The On-X® Experience

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From the Editor

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This issue of "The On-X® Experience" provides an update of clinical implantations of the On-X Valve, a report on the regulatory status, a comparison of linearized complication rates, a listing of recent publications and presentations and ancillary studies on the On-X Valve and On-X Carbon.

On-X Valve Update

The first clinical implant of an On-X® Prosthetic Heart Valve occurred on September 12, 1996. Since that time, approximately 3500 On-X valves have been implanted worldwide. Total valve implant experience now exceeds 3300 patient years.

The number of implanting centers continues to grow and is now more than 200 centers. The On-X valve has now been implanted in 33 countries. Recently, centers in Belgium, Slovakia, Croatia, Iraq and Iran have begun implanting the On-X valve. Implants in the US clinical centers continue under the IDE granted by the US FDA in December 1998.

Regulatory Status

The CE mark was obtained for the On-X valve from the TÜV in Munich on July 24, 1998. Regulatory approval to allow implantation of the On-X valve has been obtained in other countries as required. Applications are pending in Japan, Canada and the United States.

MCRI's interaction with the US FDA continues to proceed favorably. On Sept. 16, 1999, the FDA accepted the first module of MCRI's modular Pre-Market Approval (PMA) Application. The final module was submitted August 30, 2000. The FDA staff will require some time to complete the application review. Clinical study data submitted to the FDA are summarized as follows.

Two Year Follow-Up Data

Patient population and surgery

From September 1996 to May 2000, 301 patients had isolated valve replacement at 11 European centers under a standardized protocol. Isolated aortic valve replacement (AVR) occurred in 184 (61%) patients and isolated mitral valve replacement (MVR) in 117 (39%). There were 21 double valve implants to give a total population of 322 patients.

In AVR, 66% of patients were male, while in MVR 46% were male. The mean age at implant was 60.2 ± 8.4 years in AVR (range 20-80) and 60.0 ± 10.2 years in MVR (range 21-76).

Preoperatively, approximately half of the AVR patients were in NYHA Class II, while 62% of the MVR patients were in Class III indicating that the mitral population was more severely ill to start. Additionally, only 2.2% of AVR patients had previous cardiac surgery, while 17.1% of MVR patients had previous cardiac surgery.

The most common disease etiology was calcific degeneration in AVR (50.0%) and rheumatic heart disease in MVR (38.5%). Other common etiologies were degenerative: 27.7% AVR and 27.4% MVR and endocarditis: 4.4% AVR and 11.1% MVR. The valve lesion leading to replacement was 46.7% stenosis, 21.2% regurgitation and 32.1% mixed in AVR and 17.1% stenosis, 51.3% regurgitation and 31.6% mixed in MVR. Typical of these populations, 87.5% of AVR patients were in sinus rhythm at surgery, while 53.9% of MVR patients were in atrial fibrillation. In both AVR

and MVR, all demographic variables examined indicated a usual adult mechanical valve replacement population.

Follow-up and data analysis

Follow-up in the study was obtained entirely through office visits. In accordance with the protocol, patients were maintained on anticoagulant therapy with a target therapeutic international normalized ratio (INR) range of 2.5 to 3.5 for AVR. For MVR, the INR target range was 3.0 to 4.5. The target range of anticoagulant therapy was maintained unless a contraindication to such therapy arose. A review of the INR measurements showed a median INR of 2.49 AVR. Mitral INR measurements showed a median INR of 2.68. For both the aortic and mitral measurements one-third were below 2.0. Thus, the On-X valve is already performing well in a population with low-end anticoagulant levels without apparent increase in TE or thrombosis rates.

Total follow-up in the study was 405.6 patient years (pt-yrs) AVR and 219.5 pt-yrs MVR. The average follow-up for all patients was about 24 months, 48 patients have been followed 3 years.

Morbid events were identified and classified in accordance with the AATS/STS guidelines for cardiac valve operations. Linearized rates for morbid events were calculated as percent per patient-year of follow-up (or number per 100 years of follow-up). Morbid event rates were compared to rates from the literature for other mechanical valves over comparable follow-up periods.

Results

Morbid events related to thrombosis and bleeding for isolated replacements are summarized in Table 1. The On-X valve has lower rates of thrombosis, thromboembolism and hemorrhage compared to literature reports on other mechanical valves.

Medical outcome

Outcome of valve replacement was determined by examining the preoperative and postoperative NYHA classification of each patient. Cross-tabulation at the 2 year interval shows that 75.8% of AVR patients and 70.6% of MVR patients improved one or more classes, 21.2% of AVR patients and 17.6% of MVR patients stayed the same and 3% AVR and 3.9% MVR showed a higher classification.

Quality of Life

Quality of life surveys demonstrated that both AVR and MVR patients with preoperative serious complicated disease states were restored to a minor, uncomplicated chronic disease state, especially with regard to physical function.

On-X Valve, Bioprosthetic Stented and Stentless Valve Hemodynamics

The purported superior hemodynamics of some stented and stentless bioprosthetic valves has been used to rationalize implantation of these valves rather than mechanical valves. However, a detailed comparison of hemodynamic results for bioprosthetic valves (from the literature) to those of the On-X valve strongly suggests that this prima facia assumption of superior bioprosthetic hemodynamics is not true. In fact, the hemodynamic performance of the On-X valve was superior, particularly in the small aortic root sizes. Comparison results are given in Tables 2 through 4. Hemodynamic study citations used in this comparison were all performed in resting patients using the full Bernoulli equation form and the velocity-time integral form of the continuity equation.

Recent On-X Publications/Presentations

Performance of the On-X® Valve in the Small Aortic Root: A Multicenter Trial

A. Haverich, and the Multicenter Investigators
Medizinische Hochschule Hannover, Hannover, Germany

Presented to the Asian Society for Cardiovascular Surgery, Fukuoka, Japan, September 6 – 8, 2000

A clinical trial of the performance of the On-X® Prosthetic Heart Valve, particularly in the small aortic root, was conducted at 11 centers in Europe. From September 1996 to January 2000, 184 aortic valves were implanted, including 17 19mm and 35 21mm valves. All patients were followed with a mean of 11 months. Hemodynamic values were measured at discharge and 1 year, and blood studies were done at each visit. Clinical outcome was evaluated by NYHA classification. Mean pressure gradient for the valve at dis-

charge was 12.6 ± 4.7 and 9.0 ± 5.3 mmHg for 19 and 21mm valves, while their effective orifice areas were 1.5 ± 0.2 and 1.8 ± 0.4 cm^2. Blood damage was low with LDH levels of 214 ± 46 - 196 ± 33 for size 19 and 212 ± 33 - 215 ± 33 for size 21 at 3-6 months and 1 year (upper normal = 250). NYHA improvement occurred in 75% of patients. The early performance of the On-X valve in the small aortic root is exceptional.

A Comparison of the Initial European and North American Experience With the On-X® Valve

A. Laczkovics, and the Multicenter Investigators
Klinikum Bergmannsheil, Ruhr University-Bochum, Bochum, Germany

Presented to The International Society of Cardiothoracic Surgeons, Vancouver, August 13-16, 2000

A multicenter clinical investigation of the On-X® Prosthetic Heart Valve was conducted in Europe (EU) and an identical trial was started in North America (NA). Through December 1999, in the EU trial 301 patients received isolated valve implants at 11 centers and 61 isolated valve patients were entered in the NA trial at 9 centers. Follow-up averages about 2 years in EU and 1 year in NA. Demographically, the patients are sim-ilar: mean age 60.2 EU and 57.1 NA; 56% male EU and 50% male NA; primary etiology calcific degeneration for aortic valves and rheumatic or degenerative for mitral valves in both studies; valve lesion and preoperative New York Heart Association classification were also not different between studies. Follow-up is limited in the NA study, so comparison of adverse event rates is not feasible, but the rates are low in each study, for example, in the EU thromboembolism 2.2%/ptyr, paravalvular leak 0.7, and endocarditis 1.4. The principle early comparisons between the studies come from postoperative echocardiographic hemodynamics and blood studies for hemolysis. Aortic effective orifice area in EU ranged from 1.5 to 2.7 cm^2 for 19 to 25 mm valves, and the results are similar in NA at 1.4 to 3.4 cm^2. Postoperative lactate dehydogenase at 3-6 months was 225 aortic and 268 mitral EU, and 212 aortic and 272 mitral NA (upper normal 250 I.U.). These two studies show similar patient populations, have excellent agreement in results and demonstrate the satisfactory early performance of the valve.

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Comparison of the Classical and Modified Forms of the Continuity Equation in the Aortic Position

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In Vitro Hydrodynamics of Four Bileaflet Valves In Mitral Position

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Unalloyed Pyrolytic Carbon for Implanted Mechanical Heart valves

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Assessment of Perceived Mechanical Heart Valve Sound Level in Patients

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Table I
Linearized Rate (% / pt.yr.) Comparison

Morbid Event	**On-X:** Aortic	Mitral	**SJM:** Aortic	Mitral	**CMI:** Aortic	Mitral	**Med-Hall:** Aortic	Mitral
Thromboembolism	1.73	1.82	1.71	1.86	1.11	2.05	1.50	2.00
Thrombosis	0.00	0.00	0.19	0.14	0.03	0.47	0.20	0.40
Hemorrhage	0.74	0.00	2.00	1.34	1.82	1.92	0.80	1.90
TOTALS	2.47	1.82	3.90	3.34	2.96	4.44	2.50	4.30

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Hemodynamic Comparison of Stented Pericardial, Stentless Porcine and On-X Valves

Table II
Valve Effective Orifice Area (cm^2)

Size	Mitroflow	Perimount	Toronto	Freestyle	On-X
19.0	1.14 ± 0.16	0.90 ± 0.13		1.26 ± 0.27	1.5 ± 0.3
19.0		1.1 ± 0.23			
21.0				1.52 ± 0.54	1.9 ± 0.5
22.0			1.3 ± 0.7		
23.0			1.5 ± 0.5	1.77 ± 0.59	2.47 ± 0.67
25.0			1.7 ± 0.4	2.08 ± 0.62	2.7 ± 0.7
27.0			2.0 ± 0.4	2.54 ± 0.74	2.9 ± 0.7
29.0			2.4 ± 0.6		2.9 ± 0.7

Table III
Mean Gradient (mmHg)

Size	Mitroflow	Perimount	Toronto	Freestyle	On-X
19.0	14.9 ± 3.5	19.1 ± 4.9		12.1 ± 4.9	8.9 ± 3.1
19.0		18.0 ± 6.9			
21.0				9.6 ± 7.3	7.6 ± 2.96
22.0			7.3 ± 4.4		
23.0			7.4 ± 4.5	8.7 ± 7.8	6.6 ± 3.1
25.0			6.1 ± 3.1	5.9 ± 4.4	4.3 ± 2.4
27.0			4.9 ± 2.4	4.2 ± 3.0	5.6 ± 3.1
29.0			4.0 ± 2.1		5.6 ± 3.1

Table IV
Peak Gradient (mmHg)

Size	Mitroflow	Perimount	Toronto	Freestyle	On-X
19.0	20.3 ± 5.8	25.4 ± 6.4			17.1 ± 5.3
19.0		31.0 ± 11.2			
21.0					14.2 ± 5.4
22.0			18.4 ± 11.8		
23.0			15.1 ± 8.8		12.4 ± 6.2
25.0			11.6 ± 6.6		8.9 ± 4.6
27.0			9.6 ± 5.0		9.8 ± 5.3
29.0			7.2 ± 4.1		9.8 ± 5.3

** All data late post operation.*

Hemodynamic Comparison Data Sources:

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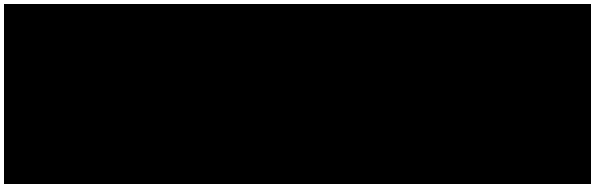
Your comments, questions and ideas regarding "The On-X® Experience" should be directed to Robert More (512) 339-8000 or rmore@mcritx.com.



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