stony Brook University Hospital, New York, NY.

Received for publication Feb 12, 2017; revisions received July 4, 2017; accepted for publication July 30, 2017; available ahead of print Sept 21, 2017.

Address for reprints: Joanna Chikwe, MD, Department of Cardiovascular Surgery, Mount Sinai Medical Center, 1190 Fifth Ave, New York, NY 10029 (E-mail: Joanna.Chikwe@mountsinai.org).

0022-5223/$36.00

http://dx.doi.org/10.1016/j.jtcvs.2017.07.077

Scanning this QR code will take you to supplemental figures and tables for this article.

Abbreviations and Acronyms
CI = confidence interval
HR = hazard ratio
ICD-9-CM = *International Classification of Disease, 9th Revision, Clinical Modification*

native valve endocarditis.[1-3] The long-term outcomes of repair and replacement for native mitral valve endocarditis in contemporary, real-world practice largely are unknown, in part because of the low frequency of infective endocarditis. We therefore conducted a population-based study encompassing patients operated on for active native mitral valve endocarditis in California and New York State.

METHODS

Study Design and Population

This retrospective cohort study analyzed long-term outcomes after primary, isolated mitral valve surgery for active native valve endocarditis in patients aged 18 years or older in New York State and California State between 1998 and 2010, according to whether patients underwent mitral valve repair or replacement. Patients were identified with *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) procedure codes for mitral valve surgery and replacement (35.12, 35.23, 35.24, or 35.33) and diagnosis codes indicating active infective endocarditis (421.0, 421.1, 421.9, 036.42, 098.84, 112.81, 115.04, 115.14, or 115.94) in mandatory patient discharge databases collated by the New York Statewide Planning and Research Cooperative System and the Office of Statewide Health Planning and Development in California State. These all-payer, administrative databases prospectively collect data on every hospital discharge, ambulatory surgery, and emergency department visit in their respective states. A unique identifier allocated to each patient in each database permits analysis of clinical outcomes after the index admission. The proportion of patients who underwent mitral valve repair versus replacement for infective endocarditis was calculated including 1998 to 2014 data.

Patients were excluded if they underwent concomitant aortic or tricuspid valve surgery; if they had a history of valve surgery, heart transplantation, ventricular assist device placement, or drug abuse; or had surgery more than 6 weeks after admission (Figure E1). Details of exclusion criteria definitions were included in Table E1. Baseline comorbidities were identified from the index hospitalization and all previous hospitalizations (a detailed definition is given in Table E2). Drug abusers were analyzed as a separate subgroup, and the outcomes were compared with the nondrug abuse study cohort. This study was approved by the Data Protection Review Boards of New York State Department of Health; the Committee for the Protection of Human Subjects of California State; and the Program for Protection of Human Subjects at the Icahn School of Medicine at Mount Sinai. The approval included a waiver of informed consent.

Definitions and Code Validation

ICD-9-CM codes for active infective endocarditis were validated in a subset of patients' medical records. The sensitivity, specificity, and positive predictive value of ICD-9-CM codes to identify active infective endocarditis defined by the modified Duke criteria[4] were 94%, 99%, and 94%, respectively.[5] Causative micro-organisms were categorized by the use of primary and secondary diagnosis codes as follows: *Staphylococcus aureus* (including methicillin-resistant species), other *Staphylococcus* species, *Streptococcus* species, Gram-negative bacilli, fungus, and unknown (which included culture negative and cases where the organism was not specified).

Study End Points

The primary endpoint was all-cause mortality, and secondary endpoints were recurrent endocarditis and mitral valve reoperation. Deaths were ascertained from linked state's vital statistics death records, deceased discharge disposition at any subsequent in-hospital and emergency department and ambulatory surgery visits, and additionally from the Social Security Death Master File; recurrent infective endocarditis was defined as a diagnosis of infective endocarditis in the subsequent admissions at least 6 weeks after discharge, based on the period of antibiotics treatment recommended in the current guidelines.[6] Reoperation was identified as any subsequent mitral valve repair or replacement.

Statistical Analysis

Normally distributed continuous variables were reported as means with standard deviation and compared with the *t* test. Categorical variables were expressed as proportions and compared with the χ^2 test. Trends in mitral valve surgery were analyzed with the Cochran-Armitage trend test. Survival curves of the primary end point of all-cause mortality were constructed with Kaplan-Meier methodology and compared with log-rank test. Cumulative incidence curves for the secondary end points of recurrence of infective endocarditis and mitral reoperation were constructed with competing risk analysis as death as a competing event and compared with the Gray test. For each endpoint, multivariable Cox regression models were fit controlling for the surgery type (repair vs replacement), baseline comorbidities (age, sex, race, history of hypertension, diabetes, congestive heart failure, chronic kidney disease, coronary artery disease, atrial fibrillation, peripheral vascular disease, chronic obstructive pulmonary disease, liver disease, cancer, cerebrovascular disease, and coagulation disorders), causative organisms, admission year, state of residency, and concomitant coronary artery bypass graft and clustering patients within hospitals. For secondary outcomes with limited number of events, models were selected based on stepwise selection and fit assessed with Akaike Information Criteria. Patient demographics (age, sex, race, state of residency), admission year, and the surgery type were retained and forced into the model. In each model, proportional hazard assumption was evaluated and if violated, the interaction term between time-to-event and the surgery type were incorporated into the model and hazard ratios were calculated at different follow-up time points. For the analysis of recurrence, patients who had mitral valve reoperation before the date of recurrence or last follow-up were not censored at the time of reoperation and remained in the analysis.

As a validation of the results of multivariable analyses, the analyses described previously were repeated for all study end points using inverse probability weighting and propensity score adjustment and cohorts created by propensity score matching (Figure E3).[7,8] Propensity scores were calculated with a multivariable hierarchical logistic regression model with repair as the outcome and with patients clustered by hospitals. Patients' demographics, baseline comorbidities, causative organisms, and admission year were included in the model as covariates. The area under the receiver operating curve for the model was 0.78. For propensity matching, 1:2 match was conducted. Each outcome was assessed by fitting Cox regression models with each outcome as a dependent variable and the surgery type as a covariate with a robust sandwich variance estimator. Marginal Cox models with a robust sandwich variance estimator were used to assess the difference in outcomes in matched cohort. The results of this sensitivity analysis confirmed the main findings and are listed in Table E5.

A subgroup analysis of the effect of individual surgeon volume on reoperation within 1 year after repair was conducted with New York State patients (individual surgeon identifiers for California were not available). Surgeons were divided into 2 groups according to whether they performed fewer or more than 25 operations for any etiology on the mitral valve annually. We selected 25 cases as the cut-off based on previous data