

# The On-X® Heart Valve: Mid-Term Results in a Poorly Anticoagulated Population

Mervyn A. Williams, Sonia van Riet

Provincial Hospital, Port Elizabeth, South Africa

**Background and aim of the study:** The study aim was to evaluate the clinical performance of the On-X® heart valve in a socioeconomically disadvantaged population. Most patients were from an indigenous, poorly educated and geographically dispersed segment of the population where anticoagulation therapy was generally erratic.

**Methods:** Between 1999 and 2004, a total of 530 valves (242 mitral valves, 104 aortic valves, 92 double valves) was implanted in 438 patients (average age 33 years; range: 3-78 years). The most common reason for surgery was rheumatic valve disease (57%), followed by degenerative valve disease (11%) and infective endocarditis (9%). Follow up was 95% complete for a total of 746 patient-years (pt-yr). Among the patient population, 40% were either not anticoagulated or were unsatisfactorily anticoagulated.

**Results:** Hospital mortality was 2.3%, and none of the hospital deaths was valve-related. Mean ( $\pm$  SE) actu-

arial survival (including hospital deaths) at four years was: AVR  $73.8 \pm 8.1\%$ , MVR  $83.4 \pm 5.7\%$  and DVR  $60.9 \pm 10.3\%$ . Linearized rates (for AVR, MVR and DVR, respectively) for late complications (%/pt-yr) were: bleeding events 0.6, 1.0, and 2.3; thrombosis 0.0, 0.2, and 0.0; endocarditis 0.6, 1.0, and 2.3; paravalvular leak 0.6, 0.2, and 0.0; systemic embolism 1.1, 1.5, and 3.5. Most systemic emboli were related to infective endocarditis. Among patients there were seven uncomplicated, full-term pregnancies.

**Conclusion:** Bearing in mind the erratic anticoagulation coverage and high incidence of infective endocarditis, the results of this study may be regarded as encouraging. The low incidence of valve thrombosis (one case) was noteworthy. These data also suggest that the On-X valve may be implanted with relative safety in women wishing to have children.

The Journal of Heart Valve Disease 2006;15:80-86

The enthusiasm following the introduction of mechanical valves during the early 1960s was rapidly dampened by the documentation of a high incidence of thromboembolic complications (1,2). Although the use of anticoagulants reduced the incidence of thrombosis and thromboembolism, it introduced the problem of anticoagulant-related hemorrhage. Consequently, physicians involved in the care of

patients with mechanical valves must steer a course between the Scylla and Charybdis of anticoagulant hemorrhage and thrombotic complications. Among the large number of mechanical valves that have been introduced into clinical practice - all of them in the hope that the incidence of valve-related complications would be reduced - few have lasted the course, and currently only a handful are implanted on a regular basis.

The On-X bileaflet valve was first used clinically in September 1996 (3). The valve is manufactured from On-X carbon, a silicone-free pyrolytic compound. The elimination of silicone from the manufacturing process results in a much smoother and, in theory, a less-thrombogenic surface. The valve housing is of a tubular configuration rather than the washer configuration used in other devices. The valve has a flared inlet and a natural length-to-diameter ratio. This design, when combined with fully opening leaflets, results in linear flow with minimal turbulence. These innovative design features suggest that the On-X heart valve

---

## Disclosure

Mrs. B. Williams, wife of Mr. Mervyn A Williams is the sole distributor of the On-X valve in South Africa.

Presented as a poster at the Third Biennial Meeting of the Society for Heart Valve Disease, 17th-20th June 2005, Vancouver Convention and Exhibition Centre, Vancouver, Canada

## Address for correspondence:

M. A. Williams, 314 Greenacres Hospital, Port Elizabeth, Greenacres, Port Elizabeth 6045, South Africa  
Tel: 041 3633733  
Fax: 041 3633401  
e-mail: drmwiliams@telkomsa.net

should have a lower incidence of thrombosis and thromboembolism compared to other valves.

The population of South Africa is both multi-cultural and ethnically complex. Historical imbalances and the ravages of the previous apartheid era have resulted in a large part of the population being socioeconomically disadvantaged. Overcrowding, inadequate sanitation, poor nutrition and an unemployment rate variously estimated at 30-50% result in a population in which diseases such as pulmonary tuberculosis and rheumatic fever are common. HIV/AIDS, the scourge of Africa, occurs in more than five million of a population of 45 million. The nature of the population is such that one would expect a high rate of valve-related complications, especially thromboembolism and valve thrombosis.

The data presented here relate to the authors' experience with On-X valve implantation in a poorly anticoagulated group of South African patients.

## Clinical material and methods

### Patients

Between October 1999 and November 2004, a total of 530 valves was implanted in 438 patients. Among these patients, 104 had aortic valves replaced, 242 had mitral valves replaced, and 92 had both mitral and aortic valves replaced. The patient demographics are listed in Table I. The etiology of the valve disease is detailed in Table II, the most common cause being rheumatic carditis. Infective endocarditis was the indication for surgery in 9% of patients; the highest incidence of endocarditis was among those patients requiring double valve replacement (16.3%). The sites and sizes of the implanted valves are shown in Figure 1.

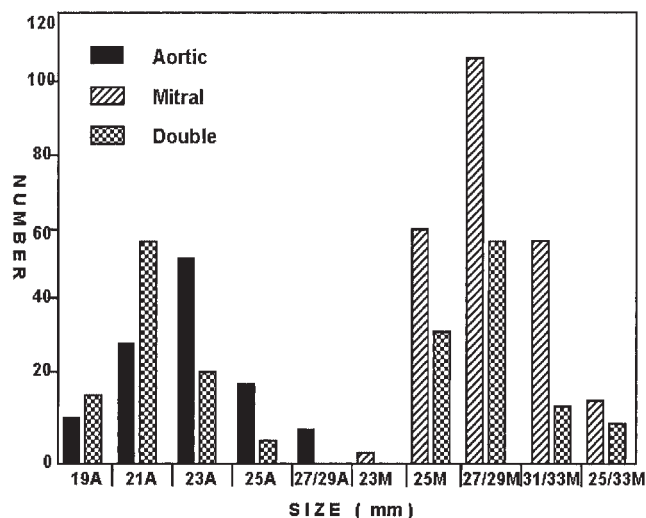


Figure 1: Size distribution of implanted valves. A: Aortic; M: Mitral.

### Surgical technique

All valves were implanted by one of four surgeons using similar techniques. Surgery was undertaken using standard cardiopulmonary bypass with moderate hypothermia and crystalloid cardioplegic arrest. In the mitral position, the valve was implanted using pledgetted interrupted mattress sutures. In the aortic position, the valve was inserted either with simple interrupted sutures or with vertical pledgetted mattress sutures. The valve was oriented in the anti-anatomic position in the mitral annulus, whilst in the aortic position the valve axis was placed perpendicular to the ventricular septum.

Table I: Clinical characteristics of patients.

Parameter	AVR	MVR	DVR
No. of patients	104	242	92
Age (years)*	39.7 (9-78)	33.8 (3-69)	28.7 (9-77)
Gender (% male)	69.2	34.3	57.6
Follow up (pt-yr)			
Total	172.5	402.7	171.5
Mean	1.8	1.8	1.9
Maximum	4.8	5.1	4.4
% complete	96	94	98
Rhythm			
Sinus (%)	80.8	52.9	75.0
Atrial fibrillation (%)	8.7	26.2	19.6
Full-term pregnancies (n)	1	3	3

\*Values are mean (range).

AVR: Aortic valve replacement; DVR: Double valve replacement; MVR: Mitral valve replacement.

### Follow up

The unreliable nature of the study population made follow up difficult and somewhat erratic. Follow up was closed in January 2005, and all patients seen between July 2004 and January 2005 were included for the purposes of statistical analysis of late results. Ultimately, follow up was 95% complete. Patients were examined at a number of local and rural clinics, or contacted by telephone or by letter. The importance of anticoagulation was stressed prior to discharge, and on every occasion that the patient was either examined or contacted.

### Anticoagulation

Before discharge, all patients were anticoagulated using warfarin, the target INR being 1.5-2.5. Patients who attended regularly at clinics and whose INR values fell within the target range were regarded as adequately anticoagulated. Among those who attended regularly, some had INR values of 1.0 while protesting that they were taking their medication, and clearly were not anticoagulated. Some patients attended occasionally, perhaps once or twice each year, and these patients were not anticoagulated. Many of the patients who were contacted by telephone did not attend clinics, and of those who did attend rural clinics the INR values were unknown. The anticoagulation status of the patients is detailed in Table III.

### Statistical analysis

Operative events were summarized as simple percentages, equal to the number of events divided by the number of patients. Valve-related events were defined according to the published guidelines for reporting mortality and morbidity after valve operations (4). Results were expressed as linearized rates, obtained by dividing the number of late events by the total patient years of follow up. Actuarial event free rates were computed using the Kaplan-Meier product limit method (5).

## Results

### Hospital mortality

Hospital mortality was 2.3%. None of the deaths was valve-related.

### Survival

Among 34 deaths which occurred during the follow up period, 12 were valve-related (Table IV) and seven non-valve-related. There were 15 sudden or unexplained deaths. Of the seven non-valve-related deaths, three were linked to AIDS, two patients died from pulmonary tuberculosis, and two following trauma. As sudden or unexplained deaths were considered to be

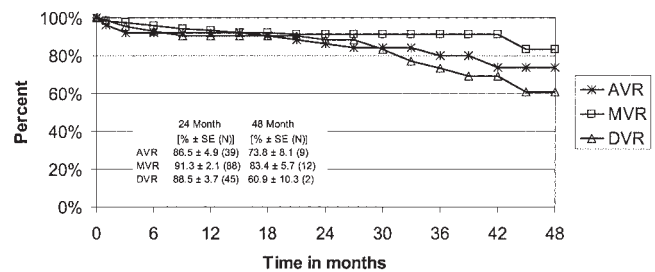


Figure 2: Actuarial prediction of survival at four years. AVR: Aortic valve replacement; DVR: Double valve replacement; MVR: Mitral valve replacement.

Table II: Etiology: indications for valve replacement (%).

Etiology	AVR	MVR	DVR
Rheumatic	32.7	64.0	68.5
Degenerative	28.8	6.2	7.6
Congenital	5.8	1.2	1.1
Endocarditis	8.6	7.0	16.3
Previous valve	8.6	18.6	12.0
Calcification	0.0	0.0	1.1
Other	8.6	2.5	3.3

AVR: Aortic valve replacement; DVR: Double valve replacement; MVR: Mitral valve replacement.

Table III: Anticoagulation status of patients.

Condition	No. of patients
Attended regularly, INR within target range 1.5-2.5	237 (56.4)
Attended irregularly with most INRs <1.5	60 (14.3)
Not anticoagulated or anticoagulation status unknown	123 (29.3)

Values in parentheses are percentages. INR: International normalized ratio.

Table IV: Causes of valve-related deaths.

Surgery	Endocarditis	CVA	Hemorrhage
MVR	1	2	0
AVR	2	1	0
DVR	5	0	1

AVR: Aortic valve replacement; CVA: Cerebrovascular accident; DVR: Double valve replacement; MVR: Mitral valve replacement.

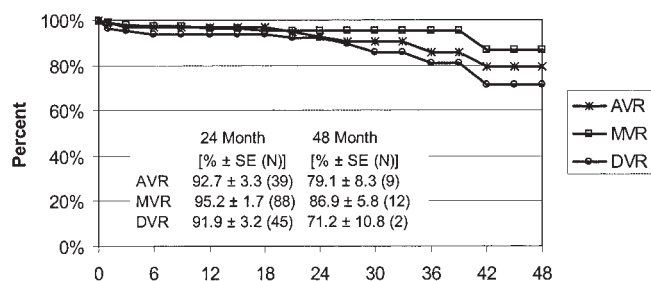


Figure 3: Actuarial prediction of freedom from valve-related mortality and sudden death at four years. Abbreviations as Figure 1.

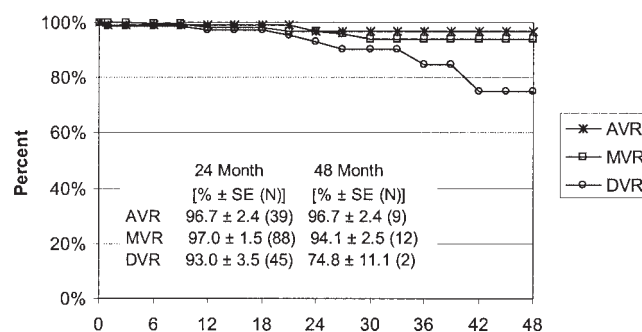


Figure 4: Actuarial prediction of freedom from thromboembolism at four years. Abbreviations as Figure 1.

valve-related, the total of such deaths was 27. Overall actuarial survival at four years (including hospital deaths) is shown in Figure 2, and Kaplan-Meier prediction of freedom from valve-related death at four years in Figure 3.

### Adverse events

#### Thromboembolism

There were 14 systemic embolic events, five of which were transient and patients made a full recovery. The linearized rates for thromboembolism are shown in Table V, and the actuarial prediction of freedom from thromboembolism at four years in Figure 4. Three cerebral emboli were fatal.

#### Thrombosis

A single occurrence of thrombosis was recorded in the mitral position. Actuarial freedom from thrombosis at four years is shown in Figure 5.

### Bleeding events

There were nine bleeding events, one of which was fatal. The actuarial prediction of freedom from bleeding at four years is shown in Figure 6.

### Endocarditis

Endocarditis was a common reason for valve surgery (see Table II), and was also the most common cause of valve-related death. Of eight patients who died from infective endocarditis, five died from ongoing disease. Actuarial freedom from endocarditis at four years is shown in Figure 7.

### Mechanical failure

Structural valve deterioration was not observed in any of the prostheses implanted. Two trivial periprosthetic leaks were recorded.

Table V: Adverse events: rates of early (%) and late (%/pt-yr) complications.

Event	AVR		MVR		DVR	
	Early	Late	Early	Late	Early	Late
TE						
Total	-	1.1 (2)	-	1.5 (6)	-	3.5 (6)
Transient	-	0.6 (1)	-	0.5 (2)	-	1.2 (2)
Permanent	-	0.6 (1)	-	0.5 (2)	-	1.7 (3)
Peripheral	-	-	-	0.5 (2)	-	0.6 (1)
Thrombosis	-	-	-	0.2 (1)	-	-
Bleeding event	-	0.6 (1)	-	1.0 (4)	-	2.3 (4)
Endocarditis	-	0.6 (1)	-	1.0 (4)	2.2 (2)	2.3 (4)
Paravalvular leak	-	0.6 (1)	-	0.2 (1)	-	-
Explant	-	-	-	0.5 (2)	-	-
Valve-related death	-	1.7 (3)	-	0.7 (3)	2.2 (2)	2.3 (4)
Sudden death	-	2.3 (4)	0.4 (1)	1.2 (5)	-	2.9 (5)
Total mortality	2.9 (3)	6.4 (11)	1.7 (4)	3.5 (14)	3.3 (3)	7.6 (13)

Values in parentheses are numbers of patients.

AVR: Aortic valve replacement; DVR: Double valve replacement; MVR: Mitral valve replacement; TE: Thromboembolism.

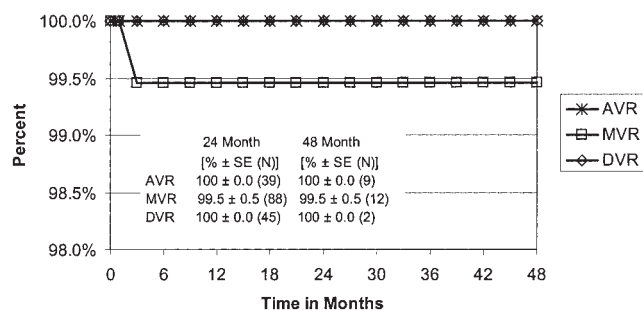


Figure 5: Actuarial freedom from thrombosis at four years. Abbreviations as Figure 1.

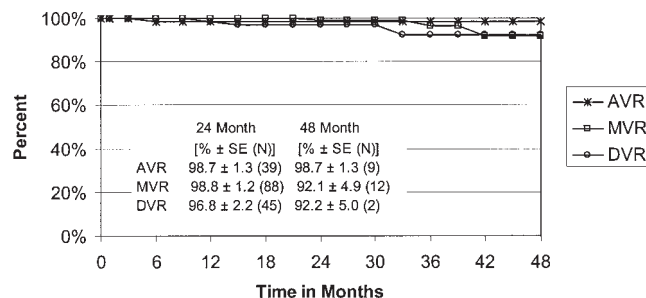


Figure 6: Actuarial freedom from bleeding events at four years. Abbreviations as Figure 1.

### Echocardiographic gradients

Echocardiographic data were collected from 32 aortic valve patients, and from 16 mitral valve patients. These data were collected at approximately one year after surgery. The average gradient in the mitral position was 2.3 mmHg, whilst that in the aortic position varied according to valve size as follows: 19 mm valve (peak 23 mmHg, mean 10.5 mmHg); 21 mm valve (peak 19 mmHg, mean 9.9 mmHg); 23 mm valve (peak 16 mmHg, mean 7 mmHg).

### Pregnancy

There were seven uncomplicated full-term pregnancies, and four of these patients were anticoagulated.

### NYHA functional class

Preoperative and postoperative NYHA functional class data are shown in Figures 8 and 9, respectively.

### Discussion

There is evidence that the incidence of valve thrombosis varies among different ethnic groups. The 25-year follow up of the St. Jude Medical (SJM) valve from the unit in the USA where the first SJM valve was implanted recorded a low incidence of valve thrombosis (6). In the SJM valve series reported by Stevens

from Cape Town, South Africa, the incidence of thrombotic complications was 12% per patient-year (pt-yr) (7). Deviri et al., in Johannesburg, noted a high incidence (1.96%/pt-yr) of valve thrombosis using the SJM valve (8).

The present authors reported an unacceptably high incidence of valve thrombosis using the CarboMedics valve (9), whilst a similar high incidence was recorded in an Indian patient population by Reddy et al. (10). In contrast, a low incidence of thrombotic complications in patients in whom the CarboMedics valve was used was recorded from Japan (11,12). In one of these reports, the level of anticoagulation was similar to that used previously (12), and there were no thrombosed valves.

Butchart et al., in reporting a 20-year experience in the UK with the Medtronic Hall valve, found a negligible incidence of valve thrombosis (13), whilst Antunes et al., reporting from Johannesburg, recorded a thrombosis rate of 1.2% per pt-yr in a population similar to the present group, with the Medtronic Hall

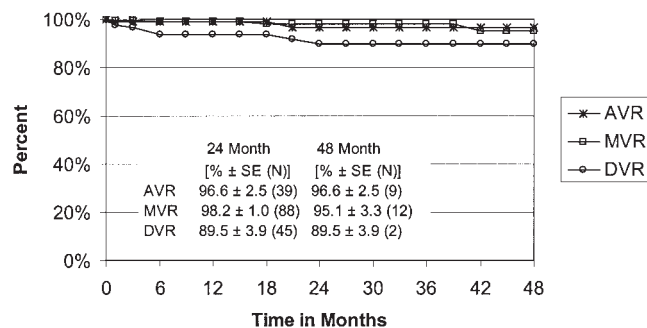


Figure 7: Actuarial freedom from endocarditis at four years. Abbreviations as Figure 1.

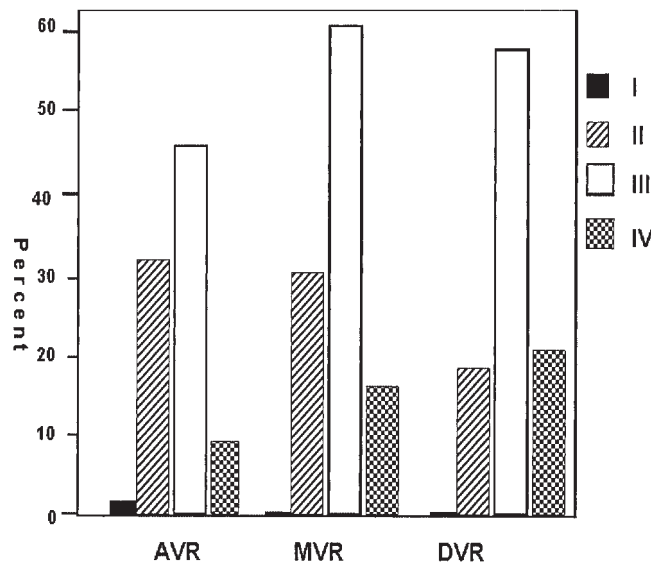


Figure 8: Preoperative NYHA classification.

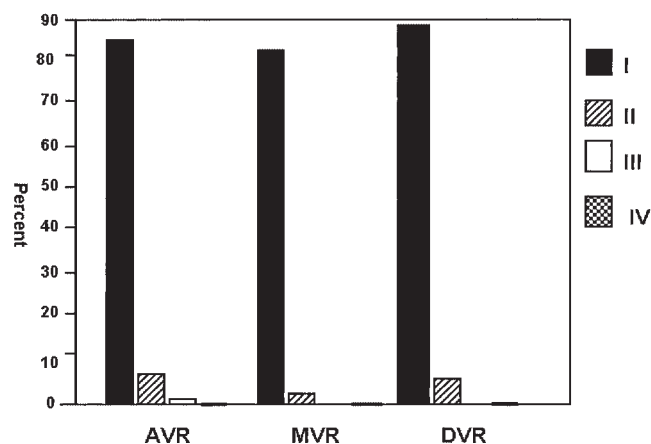


Figure 9: Postoperative NYHA classification.

valve (14). The latter patients were followed for five years, and since pannus ingrowth was not mentioned it was assumed that reference was being made to primary thrombosis. A linearized rate of 2.0% per pt-yr in the mitral position using the same device was reported (9). In that series, valve thrombosis was most often related to aggressive pannus ingrowth. The patients were followed for 10 years, and pannus obstruction was most common after five years. The interpretation of these data was that some population groups were more prone to valve thrombosis and pannus ingrowth than others. In this regard, the South African indigenous population appears to fall into a 'worst-case scenario'.

The present experience with the On-X valve has been rewarding, with only one episode of valve thrombosis recorded. This occurred in a patient who was adequately anticoagulated, though an excessive consumption of spinach during the previous week might have been a predisposing factor. In this patient the valve was removed and replaced with a second On-X valve, and the patient is currently alive and well. Pannus ingrowth has not been encountered in the present patient series. However, whilst it is possible that its absence is related to the tubular design of the leaflet housing, it must be remembered that pannus ingrowth is usually a late phenomenon that often occurs five or more years after valve implantation.

Infective endocarditis was a common reason for valve surgery, and particularly so in patients requiring double valve replacement. In most of these patients there were large and friable vegetations, with the infective process involving the anterior leaflet of the mitral valve. Ongoing infective endocarditis was the most common cause of systemic embolism and valve-related death. Five patients died from ongoing endocarditis, and three died later from endocarditis without

previous evidence of infection. Although it is customary to record infective endocarditis as a valve-related complication, its occurrence is usually patient- rather than prosthesis-related.

Seven full-term pregnancies were recorded among the present patient group, and in none of these patients was heparin used during the first trimester. It is possible that the danger of teratogenesis might have been exaggerated, and this view has been echoed by others (16,17). Although three of the seven patients who delivered normal full-term infants were not anticoagulated, it would be reckless to suggest that delivery would be safe without anticoagulation. Today, many South African female patients who require valve replacement are prepubescent or in their teenage years. In these patients, the tissue valves calcify early (18), and there is no alternative to valve replacement with a mechanical device. Although advising against pregnancy, cultural demands in this population are such that this advice is usually ignored. Oakley (19) pointed out that tissue valves were not free of thrombotic and thromboembolic occurrences in relation to pregnancy, and recommended that mechanical valves be used in young females, with oral anticoagulation being changed to systemic heparin during the last two weeks of pregnancy. In a previous report with the Medtronic Hall valve (15), nine normal births were recorded, while Sareli et al. (20) reported 49 pregnancies with no thromboembolic complications or maternal deaths in patients in whom either SJM or Medtronic Hall valves were implanted. Sareli concluded that, with new-generation valves, the maternal risk is low. It is the present authors' view that most currently used mechanical valves, including the On-X, can be used with relative safety in young women wishing to have children.

The present echocardiographic data demonstrated low gradients across both the mitral and aortic prostheses. These data were similar to those recorded by Moidl et al. in their analysis of data submitted for FDA approval of the On-X valve (3).

**In conclusion**, despite the 'unreliable' nature of the present population, the incidence of thrombosis and thromboembolism was similar to that obtained with other devices in developed countries. These results suggest that the On-X valve may well be the valve of choice in communities where anticoagulation regimes are uncertain. Furthermore, these data suggest that in a well-controlled population, anticoagulation at a lower level than that usually recommended would adequately mitigate thrombosis and thromboembolism, with a low incidence of anticoagulant hemorrhage. These data also confirm the excellent hemodynamics of the On-X valve, and suggest that

where there is no alternative to replacement with a mechanical device - and provided that the recommended guidelines for anticoagulation are followed - the On-X valve may be used with relative safety in women of child-bearing age.

#### References

1. Starr A, Edwards ML. Mitral replacement: Clinical experience with ball valve prosthesis. *Ann Surg* 1961;154:726-740
2. Starr A, Herr RH, Wood JA. Mitral replacement: Review of 6 years' experience. *J Thorac Cardiovasc Surg* 1967;54:333-358
3. Moidl R, Simon P, Wolner E, and Members of the On-X Prosthesis Heart Valve Trial. The On-X prosthetic heart valve at five years. *Ann Thorac Surg* 2002;74:S1312-S1317
4. Edmunds LH, Clark RE, Cohn LH, et al. Guidelines for reporting morbidity and mortality after cardiac valvular operations. *Ann Thorac Surg* 1988;46:257-259
5. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J Am Statist Assoc* 1958;53:457-481
6. Emery RW, Krogh CC, Arom KV, et al. The St. Jude Medical cardiac valve prosthesis: A 25-year experience with single valve replacement. *Ann Thorac Surg* 2005;79:776-783
7. Stevens JE. The Cape Town experience with the St. Jude prosthetic valve. Abstract, XIIIth Southern Africa Cardiac Congress, 6th-8th September 1982
8. Deviri E, Sareli P, Wisenbaugh T, Cronje SL. Obstruction of mechanical heart valve prostheses: Clinical aspects and surgical management. *J Am Coll Cardiol* 1991;17:646-650
9. Williams MA, Crause L, Van Riet S. A comparison of mechanical valve performance in a poorly anticoagulated community. *J Card Surg* 2004;19:410-414
10. Reddy N, Padmanabhan T, Singh S, et al. Thrombolysis in left-sided prosthetic valve occlusion: Immediate and follow up results. *Ann Thorac Surg* 1994;58:462-471
11. Tominaga R, Kurisu K, Ochiai Y, et al. A 10-year experience with the CarboMedics cardiac prosthesis. *Ann Thorac Surg* 2005;79:784-789
12. Soga Y, Okabayashi H, Nishina T, et al. Up to 8-year follow-up of valve replacement with CarboMedics valve. *Ann Thorac Surg* 2002;73:474-479
13. 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
14. Antunes MJ, Wessels A, Sadowski RG, et al. Medtronic Hall valve replacement in a Third World population group. *J Thorac Cardiovasc Surg* 1988;95:980-993
15. Williams MA. Anticoagulation in developing countries. In: Butchart EG, Bodnar E (ed.). *Current Issues in Heart Valve Disease: Thrombosis, Embolism and Bleeding*. 1st edition. ICR Publishers, London, 1992:362-368
16. Geelani MA, Singh S, Verma A, Nagesh A, Betigeri V, Nigam M. Anticoagulation in patients with mechanical valves during pregnancy. *Asian Cardiovasc Thorac Ann* 2005;13:30-33
17. Al-Lawati AA, Venkitraman M, Al'Delmaine T, Valliathu J. Pregnancy and mechanical valves replacement; dilemma of anticoagulation. *Eur J Cardiothorac Surg* 2002;22:223-227
18. Williams MA. Tissue valves in young patients: A recipe for disaster. *J Card Surg* 1991;6(4 Suppl.):620-623
19. Oakley CM. Anticoagulation during pregnancy. In: Butchart EG, Bodnar E (ed.). *Current Issues in Heart Valve Disease: Thrombosis, Embolism and Bleeding*. 1st edition. ICR Publishers, London, 1992:339-345
20. Sareli P, England MJ, Berk MR, et al. Maternal and fetal sequelae of anticoagulation during pregnancy in patients with mechanical valve prostheses. *J Am Coll Cardiol* 1989;63:1462-1466