Late outcomes comparison of nonelderly patients with stented bioprosthetic and mechanical valves in the aortic position: A propensity-matched analysis

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Objective: Our study compares late mortality and valve-related morbidities between nonelderly patients (aged <65 years) undergoing stented bioprosthetic or mechanical valve replacement in the aortic position.

Methods: We identified 1701 consecutive patients aged <65 years who underwent aortic valve replacement between 1992 and 2011. A stented bioprosthetic valve was used in 769 patients (45%) and a mechanical valve was used in 932 patients (55%). A stepwise logistic regression propensity score identified a subset of 361 evenly matched patient-pairs. Late outcomes of death, reoperation, major bleeding, and stroke were assessed.

Results: Follow-up was 99% complete. The mean age in the matched cohort was 53.9 years (bioprosthetic valve) and 53.2 years (mechanical valve) ($P = .30$). Fifteen additional measurable variables were statistically similar for the matched cohort. Thirty-day mortality was 1.9% (bioprosthetic valve) and 1.4% (mechanical valve) ($P = .77$). Survival at 5, 10, 15, and 18 years was 89%, 78%, 65%, and 60% for patients with bioprosthetic valves versus 88%, 79%, 75%, and 51% for patients with mechanical valves ($P = .75$). At 18 years, freedom from reoperation was 95% for patients with mechanical valves and 55% for patients with bioprosthetic valves ($P = .002$), whereas freedom from a major bleeding event favored patients with bioprosthetic valves (98%) versus mechanical valves (78%; $P = .002$). There was no difference in stroke between the 2 matched groups.

Conclusions: In patients aged <65 years, despite an increase in the rate of reoperation with stented bioprosthetic valves and an increase in major bleeding events with mechanical valves, there is no significant difference in mortality at late follow-up. (J Thorac Cardiovasc Surg 2014;148:1931-9)

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The emphasis to place on patient age with regard to valve choice in aortic stenosis remains a perplexing dilemma in select situations. The recent guidelines for aortic valve replacement have removed age as an absolute determinant in the decision-making process. Still, whether implicitly stated or not, when deciding to implant a mechanical or bioprosthetic heart valve into a patient, age will always be a consideration. The quandary between mechanical prostheses and bioprostheses endures—superior prosthesis durability and low likelihood of future reoperations with mechanical implants at the expense of lifelong anticoagulation and the associated increase in bleeding attributed to warfarin therapy. Quality of life infringements related to labor-intensive monitoring with warfarin are also not negligible.

Prior renditions of valve guidelines recommended that patients younger than age 65 years undergo implantation of a mechanical prosthesis (barring contraindications to anticoagulation therapy) whereas patients older than age 65 years receive a bioprosthesis.[1] The threshold of 65 years was considered the inflection point where the risk of reoperation secondary to structural valve deterioration (SVD) was low enough that the advantage of a bioprosthesis (ie, removal of warfarin therapy) outweighed the long-term durability inherent to a mechanical prosthesis. Improvements in surgical outcomes for reoperations,[2,3] perceived improvements in the durability of newer-generation bioprostheses,[4,5] and the currently untested yet highly anticipated future use of percutaneous valve-in-valve technology to treat SVD[6] have contributed to a steady trend toward implanting bioprostheses into younger patients instead of mechanical prostheses.[7,8]

Despite this trend, there are contemporary single-institution observational studies that suggest a mortality benefit of mechanical prostheses over bioprosthetic prostheses in nonelderly patients.[9-11] These studies suggest caution when implanting bioprostheses into patients aged younger than 65 years. In contrast, the only contemporary randomized clinical trial to assess the issue revealed no difference in survival out to 13 years.[12] Considering the

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Abbreviations and Acronyms
AVR = aortic valve replacement
EMR = electronic medical record
SVD = structural valve deterioration

paucity of data and conflicting conclusions in the contemporary literature, we set out to compare late mortality and valve-related morbidity between nonelderly patients undergoing implantation of a stented bioprosthetic or mechanical valve in the aortic position at the Brigham and Women's Hospital. The purpose of our study was to delineate differences in outcomes at late follow-up and to see if the current trend toward implanting bioprosthetic valves into younger patient populations is justifiable.

PATIENTS AND METHODS

With approval from an institutional review board, a review of the electronic medical record (EMR) was conducted to identify all patients aged younger than 65 years undergoing an isolated aortic valve replacement (AVR) with a bileaflet mechanical or stented bioprosthesis from January 1992. An isolated AVR was defined as an AVR without additional concomitant valvular, coronary, or ventricular procedures at the time of the indexed operation. Concomitant aortic root and/or ascending aortic repair procedures were included in the isolated AVR cohort, as were patients having had cardiac surgery before the indexed operation. Exclusion criteria were AVR using a pulmonary autograft, homograft, or stentless bioprostheses. Of 6794 patients who underwent an AVR within the specified time frame, 1701 patients met the inclusion criteria. The primary outcome was late survival. Secondary outcomes included stroke, major bleeding, and reoperations at late follow-up.

The study cohort underwent a propensity-matched analysis to create evenly matched patient-pairs with respect to measurable covariates, with type of prosthesis implanted (ie, bileaflet mechanical or a second-generation stented bioprosthetic prosthesis) at the time of the indexed operation being the only discernible difference. The remaining unmatched patients were placed into a separate database and their outcomes were also assessed. The investigators were blinded to any outcomes during the matching process (Figure 1).

Unless warfarin therapy was indicated for other reasons (eg, atrial fibrillation or pulmonary embolism), patients receiving a bioprosthetic valve were managed solely with antiplatelet therapy (ie, daily aspirin), whereas patients receiving a mechanical valve received both antiplatelet and anticoagulation therapy in combination (ie, daily aspirin and warfarin). Goals for warfarin therapy were to maintain an international normalizing ratio between 2.0 and 3.0. The decision to implant a bioprosthetic or mechanical valve was at the discretion of the primary surgeon and the patient at the time of implantation.

Data Collection

Patient characteristics, medications, laboratory values, and in-hospital outcomes of the index surgery were collected at the time of presentation and extracted from the hospital's EMR. Data on long-term outcomes were collected by questionnaires, records requested from referring physicians, and extraction from the EMR at follow-up visits. Mortality data, including date and cause of death, were collected from the following sources: the Social Security Death Index, EMR, and the state Department of Public Health and Registry of Vital Statistics. Nineteen patients with an international residence were lost to follow-up.

To acquire up-to-date data for the secondary outcomes of stroke, major bleeding, and reoperations, questionnaires were mailed to all eligible study patients residing in the United States and presumed alive as of October 2011 (N = 1391). Questionnaires were mailed in serial succession beginning in November 2011. Two additional mailings were sent in January 2012 and March 2012 for nonresponders. Patient-reported responses were cross-referenced and corroborated with the most current EMR records on file. For those patients where a questionnaire was unattainable, the time point used for secondary outcomes was the last recorded visit on file in the EMR. A responder bias analysis was performed to assess for potential differences between patients who responded to the survey and those who elected not to participate.

Patient demographics and hospital outcomes were coded and defined according to the Society for Thoracic Surgeons Adult Cardiac Surgery database specifications, version 2.52. In addition to late mortality and valve-related morbidities, short-term outcomes were also assessed. Short-term outcomes of interest were 30-day mortality, re-exploration for bleeding, postoperative stroke, in-hospital cardiac arrest, complete heart block, time on the ventilator, intensive care unit length of stay, and hospital length of stay. Sudden, unexplained death was considered a cardiac-related mortality.

Propensity-Matched Cohort

We conducted a matched group analysis using propensity-matched cases (stented bioprostheses) and controls (mechanical valves). Propensity to receive bioprosthetic valves was evaluated using logistic regression analyses done in 2 steps. Variables to be evaluated as predictors were selected based on literature review, known confounding covariates for the outcomes of interest, differences between the 2 patient groups (Table 1), and clinical judgment. These variables were then classified as patient-dependent or treatment-dependent and separate forward-stepwise regression analyses were conducted for each variable set, including examinations for interaction effects. Any variable with a $P \leq .15$ was entered into the final model, which was an enter-method logistic regression. The final model consisted of 11 variables: age, year of surgery, cardiopulmonary bypass time, etiology of disease (ie, calcific, endocarditis, congenital, rheumatic, primary aorta, or other), body mass index, reoperation, gender, hypertension, congestive heart failure, operative status (elective, urgent, or emergent), and ejection fraction. An interaction variable between the surgeon and the year of surgery was also included to control for differences in patient mix and clinical practice over time. The resulting adjusted predicted probability score for each patient was then used to select matched pairs based on probability scores <.01 (a priori algorithm).

Statistical Analysis

Normally distributed continuous variables are presented as mean ± standard deviation. Non-normally distributed continuous variables are presented as median with interquartile range. Analyses of continuous variables were done using the Student *t* test with Levine's homogeneity of variance or Mann-Whitney *U* test, as appropriate. Dichotomous variables were evaluated using the Fisher exact test and are presented as a numerical value as well as a percentage. Outcomes of interest were analyzed by Kaplan-Meier analysis. Failure time date was compared using the log-rank test. Life-table estimations of 5-year, 10-year, 15-year, and 18-year survival curves are presented as cumulative percent ± standard error. Statistical analyses were done using SPSS (version 13.0; IBM-SPSS Inc, Armonk, NY).

RESULTS

Our study included 1701 patients (769 stented bioprosthetic cases, 932 mechanical cases; 14,848 patient-years of data; median follow-up 8-years). Baseline characteristics for the complete cohort are presented in Table 1. Patients receiving a bioprosthesis were older and had more hypertension and