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Fisics-Incor Bovine Pericardial Bioprostheses: 15 Year Results

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ABSTRACT

Background: From March 1982 to December 1995, 2,607 Fisics-Incor bovine pericardial bioprostheses were implanted in 2,259 patients. Mean age was 47.2 ± 17.5 years, and 55% were male. Rheumatic fever was present in 1,301 (45.7%) patients.

Methods: One thousand and seventy-three aortic valve replacements, 1,085 mitral replacements, 27 tricuspid replacements, 195 mitral-aortic replacements, and 16 other combined valve replacements were carried out. Combined procedures were performed in 788 (32.9%) patients, the most frequent being tricuspid valve repair (9.2%) and coronary artery bypass grafting (7.7%).

Results: Hospital mortality was 8.6% (194 patients), 8.6% for the mitral group, 4.7% for the aortic group, and 12.8% for double-valve replacements. The linear rates for calcification, thromboembolism, rupture, leak and endocarditis were, respectively, 1.1%, 0.2%, 0.9%, 0.1% and 0.5% patient-year. The actuarial survival curve was 56.7 ± 5.4% in 15 years. Survival free from endocarditis was 91.92%, survival free from thromboembolism was 95 ± 1.7%, survival free from rupture was 43.7 ± 9.8%, survival free from leak was 98.9 ± 4.5%, and survival free from calcification was 48.8 ± 7.9% in 15 years. In the late postoperative period, 1,614 (80.6%) patients were in New York Heart Association functional Class I.

Conclusions: We conclude that the results with the Fisics-Incor bovine pericardial prostheses were satisfactory in our group of patients.

INTRODUCTION

In 1969, Carpentier et al. [Carpentier 1969], introduced low concentrations of glutaraldehyde to preserve biological tissues. To describe the valves manufactured with biological tissues modified by glutaraldehyde, Carpentier suggested the word bioprosthesis. In the early 1970s, Ionescu et al. [Ionescu 1972] manufactured an aortic valve with bovine pericardium fixed in glutaraldehyde. In 1977, Ionescu et al. [Ionescu 1977] reported their initial clinical experience with bovine pericardial bioprosthesis. At the Heart Institute, Hospital das Clínicas, Medical School, University of São Paulo, bovine pericardial bioprostheses have been used since 1982 [Pomerantzeff 1989].

This study is aimed at evaluating our experience with bovine pericardial bioprostheses from 1982 to 1995.

MATERIALS AND METHODS

From March, 1982, to December, 1985, 2,607 bovine pericardial bioprostheses were implanted at the Heart Institute, Hospital das Clínicas, Medical School, University of Sao Paulo, in 2,259 patients, in a total of 2,396 surgical procedures. Xenografts fixed in glutaraldehyde at 0.56% and preserved at 4% were used. From March, 1982 to March, 1984 high profile (HP) bioprostheses with polypropylene rings were implanted; from March, 1984 to August, 1992 low profile (LP) bioprostheses with Delrin flexible rings (see Figure 1 ◎) were used; and, since August 1992, low profile bioprostheses with bovine pericardium covered rings (CR) have been used (see Figure 2 ◎).

Two thousand six hundred and seven bovine pericardial bioprostheses were implanted in 2,259 patients with ages ranging from 3 to 87 years (mean 47.2 ± 17.5 years). Two hundred and thirty-five (9%) were HP bioprostheses, 1,503 (57.6%) were LP bioprostheses and 869 (33.4%) were CR. One thousand two hundred and fifty (55%) patients were male and 1,009 (45%) were female.

One thousand and seventy-three (44.8%) aortic valve replacements, 1,085 (45.3%) mitral valve replacements, 195 (8.1%) mitral-aortic replacements, 27 (1.2%) tricuspid valve replacements, 10 (0.4%) mitral-tricuspid replacements, 3 (0.1%) aortic-tricuspid replacements, 1 (0.04%) mitral-aortic-tricuspid replacement, 1 (0.04%) pulmonary

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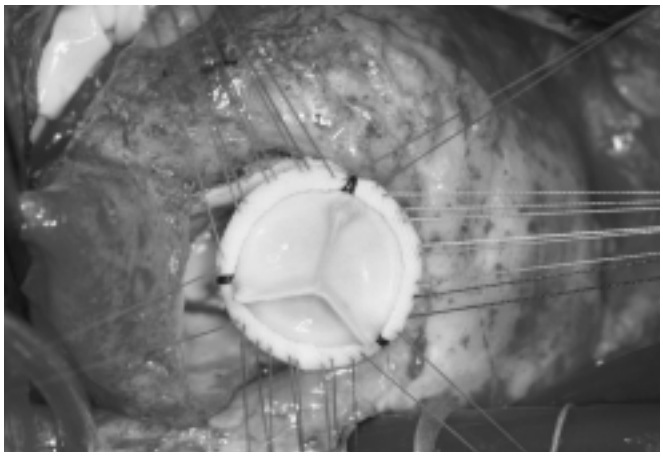


Figure 1.

replacement, and 1 (0.04%) tricuspid-pulmonary replacement were carried out.

Combined procedures were performed in 788 (32.9%) patients, including 207 (9.2%) plastic surgeries of the tricuspid valve, 174 (7.7%) coronary artery bypass grafting, 55 (2.4%) mitral valve plastic surgery, 61 (2.7%) mitral commissurotomies, 27 (1.2%) aortic valve plastic surgeries, 59 (2.6%) aortic commissurotomies, 35 (1.5%) corrections of aortic ring abscess and 170 (7.5%) additional procedures.

The lesions observed were: mitral insufficiency in 290 (12.8%) patients, double mitral lesion in 274 (12.1%), mitral stenosis in 211 (9.3%), aortic insufficiency in 316 (13.9%), aortic stenosis in 370 (16.4%), double aortic lesion in 277 (12.3%), tricuspid insufficiency in 19 (0.8%), mitral prosthesis dysfunction in 329 (14.6%), aortic prosthesis dysfunction in 129 (5.7%), tricuspid prosthesis dysfunction in 5 (0.2%), pulmonary stenosis in 1 (0.04%), mitral restenosis in 71 (3.1%), and aortic restenosis in 6 (0.25%) patients.

Figure 2.

The etiology was rheumatic fever in 1,301 (57.6%) patients, calcified valvulitis in 220 (9.7%), endocarditis in 199 (8.8%), chronic non-specific valvulitis in 73 (3.2%), myxomatous degeneration in 65 (2.9%), congenital degeneration in 16 (0.7%), ischemic mitral insufficiency in 14 (0.6%), endomyocardial fibrosis in 9 (0.4%), and unknown in 630 (27.8%) patients.

The clinical symptoms were classified according to the New York Heart Association (NYHA) functional class. In the preoperative period, 48.5% of the patients were in functional Class IV, 45.9% in Class III, 4.9% in Class II and 0.7% in Class I.

Clinical visits, telephone interviews or questionnaires sent by mail were used for the postoperative follow-up.

Data are presented according to literature rules and nomenclature [Edmunds 1996]. Survival curves and survival free from events were calculated by Kaplan-Meier's method [Anderson 1974]. Linear rates were presented as percentage per patient-year (% pat/year) (see Tables 1 and 2 ◎). Statistical analysis was carried out by Student's T test and Fisher's test.

RESULTS

Hospital mortality was 8.6%, 4.7% for aortic valve replacement (AVR), 8.6% for mitral valve replacement (MVR) and 12.8% for mitral-aortic double replacement (MADR). In terms of the type of prosthesis, mortality in the HP group was 8.3%, 9.8% in the LP group and 6.4% in the CR group. The major cause of hospital mortality was low cardiac output (43.3%). Other causes of mortality were multiple organ failure (10.3%), septicemia (10.3%), coagulation disorders (5.2%), neurologic complications (4.1%), respiratory insufficiency (5.7%), acute myocardial infarction (3.6%), endocarditis (2.1%), arrhythmias (2.6%), mediastinitis (1%), cardiac tamponade (1%) and others.

Of the patients who had hospital discharge, 90.4% were followed up for an average of 6.3 ± 2.4 years. Actuarial survival was 49.1 ± 4% in 15 years. For the HP group, survival was 48.0 ± 5.4% in 15 years, 59.2 ± 3.4% for the LP group in 12 years, and 72.7 ± 7% for the CR group in 5 years (p = NS).When the position of the graft is analyzed, the survival was 53.5 ± 5.9% for the mitral position, 49.6 ± 6% for the aortic position and 43.1 ± 9.3% for the mitral-aortic position (p = NS) in 15 years (see Graph 1 ◎).

The linear rates for late complications, comparing the three groups and the different positions are shown in Tables 1 and 2 ◎, respectively. Survival rates are shown in Graph 2 ◎.

Survival rates free from calcification in 15 years were 96.3 ± 1.9% in the group with age over 60 years and 26.3 ± 21.6% in the group with less than 21 years (p = 0.0001), as shown in Graph 3 ◎. In the HP group, the survival was 50.3 ± 8.5% in 15 years; in the LP group it was 78.7 ± 7.8% in 12 years, and 97.0 ± 5.8% in the CR group in 5 years. Survival free from calcification in 15 years was 72.5 ± 5.2% for the AVR group, 62.2 ± 12.7% for the MVR group, and 78.7 ± 9.9 for the MADR group (see Graph 4 ◎).

Table 1. Linear Rates of Events in Accordance with the Bioprosthesis Model

Linear Rates (Pat/year)	High Profile (HP)	Low Profile (LP)	Covered Ring (CR)
Calcification	1.5%	1.3%	0.2%
Thromboembolism	0.3%	0.2%	0.1%
Leak	0.1%	0.1%	0.1%
Rupture	1.2%	1.2%	0.3%
Endocarditis	0.4%	0.4%	1.0%
Manufacture defect	0.08%	0.04%	0.05%
Death	2.3%	2.7%	1.8%

Survival free from rupture was 43.7+9.8% in 15 years. The rates were 44.9 ± 20.3% in 15 years in the HP group, 87.4 ± 2.5% in 12 years in the LP group and 97.9 ± 2% in 5 years in the CR group. For AVR survival was 40.9 ± 29.2%; for MVR it was 54.6 ± 17.2%, and for MADR, 96.7 ± 2.4% in 15 years.

Survival free from thromboembolism was 95.0 ± 1.7% in 15 years. In terms of the bioprosthesis position, the AVR rate was 71.3+1.7%, 95.1 ± 3.5% for MVR and 87.5 ± 11.7% for MADR.

Survival free from endocarditis was 91.9 ± 2% in 15 years. The rates for the groups were: 89.4 ± 3.4% for HP in 15 years, 94.7% for LP in 12 years and 95.2 ± 2.3% for CR in 5 years. According to the bioprosthesis position, survival free from endocarditis was 88.3 ± 4.7% for AVR, 94.4 ± 1.4% for MVR, and 92.9 ± 3.6% for MADR.

Survival free from paravalvular leak was 98.9 ± 4.5% in 15 years. In the HP group, the rate was 98.3 ± 1.2% in 15 years; in the LP group, 99.3 ± 3.4% in 12 years, and in the CR group, 99.6 ± 2.9% in 5 years. In the aortic position (AVR), survival free from paravalvular leak was 99.1 ± 6.6% in 15 years, in MVR it was 99.7 ± 4%, and in MADR it was 95.0 ± 3.5%.

When the NYHA functional class was evaluated late postoperatively, 80.6% of the patients were in functional Class I, 8.7% in Class II, 7.1% in Class III, and 3.6% in Class IV.

DISCUSSION

This evaluation of 2,259 patients with a follow-up of 90.4%, allows the evaluation of the clinical course of Fisics-Incor bovine pericardial bioprosthesis.

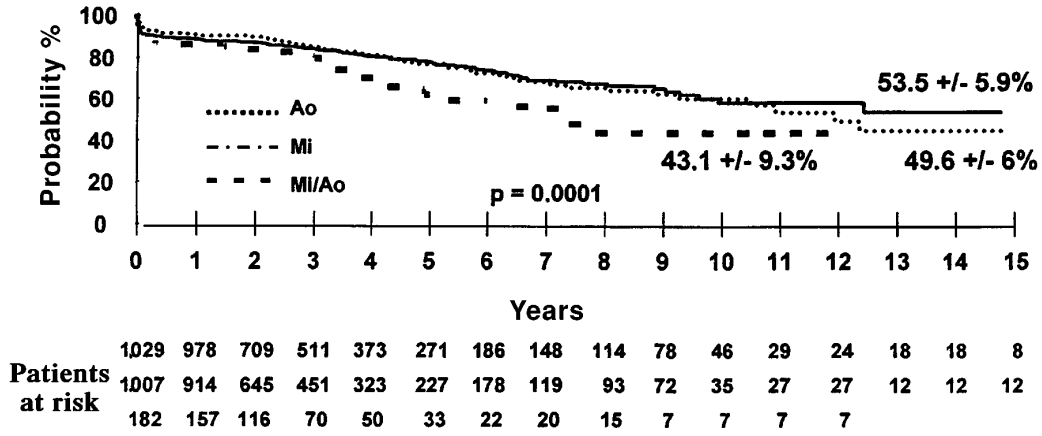
Table 2. Linear Rates of Late Events in Accordance with Bioprosthesis Position

Linear Rates (Pat/year)	Aortic	Mitral	Total
Calcification	0.7%	1.5%	1.1%
Thromboembolism	0.3%	0.2%	0.2%
Leak	0.07%	0.1%	0.1%
Rupture	0.8%	1.2%	0.9%
Endocarditis	0.4%	0.6%	0.5%
Manufacture defect	0.02%	0.09%	0.05%
Death	2.0%	2.8%	2.5%

The comparison of hospital mortality rates show a rate of 4.7% for AVR, 8.6% for MVR, and 12.8% for MADR, against a rate of 12.6% for AVR, 15.3% for MVR, and 29.5% for MADR for Ionescu-Shiley bovine pericardial bioprosthesis, as reported by Masters et al. [Masters 1991] and Braile et al. [Braile 1991] with a hospital mortality of 9.2% for mitral valve replacement alone. Pelletier et al. [Pelletier 1995] reported a mortality rate of 5.2% for aortic valve replacement alone with Carpentier-Edwards pericardial bioprosthesis. The major cause of hospital mortality was low cardiac output (49.5%). Preoperative functional class has a significant influence on hospital mortality rates ($p < 0.0001$). Several other factors may have influenced hospital mortality. Among them is the large number of combined procedures (788, 32.9%), such as coronary artery bypass grafting, tricuspid valve plastic surgery and reoperations (540, 22.5%).

The actuarial survival was 77.3 ± 1.3% in 5 years, 61.3 ± 2.8% in 10 years and 49.1 ± 4% in 15 years; in the HP group, survival was 48.0 ± 5.4% in 15 years; in the LP group it was 59.2 ± 3.4% in 12 years, and 72.7 ± 7% in 5 years in the CR group. There was no statistically significant difference between these values. Pelletier et al. [Pelletier 1989] published a study with a late survival of 79% in 5 years. Cosgrove et al. [Cosgrove 1995] reported a survival of 45.9% in 10 years. Pellerin et al. [Pellerin 1995] reported a survival of 49.9% in 12 years of follow-up. We have reported a significant difference ($p = 0.0001$) between the actuarial survival of the groups with age below 20 years (80.2 ± 7.7%) and over 60 years (41.9 ± 7.7%), as shown in Graph 5 ◎.

Calcification is due to several reasons such as age, metabolic factors, mechanical wear, time and the position of the implant. In this study, a significant difference is shown ($p < 0.0001$) between the calcification rates in the groups with age over 60 years (96.3 ± 1.9%) and below 20 years (26.3 ± 21.6%). Similar results were observed by Aupart et al. [Aupart 1995] with Carpentier-Edwards pericardial bioprostheses. When survival rates free from calcification according to bioprosthesis position were compared, we found a significantly greater ($p = 0.0001$) incidence for the mitral position (62.2 ± 12.7%) compared to the aortic position (72.5 ± 5.2%) in 15 years. Similar results were found by Masters et al. [Masters 1995]. A possible explanation for this is that mitral prosthesis is subjected to a peak of systolic pressure, whereas the aortic prosthesis is subjected to diastolic pressure.



Graph 1. Survival Rate in Accordance with Bioprosthesis Position. Ao: Aortic replacement; Mi: mitral replacement; Mi/Ao: mitral-aortic replacement.

As to the survival free from rupture, we observed a greater prevalence in the aortic position, with a rate of 40.9 ± 29.2% against 54.6 ± 17.2% for the mitral position in 15 years.

The major advantage of the bioprosthesis is the low incidence of thromboembolism in the absence of anticoagulation. Due to the characteristics of our patients, such as the low socio-economic level and the geographic dispersion, anticoagulation is frequently unachievable. Linear rates for thromboembolism were low in this study (0.2% pat/year) when compared to other studies, such as Reichenspurner et al. [Reichenspurner 1995] with 1.8% and Loisance et al. [Loisance 1993] with 0.5%. The present study shows that valvar replacement with bovine pericardial bioprosthesis may be carried out without routine anticoagulation, with a low incidence of thromboembolic events in 15 years of follow-up.

Endocarditis is usually an immediate complication of valvar replacement. In our study, we showed a linear rate of 0.5% pat/year, which is lower than in other series, as reported by Fraters et al. [Fraters 1992] with 0.8%, Pelletier et al. [Pelletier 1989] with 1.39% and Loisance [Loisance 1993] with 0.5% pat/year.

Late results with the use of bovine pericardial bioprostheses have encouraged our group to improve the treatment and the manufacture of these prostheses. We believe there shall be a great improvement with the adequacy of the geometry of each valve, in addition to the in vitro tests with "Reniform Bioprostheses" [Pomerantzeff 1992] and the initial clinical experience.

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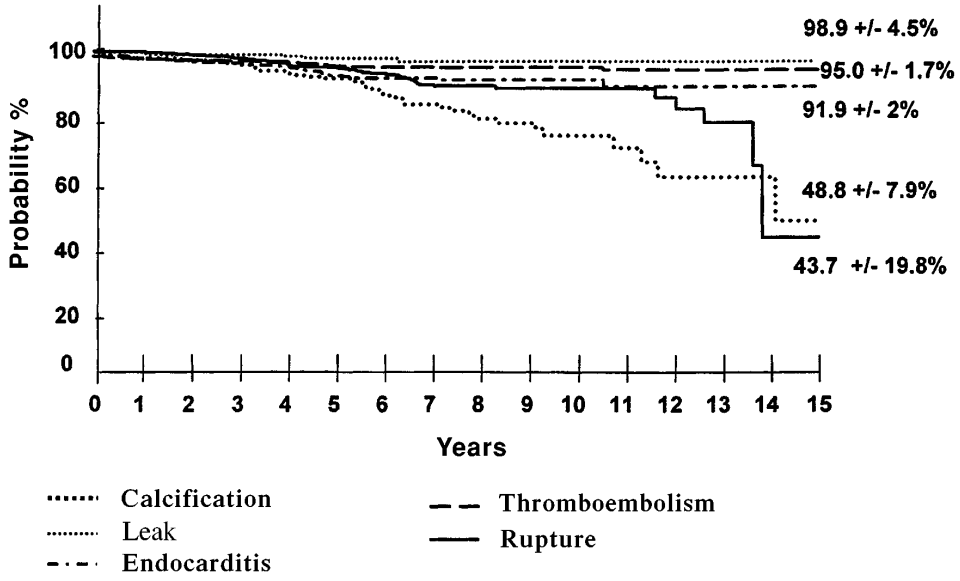
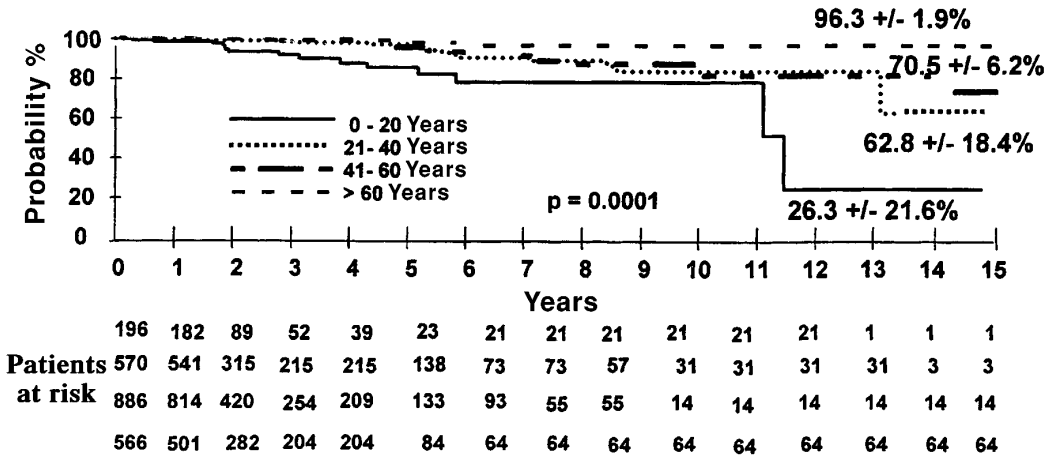


Graph 2. Actuarial Survival Free from Calcification, Leak, Endocarditis, Thromboembolism and Rupture.



Graph 3. Survival Rate Free from Calcification in Accordance with Patient Age.

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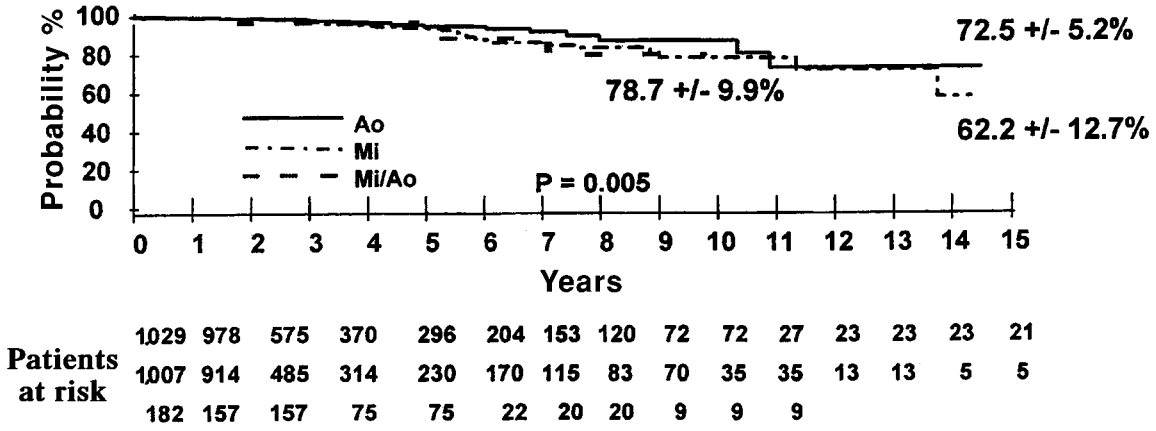
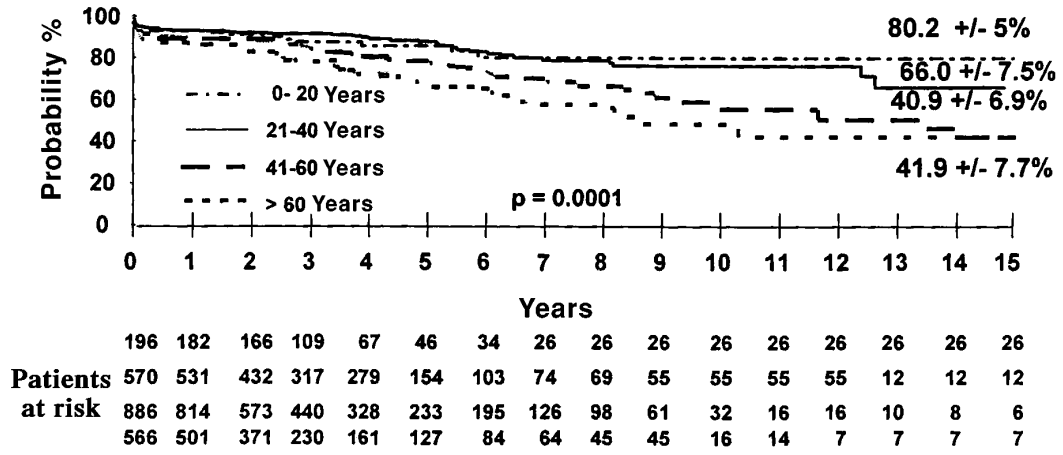


Graph 4. Survival Free from Calcification in Accordance with Bioprosthesis Position. Ao: Aortic replacement; Mi: mitral replacement; Mi/Ao: mitral-aortic replacement.



Graph 5. Survival in Terms of Patient Age. Ao: Aortic replacement; Mi: mitral replacement; Mi/Ao: mitral-aortic replacement.

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