

Surgical Management of Aortic Root Dilatation with Advanced Aortic Regurgitation: Bentall Operation versus Valve-sparing Procedure

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Background: Although the aortic valve-sparing procedure has gained popularity in recent years, it still remains challenging in patients with advanced aortic regurgitation (AR). We compared the long-term outcomes of the aortic valve-sparing procedure with the Bentall operation in patients with advanced aortic regurgitation secondary to aortic root dilatation. **Materials and Methods:** A retrospective review of 120 patients who underwent surgery for aortic root dilatation with moderate to severe AR between January 1999 and June 2009 was performed. Forty-eight patients underwent valve-sparing procedures (valve-sparing group), and 72 patients underwent the Bentall procedure (Bentall group). The two groups' overall survival, valve-related complications, and aortic valve function were compared. **Results:** The mean follow-up duration was 4.9 ± 3.1 years. After adjustment, the valve-sparing group had similar risks of death (hazard ratio [HR], 0.61; $p=0.45$), and valve related complications (HR, 1.27; $p=0.66$). However, a significant number of patients developed moderate to severe AR in the valve-sparing group at a mean of 4.4 ± 2.5 years of echocardiographic follow-up ($p < 0.001$). **Conclusion:** Both the Bentall operation and aortic valve-sparing procedure showed comparable long-term clinical results in patients with advanced aortic regurgitation with aortic root dilatation. However, recurrent advanced aortic regurgitation was more frequently observed following valve-sparing procedures.

Key words: 1. Aortic root
2. Aortic valve insufficiency
3. Bentall operation
4. Aortic valve repair

INTRODUCTION

Although the Bentall operation has been considered the 'gold standard' in the management of combined aortic valve (AV) and ascending aorta pathology [1], AV-sparing procedures have gained popularity in recent years because of benefits such as the minimum risk of systemic thromboembolic

complications, no requirements for lifelong anticoagulation, and hemodynamic superiority to the Bentall operation [2]. As the surgical techniques of the AV-sparing procedures have evolved over time, several groups have reported excellent durability of valve-sparing surgeries, comparable to the Bentall operation, in patients with aortic regurgitation (AR) associated with aortic root dilatation [3,4]. However, concerns still exist

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about the durability of AV-sparing procedures despite their advantages, especially in patients with advanced AR with aortic root dilatation. Furthermore, it remains controversial whether the advantages of AV-sparing procedures, despite the unreliable long-term durability, outweigh the benefits of the Bentall operation. We therefore compared the clinical outcomes of AV-sparing procedures and the Bentall operation in patients with advanced AR associated with aortic root dilatation.

MATERIALS AND METHODS

1) Patients

Between January 1999 and June 2009, 205 patients underwent operations for moderate to severe AR (grades 3 and 4) associated with aortic root dilatation. Patients who had a congenital anomaly of the AV or severe leaflet pathology were excluded from the present study; 120 patients were included. Of the 120, 72 underwent a Bentall operation (Bentall group) and 48 underwent AV-sparing procedures (valve-sparing group). The choice of surgical technique was at the attending surgeon's discretion.

2) Surgical techniques

Operations were performed by one of four surgeons. Patients in the Bentall group underwent aortic root replacement with a composite valve graft using standard methods. Aortic root reconstruction was made by reduction of the sinotubular junction (n=27) or sinotubular junction+annulus (n=11), or the reimplantation or remodeling technique (David I, n=7; David II, n=3). AV leaflet procedures were performed in cases of leaflet fenestration or asymmetry (n=18). The distal extent of aorta replacement was determined according to the extent of the dilated aorta.

3) Follow-up

Data were obtained up to March 2010, and were collected during regular visits to the outpatient clinic or by telephone interviews. Operative mortality was defined as death within 30 days of surgery or in-hospital death. Deaths were classified as cardiac or non-cardiac on the basis of medical records. All deaths were considered of cardiac origin unless a

non-cardiac origin was established clinically.

The end point of the study was defined as the composite of death and valve-related complications. Valve-related complications included thromboembolic events, infective endocarditis, bleeding complications secondary to anticoagulation, or the need for reoperation during follow-up. Bleeding secondary to anticoagulation was defined as any requirement for transfusion, unplanned hospital admission or a hemostatic intervention.

4) Statistical analysis

Categorical variables are presented as frequencies and percentages, and continuous variables are expressed as mean \pm standard deviation. Differences in baseline characteristics between patients who underwent a Bentall operation or valve-sparing procedures were compared using the t-test or the Mann-Whitney U-test for continuous variables and the chi-squared test or Fisher's exact test for categorical variables, as appropriate. Cumulative incidence rates of individual and composite outcomes were estimated by the Kaplan-Meier method and compared using the log-rank test. To reduce the impact of treatment selection bias and potential confounding in this observational study, we performed rigorous adjustments for the significant differences in patient characteristics by using weighted Cox proportional-hazards regression models and inverse-probability-of-treatment weighting (IPTW) [5,6]. With that technique, weights for patients receiving a Bentall operation were the inverse of the propensity score (1 minus propensity score), and weights for patients receiving AV sparing procedures were the inverse of the propensity score. The propensity scores were estimated by multiple logistic-regression analysis [5]. All prespecified covariates were included in full nonparsimonious models for AV sparing procedures, versus the Bentall operation (Tables 1, 2). The discrimination and calibration abilities of each propensity score model were assessed by C statistics and the Hosmer-Lemeshow test. The model was well calibrated (Hosmer-Lemeshow test; p=0.651) with reasonable discrimination (C statistic=0.965). The results were expressed as hazard ratio (HR) with 95% confidence interval. All reported p values are two-sided, and values of p < 0.05 were considered statistically significant. SAS ver. 9.1 (SAS Inc., Cary, NC, USA) was used for statistical analysis.

Table 1. Preoperative data

	Bentall group (n=72)	Valve-sparing group (n=48)	p-value
Sex			
Male	45 (62.5)	34 (71.3)	0.43
Age (yr)	49±16	54±13	0.102
Diabetes mellitus	4 (5.6)	3 (6.3)	1.00
Hypertension	24 (33.3)	12 (25)	0.168
Dyslipidemia	7 (9.7)	3 (6.3)	0.738
Glomerular filtration rate (mL/min)	87±22	79±26	0.356
Coronary disease	14 (19.4)	2 (4.2)	0.016 ^{a)}
Previous heart surgery	2 (2.8)	1 (2.1)	1.00
NYHA class			0.224
I	38 (52.8)	33 (68.8)	
II	19 (26.4)	11 (22.9)	
III	12 (16.7)	3 (6.3)	
IV	3 (4.2)	1 (2.1)	
Marfan syndrome	19 (26.4)	3 (6.3)	0.005 ^{a)}
Annuloaorticectasia	64 (88.9)	28 (58.3)	<0.001 ^{a)}
Aortic dissection	20 (27.8)	12 (25)	0.736
Aortitis (Takayasu's, Behcet's)	5 (7)	0	0.082
Aortic regurgitation grade			0.022 ^{a)}
3	10 (13.9)	15 (31.3)	
4	62 (86.1)	33 (68.8)	
LV ejection fraction (%)	51±12	51±10	0.527
LV systolic dimension (mm)	50±12	48±12	0.469
LV diastolic dimension (mm)	71±12	50±11	0.366
Maximal aortic root diameter (mm)	63.3±15	57.7±11	0.044 ^{a)}
Urgency or emergency	11 (15.3)	11 (22.9)	0.514

Values are presented as number (%) or mean±standard deviation. NYHA, New York Heart Association; LV, left ventricle.
^{a)}p<0.05.

RESULTS

1) Preoperative characteristics

Preoperative clinical characteristics are shown in Table 1. Patients in the Bentall group were significantly more likely to have Marfan syndrome, annuloaorticectasia, and severe AR than those in the valve-sparing group. The maximal aortic

Table 2. Operative profiles

	Bentall group	Valve-sparing group	p-value
Surgical year			<0.001
1999–2001	33 (45.8)	5 (10.4)	
2002–2005	9 (12.5)	39 (81.3)	
2006–2009	30 (41.7)	4 (28.3)	
Extent of aortic repair			0.04 ^{a)}
Ascending aorta	59 (81.9)	38 (79.2)	
Ascending aorta+hemiarch	13 (18.1)	6 (12.5)	
Ascending aorta+total arch	0	4 (8.3)	
Open distal anastomosis	14 (19.4)	12 (25.0)	0.423
Brain protection ^{b)}			0.003 ^{a)}
Selective cerebral perfusion	3 (4.2)	0	
TCA	5 (6.9)	0	
Selective perfusion+TCA	6 (8.3)	12 (25)	
Associated procedure	8 (11.1)	6 (12.5)	0.816
Coronary artery bypassing	4	1	
Mitral repair	3	3	
Tricuspid repair	1	2	
CPB time (min)	196±88	203±68	0.941
ACC time (min)	131±37	135±46	1.00
Circulatory arrest time (min) ^{b)}	25±10	32±21	0.853

Values are presented as number (%) or mean±standard deviation. TCA, total circulatory arrest; CPB, cardiopulmonary bypass; ACC, aortic cross clamp.

^{a)}p<0.05.

^{b)}For patients who underwent open distal anastomosis.

root diameter was larger in the Bentall group. Other characteristics were not significantly different between the two groups. Follow-up was complete in 103 (86%) patients with a mean follow-up duration of 4.86±3.1 years.

2) Operative profiles

Table 2 shows the perioperative profiles of the two groups. Total arch replacement was more frequently performed in the valve-sparing group. For patients who underwent open distal anastomosis, retrograde cerebral perfusion and total circulatory arrest were preferred for brain protection in the valve-sparing group whereas antegrade cerebral perfusion or

Table 3. Operative outcomes

	Bentall group	Valve-sparing group	p-value
Early outcomes			
Operative mortality	2 (2.4)	0	0.358
LCOS	2 (2.4)	0	0.358
Stroke	1 (1.4)	1 (2.1)	1.00
Requirement for dialysis	0	2 (4.2)	0.158
Bleeding re-exploration	6 (8.3)	2 (4.2)	0.474
Sternal infection	2 (2.4)	2 (4.2)	1.00
Atrial fibrillation	11 (15.3)	7 (14.6)	0.892
Pericardial effusion	0	2 (4.2)	0.158
Late outcomes			
Late death	5 (6.9)	5 (10.4)	1.00
Cardiac-related	3 (4.2)	1 (2.1)	0.114
Unknown	2 (2.4)	4 (8.3)	0.058
Reoperation	4 (5.6)	7 (14.6)	0.125
Aortic root-related	1 (1.4)	7 (14.6)	0.400
Anticoagulation-related hemorrhage	4 (5.6)	0	0.158
Thromboembolism (stroke)	0	1 (2.1)	
Infective endocarditis	0	2 (4.2)	

Values are presented as number (%).
LCOS, low cardiac output syndrome.

total circulatory arrest was used in the Bentall group. From 2002 to 2005, valve-sparing procedures were performed in a significantly larger number of patients. Since 2006, the Bentall operation has been performed more frequently at our institution due to the surgeon’s personal preference.

3) Clinical outcomes

Operative mortality occurred in two patients (2.4%) only in the Bentall group. One died of postoperative low cardiac output syndrome and the other died of an unknown cause three days after discharge. There were no significant differences in operative mortality and morbidity between the two groups, as shown in Table 3.

There were ten late deaths during follow-up including four cardiac-related deaths. The causes of the cardiac-related deaths included postoperative low cardiac output syndrome following the reoperation in two patients: one from each group, one type III aortic dissection in the Bentall group, and one warfarin-related cerebral hemorrhage in the Bentall group.

Overall 5-year survival rates were 88.4±5.2% in the Bentall

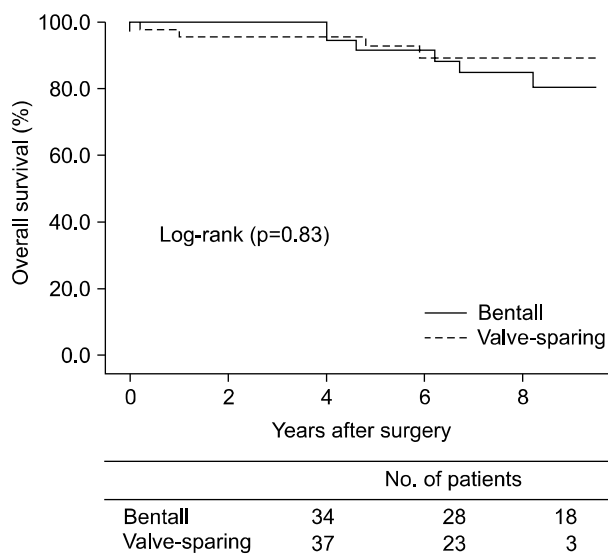


Fig. 1. Kaplan-Meier curve for overall survival.

group and 90.8±4.4% in the valve-sparing group (Fig. 1).

A total of 11 patients required reoperation during follow-up. The mean time to reoperation for the Bentall group and valve-sparing group was 4.29±3.4 years and 4.82±2.6 years, respectively (p=0.274). In the valve-sparing group, seven patients underwent reoperation for recurrence of significant AR. Among them, two patients experienced infective endocarditis with significant AR about 4 years after the valve-sparing procedure. Despite the failure of identification of the pathogen, reoperation with a mechanical prosthesis was performed without any operative complications. Among the five remaining patients, with significant AR, one underwent AV re-repair, two underwent AV replacement, and two underwent Bentall operations resulting in one operative death. In the Bentall group, four required reoperation for recurrent AR (n=1), type III aortic dissection (n=1), and other valvular diseases (n=2). Overall, freedom from reoperation at five years was 93.9±4.2% in the Bentall group and 81.8±6.3% in the valve-sparing group (Fig. 2). Although the overall reoperation rate was not significant between the groups, the rate of reoperation for recurrent significant AR was higher in the valve-sparing group with marginal significance (p=0.058).

Details of other late complications are described in Table 3. Incidences of prosthetic valve-related complications were not significantly different between the two groups. Freedom from

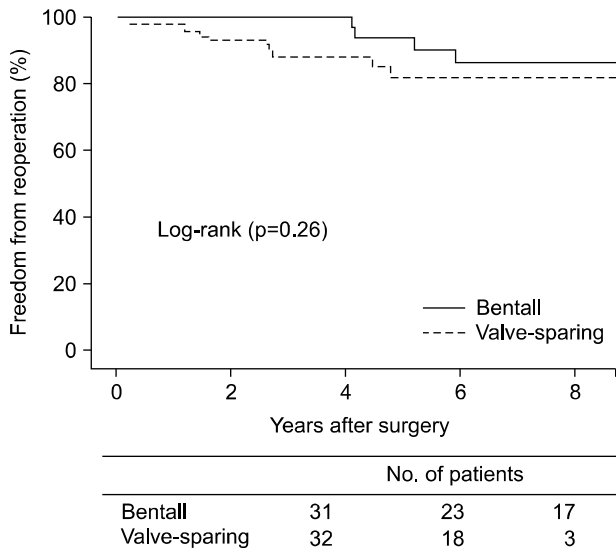


Fig. 2. Kaplan-Meier curve for freedom from reoperation.

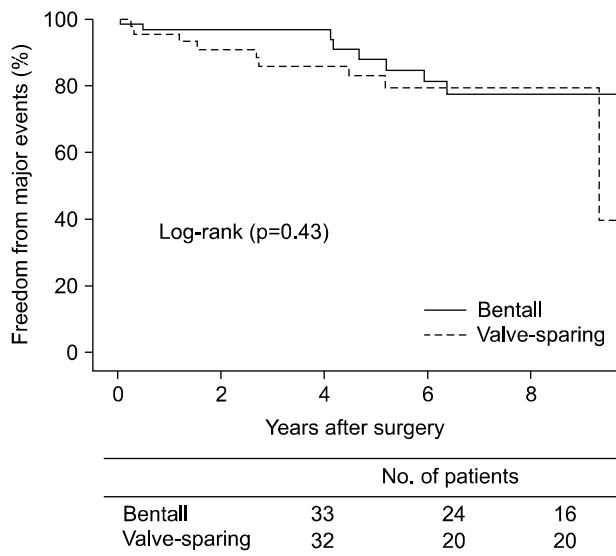


Fig. 3. Kaplan-Meier curve for freedom from major events.

major events which include valve-related complications was 88.2±5.2% for the Bentall group and 83.3±5.8% for the valve-sparing group at five years (Fig. 3).

After adjustment with the Cox-proportional hazards model and IPTW, the valve-sparing group had similar risks of death (HR, 0.61; p=0.45), of valve related complications (HR, 1.27; p=0.66), and of the composite of death and valve-related complications (HR, 0.90; p=0.82), compared with the Bentall group.

Table 4. Echocardiographic assessments for left ventricular and aortic valvular function on last follow-up

	Bentall group	Valve-sparing group	p-value
Follow-up duration (yr)	4.58±3.47	5.28±2.4	0.319
LV ejection fraction (%)	53±12	57±9	0.662
LV systolic dimension (mm)	37±10	37±10	0.781
LV diastolic dimension (mm)	53±10	55±10	0.085
Aortic regurgitation grade	1 (1.4)	10 (20.8)	<0.001 ^{a)}
3	1 (1.4)	6 (12.5)	
4	0	4 (8.3)	

Values are presented as mean±standard deviation or number (%). LV, left ventricle.

^{a)}p<0.05.

4) Echocardiographic evaluation for aortic valve function

Table 4 shows the echocardiographic parameters of the left ventricular function and the degree of AR on last trans-thoracic echocardiography (TTE) follow-up. Although there were no significant differences in the left ventricular ejection fraction and dimensions between the two groups, a greater number of patients in the valve-sparing group developed moderate to severe AR after surgery than in the Bentall group at the mean echocardiographic follow-up of 4.4±2.5 years (p <0.001). One case of significant recurrent AR in the Bentall group was associated with degeneration of a bioprosthesis.

DISCUSSION

As an alternative to the composite valve graft replacement, valve-sparing procedures for aortic root dilatation with or without AR have been performed by many surgeons and have demonstrated durable valve function [4,7]. With the evolution of the techniques of valve-sparing surgery, the indications for valve-sparing surgery have been expanded to more complex patients [8,9]. However, valve-sparing surgery remains a complex procedure and concerns remain regarding postoperative valve dysfunction, particularly in patients with severe pre-operative AR [10]. Despite several reports demonstrating the feasibility of correcting severe AR with a valve-sparing procedure [10-12], long-term outcome data with a large cohort have not been available. Badiu et al. [11] favored valve-spar-

ing surgery for severe AR and were also concerned that preoperative severe AR may play a role in the development of recurrent moderate AR after valve-sparing surgery and reoperation. In our study, the study population was limited to patients who had moderate to severe AR preoperatively. There was no operative mortality in the valve-sparing group and the immediate postoperative mean AR grade was grade 1, which was an acceptable early result. However, aggravation of AR was noticed more in the valve-sparing group during follow-up, and seven patients had to undergo reoperation for recurrent AR. In addition, except for those seven patients, a significant number of the patients in the valve-sparing group revealed AR of more than grade 3 ($p < 0.001$) in the last echocardiographic data. It is predictable that the reoperation rate would be higher in the valve-sparing group at longer follow-up with statistical significance.

In terms of the valve-sparing procedure techniques, there is a lack of standardization in the wide variety of published techniques [13]. Lansac et al. [14] suggested lesion classification for standardizing surgical management. We also applied several valve-sparing techniques according to the pathology of the AR and root dilatation. In 18 patients, an additional AV leaflet procedure was performed. As valve-sparing procedures require a surgeon's experience and comprehensive understanding of the aortic root as a dynamic unit [15], the techniques of valve-sparing procedure may influence the recurrent AR. Among the 10 patients who had significant recurrent AR following the valve-sparing procedure, 6 patients (60%) underwent David I or II operations, and the remaining ones underwent other valve-sparing techniques. However, no predictable factor for recurrent AR was identified in the valve-sparing technique. Most of the recurrent AR was eccentric AR caused by a leaflet prolapse on TTE. This may indicate that the leaflet repair procedure is important in valve-sparing surgery for patients with advanced AR.

It remains controversial that the Bentall procedure can be the preventive alternative to valve-sparing surgery in high-risk patients with advanced AR secondary to aortic root dilatation. Although the Bentall operation is considered to have a higher risk of thromboembolism, anticoagulation-related complications, and endocarditis, the actual rate of overall valve-related complications is low in the Bentall patients and similar to

that in the valve-sparing patients [16]. In addition, the Bentall operation is technically reproducible and has demonstrated favorable long-term results with a low reoperation rate [17,18]. In our study, the Bentall operation showed low mortality and morbidity and also demonstrated that the incidence of valve-related complications in the Bentall group was not significantly different than the valve-sparing group.

In conclusion, both valve-sparing procedures and the Bentall operation can be performed in patients with advanced AR secondary to aortic root dilatation with low mortality and morbidity. The incidence of valve-related complications of the Bentall operation is quite low and similar to that of the AV-sparing procedure. However, the progression of recurrent AR following the AV-sparing procedure, which may lead to an increased risk of reoperation, was noted. Therefore, AV-sparing procedures should be performed with caution in patients with advanced AR.

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