Long-term outcomes after elective isolated mechanical aortic valve replacement in young adults

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Objectives: The aim of this study was to determine long-term survival and clinical outcomes after elective isolated mechanical aortic valve replacement in young adults.

Methods: A clinical observational study was conducted in a cohort of 450 consecutive adults less than 65 years of age who had undergone elective isolated mechanical aortic valve replacement (AVR) between 1997 and 2006. Patients who had undergone previous cardiac surgery, and those undergoing concomitant procedures or urgent surgery were excluded. Follow-up was 93.3% complete with a mean follow-up of 9.1 ± 3.5 years. The primary end point was survival. Life table analyses were used to determine age- and gender-matched general population survival. Secondary end points were reoperation and valve-related complications.

Results: Overall actuarial survival at 1, 5, and 10 years was 98% ± 1%, 95% ± 1%, and 87% ± 1%, respectively, which was lower than expected in the age- and gender-matched general population in Quebec. Actuarial freedom from prosthetic valve dysfunction was 99% ± 0.4%, 95% ± 1%, and 91% ± 1% at 1, 5, and 10 years, respectively. Actuarial freedom from valve reintervention was 98% ± 1%, 96% ± 1%, and 94% ± 1% at 1, 5 and 10 years, respectively. Actuarial survival free from reoperation at 10 years was 82% ± 2%. Actuarial freedom from major hemorrhage was 98% ± 1%, 96% ± 1%, and 90% ± 2% at 1, 5, and 10 years, respectively.

Conclusions: In young adults undergoing elective isolated mechanical AVR, survival remains suboptimal compared with an age- and gender-matched general population. Furthermore, there is a low but constant hazard of prosthetic valve reintervention after mechanical AVR. (J Thorac Cardiovasc Surg 2014;148:1341-6)

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Aortic valve disease is one of the most common indications for surgery in patients less than 65 years of age. However, the ideal aortic valve substitute remains unknown. This is partly due to the lack of data on long-term outcomes in this specific patient population. More importantly, most long-term studies of aortic valve replacement (AVR) include patients at higher risk (urgent operations, concomitant coronary revascularization, reoperations), which makes it more challenging to assess outcomes related to the actual procedure.[1-3] Nevertheless, recent evidence has shown excess long-term mortality in patients undergoing AVR compared with an age- and sex-matched general population, and this discrepancy was most pronounced in the youngest age group.[4]

A longer life expectancy exposes young adults to a higher lifelong risk of prosthesis-related complications after AVR, most notably in the form of thromboembolic events, hemorrhage, and reoperation. Bioprosthetic valves have limited long-term durability and therefore carry an inherent risk of reoperation in young adults. Nevertheless, they have a low thrombogenic risk and have the advantage of avoiding anticoagulation. In contrast, mechanical prostheses provide better long-term durability with low risk of prosthesis reintervention, and are thus often considered the option of choice in young adults with aortic valve disease.[5] Nevertheless, mechanical prostheses carry a thrombogenic risk and therefore mandate long-term anticoagulation with an associated risk of major bleeding. Although some studies have examined long-term results after AVR, few have focused on contemporary results of isolated mechanical AVR in young adults.

The aim of this study was to assess long-term survival in a contemporary series of consecutive young adults undergoing elective isolated mechanical AVR compared with the age- and gender-matched general population in Quebec. The secondary objective was to describe the occurrence of long-term valve-related complications after AVR in this patient population.

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Abbreviations and Acronyms
AVR = aortic valve replacement
INR = international normalized ratio
MAPE = major adverse prosthetic events
MHI = Montreal Heart Institute

MATERIALS AND METHODS

Patients

All patients less than 65 years old undergoing AVR at the Montreal Heart Institute (MHI) between January 1997 and October 2006 were screened. Mechanical AVR was the procedure of choice in this patient population unless there was a specific contraindication for anticoagulation or because of patient preference. In total, 1158 patients were identified. Of those, 208 underwent bioprosthetic valve replacement (18%; mean age, 55 ± 10 years) and 950 underwent mechanical valve replacement (82%; mean age, 53 ± 9 years). All patients were followed on a yearly basis by mail questionnaires and phone interviews at our institution's dedicated Valve Clinic. Patients undergoing emergency surgery, concomitant procedures (including coronary bypass, other valve repair, ascending aorta replacement, Bentall procedure, annular enlargement procedures, Maze radiofrequency ablation, and atrial or ventricular septal defect closure) and those who had undergone previous cardiac surgery were excluded (n = 500 patients). The study population consisted of 450 consecutive patients undergoing elective isolated mechanical AVR. Preoperative baseline characteristics are presented in Table 1. Mean age at surgery was 53 ± 9 years (68% male). Aortic stenosis was the indication in 337 patients (75%), aortic regurgitation in 68 patients (15%), and mixed aortic disease in 45 patients (10%). The mean EuroSCORE II[6] was 1.1% ± 0.6%.

Operative Data and Anticoagulation Management

Implanted mechanical prostheses were distributed as follows: Carbomedics (Sorin Group, Milan, Italy) in 402 (89%) patients, St Jude Medical (St Jude Medical Inc, St Paul, Minn) in 35 (8%) patients, and Medtronic Advantage (Medtronic, Minneapolis, Minn) in 13 (3%) patients. The mean clamping time was 62 ± 15 minutes and the mean cardiopulmonary bypass time was 83 ± 20 minutes. Anticoagulation therapy with warfarin was started in all patients on the second postoperative day. Close anticoagulation follow-up in specialized clinics was performed and the target internationalized normalized ratio (INR) ranged between 2 and 3.

Follow-up and Data Collection

Approval was obtained from our local ethics committee. All data were prospectively collected through the MHI Valve Clinic. Additional data were gathered from medical records. The follow-up period for this study ended in September 2012. Mean follow-up time was 9.1 ± 3.5 years (total follow-up was 4099 patient-years). Follow-up was 93% complete.

Reference population survival estimates were generated from publicly available Province of Quebec survival tables for each patient according to age and sex.

Outcomes

Outcomes were recorded according to the Society of Thoracic Surgery *Guidelines for Reporting Mortality and Morbidity Mortality After Cardiac Valve Interventions*.[7] The primary outcome of this study was death from any cause and was divided into early mortality (30 days after surgery) and late mortality. Secondary outcomes reported were prosthesis dysfunction including structural and nonstructural valve dysfunction, thromboembolic events (stroke, transient ischemic attack, and noncerebral embolic events), endocarditis, valve thrombosis, and significant hemorrhage, which was defined as major bleeding requiring hospitalization or transfusion. Major adverse prosthetic events (MAPE) included a composite of all the aforementioned outcomes. Causes of death were reported as valve-related, cardiac, and noncardiac.

Statistical Analysis

Continuous variables are presented as the mean ± standard deviation and categorical variables are reported as frequency (percentage). All outcomes were analyzed using actuarial methods. Patients were censored at the time of death or at the time of their last follow-up if the outcome of interest had not occurred. Expected survival of a sex- and age-matched population was obtained using the Hakulinen method.[8]

Predictors of mortality were assessed using a multivariable logistic regression model. Variables screened as potential confounders were the preoperative baseline characteristics. All variables with a P value <.20 on univariate analysis were considered as having a potential confounding effect. A nonautomated variable selection was performed. Variables with a P value <.05 were retained in the multivariate Cox regression. Data were analyzed using SAS 9.3 (SAS Institute, Inc, Cary, NC).

RESULTS

Early Complications

Thirty-day mortality was 1.1% (n = 5). Causes of early death were myocardial infarction (n = 2), endocarditis (n = 1), malignant arrhythmia (n = 1), and massive bleeding (n = 1). New onset of atrial fibrillation or flutter was reported in 141 patients (31%). Postoperative bleeding (<48 hours) requiring reintervention occurred in 23 patients (5%). Late pericardial effusion necessitating surgical drainage after the start of anticoagulation (48 hours to 30 days after surgery) was observed in a further 43 patients (10%). Although anticoagulation was started progressively on the second postoperative day, INR rates were >3 in 47% of patients at the time of drainage. A pacemaker was implanted for atrioventricular block in 17 patients (4%). Stroke occurred in 7 patients (2%). Details on postoperative complications are summarized in Table 1.

Long-Term Survival

Late mortality occurred in 58 patients (13%) during the follow-up period. The cause of death was valve related in 31 patients (53%), cardiac related in 10 patients (17%), and noncardiac related in 17 patients (30%). Details on causes of late deaths are presented in Table 2. Actuarial survival at 1, 5, and 10 years was 98% ± 1%, 95% ± 1%, and 87% ± 1%, respectively. At each time point, survival was lower than in the age- and gender-matched general population of Quebec (Figure 1). Expected survival in the age- and-gender-matched general population was 99.6%, 97.6%, and 94.2% at 1, 5, and 10 years, respectively.

On multivariate analysis, decreased preoperative left ventricular ejection fraction (P = .001), decreased preoperative glomerular filtration rate (P = .002), diabetes (P < .0001), obesity (P = .008), hypothyroidism (P = .007), and asthma (P = .014) were independent predictors of long-term mortality. Patient age at the time of surgery was not associated with late mortality.