Biological Aortic Valve Replacement. Long-Term Follow-Up and Predictors of Mortality, Rehospitalization and Reintervention

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Received: 10/22/2007
Accepted: 04/17/2008

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ABSTRACT

Background
Aortic valve replacement is the conventional procedure in aortic valve disease; nevertheless, choosing the most suitable model of prosthesis is a complex decision. The use of novel biological models specially treated to reduce long-term structural deterioration has been encouraged, even in young populations.

Objective
To assess long-term survival of biological valve replacement, quality of life, rates of readmission and reintervention and to identify predictors of those events. We analyzed a population of patients who had undergone aortic valve replacement with bioprosthesis, alone or combined with revascularization, between June 1996 and December 2005. Excluding those who were dead within 30 days after surgery, 256 patients were included, and 94.2% completed follow-up at 1158 days.

Results
Overall survival was 94.8%, 88.6%, 85% and 82.4% at 1, 3, 5 and 7 years, respectively; and 97.2%, 94.6%, 91.2% and 89.4%, respectively, excluding cardiovascular deaths. Freedom from readmission was 86%, 75.7%, 70.6% and 65.9% for the same period. Freedom from reintervention was 97.4%, 95.2%, 92.1% and 92.1% at 1, 3, 5 and 7 years. Non-sinus rhythm was identified as a predictor for mortality (OR 3.4; p = 0.012) and carotid disease (OR 7.6; p = 0.002), COPD (OR 7; p = 0,004 and male gender (OR 2.18; p = 0.039) were recognized as predictors for readmission. Predictors for reintervention were not identified due to the low incidence of this endpoint.

Conclusions
Long-term survival is acceptable for the age group and non-sinus rhythm, the only predictor of mortality identified. Readmission rate at one year is high and male gender, carotid stenosis, history of respiratory and cerebrovascular diseases and non-elective surgery are predictors for this outcome. Reintervention rate during follow-up is low, encouraging the indication of this type of prosthesis.

Rev Argent Cardiol 2008;76:266-271.

Key words > Aortic Valve - Heart Valve Prosthesis - Prognosis

Abbreviations >

S	Stroke	**IE**	Infective endocarditis
PTCA	Percutaneous transluminal coronary angioplasty	**COPD**	Chronic obstructive pulmonary disease
ICD	Implantable cardioverter-defibrillator	**LVSF**	Left ventricular systolic function
ECC	Extracorporeal circulation	**AMI**	Acute myocardial infarction
CABGS	Coronary artery bypass-graft surgery	**CHF**	Congestive heart failure
LVDD	Left ventricular diastolic diameter	**AVR**	Aortic valve replacement
LVSD	Left ventricular systolic diameter		

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BACKGROUND

During the last decades, the therapeutic options in patients with mixed aortic valve disease have included a variety of techniques, such as mechanical or stented/stentless biological heart valve prostheses implant, aortic homografts implant or Ross procedure surgery.

Isolated valve replacement is a simple and reproducible procedure for patients with severe valvular disease, and is associated with a significant improvement in symptoms and in life expectancy.

Several randomized clinical trials have assessed the outcomes of valve replacement according to the type of valve implanted; however, in daily practice the selection of the valve prosthesis depends on multiple factors, such as patient's age, valve implant position, presence of comorbidities, association with coronary artery disease, life expectancy and risk/benefit ratio of anticoagulation therapy.

The benefits and disadvantages of mechanical and biological heart valve prostheses available on the market are well known. Biological heart valve prostheses are subjected to non-physiological mechanical stress, calcification and valve dysfunction. As a result of valve dysfunction, reinterventions are necessary at long-term follow-up, constituting the principal limitation to use these types of prostheses. Nevertheless, third generation models with improved hemodynamic profile and anti-calcification treatment seem to revert the traditional and almost dogmatic criteria of indication of biological prostheses and encourage their use in younger populations. (1-6)

In our country, there is few data on long-term survival and quality of life in patients subjected to aortic valve replacement with biological prosthesis. This may be related to the fact that, during the last decades, several and complicated satisfaction and well-being questionnaires have developed instead of using more simple expressions such as event rates (readmissions and reinterventions related to the implanted valve) (7)

The aim of the present study is to assess long-term survival of aortic valve replacement with biological prosthesis in terms of rates of readmission, reintervention and mortality, and to identify perioperative predictors of those events.

MATERIAL AND METHODS

Between June 1996 and December 2005, 3186 patients underwent heart surgery at our institution. Patients' data were consecutively and prospectively added to a general database. Six hundred and twenty six patients underwent aortic valve replacement, isolated or combined with revascularization. In this special subgroup, 289 patients (46.2%) received biological valve prostheses which constituted the aim of this review. After excluding patients with symptomatic carotid artery disease, patients subjected to associated procedures for atrial fibrillation ablation and/or surgical repair of the ascending aorta, and those who were dead within 30 days after surgery (7.56%), the final population included 256 patients.

Preoperative variables (age, sex, body surface area, comorbidities, prior cardiovascular and non cardiovascular history, heart rhythm, cardiac diameters, physiopathology and valvular etiology, coronary artery disease and priority of surgery), *intraoperative* variables (LV function, prosthesis type and size, elective or urgent revascularization, operative time) and *postoperative* variables (major complications, length of hospital stay) were analyzed. During hospitalization, data were retrieved from the corresponding clinical records. At long-term follow up, data were collected from the medical records of clinical cardiologists, interventional cardiologists, hematologists, nutritionists, physicians from cardiac rehabilitation programs, primary-care physicians and/or results of telephone surveys.

The following issues were analyzed: patients' current clinical state, the presence of outpatient events (readmission, reintervention and death), the Duke Activity Status Index, the results of annual screening with image tests and the medication at the time contacted. The presence of associated events at follow-up was reported and predictors of events were assessed in univariate and multivariate analysis. The results are expressed as mean ± standard deviation for numerical variables, and categorical variables are expressed as percentages. The association between the variables and outcomes are expressed as OR with their corresponding 95% CI. A p value < 0.05 was considered statistically significant.

RESULTS

Mean age was 74.6 ± 6.05 years (range, 42 to 89 years), and 58.6% were men. Body surface area was 1.83 ± 0.31 m^2. Table 1 shows the remaining demographic characteristics, as well as mean values of preoperative echocardiograms.

Eighty two percent of patients underwent elective surgery (n = 210); the operative times were as follows: clamp time 85 ± 26 min, ECC time 114 ± 34 min, total operative time 247 ± 62 min. The size of prostheses used was 23 (38.3%), 21 (33.6%) and 19 (19.2%). Patients subjected to combined procedures due to coronary artery disease received 2.06 ± 0.6 bypass grafts. Although the analysis of perioperative complications was not the aim of this study, adverse outcomes are shown in Figure 1.

Median follow-up was 1158 days and was completed by 94.2% of patients. Overall survival was 94.8%, 88.6%, 85% and 82.4% at 1, 3, 5 and 7 years, respectively; and 97.2%, 94.6%, 91.2% and 89.4%, respectively, excluding cardiovascular deaths (Figure 2). Freedom from readmission was 86%, 75.7%, 70.6% and 65.9% for the same period (Figure 3). The causes of readmission were reported and will be discussed later. Intervention-free rate was 94.3%, 87.6%, 83.5% and 79% at 1, 3, 5 and 7 years, respectively, including procedures as coronary angioplasty, definite pacemaker and/or ICD implant and supraventricular arrhythmias ablation. Freedom from reintervention increased to 97.4%, 95.2%, 92.1% and 92.1% for the same periods when the need of a new surgery, such as

Table 1. Demographic characteristics

VARIABLE	n = 256	%
Risk factors		
Hypertension	166	65.8
Dyslipemia	115	45
Smoking habits	81	31.5
Family history	5	2
Personal history		
Diabetes	46	17.9
Previous myocardial infarction	31	12.1
Previous PTCA	20	7.8
Previous renal failure	16	6.2
Peripheral vascular disease	13	5
CORD	11	4.3
Previous S	8	3.2
Previous CABGS	13	5
Previous valvular surgery	1	0.4
AAA	4	1.6
Clinical picture		
Asymptomatic	38	14.8
Chronic stable angina	35	13.6
Unstable angina	61	23.8
AMI < 7 days	5	1.9
CHF	18	7
FC III-IV dyspnea	89	34.7
Syncope	23	9
IE	9	3.5
Coronary artery disease	138	54
Moderate-to-severe LVD	46	18
Echocardiographic characteristics		
LVDD	51 ± 6,7 mm	
LVSD	31.8 ± 7 mm	
Septum	13.3 ± 1.9 mm	
Posterior wall	9.5 ± 1.4 mm	
Aortic ring	32 ± 2 mm	
Peak aortic gradient	80 ± 12 mm Hg	
Mean aortic gradient	49 ± 9.8 mm Hg	

For echocardiographic variables, units are expressed as median and standard deviation. PTCA: Percutaneous transluminal coronary angioplasty. S: Stroke. COPD: Chronic obstructive pulmonary disease. CABS: Coronary artery bypass graft surgery. AMI: Acute myocardial infarction. CHF: Congestive heart failure. IE: Infective endocarditis. LVD: Left ventricular dysfunction. LVDD: Left ventricular diastolic diameter. LVSD: Left ventricular systolic diameter.

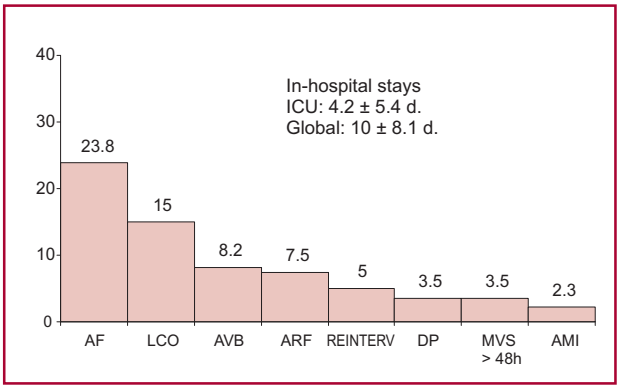

Fig. 1. Perioperative complications. Units are expressed in percentages.

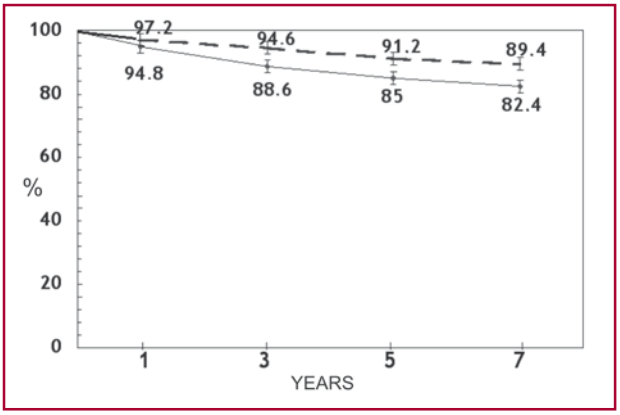

Fig. 2. Survival during follow-up. Full line: global survival. Dotted line: survival related to cardiovascular deaths.

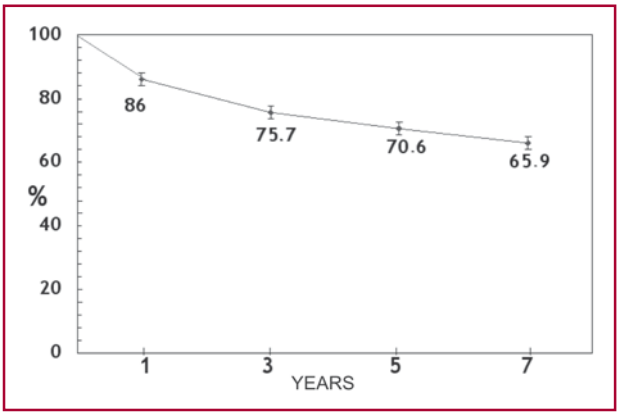

Fig. 3. Readmission during follow-up.

myocardial revascularization and/or valve replacement was considered (Figure 4).

The Duke Activity Status Index was used to assess the quality of life according to the type of activities and gradual difficulties which could be estimated with a score. (8) The average value obtained was 26.95 ± 12.46 and corresponded to a good quality of life. During follow-up, 96.3% of patients were receiving three drugs, and only 8.1% were treated with oral anticoagulant agents due to arrhythmia and/or associated thromboembolic events.

Several publications have identified heart failure, atrial fibrillation, gastrointestinal disorders, involvement of the lower limbs and metabolic disorders as predictors for readmission at 30 days. (9, 10) The mean surgery-readmission interval was 787.77 days, and values vary according to the different follow-up periods and causes. Readmission rate is high during the first period, mainly due to congestive heart failure, supraventricular arrhythmias, infections, stroke (S), syncope and infective endocarditis (IE); the latter is

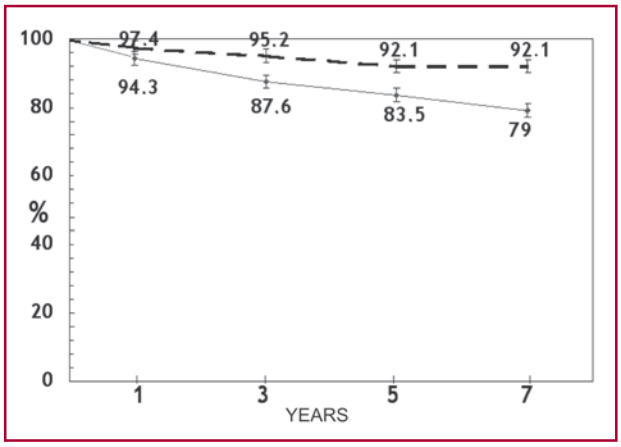

Fig. 4. Reintervention during follow-up. Full line: global reintervention (ablation, definite pacemaker, PTCA) Dotted line: new CABGS and/or valvular replacement.

the principal cause of readmission since the fourth year of follow-up. Nevertheless, as IE has an excellent response to medical treatment, the reintervention rate is very low. (11-14)

Univariate analysis identified several variables as predictors of mortality (overweight, sex, hypertension, prior renal disease, non-sinus rhythm, LVSD, prosthesis size); however, non-sinus rhythm was the only variable identified at multivariate analysis (OR 3.45; 95% CI 1.31-9.05, p = 0.012). Readmission variables recognized at univariate analysis were sex, carotid artery disease, CORD, previous stroke, non-elective priority and prolonged operative time; when a multivariate analysis was performed, only carotid artery disease (OR 7.6; 95% CI 2.15-27.04, p = 0.002), CORD (OR 7.08, CI 95% 1.85-27.04; p = 0,004) and sex (OR 2.18; CI 95% 1.04-4.58, p = 0.039) were recognized as predictors for readmission. Predictors for reintervention (CABGS or AVR) were not identified due to the low incidence of this endpoint.

DISCUSSION

Patients' demographic characteristics were not remarkable. The presence of elder patients in this population is a consequence of a selection bias for biological valve prosthesis implant; in addition, the great mean value of body surface area defines the phenotype of our sample. The selection of patients in this study includes those subjected to isolated aortic valve replacement and/or to procedures combined with coronary revascularization. Our team presented a previous study during the Congress of the Argentine Society of Cardiology in 2003, demonstrating that programmed revascularization combined with aortic valve replacement does not imply a greater 30-day morbidity and mortality; for this reason this group of patients has been included in the analysis. (15) On the other hand, urgent revascularization secondary to intraoperative complications (coronary occlusion after heart valve prosthesis implant, embolism, ventricular dysfunction unresponsive to treatment, etc.) increases in-hospital mortality and morbidity. In this series, only 4 patients (1.56%) required urgent revascularization with no impact on survival or rate of events during follow-up.

The relationship between the median value of the body surface area and the great number of prostheses size 21 or less is interesting. The assessment of the effective orifice area indexed for body surface area was not the aim of the present study; however, as the incidence of patient-prosthesis mismatch defined by a ratio < 0.85 cm^2/m^2 (18.3%), and of severe mismatch (< 0.65 cm^2/m^2, 1.95%) was higher than expected, we felt obliged to analyze this subgroup of patients. The heterogeneity of the valve models used and the lack of information supplied by the manufacturers of the real measure of the effective orifice area are two important difficulties. Several papers have been published on different experiences with mismatch. Pibarot (16, 17) emphasized the importance of patient-prosthesis mismatch and the necessity and possibility to prevent it during the intervention. The relationship between moderate or severe mismatch and greater perioperative mortality has been discussed in a lesser extent; we have confirmed this situation in our experience for 30-day mortality and patients who were dead 30 days after surgery were excluded from the present study. We did not find statistically significant differences in mortality, readmission and/reintervention among patients with valvular diameter in accordance with body surface area, even in the group of patients with new hospitalizations due to CHF at the first year of follow-up; this situation had been previously reported by Frapier (18) for a specific model of aortic heart valve prosthesis.

Survival rate in our study is greater than the one reported in other series of comparable patients. Gross et al. reported survival rates of 87.5% and 74% at 1 and 4 years, respectively, for biological prosthetic models; Kahn et al. informed survival rates of 88%, 71%, 40 % and 17% at 1, 5, 10 and 15 years in patients older than 65 years and 94%, 80%, 67% and 55% for patients younger than 65 years at similar intervals of time in subjects who underwent aortic valve replacement with mechanical or biological valve heart prosthesis. (19, 20)

We did not estimate Duke's score prior to surgery, so we are not able to analyze the real impact of the procedure; however, its value during late follow-up represents a clear estimation of the postoperative functional class. Occasionally, medical therapy during follow-up expresses patients' discomfort and limitation, especially if the drug administrated requires permanent screening or presents considerable adverse outcomes. The incidence of anticoagulation therapy

is low and supports the choice of this type of prosthesis. This rate is similar to the one reported by Goldman and David for biological valvular models comparable to those used in our series. (21) The association between drug therapy and rate of events during follow-up has not been established yey and constitutes the starting point for further communications.

The rate of reintervention was similar to published series with second generation models of biological prostheses. (19, 20) Different publications analyze variables for reintervention, such as early age, learning curve, diameter of the implanted prosthesis, previous coronary artery disease, low ejection fraction and moderate dilation of the ascending aorta. (22) In our series, predictors for reintervention were not identified due to the low incidence of this endpoint.

CONCLUSIONS

Aortic valve replacement with biological heart valve prosthesis is a standardized procedure with acceptable rates of morbidity and mortality. The election of a biological prosthetic model is related to an adequate quality of life in terms of freedom from symptoms, absence of cardiac events requiring repetitive readmission and/or survival in absence of new interventions.

Reintervention rate at 7 years follow-up is low, encouraging the indication of biological prosthesis in this kind of patients. It is advisable to perform a longer follow-up taking into account that valvular degenerative processes and structural deterioration of the biological models take place 10 years after the valve replacement.

This population of patients should be followed-up at long-term discriminating the different prosthetic models (porcine, bovine, pericardial, prosthesis with decalcification treatment, etc.); this behaviour is widely justified and might enable us to identify the adequate prosthesis in terms of survival free from rehospitalization. In addition, follow-up should discriminate age groups within this population, as an attempt to extrapolate these favorable outcomes to the follow-up of patients younger than 65 years as a way to justify biological heart valve implants in younger patients.

RESUMEN

Reemplazo valvular aórtico biológico. Seguimiento a largo plazo y predictores de mortalidad, reinternación y reintervención

Introducción
El reemplazo valvular aórtico es el procedimiento convencional en la enfermedad valvular y el modelo protésico que se ha de implantar resulta una decisión compleja. Nuevos modelos biológicos, cuyo especial tratamiento reduce el deterioro estructural alejado, han alentado su uso, aun en poblaciones jóvenes.

Objetivo
Evaluar la sobrevida alejada del recambio valvular aórtico biológico, la calidad de vida, las tasas de reinternación y reintervención, así como identificar predictores para tales eventos.

Material y métodos
Se analizó una población sometida a cirugía aórtica aislada o combinada con revascularización, con modelos biológicos, entre junio de 1996 y diciembre de 2005. Excluidos los fallecidos a los 30 días, se analizaron 256 pacientes, con un seguimiento del 94,2% a 1.158 días.

Resultados
La sobrevida global fue del 94,8%, 88,6%, 85% y 82,4% a 1, 3, 5 y 7 años; sobrevida libre la mortalidad cardíaca, fue del 97,2%, 94,6%, 91,2% y 89,4%, respectivamente. La sobrevida libre de reinternación fue del 86%, 75,7%, 70,6% y 65,9% para igual período. La sobrevida libre de reintervención fue del 97,4%, 95,2%, 92,1% y 92,1% a 1, 3, 5 y 7 años. Fueron predictores para *mortalidad* el ritmo no sinusal (OR 3,4; p = 0,012) y para *reinternación* la enfermedad carotídea (OR 7,6; p = 0,002), la EPOC (OR 7; p = 0,004) y el sexo masculino (OR 2,18; p = 0,039). La baja incidencia de reintervenciones no permitieron identificar predictores.

Conclusiones
La sobrevida alejada es aceptable para el grupo etario y el ritmo no sinusal es el único predictor de mortalidad identificado. La tasa de reinternación al primer año es elevada y el sexo masculino, la estenosis carotídea y los antecedentes respiratorios y cerebrovasculares, así como la prioridad no electiva, son sus predictores. La tasa de reintervención al seguimiento es baja y alienta la utilización de este tipo de prótesis.

Palabras clave > Válvula aórtica - Prótesis valvular cardíaca - Pronóstico

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