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ORIGINAL ARTICLE

Long-Term Clinical Outcomes of the On-X Mechanical Prosthetic Valve in the Aortic or Mitral Position

— A Single-Center Experience of up to 20 Years' Follow up —

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Background: This study evaluated the long-term outcomes for up to 20 years after On-X mechanical valve implantation in the left side of the heart.

Methods and Results: Between 1999 and 2015, 861 patients (mean age=51.6±10.9 years) who underwent prosthetic valve replacement using the On-X valve in the aortic or mitral position were enrolled (aortic=344, mitral=325, double=192). The mean clinical follow-up duration was 10.5±5.3 (median 10.9) years. Operative mortality occurred in 26 patients (3.0%), and linearized late cardiac mortality was 0.9%/patient-year without an intergroup difference. Linearized thromboembolism, bleeding, prosthetic valve endocarditis, non-structural valve deterioration (NSVD), and reoperation rates were 0.8%/patient-year, 0.6%/patient-year, 0.2%/patient-year, 0.5%/patient-year, and 0.5%/patient-year, respectively. Prosthetic valve endocarditis was more frequent after double valve replacement than after aortic or mitral valve replacement (P=0.008 and 0.005, respectively). NSVD and reoperation rates were significantly lower aortic valve replacement than after mitral or double valve replacement (P=0.001 and 0.002, P=0.001 and <0.001, respectively). Valve replacement in the mitral position was the only risk factor for NSVD (hazard ratio [95% confidence interval]=5.247 [1.608–17.116], P=0.006).

Conclusions: On-X valve implantation in the left side heart had favorable clinical outcomes with acceptable early and late mortality and a low incidence of prosthetic valve-related complications. Particularly in the aortic position, the On-X valve had better long-term non-structural durability.

Key Words: Aortic valve; Long term adverse effects; Mitral valve; Prosthesis

Since the first implantation in September 1996, the On-X bileaflet mechanical valve (CryoLife Inc., Kennesaw, GA, USA) has been widely used owing to its pure pyrolytic carbon material properties, flared inlet design, hemodynamic stability with an elongated orifice, and 90° leaflets promoting laminar flow (**Figure 1**).[1] Several reports have shown that On-X valve implantation in the aortic or mitral position resulted in good hemodynamic function and low rates of adverse events in short- and mid-term clinical studies.[2–6] However, there are few long-term clinical results including echocardiographic follow-up data evaluating structural and non-structural valve deterioration (NSVD). The aim of this study was to evaluate the long-term outcomes for up to 20 years after On-X bileaflet mechanical valve implantation in the left side of the heart.

Methods

Patient Characteristics

The study protocol of this retrospective observational study was reviewed and approved by our institutional review board (approval date: August 19, 2019, approval number: 1907-165-1050). Individual informed consent was not required based on the institutional guidelines for waiving consent. Between February 1999 and December 2015, 1,029 patients at our institution underwent prosthetic valve replacement using the On-X valve in the aortic or mitral position. The following patients were excluded: 97 patients with a second valve implantation other than the On-X valve, 16 patients with triple valve replacement, 16 patients who underwent an emergency or urgent operation, 8 reoperation cases for enrolled patients during the study period,

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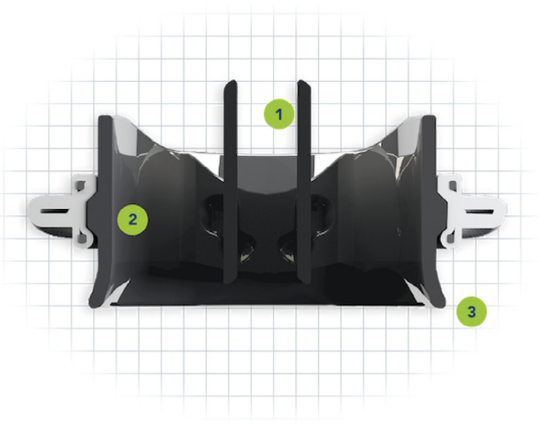

Figure 1. Design and features of the On-X heart valve. (1) 90° leaflets: promotes laminar flow; (2) Pure pyrolytic carbon: reduces thrombogenicity; (3) Flared inlet: organizes flow; prevents pannus. (Reprinted with permission from CryoLife Inc.)

3 patients with incomplete medical records, and 28 patients who underwent surgery for paravalvular leakage (PVL) of a previously implanted prosthetic valve. Finally, a total of 861 patients (mean age=51.6±10.9 years) were enrolled in this study. The patients were divided into 3 groups: the aortic valve replacement group (AVR, n=344), the mitral valve replacement group (MVR, n=325), and the double valve replacement group (DVR, n=192) (**Table 1**). There were 773 concomitant procedures including anti-arrhythmia procedures (n=281), tricuspid valve repairs (n=251), aorta procedures (n=148), mitral valve repairs (n=35), aortic valve repairs (n=31), and coronary artery bypass grafting (n=27) (**Table 2**). The preoperative patient demographics and operative data are summarized in **Tables 1** and **2**.

Surgical Procedure and Operative Data

Most operations were performed under moderate systemic hypothermia (28–32°C), except for 1 case that required deep hypothermic circulatory arrest (<28°C) for concomitant aortic arch replacement. Cold cardioplegia and local cooling with ice slush were used to maintain myocardial

Table 1. Preoperative Patient Demographics

	AVR (n=344)	MVR (n=325)	DVR (n=192)		P value
Age, years	53.2±11.8	50.4±10.1	51.1±10.3		0.003[a]
Sex, n (%)					<0.001[b]
Male	217 (63.1)	107 (32.9)	99 (51.6)		
Female	127 (36.9)	218 (67.1)	93 (48.4)		
Body surface area (m²)	1.66±0.20	1.58±0.17	1.62±0.16		<0.001[a]
Risk factors, n (%)					
Body mass index ≥25 kg/m²	103 (29.9)	59 (18.3)	36 (18.8)		<0.001[c]
Smoking	81 (23.8)	38 (11.7)	34 (17.7)		<0.001[a]
Hypertension	103 (29.9)	28 (8.6)	30 (15.6)		<0.001[b]
Diabetes mellitus	40 (11.6)	23 (7.1)	22 (11.5)		0.101
History of stroke	12 (3.5)	51 (15.7)	26 (13.5)		<0.001[c]
Chronic renal failure on HD	18 (5.2)	1 (0.3)	1 (0.5)		<0.001[c]
Coronary artery disease	37 (10.8)	12 (3.7)	8 (4.2)		<0.001[c]
Dyslipidemia	20 (5.8)	14 (4.3)	10 (5.2)		0.675
NYHA Fc class ≥III	77 (22.4)	110 (33.8)	71 (37.0)		<0.001[c]
Atrial fibrillation	42 (12.2)	236 (72.6)	131 (68.2)		<0.001[c]
Previous surgery	57 (16.6)	81 (24.9)	29 (15.1)		0.006[d]
Etiology, n (%)			**AV etiology**	**MV etiology**	
Rheumatic	66 (19.2)	211 (64.9)	128 (66.7)	148 (77.1)	
Degenerative	43 (12.5)	13 (4.0)	10 (5.2)	6 (3.1)	
Endocarditis	32 (9.3)	19 (5.8)	13 (6.8)	13 (6.8)	
Congenital	161 (46.8)	1 (0.3)	24 (12.5)	1 (0.5)	
Prosthetic valve failure	38 (11.0)	78 (24.0)	15 (7.8)	22 (11.5)	
Others	4 (1.2)	3 (0.9)	2 (1.0)	2 (1.0)	
Preoperative echocardiography					
LVESD (mm)	39.2±11.5	34.7±7.6	38.4±9.6		<0.001[d]
LVEDD (mm)	58.7±11.8	52.5±9.5	57.3±10.4		<0.001[d]
LVEF (%)	55.6±11.7	56.2±8.5	55.2±9.8		0.556
LV dysfunction, n (%)	34 (9.9)	12 (3.7)	13 (6.8)		0.006[a]
Left atrial size (mm)	44.4±10.0	60.2±14.0	59.8±13.0		<0.001[c]

[a]Indicates significant difference between AVR and MVR groups. [b]Indicates significant difference between all 3 groups. [c]Indicates significant difference between AVR and the other 2 groups, respectively. [d]Indicates significant difference between MVR and the other 2 groups, respectively. AVR, aortic valve replacement; DVR, double valve replacement; HD, hemodialysis; LVEDD, left ventricle end-diastolic dimension; LV, left ventricular; LVEF, left ventricular ejection fraction; LVESD, left ventricle end-systolic dimension; MVR, mitral valve replacement; NYHA Fc, New York Heart Association Functional class.

Table 2. Operative Data of the Study Patients

	AVR (n=344)	MVR (n=325)	DVR (n=192)		P value
CPB time (min)	178.7±81.0	181.1±57.3	236.2±65.0		<0.001[a]
ACC time (min)	113.5±46.5	120.7±40.0	174.0±47.3		<0.001[a]
Valve sizes (mm), n (%)			**AV size**	**MV size**	
19	23 (6.7)	0 (0.0)	20 (10.4)	0 (0.0)	
21	95 (27.6)	0 (0.0)	81 (42.2)	0 (0.0)	
23	110 (32.0)	1 (0.3)	64 (33.3)	0 (0.0)	
25	78 (22.7)	84 (25.8)	21 (10.9)	38 (19.8)	
27	12 (3.5)	5 (1.5)	1 (0.5)	4 (2.1)	
27/29	22 (6.4)	142 (43.7)	5 (2.6)	90 (46.9)	
29	1 (0.3)	1 (0.3)	0 (0.0)	2 (1.0)	
31	1 (0.3)	2 (0.6)	0 (0.0)	2 (1.0)	
31/33	2 (0.6)	90 (27.7)	0 (0.0)	56 (29.2)	
Concomitant procedure, n (%)					
AV repair	–	31 (9.5)	–		
MV repair	35 (10.2)	–	–		
Tricuspid valve repair	11 (3.2)	161 (49.5)	79 (41.1)		<0.001[b]
CABG	18 (5.2)	6 (1.8)	3 (1.6)		0.016[b]
Anti-arrhythmic procedure	18 (5.2)	172 (52.9)	91 (47.4)		<0.001[b]
Aorta procedure	128 (37.2)	4 (1.2)	16 (8.3)		<0.001[c]

[a]Indicates significant difference between DVR and the other 2 groups, respectively. [b]Indicates significant difference between AVR and the other 2 groups, respectively. [c]Indicates significant difference between all 3 groups. ACC, aortic cross clamp; AV, aortic valve; AVR, aortic valve replacement; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; DVR, double valve replacement; MV, mitral valve; MVR, mitral valve replacement.

protection. Aortic valve replacement was performed using non-everted mattress sutures, and mitral valve replacement was performed using everted mattress sutures. All sutures in both positions were buttress reinforced with polytetrafluoroethylene as a tubule or pledget.

Anticoagulation Strategy

If there was no evidence of active bleeding, subcutaneous low molecular weight heparin injection was started as soon as possible after surgery. Oral vitamin K antagonist (VKA) therapy was started after beginning oral feeding. Both low molecular weight heparin and oral VKA were used together when the international normalized ratio (INR) was <1.7. After the value of INR was >1.7, the low molecular weight heparin was stopped.

The prothrombin time test was performed daily before discharge and the patient was followed regularly in the outpatient department after discharge. Apart from clinical follow up for surgery, all the patients taking oral VKA visited independent anticoagulation services (ACS) and had face-to-face consultations with physicians in our department. Follow up was observed every 1–4 weeks until INR levels reached the target range. After the INR level was firmly stabilized, follow-up intervals were lengthened up to a maximum of 3 months. The target INR was controlled between 2.0 and 2.5 in the isolated AVR and between 2.5 and 3.0 in the MVR and DVR. Target INR was modified to 3.0–3.5 in some higher-risk patient groups with previous thromboembolic events according to neurologist consultations. In our institution, the same target INR was applied to all mechanical valves.

Evaluation of Clinical Outcomes

Operative mortality was defined as all-cause death within 30 days after surgery or before discharge in the same hospital admission. Early postoperative echocardiography was performed before discharge (mean 7.8±4.7 days, range 1–49 days). Patients returned to the outpatient department clinic 2–4 weeks after discharge, and regular follow-up intervals were extended to 3–6 months according to the patient's condition. Routine echocardiographic follow up was performed at the discretion of the operating surgeons or referring medical physicians. If there was any change in clinical manifestation such as a newly found abnormal cardiac murmur, aggravated dyspnea, or signs implying hemolytic anemia, additional transthoracic or transesophageal echocardiographic evaluation was performed for further evaluation. Survival data for all patients were obtained solely from the national database of death statistics. The clinical follow-up period ended in June 2019. Follow up was complete in 93.4% of patients, and the cumulative follow-up period was 8,405.8 patient-years. The mean clinical follow-up period was 10.5±5.3 (median 10.9) years. At least 1 follow-up echocardiography was performed in 90.9% of patients, and the mean duration from the discharge date to the last follow-up echocardiography date was 109.1±74.5 (median 106.2) months. Left ventricular (LV) dysfunction was defined as LV ejection fraction (LVEF) of <40%.

Late mortality and morbidities were defined and counted by the Society of Thoracic Surgeons/American Association for Thoracic Surgery/European Association for Cardiothoracic Surgery definitions.[7] Structural valve deterioration (SVD), especially in this study for mechanical prosthesis, was defined as any intrinsic valve change resulting in stenosis or regurgitation such as rocking motion of leaflet, fracture, escape, and any type of valve rupture. Thromboembolic event was defined as valve thrombosis, any cere-

Table 3. Early Clinical Outcomes

	Total (n=861)	AVR (n=344)	MVR (n=325)	DVR (n=192)	P value
Operative mortality, n (%)	26 (3.0)	9 (2.6)	12 (3.7)	5 (2.6)	0.668
Complications, n (%)					
Low cardiac output syndrome	65 (7.5)	17 (4.9)	29 (8.9)	19 (9.9)	0.057
Bleeding reoperation	38 (4.4)	10 (2.9)	13 (4.0)	15 (7.8)	0.027
Acute kidney injury	26 (3.0)	12 (3.5)	7 (2.2)	7 (3.6)	0.510
Stroke	22 (2.6)	10 (2.9)	8 (2.5)	4 (2.1)	0.838
Respiratory complication	42 (4.9)	15 (4.4)	15 (4.6)	12 (6.3)	0.599
Mediastinitis	7 (0.8)	4 (1.2)	2 (0.6)	1 (0.5)	0.643
Infective endocarditis	5 (0.6)	1 (0.3)	1 (0.3)	3 (1.6)	0.127

Abbreviations as in Table 2.

bral embolic event including ischemic stroke and transient ischemic attack, or any non-cerebral embolic event with documented embolus operatively or clinically. Bleeding event was defined as any episode of major internal or external bleeding associated with death, hospitalization, permanent injury or transfusion not caused by major trauma or major surgery. NSVD was defined as any abnormality without intrinsic valve change resulting in valve dysfunction such as peri-prosthetic pannus formation, PVL, patient-prosthesis mismatch (PPM) and clinically important hemolytic anemia.

For the comparison of long-term results between On-X and other valves, we conducted a sub-analytic comparison with long-term results relating to the St. Jude mechanical valve (Abbott, Chicago, IL, USA), which was the second most common mechanical valve in our institution between 1990 and 2015 (AVR; n=114, MVR; n=157, DVR; n=59, total patient-year=4,550.7).

Statistical Analysis

All statistical analyses were conducted using SPSS statistical software (version 25.0; IBM Corp., Armonk, NY, USA). Continuous values are expressed as mean±standard deviations or medians, and categorical variables are expressed as proportions. The chi-squared test or Fisher's exact test was used to compare the categorical variables, and the Student's t-test was used to compare the continuous variables. To compare continuous variables between the 3 groups, 1-way analysis of variance was performed. Multivariable analyses for early operative outcomes were performed with logistic regression analysis. Survival rates and freedom from morbidities were estimated using the Kaplan-Meier method. Risk factors for time-related events were analyzed using the Cox proportional hazard model. Variables with a P value <0.05 in the univariate analysis were entered into the multivariable model. A probability value < 0.05 was considered statistically significant.

Results

Early Outcomes

Operative mortality occurred in 3.0%, and there was no significant difference in operative mortality between the 3 groups (P=0.668) (**Table 3**). Multivariable logistic regression analysis revealed that age (odds ratio (OR) [95% confidence interval (CI)]=1.050 [1.050–1.094], P=0.024) and preoperative chronic renal failure on hemodialysis (OR [95% CI]=4.223 [1.097–16.265], P=0.036) were associated with operative mortality.

Early postoperative complication rates are shown in **Table 3**. Reoperation for bleeding rates were significantly higher in the DVR (7.8%) than in the AVR (2.9%) group (P=0.010). However, risk factor analyses of the incidence of reoperation for bleeding revealed that the type of surgery was not a significant risk factor. There were no significant differences in low cardiac output syndrome, acute kidney injury, stroke, or respiratory complications between groups (**Table 3**).

Late Mortality and Risk Factors

The overall survival and freedom from cardiac mortality rates are shown in **Figure 2**. Late mortality occurred in 133 patients during the follow-up period. Linearized overall late mortality rates were 2.1%/patient-year in the AVR group, 1.2%/patient-year in the MVR group, and 1.5%/patient-year in the DVR group. The linearized cardiac mortality rates were 1.2%/patient-year in the AVR group, 0.7%/patient-year in the MVR group, and 0.9%/patient-year in the DVR group (**Table 4**). There was no significant difference in overall mortality or cardiac mortality between the 3 groups (P=0.072 and 0.236, respectively) (**Figure 2**). An age-adjusted multivariable analysis demonstrated that male sex (hazard ratio (HR) [95% CI]=1.622 [1.181–2.227], P=0.003), underlying diabetes mellitus (HR [95% CI]=1.966 [1.308–2.953], P=0.001), and preoperative chronic renal failure on hemodialysis (CRF on HD) (HR [95% CI]=5.772 [3.359–9.918], P<0.001) were risk factors for overall mortality, and preoperative CRF on HD (HR [95% CI]=2.308 [1.256–6.195], P=0.012), coronary artery disease (HR [95% CI]=2.308 [1.297–4.108], P=0.004), and New York Heart Association (NYHA) functional class ≥III (HR [95% CI]=1.507 [1.005–2.259], P=0.047) were risk factors for cardiac mortality. The valve implant position was not associated with either overall or cardiac mortality.

Late Morbidities and Risk Factors

No patients experienced late SVD. Thus, valve-related late morbidities were evaluated as follows: thromboembolic events, bleeding events, prosthetic valve endocarditis (PVE), NSVD, and reoperation.

Late thromboembolic events occurred in 69 patients in all groups. There were 58 patients who had an ischemic stroke or TIA event, 2 patients with prosthetic valve thrombosis (only in the MVR), 2 patients with coronary thromboembolism (1 in the MVR and 1 in the DVR), and 7 patients with peripheral thromboembolism such as retinal

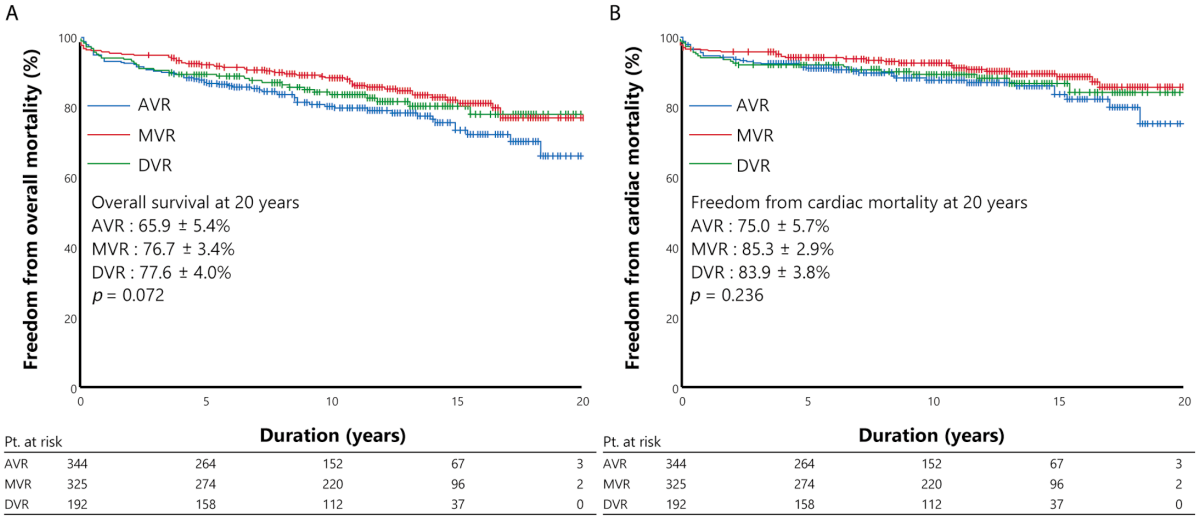

Figure 2. (**A**) Kaplan-Meier curve for freedom from overall mortality. Freedom rates by groups at 20 years are given. (**B**) Kaplan-Meier curve for freedom from cardiac mortality. Freedom rates by groups at 20 years are given. AVR, aortic valve replacement; MVR, mitral valve replacement; DVR, double valve replacement.

Table 4. Late Clinical Outcomes

	Total (Pt-yr=8,405.8)	AVR (Pt-yr=2,976.2)	MVR (Pt-yr=3,528.5)	DVR (Pt-yr=1,901.1)
	N (%/patient-y)	N (%/patient-y)	N (%/patient-y)	N (%/patient-y)
Overall mortality, n (%)	133 (1.6)	63 (2.1)	41 (1.2)	29 (1.5)
Cardiac mortality	78 (0.9)	37 (1.2)	23 (0.7)	18 (0.9)
Late morbidities, n (%)				
Thromboembolic event	69 (0.8)	25 (0.8)	26 (0.7)	18 (0.9)
Bleeding event	50 (0.6)	12 (0.4)	27 (0.8)	11 (0.6)
Prosthetic valve endocarditis	18 (0.2)	4 (0.1)	4 (0.1)	10 (0.5)
Non-structural valve deterioration	39 (0.5)	3 (0.1)	25 (0.7)	11 (0.6)
Reoperation	38 (0.5)	2 (0.1)	21 (0.6)	15 (0.8)

Pt-yr, patient-year; y, year. Other abbreviations as in Table 2.

artery occlusion. The linearized late thromboembolism event rates were 0.8%/patient-year in the AVR group, 0.7%/patient-year in the MVR group, and 0.9%/patient-year in the DVR group. There was no statistical difference in the late thromboembolism event rate between the 3 groups. The INR at the time of thromboembolic events was available for 50 of 69 patients and was 1.9±0.6 (range 1.1–3.5). Among these, 40 patients (80.0%) had INR levels <2.0 in the AVR group and <2.5 in the MVR and DVR groups. There were 5 patients with INR >3.0 at the time of thromboembolic events (1 in the AVR group, 3 in the MVR group, 1 in the DVR group).

Late bleeding events occurred in 50 patients in all groups. There were 20 patients with intracranial hemorrhage, 13 patients with gastrointestinal bleeding, 12 patients with spontaneous internal bleeding, 2 patients with hemoptysis, and 3 patients with bleeding caused by minor trauma. The linearized late bleeding event rates were 0.4%/patient-year in the AVR group, 0.8%/patient-year in the MVR group, and 0.6%/patient-year in the DVR group. There was no statistical difference in the rate of late bleeding events between the 3 groups. The INR at the time of bleeding events was available for 39 of 50 patients and was 4.7±3.6 (range 1.9–21.1). Among these, 31 patients (79.5%) had INR levels >2.5 in the AVR group and >3.0 in the MVR and DVR groups. There were 2 patients with an INR <2.0 at the time of bleeding events (only in the MVR group).

The rate of freedom from the composite of thromboembolism and bleeding (CTEB) at 20 years was 78.6±4.0% in the AVR group, 77.0±3.0% in the MVR group, and 80.5±3.5% in the DVR group. There was no significant difference in the CTEB event rate between the groups (P=0.500) (**Figure 3**). Multivariable analyses using patient characteristics including preoperative atrial fibrillation and echocardiographic data demonstrated that underlying diabetes mellitus (HR [95% CI]=1.856 [1.035–3.327], P=0.038) and preoperative stroke history (HR [95% CI]=1.900 [1.171–3.082], P=0.009) were risk factors for late CTEB events.

There was a total of 18 cases of late PVE (4 in the AVR group, 4 in the MVR group, and 10 in the DVR group),

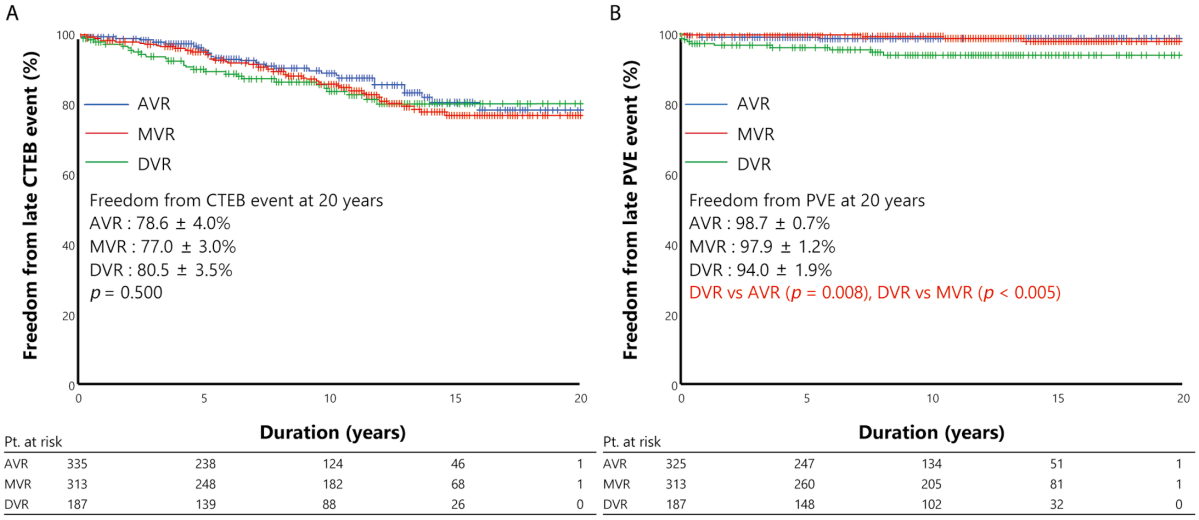

Figure 3. (**A**) Kaplan-Meier curve for freedom from composite of thromboembolism and bleeding (CTEB) event. Freedom rates by groups at 20 years are given. (**B**) Kaplan-Meier curve for freedom from prosthetic valve endocarditis (PVE). Freedom rates by groups at 20 years are given. AVR, aortic valve replacement; MVR, mitral valve replacement; DVR, double valve replacement.

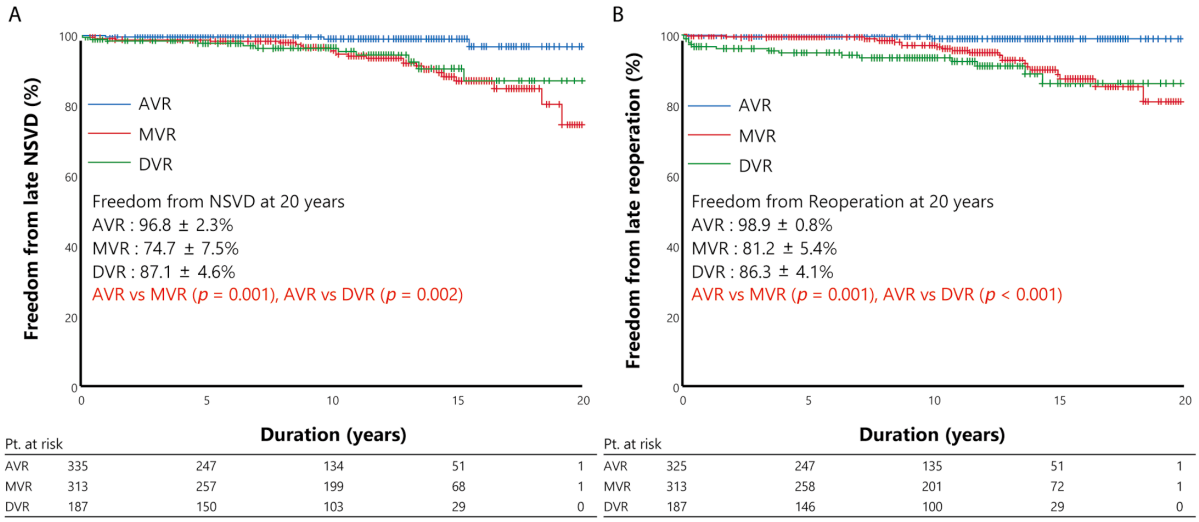

Figure 4. (**A**) Kaplan-Meier curve for freedom from non-structural valve deterioration (NSVD). Freedom rates by groups at 20 years are given. (**B**) Kaplan-Meier curve for freedom from reoperation. Freedom rates by groups at 20 years are given. AVR, aortic valve replacement; MVR, mitral valve replacement; DVR, double valve replacement.

and the DVR group had a statistically significant higher rate of late PVE compared to that in the AVR and MVR groups (P=0.008 and P=0.005, respectively) (**Figure 3**).

Late NSVD events occurred 3 patients in the AVR group (1 PPM and 2 prosthetic aortic valve [pAV] PVL), 25 patients in the MVR group (all cases with prosthetic mitral valve [pMV] PVL), and 11 patients in the DVR group (1 pAV PPM, 1 subaortic pannus formation, 1 pAV PVL and 8 pMV PVL). The linearized rates of NSVD were 0.1%/patient-year in the AVR group, 0.7%/patient-year in the MVR group, and 0.6%/patient-year in the DVR group. The freedom from a late NSVD rate was significantly higher in the AVR group than in the MVR and DVR groups (P=0.001 and P=0.002 respectively) (**Figure 4**). The Cox proportional hazard model demonstrated that MVR was the only risk factor related to late NSVD (HR [95% CI]=5.247 [1.608–17.116], P=0.006).

Late reoperation was performed in 38 patients; the reasons for reoperation were PVE in 12 patients (1 in the AVR group, 2 in the MVR group, and 9 in the DVR group) and

NSVD in 26 patients (1 in the AVR group, 19 in the MVR group, and 6 in the DVR group). The freedom from reoperation rate was also significantly higher in the AVR group than in the MVR and DVR groups (P=0.001 and P<0.001, respectively) (**Figure 4**).

Direct Comparisons of Long-Term Results Between On-X and St. Jude Mechanical Valves

Of the 330 patients who had implanted St. Jude mechanical valves in aortic or mitral positions, there were 9 cases of early mortality (2.7%), 90 cases of late overall mortality, 67 cases of CTEB events, and 32 cases of reoperations related to operated prosthetic valves. The St. Jude mechanical valve showed a linearized overall late mortality rate of 2.0%/patient-year, a late CTEB event rate of 1.5%/patient-year, and a late reoperation rate of 0.7%/patient-year in our institution. There was no statistically significant difference compared to the On-X valve for late overall mortality, late CTEB event, and late reoperation (P=0.147, 0.718, and 0.543, respectively) (**Supplementary Figure**).

Discussion

This study reported 2 main findings. First, the On-X valve in the left side of the heart had satisfactory long-term results in terms of long-term survival and valve-related complications. Second, the On-X valve in the aortic position had better long-term durability regarding NSVD and reoperation compared to those in the mitral position.

This study is the largest clinical report on the use of the On-X bileaflet mechanical valve, with 861 patients, and it has the longest follow-up duration, up to 20.3 years (mean 10.5±5.3 years). Several mid-term reports of the On-X valve have reported a mean follow-up duration of up to 5.6 years; however, no long-term results have been reported.[2,3,5]

Thromboembolism and anticoagulation-related bleeding events are the major concern in patients with mechanical valve prostheses. In a prospective multicenter study, Chan et al reported that the On-X valve provides favorable mid-term results for major thromboembolism and hemorrhage compared with several bileaflet mechanical valves.[8] Our study also showed satisfactory thromboembolism and bleeding event rates <1.0%/patient-year, respectively, which is similar to the results of a previous mid-term report.[3] Although all bleeding events requiring hospitalization were included in this study, whether associated with anticoagulation or not, fewer bleeding events occurred in our study than in studies about other mechanical prostheses.[9,10]

Overall, 77.8% (70 of 90) of patients who developed CTEB were outside the target range. These results show the importance of maintaining a therapeutic range of anticoagulation. In our institution, patients with a mechanical prosthetic valve who were taking oral VKA visited the ACS every 1–4 weeks before reaching the target INR range. After firm stabilization of INR, follow-up intervals were gradually lengthened up to 2–3 months. However, because oral VKA has many food and drug interactions, and maintaining regular clinical follow up is quite difficult for some patients, unsuspected INR fluctuation might be common. Also, it is known that the risk of oral VKA-related intracranial hemorrhage is particularly high in Asians, and for this reason, studies have also reported that a lower INR target is safe compared to the European and US guidelines for mechanical valve implanted patients.[11,12] In this respect, consideration was given to reducing the CTEB in patients with the implanted On-X valve. Although we applied the same INR strategy as other conventional mechanical valves to the On-X valve, in some reports, a low INR target (1.5–2.0) with a low-dose aspirin strategy also showed a low CTEB risk in patients with On-X valve placement for AVR.[13,14] Moreover, a randomized controlled trial comparing the anticoagulation efficacy between direct oral anticoagulants and oral VKAs is currently underway in patients who have undergone AVR using the On-X valve (PROACT Xa; US ClinicalTrials.gov no. NCT04142658). In addition, it is generally known that self-monitoring and self-management using point-of-care tests was helpful not only in terms of cost-effectiveness but also in reducing CTEB events and overall mortality in patients with mechanical heart valves.[15,16] Considering these factors, further efforts to develop an ideal anticoagulation strategy based on the patients' characteristics should be performed. We expect that we can safely apply the new anticoagulation strategy with lower INR to patients with the On-X mechanical valve.

The late PVE rate was very low, in agreement with previous short- and mid-term reports.[3,5] Ten of the 18 patients with late PVE underwent reoperation, and 2 patients expired after reoperation. The higher PVE rate in the DVR group is presumably due to the double implantation of the foreign body.

There was no SVD during the follow-up period in this study. SVD of the bileaflet mechanical valve is extremely rare, and only 2 cases have been reported with the On-X valve.[17,18] Otherwise, there were 39 NSVD events during follow-up period. The late NSVD rate was significantly lower in the AVR group than in the MVR or DVR groups. When reviewed from the valve position, late NSVD occurred in 6 cases in the aortic position and in 33 cases in the mitral position. In the aortic position, only 1 patient underwent reoperation owing to more than moderate PVL. Considering the flared inlet and elongated orifice design of the On-X valve, there is a probability to have low incidence of subaortic pannus formation with the On-X valve. However, because the duration of subaortic pannus formation requiring surgical treatment was approximately 10–15 years after the index surgery, a longer follow-up period will be required to evaluate the advantage regarding subaortic pannus formation of the On-X valve.[19–21] In this study, all cases of NSVD in the mitral position were PVL (6.4%, 33 of 517). This incidence was comparable with that in our previous study reporting the long-term incidence of PVL after bioprosthetic or mechanical MVR.[22] Considering that the valve durability would depend on the incidence of NSVD in mechanical prosthesis, further study is needed on the valve design or surgical techniques to prevent NSVD in the mitral valve location.

The present study has several limitations. First, it was a retrospective single-center study; therefore, our perioperative strategies including anticoagulation could have affected the surgical outcomes. Second, this study was basically a single-arm study. Although we demonstrated the long-term results of St. Jude mechanical valves and compared the long-term outcomes, direct comparisons using appropriate statistical methods were not performed because of different timing of prosthetic valves in use and an unclear indication of valve choice.

In conclusion, On-X valve implantation in the left side of the heart showed favorable clinical outcomes with acceptable early and late mortality rates and a low incidence of prosthetic valve-related complications. Especially

in the aortic position, the On-X valve showed better long-term durability regarding NSVD and reoperation compared to those in the mitral position.

Disclosures

The authors declare no conflicts of interest.

IRB Information

The study was approved by the institutional review board of Seoul National University Hospital (Approval date: August 19, 2019, Approval number: 1907-165-1050).

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Supplementary Files

Please find supplementary file(s);
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