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Outcomes of patients subjected to aortic valve replacement surgery using mechanical or biological prostheses

Resultados de pacientes submetidos à cirurgia de substituição valvar aórtica usando próteses mecânicas ou biológicas

Adriana Silveira de Almeida[1], Paulo Dornelles Picon[2], Orlando Carlos Belmonte Wender[3]

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Abstract

Objective: **This paper evaluates outcomes in patients subjected to surgery for replacement of the aortic valve using biological or mechanical substitutes, where selection of the type of prosthesis is relevant.**

Methods: **Three hundred and one patients, randomly selected, who had been subjected to aortic valve replacement surgery between 1990 and 2005, with a maximum follow-up period of 20 years.**

Results: **Survival at 5, 10 and 15 years after surgery using mechanical substitute was 83.9%, 75.4% and 60.2% and, for biological substitute, was 89.3%, 70.4% and 58.4%, respectively (*P*=0.939). Factors associated with death were: age, obesity, pulmonary disease, arrhythmia, bleeding and aortic valve failure. Probability free of reoperation for these patients at 5, 10 and 15 years after surgery using mechanical substitute was 97.9%, 95.8% and 95.8% and, for those using bioprostheses, was 94.6%, 91.0% and 83.3%, respectively (*P*=0.057). Factors associated with reoperation were: renal failure, prosthesis endocarditis and age. Probability free of bleeding events at 5, 10 and 15 years after surgery using mechanical substitute was 94.5%, 91.7% and 91.7% and, for bioprostheses, was 98.6%, 97.8% and 97.8%, respectively (*P*=0.047). Factors associated with bleeding events were: renal failure and mechanical prostheses.**

***Conclusions*: The authors have concluded that: 1) mortality was statistically similar in the groups; 2) patient characteristics at baseline were a major determinant of late mortality after surgery; 3) there was a tendency toward reoperation in the bioprostheses group; 4) patients using mechanical prosthesis had more bleeding events as time passed; 5) data presented in this paper is in accordance with current literature.**

***Descriptors*: Bioprosthesis. Heart Valve Prosthesis Implantation. Aortic Valve. Heart Valve Prosthesis.**

1. Specialist in Cardiovascular Surgery at MEC/Master's Degree in Cardiology and Cardiovascular Sciences at Federal University of Rio Grande do Sul (UFRGS); Cardiovascular Surgeon Physician of the Cardiovascular Surgery Service at Hospital Nossa Senhora da Conceição, Grupo Hospitalar Conceição, Porto Alegre, RS, Brazil.
2. PhD in Cardiology at UFRGS; Adjunct Professor of the Internal Medicine Department at UFRGS Medical School, Porto Alegre, RS, Brazil.
3. PhD in Medicine at Munich University, Germany; Associate Professor of the Surgery Department of UFRGS Medical School, Head of the Cardiovascular Surgery Service at Clinics Hospital of Porto Alegre, Porto Alegre, RS, Brazil.

This study was carried out at Clinics Hospital of Porto Alegre, Porto Alegre, RS, Brazil.

Correspondence address: Adriana S. de Almeida
Av. Princesa Isabel, 729 – sala 403 – Porto Alegre, RS
Brazil – Zip Code: 90620-001.
E-mail: adriana@analisys.com.br

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Resumo

Objetivo: **Esse estudo avalia resultados em pacientes submetidos à cirurgia para troca valvar aórtica utilizando substituto biológico ou mecânico, com poder de relevância na seleção do tipo da prótese.**

Métodos: **Foram selecionados, randomicamente, 301 pacientes submetidos à cirurgia para troca valvar aórtica entre 1990 e 2005, com seguimento máximo de 20 anos.**

Resultados: **Sobrevivência em 5, 10 e 15 anos após cirurgia utilizando substituto mecânico foi de 83,9%, 75,4% e 60,2% e, para substituto biológico, foi de 89,3%, 70,4% e 58,4%, respectivamente (*P*=0,939). Fatores associados com óbito foram: idade, obesidade, doença pulmonar, arritmias, eventos hemorrágicos e insuficiência valvar aórtica. Probabilidade livre de reoperação desses pacientes em 5, 10 e 15 anos após cirurgia utilizando substituto mecânico foi de 97,9%, 95,8% e 95,8% e, para bioprótese, foi de 94,6%, 91,0% e 83,3%, respectivamente (*P*=0,057). Fatores associados com reoperação foram: insuficiência renal, endocardite de prótese e idade. Probabilidade livre de eventos hemorrágicos em 5, 10 e 15 anos após cirurgia utilizando substituto mecânico foi de 94,5%, 91,7% e 91,7% e, para bioprótese, foi de 98,6%, 97,8% e 97,8%, respectivamente (*P*=0,047). Fatores associados com eventos hemorrágicos foram: insuficiência renal e prótese mecânica.**

Conclusões: **Os autores concluíram que: 1) mortalidade foi estatisticamente semelhante entre os grupos; 2) características basais dos pacientes foram os maiores determinantes de mortalidade tardia após a cirurgia; 3) houve tendência à reoperação para o grupo com bioprótese; 4) pacientes com prótese mecânica tiveram mais eventos hemorrágicos ao longo do tempo; 5) dados encontrados no presente estudo são concordantes com a literatura atual.**

Descritores: **Bioprótese. Implante de Prótese de Valva Cardíaca. Valva Aórtica. Próteses Valvulares Cardíacas.**

INTRODUCTION

Aortic valve replacement is the standard surgical procedure for patients with symptomatic valvular heart disease [1], accounting for 13% of all cardiac surgery in adults [2], being the most common procedure for all valve surgeries in the United States [3] and the second most common heart surgery in the UK [4]. In Brazil, according to a survey of the Department of the Unified Health System (DATASUS), implantation of prosthetic valve corresponds to 17.4% of highly complex heart surgery performed in January 2008 to August 2010, being the second most frequent [5].

More than 30 years after the introduction of modern prostheses, the choice between the biological and mechanical aortic valve remains controversial [6,7]. This is because there is no ideal substitute to provide a long life, without the use of oral anticoagulants, with no increased risk of thromboembolism and operating mechanism similar to the native valve [8-14]. Still, the clinical decision becomes increasingly challenging with the increase in life expectancy and the presence of comorbidities such as advanced age, congestive heart failure, coronary artery disease, pulmonary disease and renal failure [6].

The choice between the types of prostheses in adults is determined primarily by assessing the risk of bleeding related to anticoagulation, with a mechanical prosthesis versus the risk of structural valve deterioration, with a bioprosthesis [15,16].

There are few Brazilian studies comparing biological and mechanical prostheses, as well as studies describing the influence of comorbidities on the outcome in a period of 20 years.

Within this context, the aim of this study was to assess mortality, reoperation, and bleeding events in patients undergoing surgery for aortic valve replacement by mechanical or biological, in a tertiary referral hospital for heart surgery in southern Brazil.

METHODS

The study design was observational, retrospective and cohort.

Sample and sampling

Nine hundred and thirteen patients, aged 18 years, underwent surgery for isolated aortic valve replacement at the Clinics Hospital of Porto Alegre, Rio Grande do Sul in the period from 1 January 1990 to December 31, 2005. The study excluded cases of aneurysm, and dissection of heart surgery. Of the remaining cases, 301 patients to the cohort through the PEPI software (Programs for Epidemiologists) version 4.0 were randomly selected. With the same software, it was calculated the sample of sufficient size to detect a magnitude of effect (difference between groups) compared to 15% mortality among the types of prosthesis, maintaining a statistical power of 80% and a significance of 5%. The magnitude of effect was estimated taking into account the study of Hammermeister et al. [17].

All surgeries were performed under cardiopulmonary bypass with moderate hypothermia (32°) and cardiac arrest, using standard techniques of the Department of

Cardiovascular Surgery, Clinics Hospital of Porto Alegre, including anesthetic procedures. All prostheses used were a double-leaflet and all biological prostheses implanted were provided by the National Unified Health System After surgery, all patients were transferred to the ICU for postoperative mechanical ventilation in cardiac surgery. The maximum follow-up was 20 years, averaging 9.2 ± 4.8 years and median of 8.9 years.

The main objective was to compare mortality among individuals with mechanical and biological valve substitutes. The secondary objectives were: 1) to compare the probability of reoperation-free time and bleeding events between groups, 2) to assess predictors of death, and reoperation for bleeding events.

The clinical and surgical aspects of the treatment during the study period were completed from information in the written records of these patients. The data were evaluated by at least two authors independently. For quality control of the team's performance, 10% of the protocols were randomly selected to be reviewed by the main investigator.

The methodology of this study was based on the STROBE guidelines (Strengthening the Reporting of Observational Studies in Epidemiology) [18].

The death records were searched in the State Health Secretariat of Rio Grande do Sul, Center for Health Information - NIS, in Porto Alegre.

Complications related to the prosthesis were recorded in accordance with the Guidelines for Reporting Mortality and Morbidity After Cardiac Valve Interventions [19.20].

Ethical aspects

With respect to privacy and confidentiality, the anonymity of patients and the use of data obtained in the survey only for the purpose of the project were guaranteed.

The research project received approval from the Commission on Ethics in Health Research at the Clinics Hospital of Porto Alegre, registered under n° 08-147, to obtain permission to perform the study in that hospital, with financial assistance from the Incentive Fund to Research and Events (FIPE/HCPA).

Definitions

The definitions listed below were all obtained in the Guidelines for Reporting Mortality and Morbidity After Cardiac Valve Interventions [19.20].

Total deaths represents all deaths resulting from any cause in patients undergoing aortic valve surgery.

Perioperative mortality is defined as any death within 30 days after surgery, regardless of geographic location of the patient.

Hospital mortality is death during the hospital stay after surgery.

It is understood by mortality related to the prosthesis the death caused by structural deterioration, nonstructural dysfunction, thrombosis, embolism, hemorrhage, endocarditis, or death related to reoperation of a previously operated valve. Deaths caused by heart failure in patients with advanced myocardial disease and valvular function without changes are not included.

Cardiac death are all the deaths resulting from cardiac causes, including deaths related to the valves or not. They are included in this category deaths from congestive heart failure, acute myocardial infarction and arrhythmia documented, among others.

Sudden death is considered the unexplained and unexpected deaths of unknown cause. Its relationship with the valve operated is also unknown. Item reported as a separate category of valve-related mortality if the cause can not be determined by clinical or autopsy.

Hemorrhagic event is defined as any episode of internal or external bleeding that causes higher mortality, hospitalization, permanent injury such as stroke or loss of vision, or even the need for blood transfusion.

Statistical analysis

Quantitative variables were described by mean and standard deviation in cases of symmetrical distribution, or median and interquartile range in case of skewed distribution, and qualitatives through absolute and relative frequencies. The comparison between groups was performed by Student's t test for independent samples (symmetrical distribution) or Mann-Whitney (asymmetric distribution) in the case of quantitative variables and chi-squared or Fisher's exact test for qualitative variables (rates and proportions).

To assess the survival time, the probability of reoperation for bleeding events we used the Kaplan-Meier curve. We applied the chi-square log-rank test to compare curves between groups.

To control confounding factors, we used the proportional hazards model of Cox As a measure of effect, we calculated the ratio of incidences (HR) with their respective ranges, with 95% confidence. The criterion for entering the variable in the model was to produce a *P* value less than 0.20 in the bivariate analysis, except for the type of prosthesis that was considered in all models because it was the main factor under study.

The level of significance was 5% and data were analyzed with SPSS (Statistical Package for the Social Sciences) version 17.0.

RESULTS

Of the selected patients, 158 (52.5%) underwent implantation of mechanical prostheses [St Jude (n=117),

Carbomedics (n=25) and Sorin (n=16)] and 143 (47.5%) implantation of porcine prostheses [Biocor (n=70), Flumen (n=55), Bioval (n=14) and Braile Biomédica (n=4)], $p = 0.387$. The characteristics of patients enrolled in the study are listed in Table 1.

Considering the hospital outcomes, patients who underwent implantation of a bioprosthesis were hospitalized longer (P <0.001), presented longer stay in the intensive care unit (P = 0.001), total mechanical ventilation time significantly higher (P <0.001) and a larger number of cases of pneumonia (P = 0.045), as shown in Table 2.

Table 1. Characteristics of the sample

Variables	Sample (n=301)	Mechanical prosthesis (n=158)	Biologal prosthesis (n=143)	*P*
Mean age±DP	61.4±12.9	58.0±12.9	65.1±11.9	<0.001
Age range - n (%)				
≤50 years	60 (19.9)	43 (27.2)[3]	17 (11.9)	
51 - 60 years	66 (21.9)	38 (24.1)	28 (19.6)	<0.001
61 - 70 years	97 (32.2)	50 (31.6)	47 (32.9)	
≥71 years	78 (25.9)	27 (19.1)	51 (35.7)[3]	
Gender - n (%)				
Male	183 (60.8)	88 (55.7)	95 (66.4)	0.074
Female	118 (39.2)	70 (44.3)	48 (33.6)	
BMI (kg/m²) - Mean±SD	25.8±4.4	26.5±4.5	25.0±4.1	0.005
Obesity [1] - n (%)	48 (15.9)	32 (20.3)	16 (11.2)	0.047
Morbid obesity [2] - n (%)	6 (2.0)	4 (2.5)	2 (1.4)	0.687
Functional Class (NYHA) - n (%)				
I-II	155 (51.5)	88 (55.7)	67 (46.9)	0.156
III-IV	146 (48.5)	70 (44.3)	76 (53.1)	
Chronic atrial fibrillation - n (%)	23 (7.6)	12 (7.6)	11 (7.7)	1.000
Diabetes mellitus - n (%)	35 (11.6)	20 (12.7)	15 (10.5)	0.685
COPD - n (%)	108 (35.9)	56 (35.4)	52 (36.4)	0.963
Stroke- n (%)	11 (3.7)	5 (3.2)	6 (4.2)	0.866
SAH - n (%)	244 (81.1)	122 (77.2)	122 (85.3)	0.100
MI - n (%)	14 (4.7)	8 (5.1)	6 (4.2)	0.934
Creatinine>2 mg/dL - n (%)	7 (2.3)	2 (1.3)	5 (3.5)	0.263
COPD - n (%)	1 (0.3)	0 (0.0)	1 (0.7)	0.475
Emergency surgery - n (%)	4 (1.3)	2 (1.3)	2 (1.4)	1.000
Endocarditis - n (%)	12 (4.0)	6 (3.8)	6 (4.2)	1.000
Rheumatic fever - n (%)	104 (34.6)	55 (34.8)	49 (34.3)	1.000
Pathology				
Failure	62 (20.6)	32 (20.3)	30 (21.0)	
Stenosis	164 (54.5)	85 (53.8)	79 (55.2)	0.605
DL - predominant stenosis	62 (20.6)	36 (22.8)	26 (18.2)	
DL – predominant failure	13 (4.3)	5 (3.2)	8 (5.6)	

[1] BMI≥30 Kg/m² e [2] BMI≥40 kg/m², according I Brazilian Guideline for Diagnosis and Treatment of Metabolic Syndrome [21].
[3] Statistically significant association by adjusted residual test (P≥0,05).
SD = standard deviation, BMI = body mass index, NYHA = New York Heart Association Class, COPD = chronic obstructive pulmonary disease, SAH = hypertension, AMI = acute myocardial infarction; DL = double lesion

Table 2. Hospital outcomes

Variables	Sample (n=301)	Mechanical prosthesis (n=158)	Biologal prosthesis (n=143)	*P*
CPB time (min) - mean±SD	72.2±24.2	70.6±23.2	74.0±25.1	0.218
Ischemia time (min) - mean±SD	54.8±18.1	53.4±18.5	56.3±17.7	0.166
Length of hospital stay (days) - median (P25-P75)	13 (10-21)	12(10-18.3)	15(11-23)	<0.001
Time in ICU (days) - median (P25-P75)	3.1 (2.8-4.2)	3.0 (2.7-3.9)	3.5 (2.9-5.0)	0.001
PO hospitalization time (days) - median (P25-P75)	9 (8-12)	9 (8-12)	10 (8-14)	0.064
Mechanical ventilation time (h) - median (P25-P75)	14.6 (10.2-19.3)	13.3 (8.9-16.5)	15.9 (13.5-20.9)	<0.001
Mechanical ventilation >5 days - n (%)	7 (2.3)	3 (1.9)	4 (2.8)	0.712
AMI - n (%)	1 (0.3)	1 (0.6)	0 (0.0)	1.000
Stroke - n (%)	11 (3.7)	6 (3.8)	5 (3.5)	1.000
Pneumonia - n (%)	43 (14.3)	16 (10.1)	27 (18.9)	0.045
Arrhythmias requiring cardioversion/defibrillation - n (%)	10 (3.3)	7 (4.4)	3 (2.1)	0.342
Dialysis - n (%)	4 (1.3)	3 (1.9)	1 (0.7)	0.624
Reoperation for bleeding - n (%)	12 (4.0)	4 (2.5)	8 (5.6)	0.289
Tamponade - n (%)	2 (0.7)	0 (0.0)	2 (1.4)	0.225
Permanent TAV- n (%)	4 (1.3)	1 (0.6)	3 (2.1)	0.349

CPB= cardiopulmonary bypass; SD = standard deviation; AMI = acute myocardial infarction; TAV=total atrioventricular block

Survival data

Figure 1 shows the long-term survival of patients in the study. Survival at 5, 10 and 15 years after surgical valve replacement by a mechanic substitute was 83.90% (CI 95% = 78.00% -89.80%) 75.40% (95% CI = 68, 04% -82.80%) and 60.20% (CI 95% = 45.90% -74.50%), and by biological substitute, was 89.30% (CI 95% = 84.20% - 94.40%) 70.40% (CI 95% = 62.20% -78.60%) and 58.40% (CI 95% = 48.40% - 68.40%), respectively. There was no statistically significant difference in survival of patients in both groups (*P* = .939) throughout follow-up.

Using the multivariate Cox regression, the type of prosthesis remained with no association with death (*P* = 0.556), as shown in Table 3. The factors that remained statistically associated with death were: age over 70 years,

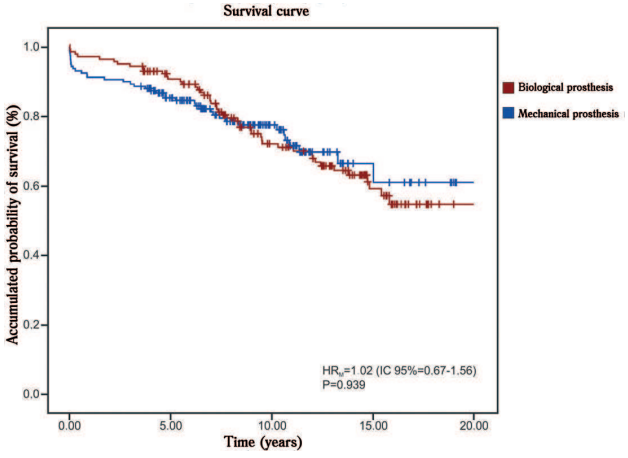

Fig. 1 - Kaplan-Meier to assess probability of survival

Table 3. Independent predictors of death by Cox regression analysis

Variables	HR (IC 95%)	*P*
Age> 70 years	2.48 (1.51-4.08)	<0.001
Aortic valve insufficiency	2.68 (1.61-4.46)	<0.001
COPD	1.97 (1.26-3.08)	0.003
Bleeding events	3.67 (1.57-8.57)	0.003
Arrhythmias with cardioversion and/or defibrillation in the ICU	3.06 (1.13-8.28)	0.027
Obesity	1.95 (1.02-3.73)	0.043
Chronic atrial fibrillation	1.79 (0.84-3.80)	0.129
Embolic events	2.41 (0.72-8.12)	0.156
Diabetes mellitus	1.47 (0.79-2.74)	0.220
SAH	1.42 (0.77-2.65)	0.264
Creatinine>2 mg/dL	1.71 (0.61-4.80)	0.310
Type of prosthesis (biological)	0.87 (0.54-1.40)	0.556
Postoperative stroke	0.76 (0.20-2.88)	0.685
Preoperative stroke	0.89 (0.28-2.80)	0.837
CHF class III and IV	1.05 (0.66-1.67)	0.843

CHF = congestive heart failure, COPD = chronic obstructive pulmonary disease, SAH = hypertension; ICU = intensive care unit

Table 4. Incidence of deaths by period

Variables	Sample (n=301) n (%)	Mechanical prosthesis (n=158) n (%)	Biologal prosthesis (n=143) n (%)	*P*
Total deaths	88 (29.2)	40 (25.3)	48 (33,6)	0,149
Perioperative	34 (11.3)	25 (15.8)	9 (6,3)	0,015
Hospitalar[1]	21 (7.0)	15 (9.5)	6 (4,2)	0,115
ICU[1]	8 (2.7)	5 (3.2)	3 (2,1)	0,726
Other	54 (17.9)	15 (9.5)	39 (27,3)	<0,001

ICU = Intensive Care Unit.

[1] None exceeded the perioperative period

obesity, chronic obstructive pulmonary disease, arrhythmias requiring cardioversion and/or defibrillation in the intensive care unit, bleeding events and aortic valve insufficiency.

The incidence of deaths by period is shown in Table 4. Considering all the perioperative period, the group with mechanical replacement had higher mortality than the group with implanted bioprostheses (*P* = 0.015). In the remaining of the follow-up period, mortality for patients with bioprostheses was higher than those with mechanical prostheses (*P* <0.001).

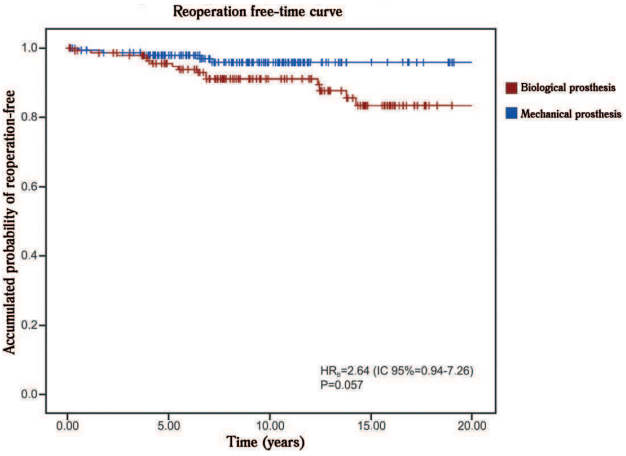

Fig. 2 - Kaplan-Meier to assess time freedom from reoperation

Regarding the causes of deaths, patients who underwent implantation of mechanical substitutes were more likely to prosthesis-related death (*P* = 0.07), which can be seen in Table 5.

As shown in Table 6, during the follow-up period, the incidence of reoperation was higher in patients with biological valve replacement (*P*=0.021). Major hemorrhagic events tended to be more frequent in patients with mechanical replacement (*P* = 0.084).

Figure 2 shows the cumulative probability of remaining free of reoperation in these patients during the follow-up. This probability in 5, 10 and 15 years after surgical valve replacement by a mechanic substitute was 97.90% (CI 95% = 95.50% -100.00%) 95.80% (95% CI = 92, 10% -99.50%) and 95.80% (CI 95% = 92.01% -99.50%), and by biological substitute, was 94.60% (CI 95% = 90.70% - 98.50%) 91.00% (CI 95% = 85.90% -96.10%) and 83.30% (CI 95% = 74.70% - 91.90%), respectively. Patients with biological substitute tended to be more likely to have another surgery, especially after the first 10 years of follow-up (*P*=0.057).

Using the multivariate Cox regression, patients with bioprosthetic remained with a greater tendency for reoperation (*P*=0.093), as shown in Table 7. The factors that remained statistically associated with reoperation were: serum creatinine levels above 2 mg/dL, prosthetic endocarditis and patients older than 70 years.

Figure 3 shows the cumulative probability of remaining free of bleeding events. This probability in 5, 10 and 15 years after surgical valve replacement by a mechanical substitute was 94.50% (CI 95% = 90.80% -98.20%) 91.70%

Table 5. Causes of death

Causes of death	Sample (n=88[1]) n (%)	Mechanical prosthesis (n=40) n (%)	Biologal prosthesis (n=48) n (%)	*P*
Cardiac	57 (64.8)	27 (67.5)	30 (62.5)	0.791
Related to the prosthesis	20 (22.7)	13 (32.5)	7 (14.6)	0.093
Sudden or unexplained	5 (5.7)	3 (7.5)	2 (4.2)	0.834
Noncardiac	31 (35.2)	13 (32.5)	18 (37.5)	0.791

[1] Deaths equivalent to 29.2% of the total sample

Table 6. Outcomes in the cohort during the follow-up period

Variables	Sample (n=301) n (%)	Mechanical prosthesis (n=158) n (%)	Biologal prosthesis (n=143) n (%)	*P*
Reoperation for valve replacement	20 (6.6)	5 (3.2)	15 (10.5)	0.021
Bleeding events [(1)]	14 (4.7)	11 (7.0)	3 (2.1)	0.084
Embolic events [(1)]	17 (5.6)	9 (5.7)	8 (5.6)	1.000
Endocarditis	8 (2.7)	3 (1.9)	5 (3.5)	0.484
Stroke	14 (4.7)	7 (4.4)	7 (4.9)	1.000
Hemorrhagic	3 (1.0)	2 (1.3)	1 (0.7)	0.803
Embolic	11 (3.7)	5 (3.1)	6 (4.2)	0.547

[(1)] *Including Stroke*

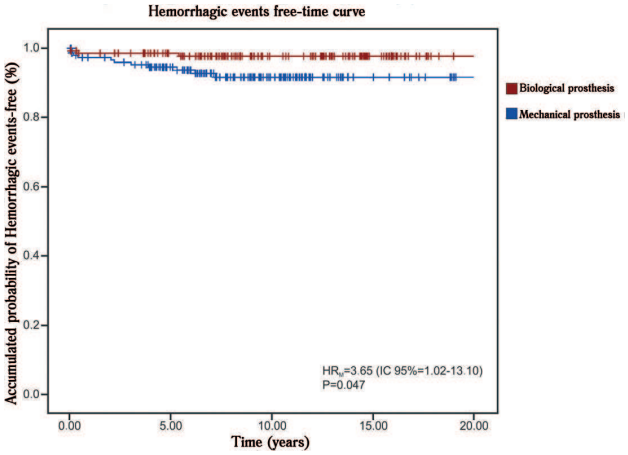

Fig. 3 - Kaplan-Meier time to assess event-free bleeding

Table 7. Independent predictors of reoperation by Cox regression analysis

Variables	HR (IC 95%)	*P*
Postoperative endocarditis	199.20 (30.70-1291.00)	<0.001
Age>70 years	0.05 (0.01-0.58)	0.016
Creatinine>2 mg/dL	9.11 (1.06-78.40)	0.044
Type of prosthesis (biological)	2.59 (0.85-7.88)	0.093
Preoperative stroke	0.25 (0.02-2.27)	0.249
Aortic failure	1.68 (0.57-5.00)	0.348

HR=Hazard Ratio

Table 8. Independent predictors of bleeding events by Cox regression analysis

Variables	HR (IC 95%)	*P*
Creatinine>2 mg/dL	33.30 (5.50-199.00)	<0.001
Type of prosthesis (mechanical)	5.52 (1.40-21.80)	0.015
Preoperative MI	4.42 (0.92-21.20)	0.063
Pneumonia in ICU	2.66 (0.74-9.56)	0.134
Morbid obesity	4.68 (0.50-44.30)	0.178
Diabetes mellitus	2.16 (0.56-8.40)	0.265
Mechanical ventilation> 5 days	2.25 (0.21-24.00)	0.503

HR=Hazard Ratio; Stroke = stroke, MI = myocardial infarction; ICU = Intensive Care Unit.

(95% CI = 86, 80% -96.60%) and 91.70% (CI 95% = 86.80% - 96.60%), and by biological substitute was 98.60% (CI 95% = 96.60% - 100.00%) 97.80% (CI 95% = 95.30% -100.00%) and 97.80% (95% CI = 95.3% -100.00%), respectively. There was a greater likelihood of patients who underwent implantation of biological substitutes to remain free of bleeding events (*P*=0.047).

Using the multivariate Cox regression, according to Table 8, the factors that remained statistically associated with hemorrhagic events were: serum creatinine levels above 2 mg/dL and mechanical prostheses.

DISCUSSION

Mortality

In this study, there was no difference in survival in both groups, considering a follow-up period of up to 20 years (*P*=0.939). This fact is due possibly to increased risk of bleeding in patients who received a mechanical prosthesis be offset in part by the increased risk of reoperation in those with biological prostheses.

The mortality observed in this cohort was 29.2% and not statistically significant when comparing the differences between the groups receiving biological and mechanical prostheses (*P*=0.149), results similar to those found in a cohort of 816 patients (24.9% in 25 years) [22]. This is possibly due to the fact that over half of the patients were older than 60 years and the presence of comorbidities such as obesity and chronic obstructive pulmonary disease, which were predictive of death in this sample. Chronic obstructive pulmonary disease was an independent predictor of death (*P* <0.05) also in the historical cohort studied by Bose et al. [23], with 68 patients older than 80 years who underwent aortic valve replacement between April 2001 and April 2004, with a mean of 712 days. Additionally, one should not forget that only 17% of the deaths were related to the prosthesis in this study, 11.3% related to mechanical prosthesis and 5.7%, biological prosthesis (*P* = 0.070). Similar data were found in the mortality study by Stassano et al. [24], observed in 27.74%.

Of these, 6.7% and 8.1% are related to mechanical and biological prostheses, respectively (*P*=0.80).

Hammermeister et al. [17] found an even higher percentage of deaths, as follows, 66 ± 3% and 79 ± 3% for patients with mechanical and biological prostheses, respectively (*P* = 0.02). This is a prospective, randomized clinical trial comparing mechanical and porcine prostheses in 394 patients, with 18 years follow-up in 13 medical centers in the United States, operated between 1977 and 1982. In this study, 37% of the deaths were related to mechanical prosthesis and 41% to the bioprosthesis. This may be because many deaths related to bioprostheses occurred in 10 to 15 years after surgery, and can be attributed to primary graft dysfunction, with or without reoperation. It is likely that the high mortality rate recorded in the study is a result of the implants performed in the late 1970s and early 1980s, when the technology of valve prostheses and surgical techniques and myocardial protection were still poorly evolved [25].

Another important clinical trial was performed in the United Kingdom in Edinburgh [26], comparing the evolution of 211 randomized patients undergoing aortic valve replacement between 1975 and 1979 to receive mechanical or porcine prostheses. The results showed a advantage regarding survival in 12 years of follow-up for the group with mechanical prosthesis, but this advantage disappeared with 20 years of follow-up (*P*=0.39). Survival at 10 and 20 years after valvar replacement surgery by mechanical substitute was 64.0% and 28.4%, and by biological substitute was 65.7% and 31.3%, respectively, showing no statistical significance (*P*=0.57). These data corroborate the results of this cohort, although they are proportionally lower.

Also, Kulik et al. [27] found a survival curve similar to the present study when evaluating a cohort of 423 patients, aged between 50 and 70 years who underwent aortic valve replacement between January 1977 and July 2002, with a mean of 4.9 ± 3.9 years and a maximum of 15.8 years. The survival at 5, 10 and 15 years after surgical valve replacement by a mechanical substitute was 89.0 ± 2.1%, 73.2% ± 4.2 and 65.3 ± 6.0% and by biological substitute was 87.6 ± 5.7%, 75.1 ± 12.6% and 37.5 ± 27.3%, respectively, with no statistically significant difference between groups (*P*=0.55).

Peterseim et al. [6] performed a retrospective analysis of a cohort of 841 patients operated from 1976 to 1996, comparing outcomes in patients undergoing aortic valve replacement with porcine and mechanical prostheses. In 10 years after surgery, survival free of health problems related to the prosthesis was higher in patients with mechanical substitute and age below 65 years and in patients with biological substitute and older than 65 years. Patients with lung disease, kidney disease, ejection fraction less than 40%, coronary disease and age over 65 years had a life expectancy of less than 10 years. In this study, as well as pulmonary disease and age over 70 years, also obesity, aortic insufficiency, bleeding events and arrhythmias were statistically significant predictors of death.

Edwards et al. [28] used data from The Society of Thoracic Surgeons National Database to identify, in a study of prevalence, risk factors associated with surgical valve replacement, including 32,968 patients operated between January 1994 and December 1997, with prevalence of mortality of 4%. Age was the only risk factor significantly related to the type of prosthesis. The factors most strongly associated with mortality were the procedures performed on an emergency, the need for reoperation and renal failure, not confirmed in this study as predictors of death.

Butchart et al. [29] followed a cohort study where they collected 82,297 blood samples for obtaining the international normalized ratio (INR) of 1,476 patients who underwent surgery for valve replacement by mechanical prostheses between 1979 and 1994 and were followed up until 1998, noting that the high anticoagulation variability is the most important independent predictor of survival. The variability of anticoagulation was expressed for each patient, the percentage of INR values †outside the limits between 2.0 and 4.0. The incidence of deaths related to the prosthesis was significantly higher in patients with high variability of anticoagulation control (changes greater than or equal to 30%) compared to those who had low variability of the intermediate control (variations between 0 and 29%, 9%), showing a linear rate of 1.4% versus 0.5% deaths per year (*P* <0.001). In this study, there was tendency for a higher number of deaths related to the prosthesis for patients who underwent implantation of mechanical prostheses compared to patients undergoing implantation of bioprostheses (*P*=0.070). It is possible that this is due to high variability of anticoagulation control, which would require further studies for confirmation.

In relation to hospital outcomes, comparing patients who underwent surgery for implantation of mechanical and biological prostheses, patients in the second group spent longer time on mechanical ventilation (*P*<0.001), probably because older age (*P* <0.001). The combination of these two factors may have resulted in higher incidence of pneumonia in these patients (*P* = 0.045). Thus, they had longer hospital stays in the intensive care unit (*P*=0.001) and, consequently, longer hospital stay (*P* <0.001). This, therefore, did not increase mortality during the perioperative period in this group. Also, in study published by Florath et al. [30], assessing determinants of mortality at 30 days postoperatively in a cohort of 2198 patients operated on between 1996 and 2003, infection was not found as a predictor of increased mortality.

Tjang et al. [3] performed a systematic review of 28 original articles published between 1985 and 2005 that

contained follow-up of patients undergoing surgery for aortic valve replacement to identify predictors of mortality. There was strong evidence that the risk of early mortality was increased in cases of emergency surgery, while the risk of late mortality was increased in older patients with preoperative atrial fibrillation. It was noted also moderate evidence that the risk of early mortality was increased by advanced age, aortic insufficiency, coronary artery disease, long cardiopulmonary bypass, left ventricular dysfunction, endocarditis, hypertension, mechanical prosthesis, preoperative pacemaker, dialysis-dependent renal failure and the diameter of the valve. Since the risk of late mortality was increased by emergency surgery and urgency of the operation. All these predictors were considered in the model of this cohort, but only age above 70 years and aortic valve insufficiency agreed with this study as predictors of mortality.

In the Mayo Clinic [31], it was studied a historical cohort of 440 patients undergoing aortic valve replacement between January 1991 and December 2000, half of whom received mechanical substitute and the other half received a biological substitute, with a mean follow up of 9.1 year for the first group and 6.2 years for the second group. The survival at 5 and 10 years was 87% and 68% for patients with mechanical prosthesis and 72% and 50% for patients with bioprostheses (P <0.001), respectively, in contrast to the present study, where there were statistically different in relation to survival for these two groups over time. Also, perioperative mortality was observed as statistically higher for the group of patients with bioprostheses (P=0.04), which was not confirmed in this study.

In a prospective randomized trial [24] performed on two Italian centers, 310 patients underwent aortic valve replacement between January 1995 and June 2003, aged 55 and 70 years, comparing events with mechanical or biological prostheses, there were also no differences in mortality between the groups at 5, 10 and 13 years of follow-up (P = 0.20), and in this cohort. In this Italian study, functional class according to the New York Heart Association was an independent predictor of mortality (P=0.01), which was not observed in this cohort.

Bleeding events

The predictors of bleeding events in this study, statistically significant, were mechanical prostheses (P=0.015) and serum creatinine levels above 2 mg/dL (P <0.001).

As stated by Geldorp et al. [32], patients with a mechanical prosthesis require anticoagulation throughout their life and the risk of bleeding events increases with advancing age, as observed in this study during the follow-up. This is often due to excessive levels of anticoagulation in patients who are not subject to adequate control, especially by low social, economic and cultural levels, or those of difficult clinical management and also due to uncertainties about the true intensity of anticoagulation. These uncertainties are due to the fact that measures of the system depend on the INR calibration of thromboplastin reagents, tissue factors whose contents vary from one commercial product to another. Moreover, although different thromboplastin reagents produce very similar results with normal blood, they can produce very different prothrombin times with anticoagulated blood [29]. According Campos et al. [33], only about a third of patients have adequate anticoagulation level in more than half of the follow-up visits, and the residence time within the desired range of anticoagulation is directly related to the occurrence of complications.

As the study of Peterseim et al. [6], whose sole predictor of bleeding events was a mechanical prosthesis (P=0.003), the study by Hammermeister et al. [19] also showed a higher incidence of bleeding events for the group with mechanical valves compared to the group of patients with bioprostheses (51 ± 4% versus 30 ± 4%, P=0.0001). The linearized rate of bleeding events was significantly lower for patients who underwent implantation of bioprostheses in comparison to patients undergoing implantation of mechanical prostheses (0.3 ± 0.1% per year versus 1.2 ± 0.3% per year; P=0.001). Oxenham et al. [26] also observed a higher incidence of bleeding events in patients receiving mechanical substitutes, being 2.0% to 2.5% per year with a mechanical prosthesis and 0.9% to 2.0% per year with a porcine prosthesis (P=0.001).

The cohort studied by Kulik et al. [27] showed no differences from bleeding events among patients with biological and mechanical substitutes (P=0.74), as well as the trial by Stassano et al. [24] (P = 0.08). This last attributed this result to the possibility of low-intensity anticoagulation for patients with mechanical prostheses in the sample and/or the possibility of patients with biological prostheses have received anticoagulation during follow-up. In contrast to these findings, Brown et al. [31] found a statistically significant difference between groups in these two types of prostheses for bleeding events, occurred in 15% of patients with mechanical prostheses and 7% of patients with bioprostheses (P=0.01), although 19% of the latter were receiving warfarin sodium.

In our sample, 2.3% of cases had renal failure and only one patient underwent dialysis prior to surgery and therefore was not considered in the model. Umezu et al. [34] studied a cohort of 63 dialysis patients undergoing surgery for valve replacement in January 1990 to July 2007, at The Heart Institute of Japan, with a mean of 49 months, and found the presence of bleeding events in 29.7 % of cases, which was much higher than found in this sample (4.7%). They also observed a higher incidence of bleeding

events in patients with mechanical valve substitutes in comparison to the biological. Still, a systematic review, also held in Japan [35], confirms the presence of bleeding complications for patients using anticoagulants in the presence of dialysis. In addition, it is stated that the mechanical prosthesis seems to be the predominant choice for hemodialysis patients in that country, because of their high life expectancy and because the studies did not show differences in long-term follow-up when comparing mechanical and biological prostheses.

Reoperation

It can be observed in most of existing publications that the risk of reoperation begins to grow after 10 years of surgery to implant of valve substitute, probably due to dysfunction of the prosthesis, and increases progressively over time, decreasing with advancing age [17,24,26,32,36-42]. In this cohort, a trend was observed for reoperation after 10 years of follow-up (P=0.057), which is probably at the borderline sample descriptive level.

The study by Peterseim et al. [6] showed no significant difference for patients older than 65 years who received bioprostheses compared to the group that received a mechanical prosthesis (P=0.4), and, according to Cox regression analysis, the use of bioprosthesis (P=0.01) and the age of 65 years (P=0.0001) were the only variables predictive of reoperation. In this cohort, only endocarditis (P<0.001) and serum creatinine levels above 2 mg/dL (P=0.044) were significantly associated with reoperation.

Hammermeister et al. [17] found a higher incidence of reoperation for patients with biological substitutes compared with mechanical (29 ± 5% versus 10 ± 3%, P= 0.004). Additionally, as the trial by Oxenham et al. [26], the risk of reoperation was significantly higher after 12 years for all patients who received a porcine prosthesis (11.3 ± 3.6% for porcine versus 4.2 ± 2.1% for mechanical, P <0 0001). Stassano et al. [24] also observed that reoperation was more frequent in the group that underwent implantation of a bioprosthesis, in agreement with other studies presented (P = 0.003).

Ruel et al. [40] studied a cohort of 2348 patients undergoing surgery for aortic valve replacement between 1970 and 2002, with a maximum follow-up period of 32.4 years. The free time of reoperation for patients with mechanical replacement was 96.2%, 94.1% and 93.8% for 10, 15 and 20 years after surgery, respectively, similar to the data presented in this cohort. As for biological substitutes, time free from reoperation was 76.1%, 61.4% and 59.6% (P <0.001) in the same periods of follow-up. Advancing age was a protective factor against reoperation due to structural dysfunction of the bioprosthesis in the aortic position (HR = 0.97, $P \leq 0.001$), attributed to less deterioration of the prosthesis in older patients.

Limitations of the Study

It is a retrospective study, performed at a single center and with insufficient sample for rare events.

CONCLUSIONS

Based on the findings of this cohort, it is concluded that:

1) The mortality rate was statistically similar between groups;

2) The baseline characteristics of patients are the most important determinants of late mortality after surgery;

3) There was a tendency to group with reoperation for bioprosthesis, especially after 10 years of follow-up;

4) Patients with mechanical prostheses presented more bleeding events over time, especially after 5 years of follow-up;

5) The data in this study are consistent with the current literature.

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