Isolated Mitral and Aortic Valve Replacement with the St. Jude Medical Valve: A Midterm Follow-up

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Summary

Background: In our country, the biological valvular prostheses predominate, considering the difficulties related to anticoagulation, even in young patients, in spite of the need for repeated operations due to the degeneration of the bioprostheses.

Objectives: To report our consecutive series of recipients of isolated St Jude Medical mechanical valve prosthesis in the mitral (MVR) or aortic (AVR) position.

Methods: Data from patients operated between January 1995 and December 2003 were revised in order to determine patient survival and prosthesis-related events up to December 2006.

Results: One hundred sixty eight patients had MVR and 117 had AVR. In the MVR cohort, the mean age was 45 years, 75% were 55 years old or younger, and 65% were females. In the ARV cohort, the mean age was 45 years, 66% were 55 years old or younger and 69% were males. Operative mortality for AVR and MVR was 7% and 7.5%, respectively. Freedom from late mortality was 81.8% at 10 years for MVR and 83% for AVR (p=0.752). Freedom from valve-related death at 10 years for the MVR cohort and AVR was 85.6% and 88.7%, respectively (p=0.698). In the MVR cohort, the freedom from reoperation was 97% and 99% in the AVR cohort (p=0.335). Freedom from thromboembolic events was 82% in the MVR cohort and 98% in the AVR cohort (p=0.049). Freedom from bleeding was 71% in the MVR cohort and 86% in the AVR cohort (p=0.534).

Conclusions: This series of predominantly young adult patients undergoing isolated MVR and AVR with the St Jude Medical mechanical prosthesis confirms the good performance of this valve prosthesis in agreement with previous reports. (Arq Bras Cardiol 2009; 93(2):XXX-XXX)

Key Words: Heart valve prosthesis; heart valve diseases; aortic valve; mitral valve.

Introduction

Mechanical prosthetic heart valves have an extremely low rate of structural failure and, with proper anticoagulation, the risk of thromboembolism is similar to the use of bioprosthetic ones without anticoagulants1. Therefore, mechanical prostheses would be the choice for patients with longer life expectancy and no contraindication for anticoagulation. However, in developing countries, anticoagulation management may be a problem due socioeconomic issues. As a result, in Brazil, valve replacement using bioprostheses prevails2,3, mainly in the mitral position, even in young patients. However, we believe that in spite of all concerns related to the anticoagulation in developing countries, the use of mechanical valve prosthesis is viable and advantageous.

Therefore, this report summarizes our experience of up to 10 years with a consecutive series of recipients of the St Jude Medical mechanical valve prosthesis in mitral (MVR) or aortic position (AVR).

Methods

Patients and follow-up

As this is a retrospective study using a database, the Ethics Committee of our institution waived the requirement for obtaining patient consent. The authors do not have any financial or commercial association with the manufacturer or distributor of the product, as well as any corporate funding or affiliations.

We revised the data from all patients having mitral or aortic valve replacement with St Jude Medical mechanical valve prosthesis (Standard model, St Jude Medical, Inc) between January 1995 and December 2003. The primary objective was to document patients’ survival and prosthesis-related events up to December 2006. Follow-up was carried out through
contact with the patient in our anticoagulation ambulatory and it comprehended 92% of the operated patients. The causes of deaths were determined based on hospital records and government-authorized death certification, when accessible. All sudden or unknown causes of death were considered valve-related. Operative techniques were not similar and relied on the surgeon’s preferences. The standard St. Jude Medical mechanical prosthesis was used in all patients.

Anticoagulation with warfarin sodium (Coumadin) was initiated 48 hours after the operation, if possible. Otherwise, Heparin administration (5,000 units subcutaneously, every 8 hours) or enoxaparin (1 mg/kg every 12 hrs) was started. The target International Normalized Ratio (INR) was 2 to 2.5 for AVR and 2.5 to 3.5 for MVR. Follow-up for anticoagulant monitoring was scheduled for discharge from the hospital at 15 days in our institution, and monthly or bimonthly postoperatively. Patients who opted to be followed in another medical facility were advised to maintain a similar schedule.

Statistical Analysis

Continuous variables are reported as means ± standard deviations and the categorical variables are represented as percentages. Proportions were compared using Fisher’s exact test or McNemar test, and continuous variables using the Mann-Whitney test. Actuarial curves were constructed to describe mortality and the incidence of prosthesis-related complications using the Kaplan-Meier technique. Long rank test was used for comparing the equality of survival and event distributions. Curves were constructed for both the AVR and MVR cohorts for the end-points of late death of any cause, prosthesis-related death, prosthesis-related reoperation, prosthesis endocarditis, thromboembolic events and anticoagulation-related hemorrhage. The proportion of patients free from prosthesis-related events and its standard error, as well as the linearized rate of valve-related events, were reported.

Results

Patients’ demographic data

Of 285 patients who had single valve replacement, 168 received a mitral prosthesis and 117 an aortic valve prosthesis. The mean age of the whole cohort was 45±15 years (ranging from 9 to 75 years); 71% were 55 years old or younger, and 51% were females. Table 1 summarizes the demographic data of the AVR and MVR cohorts.

In the MVR cohort, the mean age was 45±16 years, 75% were 55 years old or younger, and 65% were females. In the ARV cohort, the mean age was 45±16 years, 66% were 55 years old or younger and the male gender predominated (69%). The proportion of patients who experienced previous cardiac operations, had preoperative atrial fibrillation, was in functional class III (NYHA) and had systolic arterial pulmonary pressure ≥ 50 mmHg was significantly higher in the MVR cohort. On the other hand, the proportion of patients who experienced previous myocardial infarction or had endocarditis was significantly higher in the AVR cohort.

In the MVR cohort, rheumatic heart disease was the main cause of valve dysfunction (74%) followed by degenerative diseases (14%) and endocarditis (5%). In the ARV cohort, the main etiology was rheumatic fever (33%), followed by degenerative disease (15%), bicuspid aortic valve (11%), senile aortic valve disease (13%), and endocarditis (10%). The proportion of patients operated due to prosthesis dysfunction

Table 1 - Demographic data for patients having aortic or mitral valve replacement with the St. Jude Medical valve prosthesis (SPAP - systolic pulmonary arterial pressure)

<table>
<thead>
<tr>
<th></th>
<th>MVR n=159</th>
<th>AVR n=111</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>46±14</td>
<td>46±16</td>
<td>0.879</td>
</tr>
<tr>
<td>Female</td>
<td>65%</td>
<td>30%</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>Male</td>
<td>35%</td>
<td>69%</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>Previous cardiac operation</td>
<td>31%</td>
<td>8%</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>NYHA class</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>16%</td>
<td>23%</td>
<td>0.145</td>
</tr>
<tr>
<td>II</td>
<td>28%</td>
<td>40%</td>
<td>0.060</td>
</tr>
<tr>
<td>III</td>
<td>46%</td>
<td>30%</td>
<td>0.014</td>
</tr>
<tr>
<td>IV</td>
<td>10%</td>
<td>7%</td>
<td>0.503</td>
</tr>
<tr>
<td>Ejection Fraction (%)</td>
<td>62±10</td>
<td>60±13</td>
<td>0.159</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>47%</td>
<td>6%</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>30%</td>
<td>3%</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>Stroke</td>
<td>7%</td>
<td>2%</td>
<td>0.080</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>33%</td>
<td>44%</td>
<td>0.061</td>
</tr>
<tr>
<td>Peripheral arteriopathy</td>
<td>4%</td>
<td>2%</td>
<td>0.476</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8%</td>
<td>13%</td>
<td>0.225</td>
</tr>
<tr>
<td>Smoking</td>
<td>27%</td>
<td>30%</td>
<td>0.688</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>2%</td>
<td>3%</td>
<td>0.696</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0.6%</td>
<td>7%</td>
<td>0.005</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>6%</td>
<td>10%</td>
<td>0.359</td>
</tr>
<tr>
<td>SPAP (≥ 50 mmHg)</td>
<td>47%</td>
<td>12%</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>Endocarditis (acute)</td>
<td>6%</td>
<td>14%</td>
<td>0.023</td>
</tr>
<tr>
<td>Prosthesis dysfunction</td>
<td>17%</td>
<td>5%</td>
<td>0.003</td>
</tr>
<tr>
<td>Valve lesion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stenosis</td>
<td>27%</td>
<td>56%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Regurgitation</td>
<td>38%</td>
<td>25%</td>
<td>0.031</td>
</tr>
<tr>
<td>Combined</td>
<td>33%</td>
<td>25%</td>
<td>0.160</td>
</tr>
</tbody>
</table>

SPAP - Systolic pulmonary arterial pressure
was significantly higher in the MVR cohort (Table 1), and in this cohort, 89% of the prosthetic dysfunction was due to bioprosthesis degeneration (mean age 47±13 years) and 43% had chronic atrial fibrillation. However, dysfunction of the mechanical prosthesis (all non-structural) prevailed in the AVR cohort (67%). In the MVR cohort, 38% of the patients had concomitant tricuspid annuloplasty and 3% had coronary artery bypass graft (CABG) surgery. In the AVR cohort, 13% had concomitant CABG and 5% concomitant mitral valve reconstruction. Table 2 shows the distribution of prosthesis sizes.

Follow-up

Operative mortality for AVR and MVR was 7% and 7.5%, respectively. In the AVR cohort the mean age of those who died in the hospital was 50±17 years (versus 45 years, p=0.440); however, the proportion of patients presenting class III/IV of NYHA or who had history of previous myocardial infarction was higher than the one observed among those who were discharged from the hospital (75% versus 34%, p=0.049 and 37% versus 5%, p=0.010, respectively). In addition, their ejection fraction was significantly lower (0.49±0.15 versus 0.61±0.13, p=0.049). In the MVR cohort, the mean age of those who died in the hospital was 54 years (versus 44 years, p=0.005); the proportion of patients older than 60 years (25% versus 6%, p=0.024), with valve prosthesis dysfunction (37% versus 14%, p=0.030), and presenting functional class III/IV (81% versus 53%, p=0.036) was higher than the one observed among those who were discharged from the hospital.

The total follow up was 691.8 patient-years for MVR cohort and 471.3 patient-years for the AVR cohort. After the operation, the number of patients in class I of the NYHA increased significantly in both cohorts. In the MVR cohort, 68% of the patients were in class I postoperatively (versus 16% preoperatively, p<0.001; McNemar test). In the AVR cohort, 87% were in class I postoperatively (versus 23% preoperatively, p<0.001, McNemar test). The number of patients with atrial fibrillation (AF) increased after the valve replacement in both cohorts. In the MVR cohort, 49% of the patients had AF postoperatively (versus 43% preoperatively, p=0.08, McNemar test), and in the AVR cohort 14% presented AF after the operation (versus 6% preoperatively, p=0.039, McNemar test).

Late mortality

In the MVR cohort, 14 late deaths occurred (7 valve-related, 1 cardiac and 6 non-cardiac-related). In the AVR cohort, 9 late deaths occurred (6 valve-related, 1 cardiac and 2 non-cardiac-related). Survival was 82% ± 6% at 10 years for the MVR and 83% ± 8% (p=0.882) for the AVR cohort.

Valve-related mortality

In the MVR cohort, of the 7 deaths considered valve-related, 3 were due to strokes and the cause of death was unknown in 4 patients. In the AV cohort, of the 6 deaths considered valve-related, 3 were due to strokes (2 ischemic and 1 hemorrhagic), 1 was due to endocarditis, and the cause was unknown in 2 patients. Freedom from valve-related death at 10 years (figure 1) for the MVR cohort and AV were 89±7% and 85%±8%, respectively (p=0.699). The linearized rate of valve-related deaths was 1.3% per patient-year for both cohorts. Patients whose cause of death was unknown were being followed at our institution and the deaths were informed by relatives.

Reoperation

Reoperation was performed on 4 patients in the MVR cohort and 1 patient in the AV cohort. Reasons for reoperation in the MVR cohort were perivalvular dehiscence in 1 patient, endocarditis in 1 patient, and prosthesis thrombosis in 2 patients. In the AV cohort, the reason for reoperation was perivalvular dehiscence. Structural valve deterioration was not seen in either cohort. In the MVR cohort, the freedom from reoperation (Figure 2) was 97% ± 2% at 10 years and in the AV cohort was 99% ± 1% at 10 years (p=0.335). The linearized rate of reoperation was 0.6% per patient-year for the MVR cohort and 0.2% per patient-year for the AV cohort.

Thromboembolic complications

Eleven patients experienced thromboembolic events in the MVR cohort, 8 had strokes, one had a transient ischemic attack and 2 had valve thrombosis without clinically evident thromboembolism. Two patients in the AV cohort experienced embolic strokes. Kaplan-Meier analysis showed that the freedom from thromboembolic events (Figure 3) was 82% ± 8% in the MVR cohort and 98% ± 2% in the AV cohort, significantly lower than in the MVR cohort (p=0.049). The linearized rate of thromboembolism was 1.7% per patient-year for the MVR cohort and 0.5% per patient-year for the AV cohort.

Bleeding events

Bleeding events requiring medical attention occurred in 30 patients, 11 in the AV cohort and 19 in the MVR cohort. According to the Kaplan-Meier analysis, the freedom from

<table>
<thead>
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<th>Size</th>
<th>MVR n=159</th>
<th>AVR n=111</th>
</tr>
</thead>
<tbody>
<tr>
<td>19.00</td>
<td>-</td>
<td>2 %</td>
</tr>
<tr>
<td>21.00</td>
<td>-</td>
<td>16%</td>
</tr>
<tr>
<td>23.00</td>
<td>1%</td>
<td>46%</td>
</tr>
<tr>
<td>25.00</td>
<td>4%</td>
<td>28%</td>
</tr>
<tr>
<td>27.00</td>
<td>18%</td>
<td>5%</td>
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<tr>
<td>29.00</td>
<td>36%</td>
<td>1%</td>
</tr>
<tr>
<td>31.00</td>
<td>30%</td>
<td>-</td>
</tr>
<tr>
<td>33.00</td>
<td>10%</td>
<td>-</td>
</tr>
</tbody>
</table>

MVR - Mitral valve replacement, AVR - aortic valve replacement.
Figure 1A - Late mortality (any cause, panel A, p=0.882) in patients having valve replacement with the St. Jude Medical valve prosthesis; AVR – aortic valve replacement; MVR – mitral valve replacement.

Figure 1B - Freedom from prosthesis-related death (panel B, p=0.699) in patients having valve replacement with the St. Jude Medical valve prosthesis; AVR – aortic valve replacement; MVR – mitral valve replacement.
Figure 2 - Freedom from reoperation in patients submitted to valve replacement with the St. Jude Medical valve prosthesis; AVR – aortic valve replacement; MVR – mitral valve replacement, p=0.335.

Figure 3 - Freedom from thromboembolic events in patients submitted to valve replacement with the St. Jude Medical valve prosthesis; AVR – aortic valve replacement; MVR – mitral valve replacement, p=0.049.
bleeding (Figure 4) was 71% ± 8% in the MVR cohort and 86 ± 4% in the AVR cohort at 10 years (p=0.579). The linearized rate of bleeding events was 3.0% per patient-year for MVR cohort and 2.4% per patient-year for the AVR cohort.

In the MVR cohort 9 patients had gastrointestinal bleeding (3 died), 2 had menorrhagia, 3 had ovarian cyst hemorrhage, 3 had massive epistaxis, 1 had hemorrhagic stroke (died) and 1 had hemoptysis. In the AVR cohort, 7 had gastrointestinal bleeding, 1 had ovarian cyst hemorrhage, 1 had hematuria, 1 had hemarthrosis, and 1 had extensive traumatic retroperitoneal hematoma. No patients died due to bleeding in the AVR cohort.

Prosthetic Valve Endocarditis

There were 3 cases of prosthetic valve endocarditis (PVE) in the MVR cohort and one in the AVR cohort. Therefore, the freedom from PVE (figure 5) was 98% ± 1% in the MVR cohort and 99% ± 1% in the AVR cohort (p=0.534). The linearized rate of prosthetic valve endocarditis was 0.4% per patient-year for MVR cohort and 0.2% per patient-year for the AVR cohort.

Discussion

Although valve repair has become the procedure of choice for correcting valve dysfunction, its use to treat adults patients with aortic valve disease and rheumatic mitral regurgitation has remained rare. In such situations, the repair is usually technically more difficult, mainly in calcified valves, and it may be associated with a high failure rate4. Therefore, valve replacement is frequently the only option to treat many heart valve dysfunctions. However, in developing countries, heart valve replacement is always a matter of concern due to anticoagulant-related bleeding and/or thromboembolic events, mainly because of socioeconomic issues.

In Brazil, rheumatic fever is still the major cause of valve dysfunction, mainly in the mitral valve, a disease that usually affects younger populations5,6. According to the Brazilian govern*, the majority of the population relies on the public health system, as only around 25% of the population has private health insurance. Therefore, the use of mechanical valve prostheses in a non-ideal socioeconomic scenario would expose the patients to anticoagulant-related bleeding and/or thromboembolic events. Consequently, the use of bioprostheses, mainly in the mitral position, and even in young patients, prevails in Brazil1,2,3. However, although effective, bioprostheses may expose those individuals to the risk and distress of repeated valve operations8.

Our results show that in spite of the fact that the patients operated due to mitral prosthesis dysfunction were young (mean age of 47 years) and 43% of them had chronic atrial fibrillation preoperatively, 89% had received a bioprostheses, even though anticoagulation was already needed by many of them and the rate of degenerative structural dysfunction would be high. In addition, our results showed that the number of patients with atrial fibrillation was higher in the postoperative

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4http://tabnet.datasus.gov.br/cgi/idb2005/f15uf.htm

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period compared to the period prior to the intervention, indicating that new cases were added. We are not sure about the reason, but we can speculate that, as patients suffering from rheumatic heart disease and persistent atrial fibrillation usually do not return to the sinus rhythm after the operation, and that pathologic alterations caused by the rheumatic disease may still remain after the operation, some patients may have presented atrial fibrillation postoperatively, in spite of the hemodynamic advantages obtained with the valve replacement.

Even though the clinical results with bioprosthesis in a young population have been considered good, valve degeneration leading to the need of valve reoperation undoubtedly is a major issue. In the experience of Pomerantzeff et al with bioprostheses, 33% of the patients were free from reoperation, and freedom from structural valve deterioration for patients aged <50 years was 51.8%. Interestingly, Pomerantzeff et al experience shows that the freedom from thromboembolism with bioprostheses was 82.3%, similar to what we observed, although their follow-up was longer.

Ruel et al found that mitral bioprostheses offer no advantage compared to mechanical valve prostheses, with the exception of warfarin avoidance, and as the reoperation carries significant risks, they suggested that bioprostheses may be actually more hazardous. In the present cohort, we found that operation due to prosthesis dysfunction was associated with hospital mortality. In addition, Ruel et al also considered that the higher rate of embolic events might be contounded with the higher co-prevalence of atrial fibrillation in mitral valve diseases, which we agree with. Interestingly, the study by Kulik et al, comparing mechanical versus bioprosthetic valve replacement in middle-aged patients, suggests that these patients are not free from major adverse prosthesis-related events. In addition, according to Khan et al, the primary difference observed in outcomes between mechanical and tissue bioprostheses was a higher risk of hemorrhage in the aortic mechanical valve recipients and a higher risk of structural failure in all tissue valve recipients. The rate of tissue valve reoperation would outweigh the constant risk of anticoagulant-related hemorrhage with mechanical valves.

Therefore, Kulik et al suggest that the use of a mechanical prosthesis may be at least as good as, and possibly better than the use of bioprostheses in middle-aged patients. We do not think, based on all socioeconomic issues in developing countries that the mechanical prosthesis is better than the bioprosthesis, but we do believe that it may be at least as good as the bioprosthesis.

However, although heart valve bioprostheses have a limited life-span and may necessitate re-replacement due to structural deterioration, what may be associated with a higher operative mortality rate than first-time valve operation, reoperation due to mechanical valve prosthesis dysfunction may be associated with even higher perioperative mortality than tissue valve dysfunction. Hence, adequate monitoring of the anticoagulation is mandatory in patients who chose mechanical valve prostheses, mainly in the mitral position.

Our institution is a university hospital that treats a surrounding population of around 5 million inhabitants,

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**Figure 5** - Freedom from prosthesis endocarditis in patients submitted to valve replacement with the St. Jude Medical valve prosthesis; AVR – aortic valve replacement; MVR – mitral valve replacement, p=0.534.
and we have facilities for monitoring and managing oral anticoagulation. In addition, the majority of the cities and towns around offer free transportation to our institution for patients requiring secondary and tertiary medical attention. Consequently, practically the totality of our younger patients chooses mechanical valve prosthesis, and the results presented here are consistent with the good results observed by others with this mechanical bileaflet prosthesis. Nevertheless, these facilities are not a guarantee of patients’ adherence to life-long systemic anticoagulation and those caring for such patients must consider, in addition to the medical facilities, the social and cultural conditions of their patients.

Our results are comparable with other experiences with bileaflet mechanical prosthesis\textsuperscript{14-17}. In addition, the 5-year survival that we observed for each valve seems to be similar to the one observed by others\textsuperscript{15,16}. Chronic anticoagulation remains the main cause of valve-related events in patients with mechanical prostheses. The percentage of patients free of thromboembolic events was higher in the AVR cohort than in the MVR cohort, similarly to what was observed by others\textsuperscript{17}. However, the linearized rate of thromboembolic complications in this series is comparable with other series of St Jude medical, as well as the incidence of anticoagulation-related bleeding complications\textsuperscript{15,17-19}. The higher incidence of thromboembolic events in patients with mitral mechanical prosthesis is a well known fact\textsuperscript{1}, in which atrial fibrillation certainly also has an important role. Therefore, our results reflect the ability to maintain acceptable anticoagulation status within a public health system scenario, a major concern in developing countries.

The incidence of prosthetic valve endocarditis observed was low (AVR, 0.2%/patient-year; MVR, 0.4%/patient-year), similarly to other series. Oral commensal bacteria are important etiologic agents in endocarditis, and patients with periodontal disease are at risk of bacteremia\textsuperscript{20}. That is another concern in developing countries, as there is an association between low socioeconomic status and poor oral health\textsuperscript{21}. We believe that our quite low incidence of prosthesis endocarditis was probably due to a preoperative dental checkup program, routinely performed in our institution, which includes the necessary oral treatment, and supervision regarding the importance of good oral care and prophylaxis after surgery.

Regarding the prosthesis performance, although we do not have data about prosthesis hemodynamics, our results show a substantial improvement in the NYHA functional class. Additionally, the absence of structural problems and the quite low incidence of reoperation due to prosthesis-related complications also attest the good performance of this prosthesis.

We retrospectively studied a small cohort of non-randomized and non-matched patients for a relatively short interval of time. Notwithstanding these limitations, we believe that our study contributes to the debate about therapeutic options for heart valve dysfunction in developing countries, which is a dilemma, as reconstruction is not always feasible and an ideal valve substitute does not exist at the present.

In conclusion, this series of predominantly young adult patients undergoing isolated MVR and AVR with the St Jude Medical mechanical prosthesis in a developing country confirms the good performance of this valve prosthesis in agreement with previous reports.

Potential Conflict of Interest

I declare that the authors Alfredo José Rodrigues, Paulo Roberto Barbosa Évora, Adilson Scorzoni Filho and Walter Villela A. Vicente received grants from the manufacturer to participate in congresses.

Sources of funding

There were no external funding sources for this study.

Study Association

This study is not associated with any post-graduation program.

References


