Rev Bras Cir Cardiovasc 2014;29(3):316-21

Late outcome analysis of the Braile Biomédica® pericardial valve in the aortic position

Avaliação dos resultados tardios da bioprótese de pericárdio bovino Braile Biomédica® em posição aórtica

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DOI 10.5935/1678-9741.20140081

RBCCV 44205-1556

Abstract

Objective: **Aortic valve replacement with Braile bovine pericardial prosthesis has been routinely done at the Heart Institute of the Universidade de São Paulo Medical School since 2006. The objective of this study is to analyze the results of Braile Biomédica® aortic bioprosthesis in patients with aortic valve disease.**

Methods: **We retrospectively evaluated 196 patients with aortic valve disease submitted to aortic valve replacement with Braile Biomédica® bovine pericardial prosthesis, between 2006 and 2010. Mean age was 59.41±16.34 years and 67.3% were male. Before surgery, 73.4% of patients were in NYHA functional class III or IV.**

Results: **Hospital mortality was 8.16% (16 patients). Linearized rates of mortality, endocarditis, reintervention, and structural dysfunction were 1.065%, 0.91%, 0.68% and 0.075% patients/year, respectively. Actuarial survival was 90.59±2.56% in 88 months. Freedom from reintervention, endocarditis and structural dysfunction was respectively 91.38±2.79%, 89.84±2.92% and 98.57±0.72% in 88 months.**

Conclusion: **The Braile Biomédica® pericardial aortic valve prosthesis demonstrated actuarial survival and durability similar to that described in the literature, but further follow up is required to assess the incidence of prosthetic valve endocarditis and structural dysfunction in the future.**

Descriptors: **Heart Valve Prosthesis Implantation. Aortic Valve. Survival Analysis.**

Resumo

Objetivo: **A troca valvar aórtica por substitutos biológicos de pericárdio bovino Braile é realizada rotineiramente no Instituto do Coração da Faculdade de Medicina da USP desde 2006. O objetivo deste estudo é analisar os resultados da utilização da prótese aórtica Braile Biomédica® em pacientes com doença valvar aórtica.**

Métodos: **Foram analisados, retrospectivamente, 196 pacientes portadores de valvopatia aórtica submetidos à troca valvar aórtica por prótese biológica de pericárdio bovino Braile Biomé-**

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This study was carried out at Instituto do Coração (Heart Institute) of Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo InCor-HCFMUSP, São Paulo, SP, Brazil.

No financial support.

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Article received on March 17th, 2014
Article accepted on June 22nd, 2014

Abbreviations, acronyms & symbols	
NYHA	New York Heart Association

dica® entre 2006 e 2010. A idade média foi de 59,41±16,34 anos e 67,3% eram do sexo masculino. No pré-operatório, 73,4% dos pacientes estavam em classe funcional III ou IV.

Resultados: **A mortalidade hospitalar foi 8,16% (16 pacientes). As taxas linearizadas de óbito, endocardite, reoperação e disfunção estrutural foram de 1,065%, 0,91%, 0,68% e 0,075% pacientes/ano, respectivamente. A sobrevida actuarial foi de 90,59±2,56% em 88 meses. A curva livre de reoperação, endocardite e disfunção estrutural foi respectivamente de 91,38±2,79%, 89,84±2,92% e 98,57±0,72% em 88 meses.**

Conclusão: **O implante da prótese aórtica de pericárdio bovino Braile Biomédica® demonstrou sobrevida e durabilidade compatível com a literatura, porém maior seguimento é necessário para avaliar a incidência de endocardite e disfunção estrutural no futuro.**

Descritores: **Implante de Prótese de Valva Cardíaca. Valva Aórtica. Análise de Sobrevida.**

INTRODUCTION

Bovine pericardial bioprostheses have been used for aortic valve replacement since the early 70's, when first generation of bioprostheses became commercially available. Description[1], clinical use, and initial results have been known since then. A variety of models and materials have been introduced for everyday use and evaluated for long-term use[2,3].

The choice of which prosthesis to use – biological or mechanic – was not associated to a significant improvement in survival[4,5]. However, in terms of freedom from reintervention during a 20-year follow-up, bioprostheses were inferior compared to mechanical prostheses[5]. The is no consense in literature regarding long-term results of bioprosthesis, which vary not only by age group, anatomic implant position or materials used, but also by unique manufacturing and preservation techniques used by each manufacturer.

In the Heart Institute of the Universidade de São Paulo (InCOR – FMUSP) the first bovine pericardial bioprosthesis to be used was the Fisics-InCOR prosthesis[6] in 1984. Pomerantzeff et al.[7] published the results of 15-years of experience with 2607 of those prostheses. In 2001, the Braile Biomédica® bovine pericardial bioprosthesis started to be used at InCOR-FMUSP, but its everyday use began only in 2006.

The aim of this paper is to analyze the initial experience with Braile Biomédica® bovine pericardial bioprosthesis, from 2006 to 2011, concerning survival and freedom from endocarditis, structural dysfunction, and reintervention.

METHODS

This study was observational and retrospective, using a historic cohort, from April 2006 to December 2010. In that period, 196 elective consecutive aortic bioprosthesis implant surgeries were performed by the Heart Valve Surgical Team of the InCOR-FMUSP, excluding prosthetic endocarditis. Patients with previous cardiac surgery, native valve endocarditis, and mitral repair procedures were included in the analysis group. The Heart Institute Scientific Committee and the Ethics Committee of the of the University of São Paulo Medical School (FMUSP) approved the paper, with number 0453/07.

Age ranged from 16 to 85 years-old, mean of 59.41±16.41years. One hundred thirty two (67.3%) patients were male, and 64 (32.7%) were female.

Mortality rate of the analyzed group, predicted by EuroSCORE II[8] was 3.48±3.99% (ranging from 0.56 to 26.48%; median = 2.025%).

All patients were submitted to traditional surgery by median sternotomy, cardiopulmonary bypass with moderate hypothermia (28°C), aortic cannulation, and single or double venous cannulation, in cases of mitral valve involvement. Anterograde, intermittent, cold blood cardioplegic myocardial protection was performed. Aortic opening was carried out by inverted "J" aortotomy and the left atrium was opened by conventional left atriotomy. The original Braile Biomédica® sizers were used to measure the aortic annulus. Prosthetic suture in the aortic annulus was made with or without Polyester Fiber (Mersilene® or Ethibond®2-0), with pledgets at surgeon's discretion.

Main etiology of surgical aortic replacement was degenerative in 104 cases (53.1%), followed by structural dysfunction of bioprosthesis in 42 cases (21.4%), rheumatic disease in 29 (14.8%), infective endocarditis in 9 (4.6%), bicuspid aortic valve in 10 (5.1%) and other causes in 2 (1%).

Regarding prosthesis size, the prosthesis labeled number 19 by the manufacturer was used in 3 patients (1.5%), number 21 in 37 (18.9%), number 23 in 90 (45.9%), number 25 in 55 (28.1%) and number 27 in 11 (5.6%).

Associated procedures were performed in 33 patients (16.8%), 25 (12.7%) of them being mitral reconstruction and 8 (4.1%), mitral comissurotomies.

In regards to functional status (NYHA), 26 (13.3%) patients were in functional class IV, 118 (60.2%) in functional class III, 48 (24.5%) in functional class II and 4 (2.0%) in functional class I.

Follow-ups were carried out by physician's consultations at the InCOR-FMUSP, registered in the institutional electronic medical chart (sI3) or by phone interviews. Mean follow-up time was 40.29±17.05 months, and 22 patients (11.2%) failed to follow up.

The results were reported according to the Akins et al.[9] definitions in the Guidelines for reporting mortality and morbidity after cardiac valve interventions.

The GraphPad Prism6 (GraphPad Software, Inc. La Jolla, CA) software was used for the statistical analysis. Continuous data were presented as mean ± standard deviation, categorical variables as percentages (%) and exact Fisher test for comparison between groups. Survival, freedom from reintervention, endocarditis or structural dysfunction were obtained by the Kaplan-Meier estimator.

RESULTS

In-hospital mortality was 8.16% (16 patients). The *causa mortis* was cardiogenic shock in 6 patients (37.5%), pulmonary sepsis in 8 patients (50%), renal failure in 1 patient (6.25%), and hepatic failure in 1 patient (6.25%) with hepatitis C.

Patients younger than 65 years-old had 2.83% mortality (3 out of 106), while patients 65 or older had 14.4% mortality (13 out of 90). Mortality rates for the 54 reoperation cases was 7.40% whereas, while among first surgery patients, it was 8.45%.

Mortality, analyzed according to the pre-operative functional status of the patient, was 0% for NYHA I, 6.25% for NYHA II, 6.78% for NYHA III and 19.23% for NYHA IV (Table 1).

According to the procedure, isolated aortic valve replacement had the lowest mortality rate at 7.36% (12 out of 163), and the associated procedures –mitral reconstruction or comissurotomy – presented a 12.12% mortality rate (4 out of 33).

In the follow-up, there were 12 prosthesis-related deaths and 11 non-related deaths. The most common prosthesis-related death was infective endocarditis, in 10 cases, followed by one case of stroke and one unclarified death.

For the 10 cases of infective endocarditis that culminated in death, initial infection was recognized in 5 cases: one erysipelas, one pulmonary infection, and 3 urinary infections.

For the 11 non-related deaths, the main cause of death was pulmonary infection in 3 cases, followed by cardiac failure and urinary infection, both with two cases. There was one case each of abdominal sepsis, acute intestinal obstruction, pulmonary cancer, and trauma (Table 2).

The linearized event rates of reoperation, death, infective endocarditis and structural dysfunction are reported in Table 3. There was neither hemolysis nor non-structural dysfunction on this series.

Actuarial survival in 88 months was 90.59±2.56% (Figure 1). Freedom from reintervention curve (Figure 2), infective endocarditis and structural dysfunction (Figure 3) was 91.38±2.79%, 89.84±2.92% and 98.57±0.72% in 88 months, respectively.

Table 1. Subgroups in hospital mortality.

Subgroups	Mortality (%)	*P*
Functional Status (NYHA)		
I, II and III	6.47	0.433
IV	19.23	
Number of prior interventions		
First surgery	8.45	1.00
One or more	7.40	
Associated procedures		
Isolated aortic replacement	7.36	0.482
Aortic replacement and mitral procedure	12.12	
Age group		
<65 years	2.83	0.0036
≥65 years	14.4	
Ejection Fraction		
>50%	5.88	0.0931
≤50%	13.33	

Table 2. Late mortality causes.

Related Deaths	
Infective endocarditis	10
Stroke	1
Unclarified	1
Non-Related Deaths	
Pulmonary infection	3
Cardiac failure	2
Urinary infection	2
Abdominal sepsis	1
Acute abdominal obstruction	1
Pulmonary cancer	1
Trauma	1
Total	23

Table 3. Linearized event rates (late outcome).

Event	% Patients/Year
Reintervention	0.68
Death	1.065
Endocarditis	0.91
Structural dysfunction	0.075

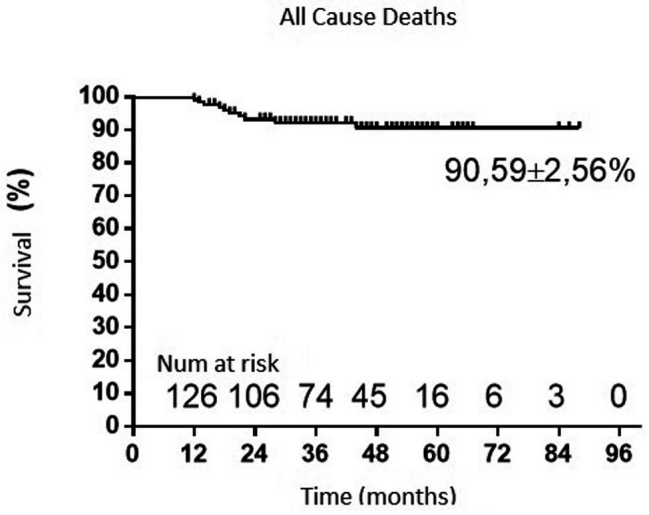

Fig. 1 - Kaplan-Meier survival curve after 88 months of aortic valve prosthetic implantation.

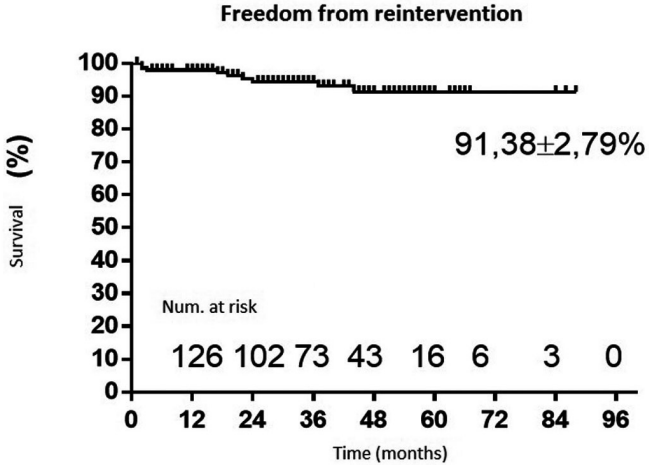

Fig. 2 - Kaplan-Meier freedom from reintervention curve after 88 months of aortic valve prosthetic implantation.

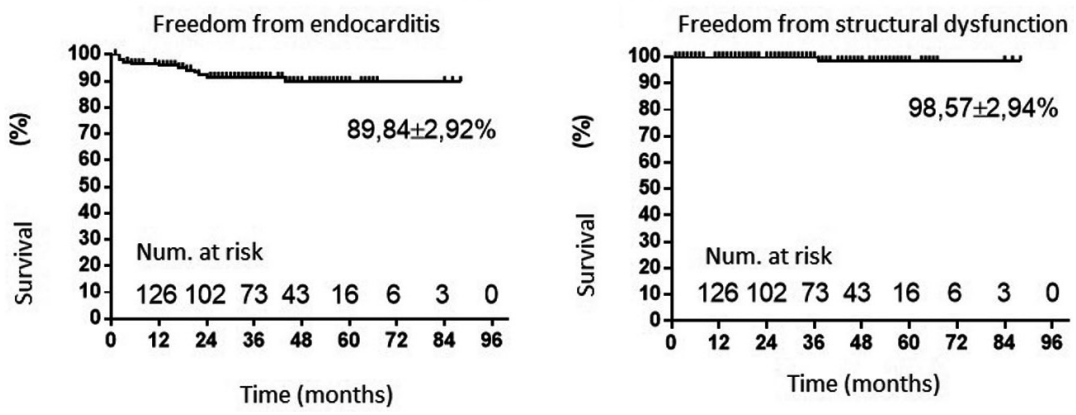

Fig. 3 - Kaplan-Meier curves, freedom from endocarditis and from structural valve dysfunction after 88 months of aortic valve prosthetic implantation.

DISCUSSION

There is few data about longevity of Brazilian bioprosthesis in comparison with other[10], and as for the Braile Biomédica® prosthesis, there are no data that show their use in an everyday basis, evaluating its performance in a consecutive group of patients that include reoperations, endocarditis and associated surgeries[11,12].

In the analyzed group, mean age was 59 years. For the most part, in the Brazilian Public Health Care System, indication of bioprosthesis in young patients is due to the inability to follow adequate medical control of anticoagulation, ruling out the use of mechanical prosthesis. As a national reference center, there is a major concern about adequate control of anticoagulation in patients coming from other regions, leading to a greater use of bioprostheses.

In-hospital mortality was 8.16%, compared to national reports of 8%[13] mortality for general cardiac surgery and from 7.0 to 15.0% for aortic valve replacement[14,15], not adjusted. Being a tertiary center with great experience in bioprosthesis implantation[6,7] and in reoperations[16,17], there is a high incidence of previous cardiac surgeries, historically rising – from 1980 to 1999, 22.8% were reoperations[16] and, from 2006 to 2010, 27.5% were reoperations. This incidence is only

comparable to Bacco et al.[15], that, with 25.6% incidence of reoperations, found 15% in-hospital mortality for aortic valve replacement. Despite mortality higher than data from the United States and the United Kingdom[18,19], it is worth mentioning the need of pairing mortality to surgical risk[8,9,20] and of internal validation of the risk score models. In Canada, Forcillo et al.[21], analyzing Carpentier-Edwards bovine pericardial bioprosthesis in aortic position, found actuarial survival of 78±2% at 5 years, lower than the 90.59±2.63% actuarial survival at 5 years found by us.

EuroSCORE II[8] mortality estimate was 3.48±3.99% and our actual mortality was 8.16%. At a concomitant period, from October 2008 to July 2009, Lisboa et al.[22] demonstrated inadequate calibration of EuroSCORE II at InCOR-FMUSP, and found better calibration of additive and logistic EuroSCORE and InsCor, a locally developed risk model. Indeed, the poorly calibrated EuroSCORE II to predict mortality in the group of patients evaluated reinforces the need for implementation, and widespread use of a Brazilian risk model.

In-hospital mortality for redo operations is considered higher than first operations[8,17], with 2.87 odds ratio (95% CI 2.03 – 4.05)[23]. However, interestingly we noted similar in-hospital mortality rates between redo's and first surgeries, 7.40% and 8.40%, respectively. In a previous historical cohort at the same institution, Brandão et al.[17] found 8.7% mortality for cardiac reoperations. The reasons for improvement are not enterily clear, but the technique standardization by Pomerantzeff et al.[16] led to progressive improvement of outcomes as well as training of a specific team, which was responsible for over 95% of the redo operations at the institution.

In agreement with the literature[8,17,23,24], our series showed mortality rates increasing according to the functional status. Associated procedures also showed higher mortality rates, but without statistical significance.

Age group and anatomic prosthetic position are the main determinant factors of calcific bioprosthesis dysfunction, with greater longevity found in the elderly with aortic prosthesis[25]. However, rising numbers of bioprosthesis implantation in younger patients, due to contra indications of oral anticoagulation or the impossibility of adequately controlling anticoagulation, have given rise to a concern about degeneration resistance of biologic prosthesis in younger patients. To ilustrate, the only case of structural dysfunction of the cohort occurred 37 months after implantation, in a 44-year-old patient, who did not receive a mechanical prosthesis because his social condition precluded adequate anticoagulation control.

We found freedom from structural dysfunction of 98.57±0.70% at 5 years, comparable to the Carpentier-Edwards prosthesis[21] at 98±0.2% and superior to the St Jude Biocor[15] at 89.2±3.5%, and a linearized rate of 0.075% patients-year.

Using Braile Biomédica® prosthesis, we found freedom from infective endocarditis at 5 years of 89.85±2.94%, while Carpentier-Edwards prosthesis[21] was 98±0.3%, the difference is partially due to the economic and social differences between the health care systems where both prostheses were analyzed (Brazil and Canada).

The present study has as limitations the retrospective cohort of a single center, with a limited number of cases and insufficient power to rare events.

CONCLUSION

Braile Biomédica® bovine pericardial prosthesis in aortic position led to similar durability and survival to that reported in the international literature. Further follow-up is required to evaluate future incidence of infective endocarditis and structural dysfunction.

Authors' roles & responsibilities	
LGA	Analysis and/or interpretation of data, statistical analysis, study conception and design, drafting of the manuscript and critical review of the content
ETV	Analysis and/or interpretation of data
JADS	Analysis and/or interpretation of data
CMAB	Analysis and/or interpretation of data, statistical analysis, study conception and design, drafting of the manuscript and critical review of the content
PMAP	Analysis and/or interpretation of data, final approval of the manuscript, study conception and design, drafting of the manuscript and critical review of the content
FBJ	Final approval of the manuscript

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