Long Term Outcomes of Aortic Root Replacement: 18 Years' Experience

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Background: We reviewed the long-term outcomes of aortic root replacement at Asan Medical Center and investigated the predictors affecting mortality. ***Materials and Methods:*** A retrospective analysis was performed on 225 consecutive adult patients undergoing aortic root replacement with mechanical conduits (n=169), porcine aortic root prosthesis (n=23), or aortic homografts (n=33) from January 1992 to September 2009. The median follow-up duration was 6.1 years (range, 0 to 18.0 years). ***Results:*** The porcine root group was older than the other groups (freestyle 55.9±14.3 years vs. mechanical 46.3±14.6 years, homograft 48.1±14.7 years; p=0.02). The mechanical group had the highest incidence of the Marfan syndrome (mechanical 22%, freestyle 4%, homograft 3%; p=0.01). Surgery performed for infective endocarditis was more frequent in the homograft group (mechanical 10%, freestyle 10%, homograft 40%; p＜0.001). The overall 30-day mortality was 5.3% (12/225). Actuarial survival rates in the mechanical, porcine root, and homograft groups were 79.4%, 81.5%, and 83.5% at 5 years and 67%, 61.9%, and 61.1% at 10 years, respectively (p=0.73). By multivariate analysis, preoperative diabetes mellitus, older age, and longer cardiopulmonary bypass time were independent predictors of mortality. Incidence of postoperative complications, including infective endocarditis and thromboembolism were comparable in all of the groups. ***Conclusion:*** Aortic root replacement can be safely performed with different types of prostheses as the outcome was not affected by the choice of prosthesis. Further studies are required to assess the long-term durability of biological prostheses.

Key words: 1. Aorta, surgery
         2. Heart valve prosthesis
         3. Follow-up studies
         4. Aortic valve, surgery

INTRODUCTION

In 1968, Bentall and DeBono described a technique for complete replacement of the aortic valve and ascending aorta with a composite graft: reimplanting the coronary ostia into the graft with the inclusion technique. The outcome was improved by later technical modifications that paid attention to avoiding tension, torsion, or kinking of the coronary reimplantation sites. There remains a concern about the long-term risk of thromboembolism, anticoagulation-related hemorrhage, endocarditis, and reoperation [1-3]. Biological prostheses such as homograft, pulmonary autograft, and stentless bioprostheses (porcine root or stentless pericardial valve) have been gaining more attention because they can minimize

the risk of thromboembolism and anticoagulation-related problems. However, few studies have directly compared the outcomes of using different prostheses in a single center. In this report we assessed the outcomes of patients who received aortic root replacement with three different types of prostheses.

MATERIALS AND METHODS

1) Study population

From January 1992 to September 2009, a total of 225 patients underwent aortic root replacement at Asan Medical Center. The follow-up ended on October 17, 2011, and current follow-up data were available for 196 of the 225 patients (87%). The median length of follow-up was 6.1 years (mechanical group, 0 to 17.8 years; freestyle group, 0 to 17.9 years; homograft group, 0 to 16.7 years). Annuloaortic ectasia (dilatation of the sinuses of Valsalva with associated moderate or severe aortic valve incompetence, cephalad displacement of the coronary ostia, and varying degrees of dilatation of the more distal descending aorta) was the most common indication for surgery (185 patients, 82.5%). Forty-nine patients had acute or chronic ascending aortic dissection. Eighteen of 49 patients with aortic dissection undergoing primary operations also had annuloaortic ectasia. The aortic root was replaced with a mechanical valved conduit (St. Jude Regent; St. Jude Medical, St. Paul, MN, USA) in 169 patients, porcine aortic root (Freestyle; Medtronic, Minneapolis, MN, USA) in 23 patients, or homograft in 33 patients. The choice of valve type depended on the preference of the surgeons. This series includes patients who underwent aortic root replacement under either elective or emergency surgical conditions.

2) Statistical analysis

Data are expressed as mean±standard deviation or median (range) for continuous variables and as number (%) for categorical variables. The cumulative survival as a function of time after the date of surgery was generated by using the Kaplan-Meier method. The equivalence of long-term mortality among the mechanical valve group, freestyle group, and homograft group survival curves was evaluated by the log-rank test. The Cox proportional hazards model was used to examine both univariate and multivariate relationships between baseline characteristics and mortality by using stepwise forward or backward selection of candidate variables at the p-value of 0.05.

Table 1. Patient demographics (n=225)

Variable	Mechanical (n=169)	Freestyle (n=23)	Homograft (n=33)	p-value
Age (yr)	46±14	55±14	48±14	0.02
Sex (male)	116 (69)	11 (48)	25 (75)	0.07
Diabetes mellitus	10 (6)	1 (4)	2 (6)	>0.99
Hypertension	50 (30)	6 (26)	5 (15)	0.22
Renal failure	2 (1)	1 (4)	4 (12)	0.01
COPD	26 (15)	1 (4)	1 (3)	0.06
NYHA class III or IV	39 (23)	4 (17)	9 (27)	0.69
Marfan syndrome	38 (22)	1 (4)	1 (3)	0.01
Emergency operation	35 (20)	1 (4)	2 (6)	0.40
Prior cardiac surgery	18 (11)	3 (13)	2 (6)	0.61
Annuloaortic ectasia	139 (80)	17 (70)	28 (80)	0.53
Infective endocarditis	15 (10)	3 (10)	14 (40)	<0.001
Aortic dissection	42 (25)	3 (10)	3 (10)	0.02

Values are presented as mean±standard deviation or number (%).
COPD, chronic obstructive pulmonary disease; NYHA, New York Heart Association.

RESULTS

1) Patient demographics

Preoperative patient characteristics are summarized in Table 1. The mechanical group had a higher degree of the Marfan syndrome (mechanical 22%, freestyle 4%, homograft 3%; p=0.01). Surgical indications for aortic root replacement differed among the three groups, with homograft aortic root replacement having been performed more frequently for infective endocarditis, while aortic dissection patients more frequently received mechanical valved conduits. However, aortic root replacement was performed for annuloaortic ectasia in similar proportions of the mechanical group, the porcine root group, and the homograft group patients (Table 1).

2) Surgical results

No differences were observed in the three groups with re-

Fig. 1. Survival of patients undergoing aortic root replacement according to the valve type.
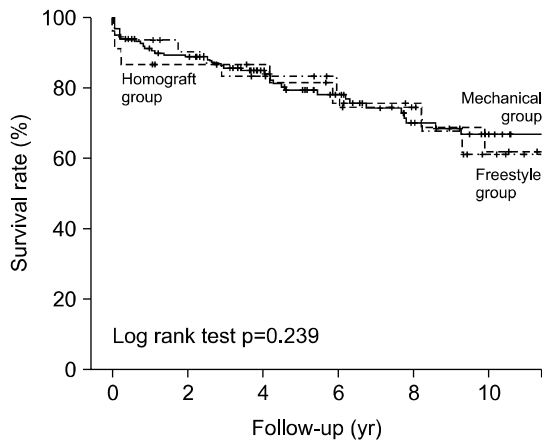
Patient at risk						
Group	0	2	4	6	8	10
Mechanical	167	140	95	66	48	34
Freestyle	22	18	16	13	11	9
Homograft	32	27	22	18	12	6

Fig. 2. Morbidity-free survival of patients undergoing aortic root replacement according to the valve type.
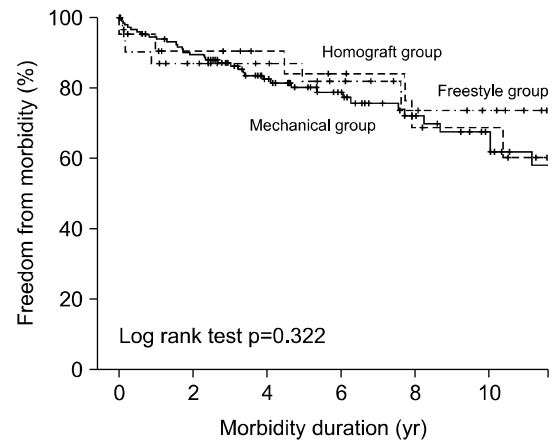
Patient at risk						
Group	0	2	4	6	8	10
Mechanical	167	123	79	55	35	24
Freestyle	22	17	14	12	9	8
Homograft	32	24	18	14	9	6

Table 2. Operative data and concomitant procedure (n=225)

Variable	Mechanical (n=169)	Freestyle (n=23)	Homograft (n=33)	p-value
CPB time (min)	236±113	225±117	200±80	0.20
ACC time (min)	148±59	156±79	152±63	0.67
TCA time (min)	6±14	3±9	2±6	0.06
Concomitant procedure				
CABG	21 (10)	2 (9)	2 (6)	0.71
MVP	8 (5)	2 (9)	6 (19)	0.02
MVR	7 (4)	0 (0)	3 (9)	0.69
TVP	6 (4)	1 (4)	1 (3)	>0.99
Total arch replacement	5 (3)	1 (4)	0 (0)	0.47
Hemiarch replacement	23 (14)	1 (4)	2 (6)	0.15

Values are presented as mean±standard deviation or number (%).
CPB, cardiopulmonary bypass; ACC, aortic cross clamp; TCA, total circulatory arrest; CABG, coronary artery bypass graft; MVP, mitral valvuloplasty; MVR, mitral valve replacement; TVP, tricuspid valvuloplasty.

gard to the aortic cross clamp or cardiopulmonary bypass times. Concurrent procedures, such as coronary artery bypass grafting, mitral valve replacement, total arch replacement, hemiarch replacement, and tricuspid valve repair were carried out in 34% (76/225) of aortic root replacement cases. A

bleeding reoperation was required in 23 patients and the incidences did not differ significantly among the three groups (p=0.52). Of the 225 patients undergoing aortic root replacements, the overall 30-day mortality was 5.3% (12/225) (Fig. 1). Of these patients, 11 patients expired of postoperative cardiogenic shock or hemodynamic instability. The one remaining patient expired due to septic shock. There was no statistically significant difference in 30-day mortality between the types of valves (p=0.86) (Table 2).

3) Long term survival

Actuarial survival rates in the mechanical, porcine root, and homograft groups were 79.4%, 81.5%, and 83.5% at 5 years and 67%, 61.9%, and 61.1% at 10 years, respectively (p=0.73) (Fig. 2). A total of 54 deaths occurred during the 16 years of follow-up. In the univariate analysis, significant predictors of long-term mortality included diabetes mellitus (DM), reoperation for postoperative bleeding, and longer aortic cross clamp and cardiopulmonary bypass times. Sex, aging, preoperative renal failure, emergency performance of aortic root replacement, Marfan syndrome, and redo operation were not statistically significant predictors of mortality. By univariate Cox model analysis, insertion of a mechanical valve

Table 3. Analysis of risk factors of mortality

Variable	Univariate analysis			Multivariate analysis		
	Hazard ratio	95% CI	p-value	Hazard ratio	95% CI	p-value
Age (yr)	1.02	1.00−1.04	0.02	1.02	1.00−1.04	0.03
Sex (male)	1.08	0.56−2.06	0.81			
Diabetes mellitus	5.16	2.28−11.6	<0.001	4.00	1.72−9.30	<0.001
Hypertension	1.01	0.53−1.92	0.97			
Preoperative renal failure	3.05	0.42−22.2	0.27			
NYHA class III/IV	1.32	0.69−2.50	0.39			
Marfan syndrome	1.45	0.64−3.20	0.36			
Emergency operation	1.58	0.67−3.72	0.30			
Redo operation	1.58	0.78−3.20	0.19			
Valve size (>33 mm)	0.27	0.04−1.80	0.20			
Bleeding reoperation	2.14	0.90−5.06	0.08			
Valve type	1.15	0.61−2.16	0.66			
CPB time	1.00	1.00−1.005	0.03	1.003	1.00−1.01	0.02
ACC time	1.01	0.01−2.01	0.07			
TCA time	1.38	0.60−3.12	0.43			
Preoperative EF (<40%)	1.01	0.99−1.03	0.27			

CI, confidence interval; NYHA, New York Heart Association; CPB, cardiopulmonary bypass; ACC, aortic cross clamp; TCA, total circulatory arrest; EF, ejection fraction.

Table 4. Valve-related complications (n=225)

Variable	Mechanical (n=169)	Freestyle (n=23)	Homograft (n=33)	p-value
Reoperation	15 (9)	4 (17)	7 (21.2)	0.01
Infective endocarditis	6 (4)	1 (4)	2 (6)	0.71
Hemorrhage	25 (15)	3 (13)	0 (0)	0.01
Thromboembolism	8 (5)	2 (9)	4 (12)	0.16

Values are presented as number (%). Hemorrhage includes postoperative intracerebral hemorrhage. Thromboembolism includes postoperative cerebral infarction.

conduit did not confer a survival benefit relative to freestyle or homograft aortic root replacement at intermediate follow-up. By multivariate analysis, preoperative DM, older age, and longer cardiopulmonary bypass time were independent predictors of mortality (Table 3).

4) Valve-related complications

Reoperation was required in 26 patients (for valve-root dehiscence, structural valve degeneration, periaortic abscess, and infective endocarditis, respectively). The overall freedom from reoperation rate at 1, 5, and 10 years was 97.5%, 91.6%, and 85.3%, respectively. There were meaningful differences in the reoperation rates of the biologic and mechanical groups (p=0.01). Nine patients (4.0%, or 0.02% per patient year) had endocarditis and fourteen patients (6.2%, or 0.3% per patient-year) experienced episodes of clinically significant thromboembolism (including cerebral infarction). No differences were observed between groups with regard to the frequency of infective endocarditis (p=0.71) or thromboembolism (p=0.16). Postoperative hemorrhage (including intracerebral hemorrhage) events occurred in 28 patients (12.4%, 0.6% per patient-year), and their incidence was higher in the mechanical group than in the other groups (Table 4).

DISCUSSION

Aortic root replacement has been the favored surgical procedure for patients with annuloaortic ectasia and other disorders of the ascending aorta that are associated with aortic regurgitation. This technique reduced the risk of recurrent proximal aortic aneurysm [1] and surgical outcomes improved dramatically. The thirty-day mortality for aortic root replace-

ment has fallen below 5% in this report and others [2,3]. These results are gratifying in light of the high mortality attending untreated ascending aortic aneurysm, dissection, and root infection. The hospital deaths that occurred in our study were similar to others reported in the literature [3]. In other comparable aortic root series, the hospital mortality has ranged between 1.7% and 18%, averaging 7% to 8% in recent studies [2-5]. Although the mortality rate for root replacement is low, risk factors for death have been identified. In this series, preoperative DM, an older age, and longer cardiopulmonary bypass time were predictors of death. Surprisingly, the era of operation, previous aortic root operation, and use of hypothermic circulatory arrest were not significant predictors of mortality.

Several clinical studies have confirmed the risk factors for mortality. In 2002, Kouchoukos et al. [6] reported that an older age, preoperative New York Heart Association (NYHA) class III and IV, non-Marfan status, urgent surgery, longer cardiopulmonary bypass time, and male gender were predictors of mortality. Baumgartner et al. [7] reported that a higher mortality rate in patients with aortic root replacement is closely related to NYHA classification III or IV, male gender, and urgent surgery. There was no in-hospital mortality among 13 patients with Marfan's syndrome in our series. The ten-year survival in this series was similar to other series [3,8]; only 60% of the patients who undergo aortic root replacement are expected to live longer than 10 years.

Up to now, the optimal choice of valved conduit for aortic valve replacement remains controversial because of a lack of prospective randomized studies. The mechanical valves offer stable hemodynamic function and longer durability, but they are thrombogenic, and patients who receive them require long-term anticoagulation, with its associated increase in the risk of hemorrhage. Bioprosthetic valves have fewer thromboembolic events and usually do not require anticoagulant agents; however, structural deterioration of the valves reduces their durability. This study represents a large series of aortic root replacements performed with aortic mechanical valve conduits or freestyle conduits or homografts. The first study of this kind, by Byrne et al. [9], included 231 elective aortic root replacements (mechanical, n=85; biologic, n=136), and concluded that there were no meaningful differences in early

or mid-term valve-related outcomes between biologic and mechanical groups. Like prior series [9], our 6-year postoperative follow-up revealed that the majority of patients were generally doing well in all three groups, and we could not find any meaningful differences regarding overall mortality or freedom from valve-related complications in the three groups.

The relatively high rates of bleeding in the mechanical groups were due largely to our policy of anticoagulant therapy according to the type of valve. The mechanical groups received coumadine for the rest of their lifetime and the homograft groups received anticoagulant therapy for only three months postoperatively. The freestyle groups had three bleeding events in our study because they needed anticoagulation therapy. One patient had postoperative atrial fibrillation and two patients were reoperated with a mechanical valve prosthesis because one patient had postoperative infective endocarditis and another patient suffered from severe mitral regurgitation. This study confirms the presence of a direct relationship between the intensity of anticoagulation and the risk of bleeding. The recommended prothrombin-time ratio in our protocol (1.8 to 2.2 times the control value) was similar to that of the Edinburgh Heart Valve Trial [10]. Increasing the prothrombin-time ratio from 1.5 to 2.5 doubles the risk of bleeding. Of the 26 major bleeding episodes in our patients, 25 occurred when the prothrombin-time international normalized ratio was over 3.0; the remaining one patient, in which the ratio was between 2.0 and 2.5 had recognizable precipitating factors.

Overall, the low rate of valve-related events in this study, such as thromboembolism and endocarditis compared favorably with the results obtained from other larger series of aortic root replacements [11]. Prasongsukarn et al. [12] recently compared mechanical and bioprosthetic valves in patients 61 to 70 years in terms of combined major valve-related complications and revealed no difference between biologic and mechanical valves in terms of valve-related reoperation and mortality.

Tyers et al. [13] have noted that patients with bioprostheses were more likely to require valve-related reoperation than were those with mechanical prostheses. However, mortality from reoperation secondary to bioprosthetic aortic struc-

tural failure can be decreased by reoperation in patients with a low, rather than medium to high, NYHA functional class [14]. Jamieson et al. [15] compared composites of valve-related complications in biologic and mechanical heart valves in terms of mitral valve replacement. In that report, mechanical prostheses had a greater than 94% actual freedom from valve-related reoperation in all age groups at 12 to 15 years. Like prior series, our study found that patients in the homograft and the freestyle groups may have had a higher risk of reoperation than those in the mechanical group, but all groups may have similar rates of causes leading to reoperation (valve failure, infective endocarditis, ascending aorta dilatation, and ascending aorta pseudoaneurysm).

The most important limitation of this study is that it is not a prospective, randomized, controlled study but a single-institution retrospective review susceptible to inherent selection biases. The patients in the mechanical group, freestyle group, and homograft group were also very heterogeneous and dissimilar with regard to preoperative characteristics and operative indications. The size of the series is also relatively small, and the extent of follow-up is limited beyond 10 years. This latter point is quite important, particularly because it is in the 10- to 15-year time interval when most of the reported cases of structural valve degeneration occur in aortic allografts [16-18]. Therefore, a specific comparison of long-term durability in the mechanical valve conduit, freestyle, homograft conduit aortic root replacement groups would require a longer period of follow-up than provided in this study.

CONCLUSION

Our data suggest that aortic root replacement with a mechanical valve conduit is safe and achieves favorable outcomes similar to those of patients receiving homograft or freestyle valve conduits. When choosing the type of valve in aortic root replacement, it is worth considering a number of patient-specific factors, including age, comorbidities, and the risk of hemorrhage and thromboembolism.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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