

# Fifteen Years' Clinical Experience with the CarboMedics Prosthetic Heart Valve

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**Background and aim of the study:** The CarboMedics bileaflet prosthetic heart valve was first implanted as part of a prospective clinical study at the authors' institution in November 1987. The patient cohort included was part of a multicenter trial set up by the manufacturer for an FDA application. The present report details findings over a 15-year period, with a continuous follow up on this patient cohort.

**Methods:** Between November 1987 and August 1990, 132 patients (68 males, 64 females; median age 56 years; range: 12-74 years) received a CarboMedics heart valve prosthesis. All patients were included in the study, whether surgery was elective or emergency, first time or reoperation. There were 69 aortic, 49 mitral and 12 double (aortic and mitral) valve replacements. Two patients had isolated tricuspid valve replacement. Concomitant surgery was performed in 15 patients. Anticoagulation with warfarin was started on postoperative day 1. After discharge, patients were examined regularly as outpatients for up to five years. Subsequent follow up was obtained prospectively by questionnaires to the patients' general practitioners and with telephone calls to the patients. Actuarial estimates of survival and freedom from morbid events were calculated using the

Kaplan-Meier method; 95% confidence limits for the distribution function were calculated according to the Greenwood formula.

**Results:** Complete follow up information was available on 94% of the patients; total follow up was 1,270.3 patient-years (pt-yr). Actuarial survival at 15 years was  $51 \pm 4.9\%$  overall;  $56 \pm 6.2\%$  for single aortic,  $51 \pm 8.0\%$  for single mitral, and  $30 \pm 15.9\%$  for double valve replacements. Actuarial rates of freedom from complications were: valve thrombosis 100%, embolism  $89 \pm 3.3\%$ , and all anticoagulant-related bleeding  $76 \pm 4.5\%$ . The linearized rates per 100 pt-yr were: embolism 0.94 (aortic 0.74, mitral 1.25); anticoagulant-related bleeding 2.28; paravalvular leakage overall 0.24 (aortic 0.29); prosthetic valve endocarditis overall 0.24 (aortic 0.29, mitral 0.21). There was no hemolysis, prosthetic valve dysfunction, or structural deterioration.

**Conclusion:** Over a 15-year time frame, the CarboMedics prosthetic heart valve has proven to be a highly reliable device with no structural failures and a low incidence of valve-related complications.

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Although the CarboMedics bileaflet prosthetic heart valve first became available in 1986, its implantation as part of a prospective clinical study did not begin at the authors' institution until November 1987. The patient cohort included in this prospective clinical study was part of a multicenter trial set up by the manufacturer for an FDA application. FDA approval was issued on September 30th, 1993. The present report details the authors' experience with the CarboMedics valve over

a 15-year time frame with continuous follow up on this patient cohort.

## Clinical material and methods

### Patients

Between November 1987 and August 1990, 132 non-selected patients (68 males, 64 females; median age 56 years; range: 12 to 74 years) each received a CarboMedics heart valve prosthesis. The low median age reflects the fact that prior to 1991 patients aged over 70 years seldom underwent cardiac surgery. All patients were included in the study, whether surgery was performed electively or on an emergency basis, and whether first time or a reoperation. At the time of

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Table I: Etiology of heart valve disease in 132 patients undergoing valve replacement with CarboMedics prostheses.

Condition	Valve location			
	Aortic (n)	Mitral (n)	Aortic/mitral (n)	Tricuspid (n)
Valve calcification/ degeneration	48	15	7	-
Rheumatic Endocarditis	7	26	4	-
Native	14	6	1	2
Prosthetic	-	2	-	-

surgery, 85% of the patients were in NYHA classes III or IV. Hemodynamic evaluation was made using echocardiography and, in selected cases, by angiography. The etiology of heart valve disease among the patients (Table I) was endocarditis in 25 (19%), of whom 16 (13 aortic, two mitral, one double valve) were in a critical state preoperatively and underwent urgent surgery because of hemodynamic instability. The other nine patients were operated on semi-urgently because of uncontrollable infection. There were 69 isolated aortic, 49 isolated mitral and 12 double (aortic and mitral) valve replacements. Two patients had isolated tricuspid valve replacement. The clinical data of patients are listed in Table II.

### Surgical technique

Three patients had a previously inserted valve prosthesis which required replacement. Concomitant procedures were necessary in 15 patients (11.4%). Coronary bypass grafting was performed in five patients, while the remaining 10 underwent tricuspid valvuloplasty (n = 2) aortic valvuloplasty (n = 2), mitral valvuloplasty (n = 2), closure of atrial or ven-

tricular septal defects (n = 3) or closure of a persistent ductus arteriosus (n = 1).

The surgical technique was standardized, and included total cardiopulmonary bypass with moderate hypothermia (30-32°C). Anterograde, cold crystalloid cardioplegia and a single aortic cross-clamp were used. The proximal anastomoses were performed after removal of the cross-clamp. Anticoagulation with warfarin was commenced on postoperative day 1. Between 1987 and 1992 the anticoagulation policy was to maintain the INR between 3.0 and 4.0; however, due to the number of bleeding events that occurred during this period the INR target level was thereafter decreased to 2.0-3.0. A differentiated INR target level has been used since 2000, namely aortic valve (2.0-3.0) and mitral valve (2.5-3.5).

### Follow up

After discharge from hospital the patients were examined at the outpatient clinic at one month, six months, and one year after surgery, and annually thereafter. At each visit the patients underwent a physical examination, blood tests, and electrocardiography

Table II: Preoperative clinical data in patients (n = 132) receiving CarboMedics heart valve prostheses.

Parameter	Valve surgery			
	AVR	MVR	DVR	TVR
No. of patients	69	49	12	2
Age (years)				
Median	55	59	59	33
Range	12-74	26-71	23-70	29
Gender				
Male	44	17	6	1
Female	25	32	6	1
Associated cardiac surgery				
CABG	3	2	0	0
Other	4	6	0	0

AVR: Aortic valve replacement; CABG: Coronary artery bypass grafting; DVR: Double (aortic + mitral) valve replacement; MVR: Mitral valve replacement; TVR: Tricuspid valve replacement.

(ECG). After five years the patients were examined by their general practitioner and local cardiologist, and the follow up was obtained annually on a prospective basis, with questionnaires to the patient's general practitioner and telephone calls directly to the patient.

**Data analysis**

Actuarial estimates of survival and freedom from morbid events were calculated using the Kaplan-Meier method; 95% confidence limits for the distribution function were calculated according to the Greenwood formula. Thromboembolic and anticoagulant-related bleeding events were calculated from postoperative day 1.

Implantation of the CarboMedics heart valve prosthesis was continued after August 1990, but these patients have not been followed on a prospective basis and were therefore excluded from the present prospective study.

**Results**

Complete follow up data were available for 124 patients (93.9%). The remaining eight patients (all of whom were immigrants) were lost to further follow up between two and five years after surgery because they had returned to their native countries and could not be traced. The median follow up period was 14.5 years (range: 12.5 to 15.5 years); the total cumulative follow up was 1,207.3 patient-years (pt-yr).

**Mortality**

The actuarial survival rate is shown in Figure 1. The overall survival at 15 years was  $51 \pm 4.9\%$  ( $56 \pm 6.2\%$  for aortic valve,  $51 \pm 8.0\%$  for mitral valve, and  $30 \pm 15.9\%$  for double valve replacements).

**Early mortality**

Twelve of the 132 patients (9.1%) died within 30 days

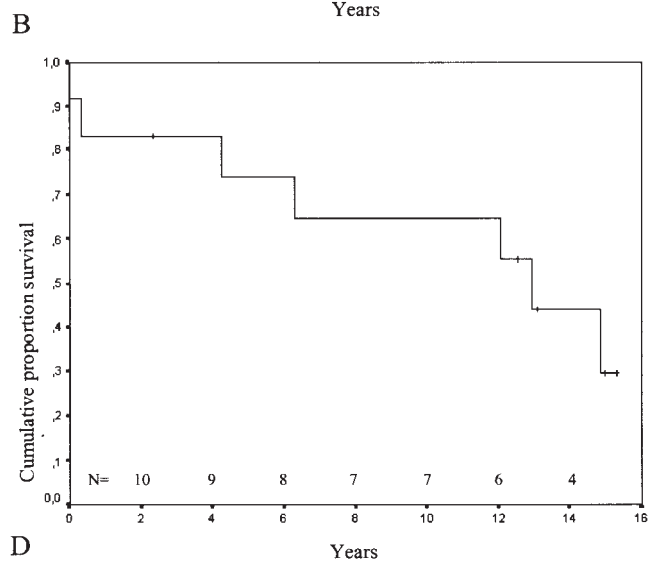
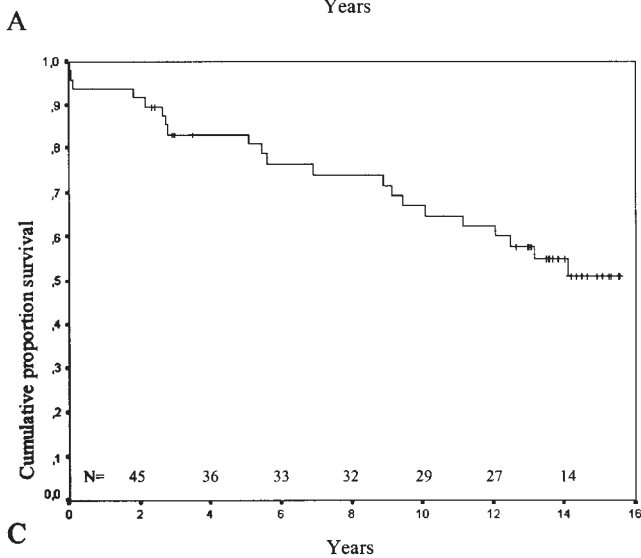
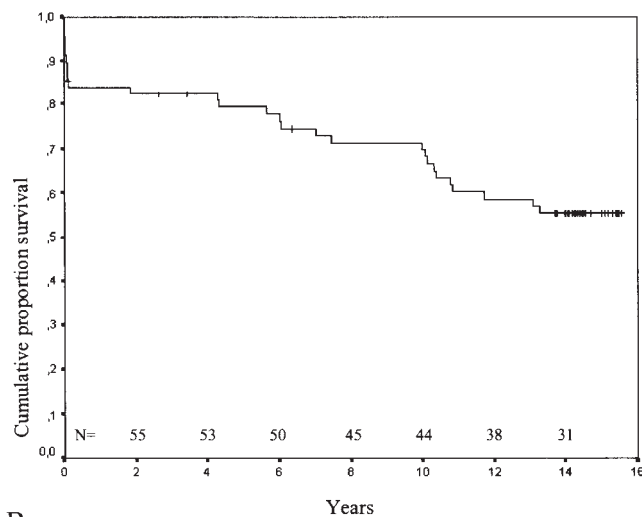
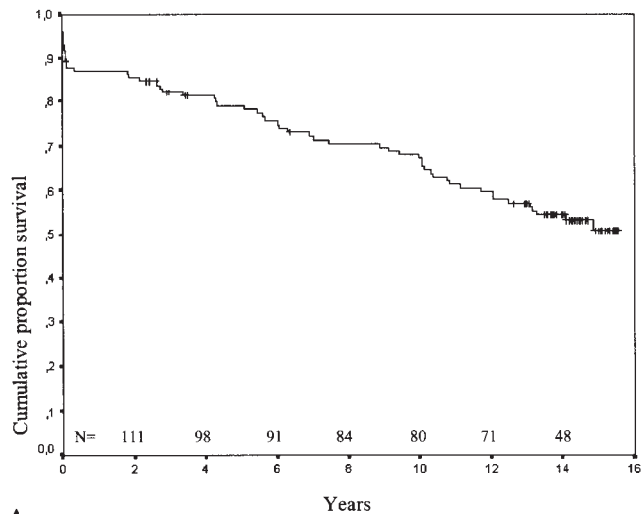


Figure 1: Actuarial survival. A) All patients (n = 132); B) aortic valve replacement patients (n = 69); C) mitral valve replacement patients (n = 49); D) aortic + mitral valve replacement (n = 12).

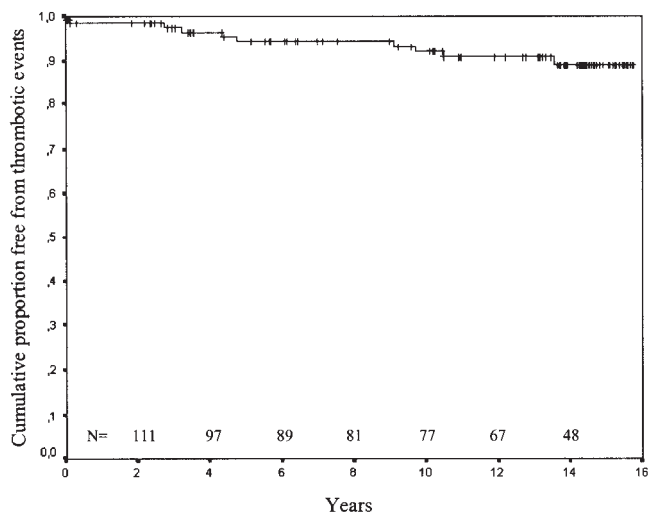


Figure 2: Actuarial freedom from thromboembolism in patients ( $n = 132$ ) after valve replacement.

of valve replacement; eight patients died after aortic valve replacement (11.6%), two after mitral valve (4.1%), one patient after tricuspid valve (50%), and one after double valve (8.3%). The high early mortality in aortic valve patients was due to the high proportion of emergency surgery for infective endocarditis, or cardiogenic shock because of end-stage aortic stenosis in this group. One patient died from a cerebral infarct (valve-related), but the other 11 deaths were considered not to be valve-related. The causes of early death are listed in Table III.

#### Late mortality

A total of 47 patients died during the follow up period. In seven cases, death was possibly related to the valve or to anticoagulation (three patients died from cerebral infarct, three from cerebral bleeding, and one patient from gastrointestinal bleeding). The other 40 deaths were not valve-related (Table III).

#### Valve-related complications

Linearized rates of valve-related complications are listed in Table IV.

Table III: Causes of death in 59 patients after heart valve replacement.

Cause of death	Early death* (n)	Late death+ (n)
Cardiac failure	11	23
Bleeding/emboli	1	7
Non-cardiac	0	17
Total	12	47

\* $<30$  days postoperatively; + $>30$  days postoperatively.

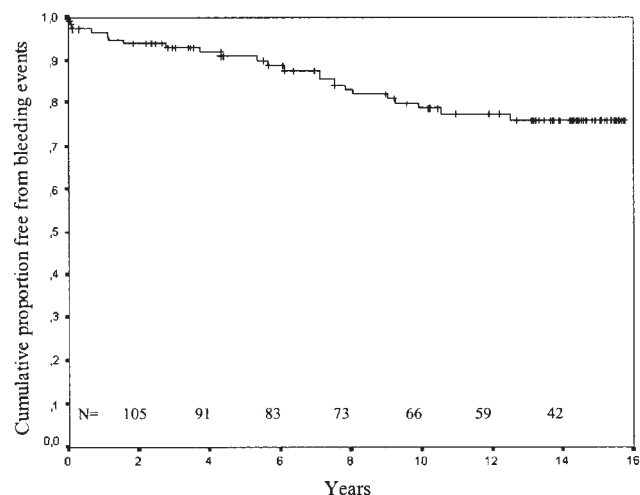


Figure 3: Actuarial freedom from anticoagulant-related bleeding in patients ( $n = 132$ ) after valve replacement.

#### Valve thrombosis

No patient experienced thrombosis of the valve.

#### Embolism

Ten patients sustained a total of 12 thromboembolic events. There were seven minor events, with no lasting disability in six patients. The minor events occurred in one patient with a double valve (aortic + mitral), in two patients with a prosthetic valve in the aortic position, and in three mitral valve patients. There were five major events in five patients: two with a prosthetic valve in the mitral position and lasting disability after a cerebral attack and an embolic event to the right eye, respectively; and three aortic valve patients who died shortly after a cerebral attack. The four mitral valve patients had atrial fibrillation and the five aortic valve patients were in sinus rhythm. One patient with double valve had atrial fibrillation. Freedom from thromboembolic events at 15 years was  $89 \pm 3.3\%$  (Fig. 2).

#### Anticoagulant-related bleeding

Twenty-three patients had a total of 29 anticoagulant-related bleeding events. Fourteen events were major bleeding that required hospital admission, and there were 15 minor episodes. Freedom from anticoagulant-related bleeding events at 15 years was  $76 \pm 4.5\%$  (Fig. 3).

#### Paravalvular leakage

Three patients developed paravalvular leakage, two after aortic valve replacement, and one after double valve replacement, with leakage in the mitral position. In the aortic valve patients, the leakage was closed with direct suture in one case, while the other patient underwent a Ross procedure. The double-valve patient

had the mitral valve prosthesis explanted and a new one inserted; the patient could not be weaned from extracorporeal circulation due to heart failure. The two other patients had an uneventful recovery, and there were no signs of infection in either case.

**Prosthetic valve endocarditis**

Excluding the three patients with persistent endocarditis, three patients - two after aortic valve replacement and one after mitral valve replacement - developed prosthetic endocarditis. One was early postoperative endocarditis after reoperation for a non-infective paravalvular leak. All three patients were treated conservatively with antibiotics for six weeks; recovery was uneventful in all three cases.

**Hemolysis**

There were no reports of clinically important hemolysis.

**Prosthetic valve dysfunction**

No cases of prosthetic valve dysfunction have been registered.

**Structural deterioration**

No structural failures were observed in this group of patients.

**Reoperations**

Six patients were reoperated on for valve-related causes. As mentioned above, three patients underwent reoperation for a non-infectious paravalvular leakage. Three patients were reoperated on because of persist-

ent endocarditis after operation for acute native valve endocarditis. All three were treated with excision of the valve, debridement and implantation of a composite graft. One patient died during the postoperative course as a result of multiple organ failure.

**Discussion**

In the present study, the CarboMedics prosthetic heart valve performed well. An early mortality rate of 11.6% in the aortic group was high compared with that in the CarboMedics studies of Fiene et al. (1) and Bernal et al. (2). The reason for this was a high number of endocarditis cases among the present cohort. Thirteen out of 14 patients with native aortic valve endocarditis were preoperatively in severe cardiac failure, and underwent urgent surgery. Some patients could not be weaned from cardiopulmonary bypass, and some died soon after surgery because of continuous cardiac failure in spite of supportive therapy. Pump failure was the main cause of early death. By contrast, in the present study the early mortality of the mitral and the aortic + mitral groups compared well with rates presented by Fiene et al. (1) and Bernal et al. (2). The long-term survival exceeded the present authors' expectations, taking into account the number of early deaths in the aortic group and the fact that only five patients (4%) who had critical coronary stenosis underwent concomitant coronary bypass surgery. The remaining patients with coronary disease developed progression of the disease during the follow up period. Actuarial survival at 15 years was 51 ± 4.9% overall; 56 ± 6.2% for single aortic and 51 ± 8.0% for

*Table IV: Complications in patients (n = 132) after heart valve replacement.*

Complication	Total follow up														
	AVR (679 pt-yr)			MVR (479 pt-yr)			DVR (109 pt-yr)			VR (3.3 pt-yr)			Total 1,270.3		
	n	Events	Rate	n	Events	Rate	n	Events	Rate	n	Events	Rate	n	Events	Rate
Mechanical failure	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Valve dysfunction	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hemolysis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Thrombosis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Embolism	5	5	0.74	4	6	1.25	1	1	0.92	0	0	0	10	12	0.94
Major events	3	3	0.44	2	2	0.42	0	0	0	0	0	0	5	5	0.39
Minor events	2	2	0.29	3	4	0.84	1	1	0.92	0	0	0	6	7	0.55
ARB	12*	13	1.91	11	16	3.34	0	0	0	0	0	0	23	29	2.28
Major events	6	6	0.88	6	8	1.67	0	0	0	0	0	0	12	14	1.10
Minor events	7	7	1.03	5	8	1.67	0	0	0	0	0	0	12	15	1.18
Paravalvular leak	2	2	0.29	0	0	0	1	1	0.92	0	0	0	3	3	0.24
PVE	2	2	0.29	1	1	0.21	0	0	0	0	0	0	3	3	0.24

Events: number of events; Rate: linearized rate per 100 pt-year.

\*One patient had both minor and major events.

ARB: Anticoagulant-related bleeding; PVE: prosthetic valve endocarditis. Other abbreviations as Table II.

single mitral valve replacement. The main cause of late death was cardiac failure secondary to coronary occlusion. Malignancy was the most common non-cardiac cause of late death. Butchart et al. (3) found, with the Medtronic Hall valve, an actuarial survival at 15 years of 45% for single aortic valve and of 36% for single mitral valve replacement, whilst Lund et al. (4) found an actuarial survival overall at 15 years of 39% with the St. Jude Medical valve.

Prosthetic valve thrombosis is generally more common after mitral valve than after aortic valve replacement, although reports have been made with the St. Jude Medical valve where the number of aortic valve thromboses exceeded the number of mitral valve thromboses (5,6). In the present cohort of patients implanted with the CarboMedics valve, there was no thrombosis when valves were fitted in either the aortic or mitral position.

Anticoagulant-related bleeding events in the present study were much more common than embolic events, and occurred at a linearized rate of 2.28 per 100 pt-yr. All bleeding events have been included, which is not the case with many reports in the literature that included only major bleeding events. More than half of the bleeding events in the present study were of a minor nature and did not require hospital admission. Bleeding events were not seen in the patient group with double (aortic + mitral) valve replacement, though this may partly be explained by the low number of patients in this group (n = 12), one of whom died during surgery.

Anticoagulation-related hemorrhage is closely linked to thromboembolism. Those patients maintained at a higher INR (3.0-4.5) have a greater incidence of anticoagulant-related hemorrhage, whereas the rate of thromboembolism is not significantly higher in patients maintained with an INR of less than 3.0 (7). When the INR exceeds 4.7, the risk of anticoagulant-related bleeding events increases dramatically (8). In the present study, an INR range of 3.0-4.0 was used during the valve implantation period, although later in the follow up period (after 1992) this was changed to 2.0-3.0. Thereafter, the incidence of anticoagulant-related bleeding events decreased, though it was a minor decrease. The embolic event rate increased slightly but remained low. During the two periods of 1987-1992 and 1993-2003, the anticoagulant-related bleeding event rates were 2.52 and 2.15, respectively, and the embolic event rates 0.69 and 1.08, respectively. During the past three years, a differentiated INR level has been used, namely 2.0-3.0 for aortic valves and 2.5-3.5 for mitral valves. The number of embolic and bleeding events in the present study compared favorably with event rates in the CarboMedics study reported by Fiane et al. (1). The St. Jude Medical heart valve pros-

thesis is often compared with the CarboMedics valve in the literature; indeed, the St. Jude Medical valve has the longest history of all the bileaflet valves, and is most likely also the most often cited valve among publications. The literature reveals a great variety in the thromboembolic event rate of the St. Jude Medical valve, with linearized rates varying from 0.5 per 100 pt-yr (9) to 6.62 per 100 pt-yr (7). The thromboembolic event rate in the present study was 0.94 per 100 pt-yr. The great variance in the rate of thromboembolic events with the St. Jude Medical valve simply reflects the multiple factors (including management of anticoagulation) that can influence thromboembolic/bleeding event ratios.

Preoperative endocarditis is a significant risk factor of early mortality in valve replacement, and this was also demonstrated in the present study by the number of early deaths in the aortic valve group. Endocarditis was the indication for surgery in 25 patients (18.9%), three of whom were reoperated on due to persistent endocarditis. The incidence of postoperative endocarditis of 0.24% was low compared with previous studies using Medtronic Hall and St. Jude Medical valves (10-13). Likewise, the incidence of paravalvular leak requiring reoperation (0.24%) was also low compared with reports of Medtronic Hall and St. Jude Medical valve implantation (10-13).

In the present study there were no patients with clinically significant hemolysis or intrinsic valve dysfunction; neither were any mechanical failures such as fractures and/or dislodgment of leaflets reported, thereby confirming data published by others (14,15).

With the current concept for anticoagulation treatment and control as well as antibiotic prophylaxis, the results obtained currently with mechanical valves are much better than those reported a decade ago. The present patient cohort, now 15 years older and with low rates of thromboembolic and major bleeding events, justifies the use of mechanical valves among the older segment of the population - a population with an increasing life-span who will outlive their biological valve prosthesis, based on the current recommended age limit for implantation of a biological valve.

*In conclusion*, it was found that - over a 15-year time frame - the CarboMedics valve prosthesis was highly reliable, with no mechanical failures and a low incidence of valve-related complications. The long-term results met - or even exceeded - those achieved with other valves.

## References

1. Fiane AE, Geiran OR, Svennevig JL. Up to eight year's follow-up of 997 patients receiving the

- CarboMedics prosthetic heart valve. *Ann Thorac Surg* 1998;66:443-448
2. Bernal JM, Rabasa JM, Gutierrez-Garcia F, Morales C, Nistal JF, Revuelta JM. The CarboMedics valve: Experience with 1,049 implants. *Ann Thorac Surg* 1998;65:137-143
  3. Butchart EG, Li HH, Payne N, Buchan K, Grunkemeier GL. Twenty years' experience with the Medtronic Hall valve. *J Thorac Cardiovasc Surg* 2001;121:1090-1100
  4. Lund O, Nielsen SL, Arildsen H, Ilkjaer LB, Pilegaard HK. St. Jude's bi-leaflet aortic valve prosthesis throughout two decades. Quality profile and risk factors. *Ugeskr Laeger* 2001;164:55-60
  5. Debétaz LF, Ruchat P, Hurni M, et al. St. Jude Medical valve prosthesis: An analysis of long-term outcome and prognostic factors. *J Thorac Cardiovasc Surg* 1997;113:134-148
  6. Zellner JL, Kratz JM, Crumbley AJ, III, et al. Long-term experience with the St. Jude Medical valve prosthesis. *Ann Thorac Surg* 1999;68:1210-1218
  7. Horstkotte D, Schulte H, Bircks W, Strauer B. Unexpected findings concerning thromboembolic complications and anticoagulation after complete 10 year follow-up of patients with St. Jude Medical prostheses. *J Heart Valve Dis* 1993;2:291-301
  8. Andersen PV, Aagaard J. Low-dose warfarin in patients with CarboMedics heart valve prostheses. *Asian Annals* 2000;8:11-14
  9. Smith JA, Westlake GW, Mullerworth MH, Skillington PD, Tatoulis J. Excellent long-term results of cardiac valve replacement with the St. Jude Medical valve prosthesis. *Circulation* 1993;88(Suppl. 2):49-54
  10. Fernandez J, Laub GW, Adkins MS, et al. Early and late phase events after valve replacement with the St. Jude Medical prosthesis in 1200 patients. *J Thorac Cardiovasc Surg* 1994;107:394-407
  11. Khan S, Chaux A, Matloff J, et al. The St. Jude Medical valve. Experience with 1,000 cases. *J Thorac Cardiovasc Surg* 1994;108:1010-1019
  12. Beaudet RL, Poirier NL, Doyle D, Nakhle G, Gauvin C. The Medtronic Hall cardiac valve: 7½ years' clinical experience. *Ann Thorac Surg* 1986;42:644-650
  13. Vallejo JL, Gonzales-Santos JM, Albertos J, et al. Eight years experience with the Medtronic-Hall Valve prosthesis. *Ann Thorac Surg* 1990;50:429-436
  14. Dalrymple-Hay MJR, Pearce R, Dawkins S, et al. Mid-term results with 1,503 CarboMedics mechanical valve implants. *J Heart Valve Dis* 2000;9:389-395
  15. Jamieson WRE, Fradet GJ, Miyagishima RT, et al. CarboMedics mechanical prosthesis: Performance at eight years. *J Heart Valve Dis* 2000;9:678-687

