

Seventeen-Year Experience with the St. Jude Medical Biocor Porcine Bioprosthesis

Pia S. Mykén

Department of Thoracic and Cardiovascular Surgery, Sahlgrenska University Hospital, Gothenburg, Sweden

Background and aim of the study: Bioprostheses in heart surgery have been investigated in recent years to reduce the long-term anticoagulant administration associated with mechanical devices. Positive results have been achieved, particularly in elderly patients who have a supposed delayed fibrocalcification and reduced life expectancy. Herein are reported 17-year data on the ongoing long-term study of the Biocor porcine prosthetic heart valve, an improved bioprosthesis with reduced stiffness and improved flexibility of the valve cusps designed to resolve issues of reduced lifespan of previous biological valves.

Methods: Data were presented for 1,455 patients who underwent aortic valve replacement (AVR) or mitral valve replacement (MVR) in Sweden with glutaraldehyde-preserved Biocor bioprostheses between 1983 and 2000. Follow up after surgery was evaluated on alternate years using hospital records, interviews, questionnaires and the Cox regression model of multivariate analysis.

Results: At 17 years, the cumulative follow up was

6,540 and 989 patient-years (pt-yr) for AVR and MVR, respectively. Late mortality accounted for 357 (28%) and 65 (38%) patients, respectively, and actuarial survival was 28.2% and 35.4%, respectively. Thromboembolic events occurred in 82 AVR (1.25%/pt-yr) and 18 MVR (1.82%/pt-yr) patients, respectively, with freedom from thromboembolism decreasing with age; 181 AVR and 44 MVR patients received anticoagulants. Reoperations due to structural valve deterioration (SVD) were required in 63 AVR and nine MVR patients. Freedom from reoperation due to SVD increased with age in both groups; actuarial freedom from reoperation was 73.9% and 81.3%, respectively.

Conclusion: Seventeen-year data confirm the low incidence of valve-related complications and improved valve durability reported at the 15-year follow up after both AVR and MVR using Biocor porcine bioprostheses.

The Journal of Heart Valve Disease 2005;14:486-492

The choice between biological and mechanical prosthetic valves remains a major dilemma in heart surgery. Mechanical prostheses have become the most popular option because they can offer a permanent solution, with a negligible risk of reoperation due to prosthetic valve failure. However, the need for long-term anticoagulant therapy for mechanical valve recipients is unwelcome to both surgeons and patients, and this has contributed to the growing popularity of bioprostheses in recent years (1,2). A recent report comparing mechanical and biological prostheses over 20 years has confirmed that there was an increased incidence of bleeding in mechanical valve recipients and an increased incidence of reoperation in patients with

a bioprosthesis, although there was no difference in survival between the two groups (3).

There is a general consensus that bioprostheses are most appropriate for elderly patients, due both to a reduced life expectancy of the patient and a supposed delayed fibrocalcification in the elderly (4). Life expectancy and average age is rising in many populations, bringing a potential increase in the number of suitable candidates for bioprosthetic valve replacement. Registry data from the UK have shown a nine-fold rise in the number of patients aged over 70 years who received valve replacements between 1986 and 1997 (2).

The Biocor porcine prosthetic heart valve (St. Jude Medical, St. Paul, MN, USA) is a third-generation, triple-composite bioprosthesis that was developed in response to the limited lifespan of previous biological valves. The Biocor valve is fixed in glutaraldehyde at a resting state, a technique that appears to reduce the

Address for correspondence:
Pia S. Mykén MD, PhD, Department of Thoracic and Cardiovascular Surgery, Sahlgrenska University Hospital, Gothenburg, Sweden
e-mail: pia.myken@swipnet.se

stiffness and improve the flexibility of valve cusps and hence improve resistance to tissue fatigue and durability (5-8). Herein are reported the 17-year data from an ongoing long-term study that aims to confirm whether these structural improvements extend the valve's longevity and enhance patient outcomes in clinical practice.

Clinical material and methods

Patients

This report includes data on 1,455 consecutive patients who underwent heart valve replacement at Sahlgrenska University Hospital in Gothenburg, Sweden between January 1983 and January 2000. Most patients (n = 1,283) underwent aortic valve replacement (AVR), while a further 172 underwent mitral valve replacement (MVR). The mean patient age at the time of implant was 70 ± 11 years for AVR, and 64 ± 12 years for MVR. Patient data at study entry are summarized in Table I. All patients in this study received a glutaraldehyde-preserved Biocor bioprosthesis, none of which had been 'No-React' treated.

Surgical procedure

During surgery, a standard operative procedure was followed using interrupted, non-everted, pledgeted sutures. Patients received three doses of prophylactic antibiotic therapy, and warfarin for three months from the second day after surgery. The goal of anticoagulation was to maintain the International Normalized Ratio (INR) value between 2.0 and 3.0.

Two procedural changes were made during the study: in 1988, a membrane oxygenator replaced the previously used bubble oxygenator, and in 1998 the

authors' institution switched from using crystal cardioplegia to blood cardioplegia.

Follow up

Follow up evaluations were performed on alternate years since the Biocor valve was first inserted in 1983 (9). Investigators obtained information from hospital records, telephone interviews and patient questionnaires. In the event of a death, the cause was established using either the hospital or attending physician's records, or autopsy records.

Data analysis

The present authors assessed patient data and defined valve-related complications according to The Society of Thoracic Surgeons and American Association for Thoracic Surgery Guidelines (1996 revision) (10). Multivariate analyses of results used the Cox regression model.

Results

Follow up was 99% complete, and ranged between one and 203 months. The mean duration of follow up was 61 and 69 months after AVR and MVR, respectively. The cumulative follow up totaled over 7,981 patient-years (pt-yr): 6,540 pt-yr for AVR and 989 pt-yr for MVR.

Patient survival

Early mortality

There were 67 (5.2%) and 22 (12.8%) early deaths following AVR and MVR, respectively (early deaths included operative mortality and all-cause mortality before hospital discharge or within 30 days of surgery).

Table I: Baseline patient data.

Parameter	Aortic valve replacement	Mitral valve replacement
No. of patients	1,283	172
Age (years)*	70 ± 11	64 ± 12
Female gender (%)	36	52
Previous CABG (%)	38	30
Follow up (pt-yr)	6,540	989
Aortic/mitral valve		
Stenosis (%)	72	18
Insufficiency (%)	13	67
Mixed (%)	15	15
Previous cardiac operation (%)	3	18
Preoperative NYHA class III/IV (%)	69	89

*Values are mean \pm SD.

CABG: Coronary artery bypass graft

Cardiac failure was the leading cause of early death for both aortic and mitral valve recipients.

Late mortality

Late mortality accounted for 422 patients (29%) overall: 357 (28%) after AVR and 65 (38%) after MVR. Actuarial survival at 17 years was $28.2 \pm 3.7\%$ after AVR, and $35.4 \pm 5.0\%$ after MVR (Fig. 1). The causes of late mortality are listed in Table II. About 40% of patients who died during this period underwent autopsy; this proportion was similar to that observed at the 15-year follow up (9).

Coronary artery bypass graft surgery was linked with impaired survival in the AVR group (17-year survival 20.7% versus 34.9%).

Thromboembolic and anticoagulant-related events

Thromboembolic events occurred in 82 aortic valve recipients ($1.25\%/pt\text{-yr}$) and 18 mitral valve recipients ($1.82\%/pt\text{-yr}$). Events causing permanent injury constituted 28% (23/82; $0.35\%/pt\text{-yr}$) and 22% (4/18; $0.40\%/pt\text{-yr}$) of the thromboembolic events in the AVR and MVR groups, respectively. The risk of thromboembolism was lowest in patients aged <50 years (at the time of surgery), who had $98.8 \pm 1.2\%$ and 100% freedom from thromboembolic events after AVR and MVR, respectively. For those patients aged 51-60 years this freedom was $84.3 \pm 6.8\%$ and $92.3 \pm 5.2\%$, respectively; for those aged 61-70 years it was $73.7 \pm 8.8\%$ and $58.9 \pm 11.1\%$, respectively, while those patients aged 71-80 years it was $78.9 \pm 3.6\%$ and $72.4 \pm 11.7\%$, respectively, after AVR and MVR. Freedom from thromboembolism decreased with age. Actuarial freedom from thromboembolic events is shown in Figure 2a and b.

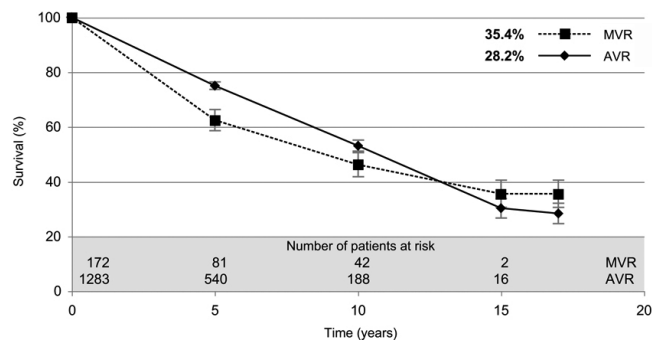


Figure 1: Actuarial survival (according to valve position).

Anticoagulant-related hemorrhage affected 49 AVR patients ($0.75\%/pt\text{-yr}$) and 18 MVR patients ($1.82\%/pt\text{-yr}$). At 17-year follow up, 181 AVR and 44 MVR patients were receiving anticoagulation treatment. After AVR and MVR, patients had $91.4 \pm 2.2\%$ and $85.7 \pm 4.9\%$ freedom from anticoagulant-related hemorrhage, respectively.

Reoperations

Structural valve deterioration

Reoperations due to structural valve deterioration (SVD) were performed in 72 patients: 63 after AVR and nine after MVR (a further four patients died due to SVD before receiving a second prosthesis). There was no early mortality associated with these procedures. Patients aged 71-80 years had $96.9 \pm 2.0\%$ and 100% freedom from reoperation for SVD after AVR and MVR, respectively; those patients aged 61-70 years had $82.1 \pm 4.3\%$ and $89.4 \pm 7.1\%$ freedom from reoperation; those aged 51-60 years had $69.5 \pm 9.7\%$ and $78.6 \pm 12.1\%$ freedom from reoperation; while those patients

Table II: Causes of late mortality.

Cause	Aortic valve replacement	Mitral valve replacement
Valve-related causes (n)		
SVD	3	1
Thromboembolism	18	3
ARH	9	4
PVE	5	0
Total	35	8
Other cardiac causes (n)		
Arrhythmia	18	5
Cardiac failure	98	20
Myocardial infarction	44	9
Cardiomyopathy	8	3
Total	168	37
Total cardiac causes (n)	203	45
Non-cardiac causes (n)	154	20

ARH: Anticoagulant-related hemorrhage; PVE: Prosthetic valve endocarditis; SVD: Structural valve deterioration

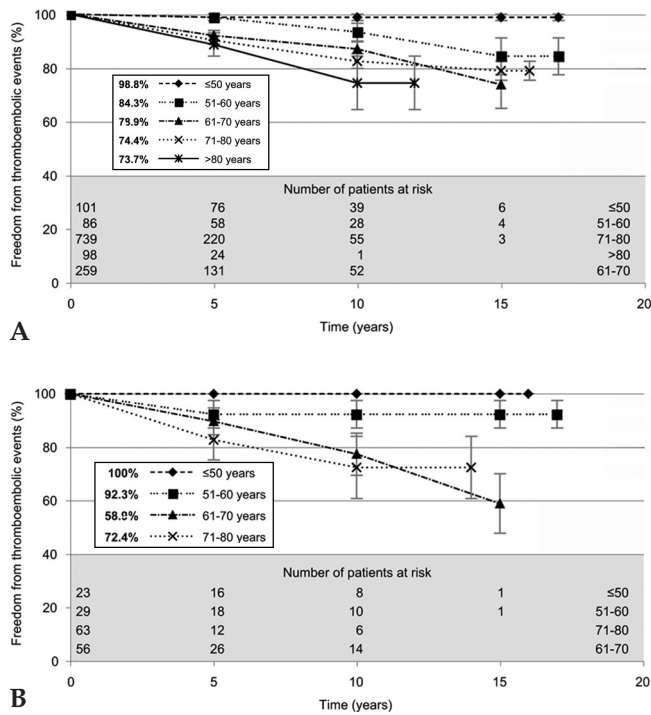


Figure 2: Freedom from thromboembolic events according to age in: a) aortic valve replacement; and b) mitral valve replacement.

aged <50 years of age had freedom from reoperation due to SVD of $43.6 \pm 8.7\%$ and $63.8 \pm 15.3\%$ after AVR and MVR, respectively (Fig. 3a and b).

Freedom from reoperation for SVD for patients aged >60 years was $90.5 \pm 2.5\%$, compared to $56.6 \pm 6.8\%$ in patients below this age. Similarly, MVR recipients aged >60 years had $95.8 \pm 3.8\%$ freedom from reoperation for SVD, with only $78.6 \pm 8.2\%$ freedom from reoperation in AVR patients aged <60 years.

Actuarial freedom from reoperation due to SVD was $73.9 \pm 4.1\%$ and $81.3 \pm 6.0\%$ in the AVR and MVR groups, respectively (Fig. 3c).

Non-structural valve dysfunction

A total of 23 patients was reoperated on due to non-structural valve dysfunction (paravalvular leak); of these patients, 20 were in the AVR group and three in the MVR group.

Prosthetic valve endocarditis

Actuarial freedom from reoperation due to prosthetic valve endocarditis (PVE) was $92.9 \pm 2.5\%$ in the AVR group and $91.7 \pm 3.4\%$ in the MVR group. There were 21 reoperations after AVR, and seven after MVR. A total of five patients died when reoperated on due to PVE; all had received aortic valves.

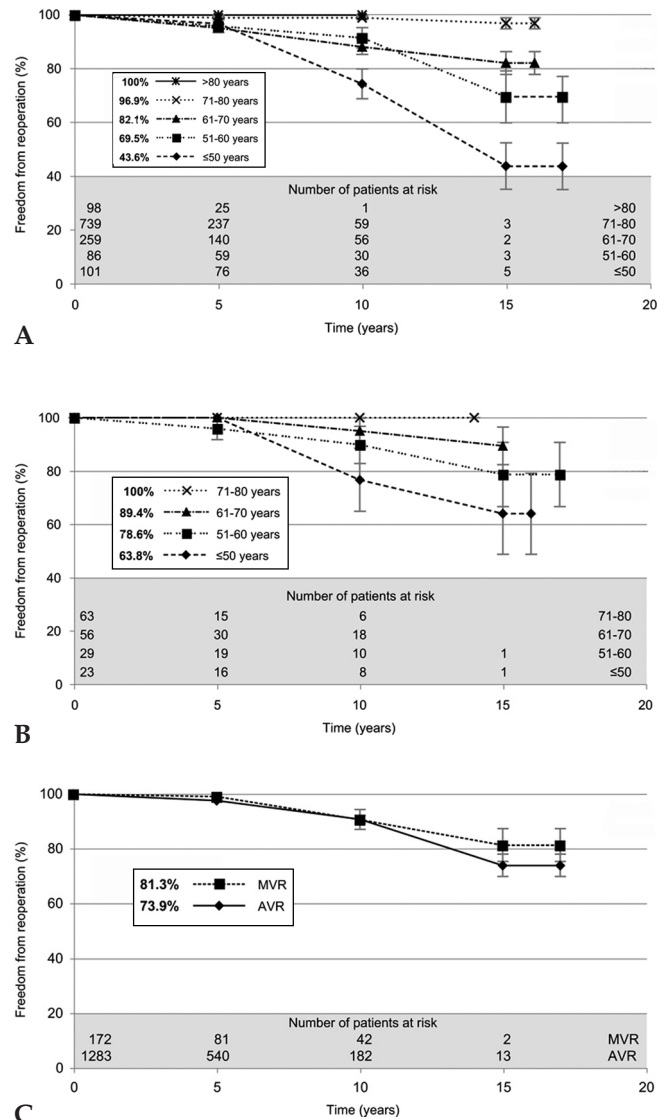


Figure 3: Freedom from reoperation for structural valve deterioration: a) by age in aortic valve replacement; b) by age in mitral valve replacement; and c) by valve position.

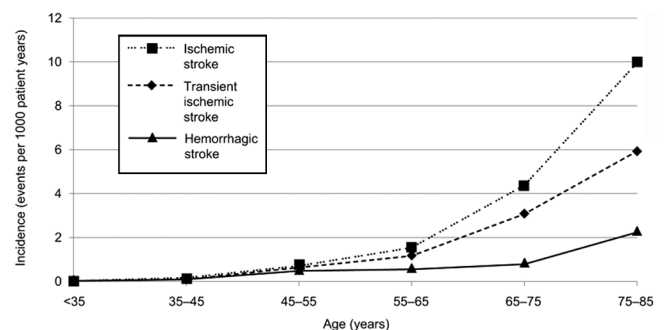


Figure 4: Increasing incidence of ischemic stroke, transient ischemic stroke and hemorrhagic stroke with age.

Discussion

The present results confirmed the favorable outcomes reported previously at the 15-year follow up with the St. Jude Medical Biocor porcine bioprosthesis (9). Indeed, both survival and freedom from reoperation due to SVD at 17 years were comparable with the 10- and 15-year results both for other porcine bioprostheses and bovine pericardial prostheses (11-13).

Perhaps the largest study of a bioprosthesis published to date is a 15-year follow up of more than 1,800 recipients of the Carpentier-Edwards SAV Bioprosthesis (Edwards Life Sciences, Irvine, CA, USA), a supra-annular porcine valve used in the aortic position (14). Overall survival was not reported, but results according to age group showed that the best survival at 15 years - in patients aged 61-70 years - was 33% (survival in patients aged >70 years was 13.5%). In the present population of 1,283 patients with AVR, 41% survival was reported at 15 years (9) and 28% survival at 17 years. There were no unexpected changes in mortality in the 61- to 70-year age group, and so survival in this subgroup followed the same pattern as at the 15-year follow up.

Bovine pericardial valve replacements were developed in an attempt to improve upon the durability of porcine bioprostheses. The long-term follow up of the most widely used pericardial valve - the Carpentier-Edwards Perimount bioprosthesis - revealed 37% survival and 69% freedom from reoperation for SVD in the mitral position at 14 years (13). In the present authors' experience, the Biocor porcine valve offers superior durability in the mitral position, with 35% survival (the present study had a mean patient age of 64 years, whereas that of Marchand et al. (13) had a mean age of 61 years) and 81% freedom from reoperation for SVD at 17 years. These favorable mitral results were confirmed by Kirali et al. (15) who used the Biocor valve and showed 76.8% freedom from SVD at 14 years in a patient population with an average age of 48.8 years. Similarly, in the aortic position, the present results compared well with those for the Perimount pericardial valve: the present patients showed 28% survival and 74% freedom from reoperation for SVD at 17 years with the Biocor valve, compared to values of 26% and 77% at 15 years with the Perimount prosthesis (11). As yet, there are no published data available beyond 15 years for the Perimount valve.

Reoperations due to non-structural valve dysfunction occurred predominantly in the earlier-treated patients of the present study because the initial Biocor valves had smaller sewing cuffs. However, this size of sewing cuff on Biocor valves has since been adjusted.

Another approach to improving outcomes has been the development of stentless aortic valves, which were

designed to accelerate left ventricular recovery by reducing transvalvular pressure gradients. Although conflicting data have been reported on whether stentless valves enhance early left ventricular mass regression (16-18), long-term studies have demonstrated early and continued regression, as well as comparable survival with age- and sex-matched population controls (19,20). The longest follow up to date with stentless valves has been nine years (21) however, so although these valves have promising durability, it is difficult to compare them with stented tissue valves in the long term.

Most surgeons agree that bioprostheses are most suitable for elderly patients while mechanical valves are appropriate for young recipients, although a number of risk factors may influence this choice for individual patients (22). The exact age threshold for choosing a biological or mechanical valve remains the subject of debate, but a recent review proposed that the cut-off ages should be 60-65 years for AVR and 65-70 years for MVR (23). The present data are consistent with age thresholds of around these values.

The age-related decrease in freedom from thromboembolism observed among the present patients may have occurred because the incidence of transient ischemic attacks, ischemic stroke and hemorrhagic stroke is augmented with age, as it has been seen to increase by more than 1% in people aged over 65 years (Fig. 4) (24,25).

In many cases, the main reason for choosing a biological valve replacement is the presumed relatively high risk of bleeding with mechanical prostheses and the resultant need for long-term anticoagulant therapy. The present data reveal freedom from anticoagulant-related hemorrhage to be 91% versus 86% after AVR and MVR, respectively. However, it would be hoped that even fewer bleeding complications would occur when using a bioprostheses, as the need for anticoagulation with these devices is low. As a considerable number of warfarin-related bleeds occur during the first three months after surgery, a switch of therapy from warfarin to aspirin could be considered. Recent data from Gherli et al. (26) suggest that there is no evidence to support the fact that warfarin is more effective than aspirin after bioprosthetic AVR, but this subject remains controversial and requires further investigation.

Outcomes are presented by actuarial analysis to optimize the power of this cumulative patient sample. There is, however, a risk of underestimating freedom from reoperation/complications using this method (11,27).

In conclusion, the present 17-year data have revealed excellent long-term outcomes using the St. Jude Medical Biocor porcine bioprosthesis in both the aortic

and mitral valve positions. The results confirm the low incidence of valve-related complications and improved valve durability reported at the 15-year follow up.

Acknowledgements

These studies were supported by grants from St. Jude Medical, Inc. and the medical faculty at Gothenburg University.

References

1. Northrup WF, III, Dubois KA, Kshetry VR, Teskey JM, Nicoloff DM. Trends in aortic valve surgery in a large multi-surgeon, multi-hospital practice, 1979-1999. *J Heart Valve Dis* 2002;11:768-778; discussion 778-779
2. Edwards MB, Taylor KM. A profile of valve replacement surgery in the UK (1986-1997): A study from the UK Heart Valve Registry. *J Heart Valve Dis* 1999;8:697-701
3. Oxenham H, Bloomfield P, Wheatley DJ, et al. Twenty year comparison of a Björk-Shiley mechanical heart valve with porcine bioprostheses. *Heart* 2003;89:715-721
4. Bonow RO, Carabello B, de Leon AC, et al. ACC/AHA Guidelines for the Management of Patients With Valvular Heart Disease. Executive Summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients With Valvular Heart Disease). *J Heart Valve Dis* 1998;7:672-707
5. Broom ND, Thomson PJ. Influence of fixation conditions on performance of glutaraldehyde-treated porcine aortic valve: Towards a more scientific basis. *Thorax* 1979;34:166-176
6. Mayne ASD, Christie OW, Smail BH, Hunter PJ, Barrett-Boyes BO. An assessment of the mechanical properties of leaflets from four second generation porcine bioprostheses using biaxial testing techniques. *J Thorac Cardiovasc Surg* 1989;98:170-180
7. Hilbert SL, Barrick MK. Porcine aortic valve bioprostheses: A morphologic comparison of the effects of fixation pressure. *J Biomed Mater Res* 1990;24:773-787
8. Vesely I. Analysis of the Medtronic Intact bioprosthetic valve: Effects of 'zero-pressure' fixation. *J Thorac Cardiovasc Surg* 1991;101:90-99
9. Mykén P, Bech-Hanssen O, Phipps B, Caidahl K. Fifteen years follow up with the St. Jude Medical Biocor porcine bioprosthesis. *J Heart Valve Dis* 2000;9:415-422
10. Edmunds LH, Jr., Clark RE, Cohn LH, Grunkemeier GL, Miller DC, Weisel RD. Guidelines for reporting morbidity and mortality after cardiac valvular operations. Ad Hoc Liaison Committee for Standardizing Definitions of Prosthetic Heart Valve Morbidity of The American Association for Thoracic Surgery and The Society of Thoracic Surgeons. *J Thorac Cardiovasc Surg* 1996;112:708-711
11. Banbury MK, Cosgrove DM, III, White JA, Blackstone EH, Frater RW, Okies JE. Age and valve size effect on the long-term durability of the Carpentier-Edwards aortic pericardial bioprosthesis. *Ann Thorac Surg* 2001;72:753-757
12. David TE, Ivanov J, Armstrong S, et al. Late results of heart valve replacement with the Hancock II bioprosthesis. *J Thorac Cardiovasc Surg* 2001;121:268-277
13. Marchand MA, Aupart MR, Norton R, et al. Fifteen-year experience with the mitral Carpentier-Edwards PERIMOUNT pericardial bioprosthesis. *Ann Thorac Surg* 2001;71(5 Suppl.):S236-S239
14. Jamieson WR, Janusz MT, Burr LH, et al. Carpentier-Edwards supraannular porcine bioprosthesis: Second-generation prosthesis in aortic valve replacement. *Ann Thorac Surg* 2001;71(5 Suppl.):S224-S227
15. Kirali K, Güler M, Tuncer A, et al. Fifteen-year clinical experience with the Biocor porcine bioprostheses in the mitral position. *Ann Thorac Surg* 2001;71:811-815
16. Walther T, Falk V, Langebartels G, et al. Regression of left ventricular hypertrophy after stentless versus conventional aortic valve replacement. *Semin Thorac Cardiovasc Surg* 1999;11(4 Suppl.1):18-21
17. Bevilacqua S, Gianetti J, Ripoli A, et al. Aortic valve disease with severe ventricular dysfunction: Stentless valve for better recovery. *Ann Thorac Surg* 2002;74:2016-2021
18. Sensky PR, Loubani M, Keal RP, Samani NJ, Sosnowski AW, Galinanes M. Does the type of prosthesis influence early left ventricular mass regression after aortic valve replacement? Assessment with magnetic resonance imaging. *Am Heart J* 2003;146:E13
19. Bach DS, Goldman B, Verrier E, et al. Eight-year hemodynamic follow-up after aortic valve replacement with the Toronto SPV stentless aortic valve. *Semin Thorac Cardiovasc Surg* 2001;13(4 Suppl.1):173-179
20. Dellgren G, Eriksson MJ, Brodin LA, Radegran K. Eleven years' experience with the Biocor stentless aortic bioprosthesis: Clinical and hemodynamic follow-up with long-term relative survival rate. *Eur J Cardiothorac Surg* 2002;22:912-921
21. Bach DS, Goldman B, Verrier E, et al. Durability and prevalence of aortic regurgitation nine years after aortic valve replacement with the Toronto SPV stentless bioprosthesis. *J Heart Valve Dis* 2004;13:64-72

22. Butchart EG, Ionescu A, Payne N, Giddings J, Grunkemeier GL, Fraser AG. A new scoring system to determine thromboembolic risk after heart valve replacement. *Circulation* 2003;108(Suppl.1):II68-II74
23. Rahimtoola SH. Choice of prosthetic heart valve for adult patients. *J Am Coll Cardiol* 2003;41:893-904
24. Kolominsky-Rabas PL, Sarti C, Heuschmann PU, et al. A prospective community-based study of stroke in Germany - the Erlangen Stroke Project (ESPro): Incidence and case fatality at 1, 3, and 12 months. *Stroke* 1998;29:2501-2506
25. Brown RD, Jr., Petty GW, O'Fallon WM, Wiebers DO, Whisnant JP. Incidence of transient ischemic attack in Rochester, Minnesota, 1985-1989. *Stroke* 1998;29:2109-2113
26. Gherli T, Colli A, Fragnito C, et al. Comparing warfarin with aspirin after biological aortic valve replacement: A prospective study. *Circulation* 2004;110:496-500
27. Jamieson WR, Burr LH, Miyagishima RT, Germann E, Anderson WN. Actuarial versus actual freedom from structural valve deterioration with the Carpentier-Edwards porcine bioprostheses. *Can J Cardiol* 1999;15:973-978