Hospital Risk Factors for Bovine Pericardial Bioprosthesis Valve Implantation

Mateus W. De Bacco, João Ricardo M. Sant'Anna, Gustavo De Bacco, Roberto T. Sant'Anna, Marisa F. Santos, Edemar Pereira, Altamiro Reis da Costa, Paulo Roberto Prates, Renato A. K. Kalil, Ivo A. Nesralla

Instituto de Cardiologia do Rio Grande do Sul/Fundação Universitária de Cardiologia – Porto Alegre, RS - Brazil

Summary

Background: Identification of preoperative heart valve surgery risk factors aim to improve surgical outcomes with the possibility to offset conditions related to increased morbidity and mortality.

Objective: Intent of this study is to identify hospital risk factors in patients undergoing bovine pericardial bioprosthesis implantation.

Methods: Retrospective study including 703 consecutive patients who underwent implantation of at least one St. Jude Medical-Biocor™ bovine pericardial bioprosthesis between September 1991 and December 2005 at the Rio Grande do Sul Cardiology Institute; 392 were aortic, 250 were mitral and 61 were mitroaortic. Characteristics analyzed were gender, age, body mass index, NYHA (New York Heart Association) functional class, ejection fraction, valve lesions, systemic hypertension, diabetes mellitus, kidney function, arrhythmias, prior heart surgery, coronary artery bypass graft, tricuspid valve surgery and elective, urgent or emergency surgery. Main outcome was in-hospital mortality. Relationship between risk factors and in-hospital mortality was analyzed using logistic regression.

Results: Were 101 (14.3%) in-hospital deaths. Characteristics with significant relationship to increased mortality were female gender (p<0.001), age over 70 years (p=0.004), atrial fibrillation (p=0.006), diabetes mellitus (p=0.043), creatinine > 2.4mg/dl (p=0.004), functional class IV (p<0.001), mitral valve lesion (p<0.001), previous heart surgery (p=0.005), tricuspid valve surgery (p<0.001) and emergency surgery (p<0.001).

Conclusion: Mortality rate observed is accepted by literature and is justifiable due to the high prevalence of risk factors, showing an increased significance level for female gender, age above 70, functional class IV, tricuspid valve repairs and emergency surgery. Offsetting these factors could contribute to reduced in-hospital mortality for valve surgery. (Arq Bras Cardiol 2007;89(2):113-118)

Key words: Thoracic surgery; hospital mortality; risk factors; bioprosthesis; heart valve prosthesis implantation.

Introduction

Literature has demonstrated variable risk for heart valve replacement surgery reporting in-hospital mortality between 1% and 15%, regardless of the type of implant replacement[1-4]. This variation is justified by differences in the demographic characteristics of the surgical patients, perioperative techniques, valve implantation position, concomitant surgical procedures and post operative care.

Surgical experience has demonstrated that factors such as advanced age, reduced body mass index, presence of kidney failure, reduced left ventricle ejection fraction, indications for emergency and repeat valve surgery, among others, contribute to increased in-hospital mortality and require greater attention from the doctors involved in the clinical and surgical patient care[5-11].

Mailing Address: João Ricardo M. Sant'Anna •
IC/FUC - Unidade de Pesquisa - Av. Princesa Isabel, 370 - 90620-001 - Porto Alegre, RS - Brazil
E-mail: santana.pesquisa@cardiologia.org.br
Manuscript received December 18,2006; revised manuscript received February 22, 2007; accepted March 13, 2007.

Nevertheless, retrospective studies involving a large number of patients could identify, with a greater degree of certainty, the characteristics that can affect surgical outcomes and create risk stratification models that could be used in different institutions[1-4]. These characteristics are called hospital risk factors and when identified and averted, can reduce surgical morbidity and mortality, as well as patient care costs.

The objective of the present study is to retrospectively analyze a series of patients who underwent St. Jude medical-Biocor™ bovine pericardial bioprosthesis heart valve implantations at the Rio Grande do Sul Cardiology Institute/Cardiology University Foundation, in order to identify characteristics that influence in-hospital mortality.

Methods

Study design - Retrospective cohort study.

Population - Between September 1991 and December 2005, 703 patients were included in the study who had undergone at least one St. Jude Medical-Biocor™ bovine pericardial bioprosthesis implantation at the Rio Grande do Sul

Cardiology Institute; of these, 359 (51%) were male and 344 (49%) were female. Ages ranged from 17 to 88 years, mean 62.5 years and standard deviation ± 12.6 years. In relation to New York Heart Association (NYHA) functional classes, 19 (2.8%) patients were class I, 151 (22.4%) class II, 348 (51.7%) class III and 155 (23.1%) were class IV. Systemic hypertension was presented by 292 (41.5%) patients, 69 (9.8%) had diabetes mellitus, 52 (7.5%) had a body mass index (BMI) lower than 20 kg/m^2 and 343 (49.8%) had a BMI greater than 25 kg/m^2. Ejection fractions were greater than 50% in 512 (80.4%) patients, between 30% and 50% in 104 (16.3%) and less than 30% in 21 (3.3%). Preoperative conditions revealed 532 (75.7%) with sinus rhythm, 152 (21.6%) with atrial fibrillation and 19 (2.7%) with atrioventricular block. Creatinine serum was greater than 2.4 g/dl in 13 (1.8%) patients and 6 (0.8%) were on dialysis.

Valve surgery - All patients underwent cardiopulmonary bypass during surgery with a membrane oxygenator and varying levels of hemodilution and hypothermia. The myocardium was preserved using hypothermic cardioplegia with ST. Thomas II solution. Intra and post operative care were administered as described above[12].

Out of the total number of patients, 506 underwent their first heart surgery, 142 had previous heart surgery and 55 had undergone two or more heart surgeries, for a total of 703 procedures. The St. Jude Medical-Biocor™ bioprosthesis implantations included 250 (35.6%) isolated mitral valve procedures, 392 (55.8%) aortic valve procedures and 61 (8.6%) mitroaortic procedures. The valve replacement surgeries were combined with 158 (22.4%) coronary artery bypass grafts or repair of mechanical defects secondary to myocardial ischemia and 42 (5.9%) procedures for concomitant tricuspid valve surgery. In relation to surgery type, 635 were elective, 17 were urgent, 5 were emergency and 20 patients required repeat surgery.

Outcomes and risk factor definitions - The main outcome considered was death during the hospital stay for the heart valve bioprosthesis implantation surgery.

The deaths were classified as: bioprosthesis related (such as thrombosis, endocarditis or dysfunction causing heart failure, regardless whether heart surgery was required); surgery related (rupture of the atrioventricular junction, bleeding); cardiac related (such as heart failure unrelated to bioprosthesis failure); or related to factors other than the heart (arising from complications of other subsystems such as neurological, renal or pulmonary).

The demographic characteristics evaluated in relation to in-hospital mortality were: gender, age, cardiac arrhythmias, ejection fraction, systemic hypertension, diabetes mellitus, body mass index, kidney failure (creatinine serum greater than 2.4 g/dl and/or on dialysis), NYHA functional class, type of valve lesion (aortic, mitral or mitroaortic) and prior heart surgery.

The surgical variables evaluated were: timeframe when surgery was performed, concomitant surgery (coronary artery bypass graft and tricuspid surgery), repeat valve surgery and type of surgery (elective, urgent or emergency).

Ethical considerations - The research project for this study was submitted to the Research Department of the Rio Grande do Sul Cardiology Institute and was approved by the institution's Research Ethics Committee. Throughout the study, patient privacy and medical information confidentiality standards were respected. Current and retrospective patient information was obtained from the medical charts for patients who were being followed-up at the institution's clinic or by telephone contact made directly or by a clinic assistant.

Data analysis - Univariate and multivariate statistical analysis to determine predominant and independent risk predictors of in-hospital mortality was conducted using the software program SPSS for Windows, version 14.0. These risk predictors were determined using the chi-square test and logistic regression. In the multivariate analysis, the greatest discriminatory power of the variables was used. All significant characteristics ($p<0.005$) in the univariate analysis were included in the multivariate analysis. Risk characteristics were determined when there was a significant association with in-hospital mortality, using a critical alpha value of 0.05.

Results

In-hospital mortality - In-hospital mortality was 14.3%. From the 101 deaths, 2 (1.9%) were bioprosthesis related (1 case of thrombosis in the prosthesis and 1 case of bacterial endocarditis confirmed by a blood culture with previous respiratory infection and infection of the venous access); 26 (25.7%) were surgery-related (25 secondary to bleeding and 1 aorta dissection); 38 (37.6%) were heart-related (30 cases of left ventricle failure, 2 cases of arrhythmia and 6 cases of intraoperatory left ventricle failure); and 35 (34.6%) were related to factors other than the heart (24 cases of sepsis causing multiple organ failure, 2 cases secondary to neurological damage, 1 case of pulmonary embolism and 8 cases of kidney failure). Between 1991 and 1995, 63 procedures were performed, with a mortality rate of 9.5% (6 deaths); between 1996 and 2000, 295 procedures were performed with a mortality rate of 14.9% (44 deaths); and between 2001 and 2005, 345 procedures were performed with a mortality rate of 14.7% (51 deaths).

Risk factors - The preoperative characteristics, called risk predictors are summarized in table 1.

The statistically significant characteristics related to increased mortality were: female gender ($p < 0.001$), age over 70 years ($p = 0.004$), atrial fibrillation ($p = 0.006$), diabetes mellitus ($p = 0.043$), creatinine serum higher than 2.4 g/dl ($p = 0.004$), NYHA functional class IV ($p < 0.001$), mitral valve lesion ($p < 0.001$) and previous heart surgery ($p = 0.005$).

The statistically significant surgical characteristics related to an elevated in-hospital mortality were: concomitant tricuspid valve surgery ($p<0.001$) and emergency surgery ($p< 0.001$). Hospital mortality was 9.4% for aortic replacement, 20.0% for mitral valve replacement and 23.0% for mitroaortic replacement. The higher mortality rate in the mitral valve replacement group agrees with data in the medical literature[13-16].

Table 1 – In-hospital mortality according to pre-operative characteristics

	Frequency	%	Mortality	%	p
Gender					
Female	344	48.9	68	19.8	< 0.001
Male	359	51.1	33	9.2	
Age					
< 50 years	100	14.2	8	8.0	0.004
50-59 years	130	18.5	18	13.8	
60-69 years	254	36.2	31	12.2	
70-79 years	192	27.4	35	18.2	
> 80 years	26	3.7	9	34.6	
BMI					
< 20 kg/m²	53	7.7	8	15.1	ns
20-25 kg/m²	293	42.5	48	16.4	
> 25 kg/m²	343	49.8	43	12.5	
Creatinine					
> 2.4 mg/dl	13	1.9	6	46.2	0.004
< 2.4 mg/dl	689	98.1	95	13.8	
Dialysis					
Yes	6	0.9	3	50.0	0.056
No	696	99.1	98	14.1	
SH					
Yes	292	41.5	39	13.4	ns
No	411	58.5	62	15.1	
DM					
Yes	69	9.8	16	23.2	0.043
No	634	90.2	85	13.4	
NYHA functional class					
I/II	170	25.3	13	7.6	< 0.001
III	348	51.7	44	12.6	
IV	155	23.0	40	25.8	
Preoperative rhythm					
Sinus	532	75.7	64	12.0	0.006
AF	152	21.6	32	21.1	
AVB	19	2.7	5	26.3	
Ejection fraction					
> 50%	512	80.4	71	13.9	ns
30-50%	104	16.3	16	15.4	
< 30%	21	3.3	5	23.8	
Valve lesion					
Aortic	392	55.8	37	9.4	< 0.001
Mitral	250	35.6	50	20.0	
Mitroaortic	61	8.7	14	23.0	

Table 1 continuation

Coronary artery bypass graft					
Yes	158	22.5	30	19.0	ns
No	545	77.5	71	13.0	
Tricuspid valve repair					
Yes	42	6.0	15	35.7	< 0.001
No	661	94.0	86	13.0	
Prior heart surgery					
No	506	72.0	60	11.9	0.005
One	142	20.2	27	19.0	
Two or more	55	7.8	14	25.5	
Repeat surgery					
Yes	20	2.8	4	20.0	ns
No	683	91.2	97	14.2	
Type of surgery					
Elective	635	96.7	77	12.1	< 0.001
Urgent	17	2.6	5	29.4	
Emergency	5	0.8	3	60.0	

BMI - body mass index; ns - p value not statistically significant; SH - systemic hypertension; DM - diabetes mellitus; NYHA - New York Heart Association; AF - atrial fibrillation; AVB - atrioventricular block.

Discussion

Valve implantation surgery is currently the second most common cardiac surgical procedure and is associated with in-hospital mortality of 1% to 15%[1-4]. Preoperative risk predictors in heart valve surgery have been studied since 1985[17]. Since then, considerable variations have been reported in the factors determined as in-hospital mortality predictors. The differences between the studies have made it more difficult for surgeons and large surgical centers to implement a risk stratification model.

Ambler et al[1] developed a risk stratification model for heart valve surgery, considering characteristics associated to an elevated in-hospital mortality, such as age, body mass index, gender, type of valve lesion, coronary artery bypass graft and/or concomitant tricuspid valve surgery, kidney failure, diabetes mellitus, hypertension, low ejection fraction, arrhythmia, number of previous heart surgeries and surgery priority. The greatest risk factors were emergency surgery followed by age over 79 years, kidney failure with dialysis and two or more prior heart surgeries.

Jamieson et al[2] identified 51 preoperative characteristics related to operative and in-hospital mortality. The greatest risk factors related to an elevated mortality rate were: emergency surgery, kidney failure (with or without dialysis), repeat surgery and NYHA functional class IV. Factors with lower risk included age over 70 years, female gender, urgent surgery, low ejection fraction, cerebral hemorrhage, congestive heart failure, arrhythmia and use of inotropic medications.

Hellgrena et al[18], found that the characteristics related to greater morbidity and mortality for heart valve surgery were: age over 70 years; elevated NYHA functional class, in particular class IV; and preoperative cardiac arrest. Edwards et al[19] identified repeat surgery, emergency surgery, kidney failure and cardiac arrest as independent risk factors for isolated valve replacement surgery.

Nowicki et al[20], in their study on independent risk factors for aortic valve replacement surgery reported the following variables: age over 70 years, small body surface, elevated creatinine, prior heart surgery, NYHA functional class IV, prior cardiac arrest, congestive heart failure, atrial fibrillation, emergency surgery, year of the surgery and concomitant coronary artery bypass graft surgery. The following characteristics were statistically significant for mitral valve surgery: female gender, advanced age, diabetes mellitus, coronary artery bypass graft surgery, previous stroke, elevated creatinine, NYHA functional class IV, emergency surgery and congestive heart failure.

Roques et al[21], using data collected from 5,762 patients between September and December 1995, published the EuroSCORE, a predictor of in-hospital mortality. The variables that were significantly associated with an elevated mortality were: advanced age, creatinine, prior heart surgery, left ventricle function, congestive heart failure, pulmonary hypertension, endocarditis, emergency surgery, multiple valve replacement or tricuspid procedure and concomitant coronary artery bypass graft surgery or thoracic surgery.

Braile et al[22], in a study including 663 patients who underwent bovine pericardial valve implantations in the

mitral position between 1977 and 1988 at the Cardiovascular Disease Institute in São José do Rio Preto (SP), identified some factors that could interfere with the durability of the bioprosthesis, such as the patient's age and metabolic conditions, the position of the implant as well as the material and technique used to prepare the valve for implantation. The authors reported that they preferred doing bioprosthesis implants in patients over 21 year of age, contradicting other studies that don't recommend the use of bioprosthesis for patients under the age of 30, except for women that wish to become pregnant[23]. In-hospital mortality was recorded as 9.2%; 13.2% was recorded for the 586 group I patients (over age 21) which is lower than the value found in this study series. The mortality rate for the 77 group II patients (under 21 years of age) was 6.3%.

Also in Brazil, Brandão et al[24] presented a study of risk factors for a series of patients who underwent bileaflet mechanical prosthesis implantations. The type of prosthesis used, which was different from that used by the authors and others reported in literature, could have modified the distribution of the patient demographic characteristics such as age, that had a lower mean (38.7 years). Nevertheless, mortality for the mitral patients was 13.5%, which was higher than that for the aortic patients (7.5%), and agrees with the values observed in the present study.

Conclusion

To determine the factors that contribute to in-hospital mortality, some risk predictors identified by other studies in literature[1-11] were used, with emphasis on those presented by Ambler et al[1]. This position was taken as the medical information considered by these authors is readily available and is routinely recorded by hospitals. Further studies on the quantification of each factor and the clinical applicability of a score based on this determination are required. Nevertheless, it must be considered that this focus excludes some known risk factors, such as pulmonary hypertension, chronic obstructive pulmonary disease and peripheral vascular disease[2,25].

The current alterations in the indication criteria for heart valve surgery is a result of at least two reasons[18]. On one hand, patients in late disease stages undergo surgery as a consequence of natural aging which causes a more severe attack on the system and increased in-hospital risk. This observation could justify the increased mortality observed during the more recent study periods.

On the other hand, the current tendency for patients with less serious valve diseases is to recommend surgery in earlier disease stages when there is lower prevalence of risk factors and therefore lower mortality. It is possible that this population, which should include younger patients, would have had mechanical prosthesis implantations and therefore would have been excluded from this study. The inclusion of these patients, with an assumed lower in-hospital mortality rate than the bioprosthesis population, could have contributed to a more favorable surgical outcome.

It is hoped that some of the surgical risk factors identified in this study (female gender, age over 70 years, atrial fibrillation, diabetes, kidney failure, NYHA functional class IV, mitral valve lesion, prior heart surgery, concomitant tricuspid valve surgery and type of surgery) will contribute to lowering the risk for altering indication criteria (earlier), improving clinical compensation or modifying surgical routines. If so, it would be possible to reduce in-hospital mortality and patient care costs.

References

1. Ambler G, Omar RZ, Royson P, Kinsman R, Keogh BE, Taylor KM. Generic, simple risk stratification model for heart valve surgery. Circulation. 2005;112:224-31.
2. Jamieson WRE, Edwards FH, Schwartz M, Bero JW, Clark RE, Grover FL. Risk stratification for cardiac valve replacement. National Cardiac Surgery Database. Ann Thorac Surg. 1999;67:943-51.
3. Jin R, Grunkemeier GL, Starr A. Validation and refinement of mortality risk models for heart valve surgery. Ann Thorac Surg. 2005;80:471-9.
4. Kuduvalli M, Grayson AD, Au J, Grotte G, Bridgewater B, Fabri BM. et al. A multi-centre additive and logistic risk model for in-hospital mortality following aortic valve replacement. Eur J Cardiothorac Surg. 2007; 31 (4): 607-13.
5. Langanay T, De Latour B, Ligier K, Derieux T, Agnino A, Verhoye JP, et al. Surgery for aortic stenosis in octogenarians: influence of coronary disease and other comorbidities on hospital mortality. J Heart Valve Dis. 2004;13(4):545-52.
6. Mistiaen W, Van Cauwelaert P, Muylaert P, Wuyts F, Harrisson F, Bortier H. Risk factors and survival after aortic valve replacement in octogenarians. J Heart Valve Dis. 2004;13(4):538-44.
7. Albeyoglu SC, Filizcan U, Sargin M, Cakmak M, Goksel O, Bayserke O, et al. Determinants of hospital mortality after repeat mitral valve surgery for rheumatic mitral valve disease. Thorac Cardiovasc Surg. 2006;54(4):244-9.
8. Litmathe J, Boeken U, Kurt M, Feindt P, Gams E. Predictive risk factors in double-valve replacement (AVR and MVR) compared to isolated aortic valve replacement. Thorac Cardiovasc Surg. 2006;54(7):459-63.
9. Florath I, Albert AA, Rosendahl UP, Hassanein WM, Bauer S, Ennker IC, et al. Body mass index: a risk factor for 30-day or six-month mortality in patients undergoing aortic valve replacement? J Heart Valve Dis. 2006;15(3):336-44.
10. Duncan AI, Lin J, Koch CG, Gillinov AM, Xu M, Starr NJ. The impact of gender on in-hospital mortality and morbidity after isolated aortic valve replacement. Anesth Analg. 2006;103(4):800-8.
11. Christiansen S, Autschbach R. Perioperative risk of aortic valve replacement after coronary artery bypass grafting. Thorac Cardiovasc Surg. 2006;54(3):157-61.
12. Nesralla I. Cardiologia cirúrgica: perspectivas para o ano 2000. São Paulo: BYK; 1994.
13. Aoyagi S, Oryoji A, Nishi Y, Tanaka K, Kosuga K, Oishi K. Long-term results of valve replacement with the St. Jude Medical valve. J Thorac Cardiovasc Surg. 1994;108:1021-9.
14. Khan S, Chaux A, Matloff J, Blanche C, DeRobertis M, Kass R, et al. The St. Jude Medical valve: experience with 1000 cases. J Thorac Cardiovasc Surg. 1994;108 (6):1010-9; discussion 1019-20.
15. Baudet EM, Puel V, McBride JT, Grimaud JP, Roques F, Clerc F, et al. Long-term results of valve replacement with the St. Jude Medical prosthesis. J Thorac Cardiovasc Surg. 1995;109:858-70.
16. Fernandez J, Laub GW, Adkins MS, Anderson WA, Chen C, Bailey BM, et al. Early and late-phase events after valve replacement with the St. Jude Medical prosthesis in 1,200 patients. J Thorac Cardiovasc Surg. 1994;107:394-407.

17. Scott WC, Miller DC, Haverich A, Dawkins K, Mitchell RS, Jamieson SW, et al. Determinants of operative mortality for patients undergoing aortic valve replacement: discriminant analysis of 1,479 operations. J Thorac Cardiovasc Surg. 1985;89:400-13.

18. Hellgrena L, Kvidalb P, Stahlea E. Improved early results after heart valve surgery over the last decade. Eur J Cardio-thorac Surg. 2002;22:904-11.

19. Edwards FH, Peterson ED, Coombs LP, DeLong ER, Jamieson E, Shroyer LW, et al. Prediction of operative mortality after valve replacement surgery. J Am Coll Cardiol. 2001;37:885-92.

20. Nowicki ER, Birkmeyer NJ, Weintraub RW, Leavitt BJ, Sanders JH, Dacey LJ, et al. Multivariable prediction of in-hospital mortality associated with aortic and mitral valve surgery in Northern New England. Ann Thorac Surg. 2004;77(6):1966-77.

21. Roques F, Nashef SA, Michel P. Risk factors for early mortality after valve surgery in Europe in the 1990s: lessons from the EuroSCORE pilot program. J Heart Valve Dis. 2001;10:572-7; discussion 577-8.

22. Braile DM, Ardito RV, Greco OT, Lorga AM. IMC bovine pericardial valve: 11 years. J Cardiovasc Surg. 1991;6(4):580-8.

23. Reul GJ Jr, Cooley DA, Duncan JM, Frazer OH, Hallman GL, Livesay JJ, et al. Valve failure with the Ionescu-Shiley bovine pericardial bioprosthesis: analysis of 2,680 patients. J Vasc Surg. 1985;2:192-204.

24. Brandão CMA, Pomerantzeff PMA, Cunha CR, Morales JIE, Puig LB, Grinberg M, et al. Substituição valvar com próteses mecânicas de duplo folheto. Rev Bras Cir Cardiovasc. 2000;15(3):227-33.

25. Roques F, Nashef SAM, Michel P, Gauducheau E, de Vincentiis C, Baudet E, et al. Risk factors and outcome in European cardiac surgery: analysis of the euroSCORE multinational database of 19,030 patients. Eur J Cardio-thorac Surg. 1999;15:816-23.