Clinical event rates with the On-X bileaflet mechanical heart valve: A multicenter experience with follow-up to 12 years

John B. Chambers, MD, FRCP, FACC,[a] Jose L. Pomar, MD, PhD, FETCS,[b] Carlos A. Mestres, MD, PhD, FETCS,[b] and George M. Palatianos, MD, FACS, FACC, FETCS[c]

Objective: The aim of the study was to establish clinical event rates for the On-X bileaflet mechanical heart valve (On-X Life Technologies Inc, Austin, Tex) using an audit of data from the 3 centers within Europe with the longest history of implanting.

Methods: All patients receiving the On-X valve between March 1, 1998, and June 30, 2009, at 3 European centers were studied. Data were collected using questionnaire and telephone surveys augmented by outpatient visits and examination of clinical records.

Results: There were 691 patients, with a mean age of 60.3 years, who received 761 valves in total: 407 mitral valve replacements, 214 aortic valve replacements, and 70 aortic + mitral valve replacements (dual valve replacement). Total follow-up was 3595 patient-years, with a mean of 5.2 years (range, 0–12.6 years). Early (≤30 days) mortality was 5.4% (mitral valve replacement), 0.9% (aortic valve replacement), and 4.3% (dual valve replacement). Linearized late (>30 days) mortality expressed per patient-year was 3.6% (mitral valve replacement), 2.2% (aortic valve replacement), and 4.1% (dual valve replacement), of which valve-related mortality was 0.5% (mitral valve replacement), 0.2% (aortic valve replacement), and 1.8% (dual valve replacement). Late linearized thromboembolism rates were 1.0% (mitral valve replacement), 0.6% (aortic valve replacement), 1.8% (dual valve replacement). Bleeding rates were 1.0% (mitral valve replacement), 0.4% (aortic valve replacement), and 0.9% (dual valve replacement). Thrombosis rates were 0.1% (mitral valve replacement), 0% (aortic valve replacement), and 0.3% (dual valve replacement). Reoperation rates were 0.6% (mitral valve replacement), 0.2% (aortic valve replacement), and 1.2% (dual valve replacement).

Conclusions: The On-X valve has low adverse clinical event rates in longer-term follow-up (mean 5.2 years and maximum 12.6 years). (J Thorac Cardiovasc Surg 2013;145:420-4)

The On-X bileaflet mechanical valve (On-X Life Technologies Inc, Austin, Tex) uses pure pyrolytic carbon and has a flared inlet designed to reduce inlet turbulence and an elongated orifice to organize flow and reduce exit losses. The valve has relatively thin leaflets that can align with flow to reduce obstruction. In the aortic position, valves 25 mm and smaller in size are implanted with the sewing cuff supra-annularly and the housing inside the annulus. The valve was first implanted in September 1996 and became commercially available in Europe in 1998. It is known to have good short- and mid-term hemodynamic function[1-3] and clinical results.[4-7] However, there is little longer-term information.

The aim of the study was to establish adverse clinical event rates for the On-X valve using an audit of data from 3 of the earliest implanting centers within Europe.

MATERIALS AND METHODS

Patients

The audit was conducted in 2010 for consecutive patients receiving On-X valve implantation between March 1, 1998, and June 30, 2009, at 3 centers: Hospital Clinico, University of Barcelona, Spain; Onassis Cardiac Surgery Center in Athens, Greece; and Guy's and St Thomas' Hospital Trust in London, United Kingdom. Included were patients with supplementary procedures, including coronary bypass grafting and mitral repair. Excluded were patients implanted with a second valve other than an On-X and those, because of small numbers, who received tricuspid valves alone or together with other valves. The On-X valve was used interchangeably with other designs, predominantly those from St Jude Medical Inc (St Paul, Minn) and Carbomedics (Sorin Spa, Milano, Italy), with no formal inclusion or exclusion criteria. Approval from the relevant local boards was obtained where required.

Management

Cardioplegic arrest and moderate cooling were used in all cases. The technique of implantation differed between the sites: inverting sutures and pledgets (Barcelona and Athens), and inverting sutures and no pledgets for the aortic position and everting for the mitral position (London). Target international normalized ratio (INR) was 2 to 3 in aortic valve replacement (AVR) and 2.5 to 3.5 in mitral valve replacement (MVR) including dual valve replacement (DVR). Patients with coexistent coronary bypass

From the Guy's and St Thomas Hospitals,[a] London, England; Hospital Clínico,[b] University of Barcelona, Spain; and Onassis Cardiac Surgery Center,[c] Athens, Greece.

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Address for reprints: John B. Chambers, MD, FRCP, FACC, Cardiothoracic Centre, St Thomas' Hospital, London SE1 7EH, England (E-mail: john.chambers@gstt.nhs.uk).

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Abbreviations and Acronyms

AVR = aortic valve replacement
DVR = dual valve replacement
INR = international normalized ratio
MVR = mitral valve replacement
NYHA = New York Heart Association
TIA = transient ischemic attack

grafting received an antiplatelet agent, usually aspirin 75-100 mg. Most patients were monitored in a clinic, and few performed home INR control. Follow-up was according to local practice at the implanting center, referring hospital, or family physician. All centers followed a common protocol using questionnaire and telephone follow-up. Preoperative and operative data were gathered from hospital records, and follow-up was augmented with clinical records to confirm adverse events and cause of death. Adverse events were defined by the Society of Thoracic Surgeons/American Association for Thoracic Surgery/European Association for Cardiothoracic Surgery definitions,[8] and other cardiovascular complications not listed in the definitions were recorded.

Statistics

Early complication rates at 30 days or less were calculated as percentages. Late rates were expressed as linearized rates per patient-year after 30 days. Descriptive statistics were computed using Microsoft Excel 2007 (Microsoft Corp, Redmond, Wash), and comparisons and life tables were calculated using MedCalc for Windows (Mariakerke, Belgium).

RESULTS

Patients

A total of 722 patients (16%) with On-X valves were identified from the total of 4556 mechanical valves implanted between 1998 and 2009. There were 8 tricuspid valve replacements with or without another valve and 23 patients with double valves, including one of a differing design that was therefore excluded from the analysis. There remained 691 patients, of whom 407 received MVR alone, 214 received AVR alone, and 70 received DVR, resulting in 761 valves in total. The most frequent valve sizes were aortic size 23 mm and mitral size 27/29 mm.

Patient information at implantation is shown in Table 1. AVR was predominantly for dominant stenosis (44%), and MVR was predominantly for insufficiency (67%). As expected, atrial fibrillation occurred more often in MVR and DVR than AVR ($P < .0001$). Patients receiving AVR had significantly lower New York Heart Association (NYHA) classifications than those receiving MVR or DVR ($P < .001$). Patients were in NYHA class III or IV preoperatively before AVR (42%), MVR (78%), and DVR (77%). The cause of the aortic disease was calcific degenerative (43%), congenital (43%), rheumatic (5%), endocarditis (5%), redo-prosthetic valve (2%), and calcific of uncertain cause (2%). The cause of the mitral disease was degenerative (39%), rheumatic (40%), redo-prosthetic (10%), endocarditis (8%), calcified annulus (2%), and congenital (1%).

TABLE 1. Patient data at implantation with mean (standard deviation) for age and number (percentage) for other measures

	AVR n = 214	MVR n = 407	DVR n = 70
Age mean (SD), y	59.7 (9.6)	60.6 (13.1)	60.2 (13.7)
Gender (M:F)	158:56	203:204	42:28
Preoperative lesion N (%)			
Stenosis	126 (44)	94 (21)	
Regurgitation	91 (32)	299 (67)	
Mixed	61 (22)	70 (16)	
NYHA N (%)			
I	39 (18)	12 (3)	4 (6)
II	79 (37)	66 (16)	9 (13)
III	71 (33)	203 (50)	38 (54)
IV	18 (8)	116 (29)	16 (23)
Previous surgery N (%)	21 (10)	116 (28)	18 (26)
Concomitant procedures N (%)	64 (30)	130 (32)	11 (16)
Rhythm N (%)			
Sinus	178 (83)	184 (45)	28 (40)
Atrial fibrillation	24 (11)	198 (49)	38 (54)
Paced	11 (5)	25 (6)	3 (4)

SD, Standard deviation.

Clinical Event Rates

Operative (≤30 days) mortality was 5.4% for MVR, 0.9% for AVR, and 4.3% for DVR (Table 2). Linearized late mortality (>30 days) was 3.6%/patient-year for MVR, 2.2%/patient-year for AVR, and 4.1%/patient-year for DVR. Figure 1 shows overall survival. Valve-related mortality was 0.5%/patient-year for MVR, 0.2%/patient-year for AVR, and 1.8%/patient-year for DVR. Survival free of valve-related mortality is shown in Figure 2. Overall survival, both early and late and survival free of valve-related mortality, was better for AVR than MVR or DVR. When patients with and without coronary bypass grafting were compared, there were no significant differences in mortality for AVR ($P = .095$), MVR ($P = .236$), or DVR ($P = .907$) groups.

There was a follow-up of 3595 patient-years. One patient was lost to follow-up after leaving the hospital 2 weeks after surgery. Overall, 53 patients (7.6%) were lost to follow-up. The range in follow-up, excluding early mortality, was 0 to 12.6 years with a mean of 5.2 years and median of 5.5 years.

Clinical event rates are shown in Table 2. There were 20 reoperations that were for paravalvar regurgitation in 14 patients, endocarditis in 3 patients, and thrombosis in 2 patients. One patient had a tight subaortic ring of fibrous tissue associated with extensive subendocardial fibrosis not seen at the time of original mitral valve implantation. There were no differences among AVR, MVR, and DVR in rates of sudden death, thromboembolism (Figure 3),

TABLE 2. Adverse events

Type	Rates					
	Aortic		Mitral		Double	
	Early N (%)	Late N (%/patient-y)	Early N (%)	Late N (%/patient-y)	Early N (%)	Late N (%/patient-y)
Death						
Sudden	0	5 (0.4)	0	4 (0.2)	0	2 (0.6)
Cardiac	2 (0.9)	4 (0.3)	14 (3.4)	30 (1.6)	3 (4.3)	3 (0.9)
Noncardiac	0	19 (1.4)	8 (1.9)	24 (1.3)	0	3 (0.9)
Valve related	0	2 (0.2)	0	10 (0.5)	0	6 (1.8)
Total	2 (0.9)	30 (2.2)	22 (5.4)	68 (3.6)	3 (4.3)	14 (4.1)
Stroke	1 (0.5)	7 (0.5)	0	4 (0.2)	0	3 (0.9)
TIA	3 (1.4)	1 (0.1)	0	12 (0.6)	0	1 (0.3)
Peripheral	0	0	0	1 (0.1)	0	1 (0.3)
Thrombosis	0	0	0	2 (0.1)	0	1 (0.3)
Total TE	4 (1.9)	8 (0.6)	0	19 (1.0)	0	6 (1.8)
Major bleed	2 (0.9)	5 (0.4)	1 (0.2)	19 (1.0)	0	3 (0.9)
Endocarditis	1 (0.5)	3 (0.2)	0	5 (0.3)	0	3 (0.9)
PVL	0	4 (0.3)	1 (0.2)	12 (0.6)	0	4 (1.2)
Nonstructural other than PVL	0	0	0	1 (0.1)*	0	0
Reoperation	1 (0.5)	2 (0.2)	1 (0.2)	12 (0.6)	0	4 (1.2)
Arrhythmia	2 (0.9)	5 (0.4)	5 (1.2)	6 (0.3)	0	0
CHF	0	2 (0.2)	0	2 (0.1)	0	1 (0.3)
MI	0	0	2 (0.5)	0	0	0

TE, Thromboembolism; *PVL,* paravalvular leak; *CHF,* congestive heart failure; *MI,* myocardial infarction. *Subaortic ring of fibrous tissue.

thrombosis, bleeding (Figure 4), endocarditis, paravalvar leak (Figure 5), or reoperation (Figure 6). AVR had greater freedom from bleeding events and reoperation than MVR and DVR, whereas all other life tables had no significant differences. There were no differences in event rates between sites.

DISCUSSION

This is the largest clinical report for the On-X valve in terms of patient-years, with 691 patients followed for a median 5.5 years and up to 12.6 years. Previous studies of the On-X valve have had a mean follow-up duration of 1.8 to 5 years.[7,9] Another study with a slightly larger population size[10] had a mean follow-up of only 2.8 years. We found low early event rates and linearized mid- and long-term event rates comparing favorably with other valve types.[11,12]

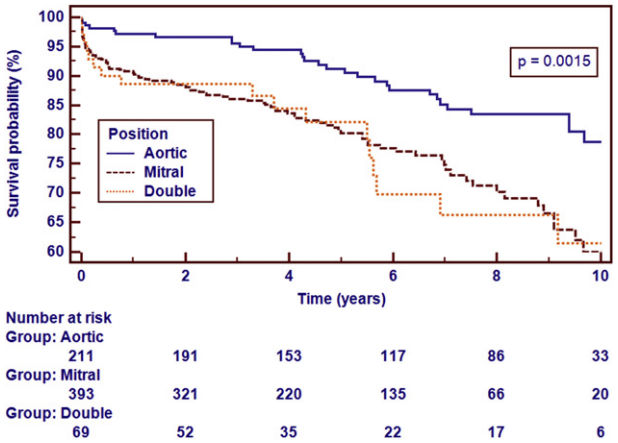

FIGURE 1. Freedom from all-cause mortality.

Transient ischemic attack (TIA) and thrombosis rates were low. Valve thrombosis was not reported in AVR in this or other series of On-X valves.[3-6,10] This compares favorably with other types of bileaflet valves in which rates of 0% to 0.5% are reported.[11] Thrombosis of the mitral position was not observed in some series.[4,5] Others report a small number associated with subtherapeutic or, usually, discontinued anticoagulation: 3 in our series, 3 in the study by Tossios and colleagues,[6] and 1 in the study by Chan and colleagues.[10] The rate of total thromboembolism including stroke, TIA, peripheral embolism, and valve thrombosis was low, with a linearized rate of 0.6% in the aortic position, 1% in the mitral position, and 1.8% for double valves. This compares with the reported thromboembolism rate alone for other valves of 0.3% to 5% in the aortic position and 1.3% to 5% in the mitral position.[10,11,12-18] However, comparison with different valve designs is difficult because of population variation in the non-prosthetic thrombotic risk factors, INR regimens, care with which follow-up is made, and method of reporting. Background rates of TIA of 1.3% in patients aged 64 to 74 years are reported,[19] which is similar to the rates in this study and therefore consistent with a degree of underreporting related to the retrospective nature of our study. However, the On-X valve may genuinely be of low

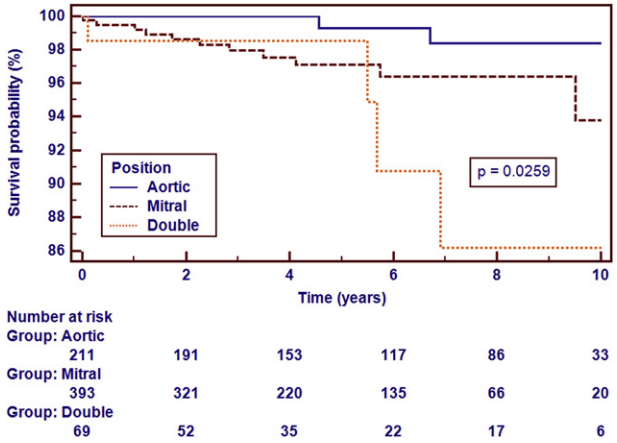

FIGURE 2. Freedom from valve-related mortality.

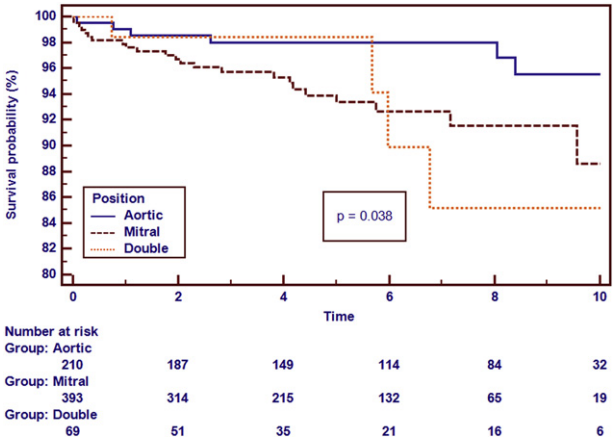

FIGURE 4. Freedom from bleeding events.

thrombogenicity, particularly in the aortic position possibly as a result of its carbon technology[20] and the design features affecting transvalve flow patterns. Reported thromboembolism is uncommon even in a population in whom 40% have no or inadequate anticoagulation.[9] Trials are in progress to investigate the safety of low anticoagulation rates in the On-X valve (PROACT; US registration NCT00291525).

No structural failures were found, and none have been reported by other studies.[3-6,10,11] This is similar to other types of bileaflet mechanical valve other than the St Jude Medical valve, the discontinued Hemex-Duromedics valve (originally Hemex Scientific Inc, Austin, Tex), and the Tekna-Edwards valve (originally Baxter Healthcare Corp, Santa Ana, Calif), for which a small number of leaflet escapes have been reported.[11-13] The endocarditis rate was low, confirming previous reports.[4,6] The incidence of reported paraprosthetic regurgitation increased with time in all positions but mainly in MVR and DVR after 2 years. This is surprising. It is possible that washing jets were misinterpreted, and there was no core laboratory to adjudicate on reports. However, most of the reoperations were for valve dehiscence or endocarditis, and the survival curves for paraprosthetic regurgitation (Figure 5) and reoperation (Figure 6) match relatively well. It is therefore likely that the regurgitation was present immediately after surgery, but that it was only detected when the patient became unwell probably after a prolonged examination including transesophageal echocardiography. The alternative explanation that the regurgitation developed as a result of cumulative stitch dehiscence is far less likely and was not shown in other series.[7] One patient required reoperation after MVR for a previously undescribed complication. There was a tight subaortic ring of fibrous tissue associated with extensive subendocardial fibrosis not seen at the time of the original mitral valve implantation. The surgeon noted that the housing of the mitral prosthesis was prominent and speculated that it had abraded the outflow tract to cause fibrosis.

The proportion of patients undergoing surgery who were in NHYA class III or IV was 42% for AVR but more than

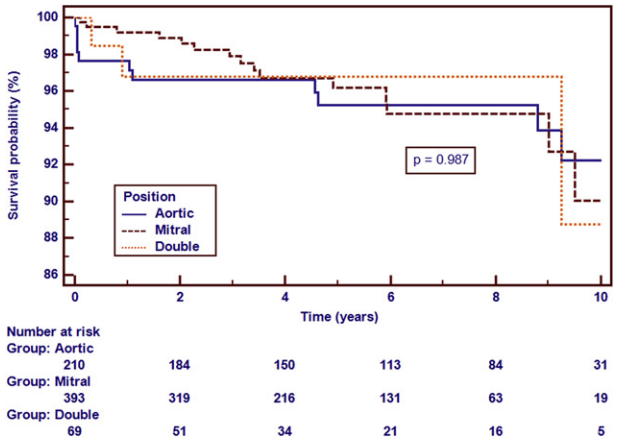

FIGURE 3. Freedom from thromboembolism.

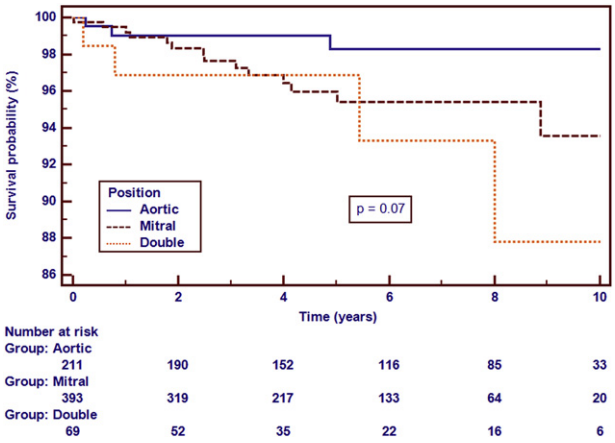

FIGURE 5. Freedom from paravalvar leaks.

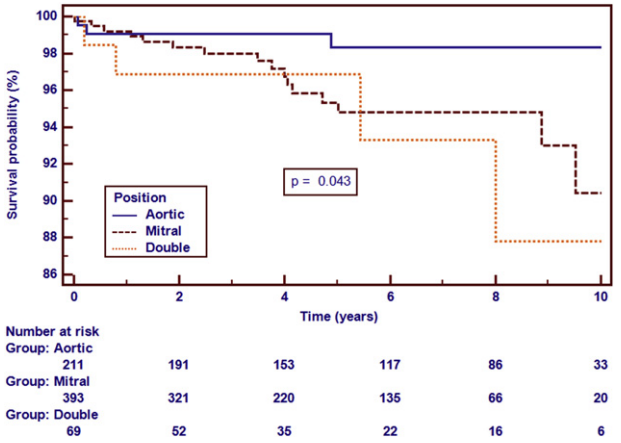

FIGURE 6. Freedom from reoperation.

70% for MVR and DVR. This is slightly better for aortic valves but slightly worse for mitral valves than in the Euro-Heart survey,[21] in which the proportions were 47% for aortic stenosis, 58% for mitral regurgitation, and 63% for mitral stenosis.

Limitations

This was a retrospective audit, so the rates of minor clinical events including minor thromboembolism and bleeds are probably underreported. However, serious events such as reoperation, valve thrombosis, or endocarditis would unlikely have been missed. There was no systematic echocardiography with core laboratory assessment of possible paraprosthetic regurgitation, so the rates of paraprosthetic regurgitation may be incorrect. Furthermore, 7.6% of patients were lost to follow-up, reflecting the mobility of our populations, and this may have introduced inaccuracies.

CONCLUSIONS

The On-X valve has low adverse clinical event rates in longer-term follow-up (mean 5.2 years and maximum 12.6 years).

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