Comparison between valve-sparing root replacement and Bentall procedure in patients with Marfan syndrome

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Background: Bentall procedure is standard procedure for aortic root aneurysm or dissection in patients with Marfan syndrome. The purpose of this study was to evaluate whether valve-sparing root replacement (VSR) can be an alternative to Bentall procedure in patients with Marfan syndrome.
Methods: Thirteen patients with Marfan syndrome underwent aortic root replacement between 1999 and 2017. Bentall procedure with a mechanical valve was performed in 9 patients and VSR was performed in 4. The mean durations of follow-up were 103.1 ± 61.6 months in Bentall and 35.0 ± 26.4 months in VSR.
Results: There was no in-hospital death in both procedures. Reoperation for bleeding was performed in one patient after Bentall procedure. One patient died because of unknown cause in the Bentall group. No death occurred in the VSR group during a follow-up period. There was no difference in mortality between two groups. In the Bentall group, subarachnoid hemorrhage was developed in one patient and cerebral hemorrhage in one, while there was no hemorrhage or thromboembolism in the VSR group. Echocardiography showed improvement of aortic valve regurgitation grade (pre-operation 2.9 ± 1.4 vs post-operation 0.5 ± 0.4, P = 0.03) in all patients of the VSR group, and there was no reoperation for aortic valve after VSR.
Conclusion: The significant inferiority of both early and late result in VSR could not be observed. VSR avoids the risk of complications associated with anticoagulation, which can be a preferable alternative to Bentall procedure in patients with Marfan syndrome.

ACTA MEDICA NAGASAKIENSIA 62: 95−100, 2019

Key words: Marfan syndrome, aortic root replacement, Bentall procedure, valve-sparing root replacement

Introduction

Marfan syndrome is a genetic connective tissue disorder due to mutation of the fibrillin 1 gene. The patients with Marfan syndrome often have dilatation of proximal aorta and annulus, which results in aortic rupture or dissection. Aortic root replacement is indicated for aortic root aneurysm or dissection. Bentall procedure was first described in 1968 by Bentall and De Bono.[1] It is complete replacement in ascending aorta with composite valve graft. It has been the standard procedure for aortic root aneurysm or dissection in patients with Marfan syndrome. Due to the relatively young age of patients with Marfan syndrome, the use of a mechanical valve is often necessary. Implantation of a mechanical valve needs life-long anticoagulation, so they are exposed to the risk of thromboembolic and hemorrhagic complications.[2] In recent years, valve-sparing root replacement (VSR) has been preferred procedure for aortic root aneurysm. Due to preservation of the native aortic valve, VSR doesn't need anticoagulation. However, in patients with Marfan syndrome, because of the presence of abnormal fibrillin in the aortic valve, the application of VSR was initially questioned.[3] Several reports have shown that the 2 procedures had similar long-term survival, freedom from reoperation, and VSR resulted in

fewer thromboembolic and hemorrhagic complications in patients with Marfan syndrome.[4, 5, 6, 7] Accordingly, in this study, the result of VSR in patients with Marfan syndrome in our institution was compared with the result of Bentall procedure to evaluate whether VSR can be an alternative to Bentall procedure in patients with Marfan syndrome.

Patients and Methods

Thirteen patients with Marfan syndrome (mean age 43.5 $\pm$ 12.2 years old) who underwent aortic root replacement between April 1999 and March 2017 at Nagasaki University Hospital were studied. All patients are diagnosed Marfan syndrome by the Ghent and/or revised Ghent criteria.[8, 9] Nine patients underwent Bentall procedure, and 4 underwent VSR. The clinical data was collected retrospectively. Operations were performed for aortic root aneurysm in 8 patients, acute dissection in 3 patients and chronic dissection in 2 patients. The primary endpoint of the study was all-cause mortality. Early mortality was defined as death before hospital discharge. The secondary endpoint of the study was major adverse events included prosthetic valve dysfunction, reoperation, thromboembolism, hemorrhage, endocarditis, or permanent

pacemaker insertion.[10] The mean duration of follow-up was 82.2 $\pm$ 61.6 months (103.1 $\pm$ 61.3 months in Bentall group and 35.0 $\pm$ 26.4 months in VSR group, P = 0.064).

Statistical analysis

Data are expressed as mean $\pm$ standard deviation or number (percentage). The student t-test, the Mann-Whitney U test or the $\chi 2$ test was performed to compare groups. A p-value less than 0.05 was considered to be statistically significant. All statistical analyses were performed with JMP for Windows (ver. 14; SAS institute Inc., Cary, NC).

Results

Preoperative characteristics

Mean pre-operative aortic valve diameter, Valsalva diameter, grade of aortic valve regurgitation (AR) in the total study patient are 29 $\pm$ 4.6 mm, 56.3 $\pm$ 12.5 mm and 2.7 $\pm$ 1.4, respectively. Table 1 shows the pre-operative clinical and echocardiographic data in each group. There was no significant difference between two groups.

Table 1. Preoperative Characteristics and echocardiographic data

Variables	Bentall (n = 9)	VSR (n = 4)	p-value
Age (years)	44.2 $\pm$ 13.6	42.0 $\pm$ 8.0	0.535
Male gender	4 (44.4%)	2 (50%)	0.859
Height (cm)	169.3 $\pm$ 8.9	171.8 $\pm$ 3.2	0.532
Weight (kg)	51.1 $\pm$ 8.8	54.9 $\pm$ 1.8	0.395
BSA (cm^2)	1.58 $\pm$ 0.2	1.65 $\pm$ 0.01	0.314
Hypertension	7 (77.8%)	1 (25%)	0.083
Surgical indication			0.723
aortic root aneurysm	5 (55.6%)	3 (75%)	
acute aortic dissection	3 (33.3%)	0	
chronic aortic dissection	1 (11.1%)	1 (25%)	
Valsalva sinus diameter (mm)	58.9 $\pm$ 12.7	50.5 $\pm$ 9.8	0.642
Aortic valve annulus diameter (mm)	30.7 $\pm$ 4.2	25.3 $\pm$ 2.8	0.639
AR grade	2.67 $\pm$ 1.3	2.88 $\pm$ 1.4	0.467
AR $\geqq$ 2	6 (66.7%)	3 (75%)	0.773

AR: aortic valve regurgitation

VSR: valve-sparing root replacement

Operative data

As shown in Figure 1, we performed Bentall procedure for 8 patients between 1999 and 2012. After 2013, 5 patients underwent operation and we accomplished VSR in 4 of them, and the other one was converted from VSR to Bentall procedure because of residual AR. Table 2 shows operative data. Operation time, Cardio-pulmonary bypass (CPB) time, Aortic cross clamp (ACC) time in the VSR group were significantly longer than Bentall group. Total or hemiarch replacement was performed in 7 patients (53.8%). All of 9 patients performed Bentall procedure with mechanical valve received an anticoagulation therapy with warfarin after surgery.
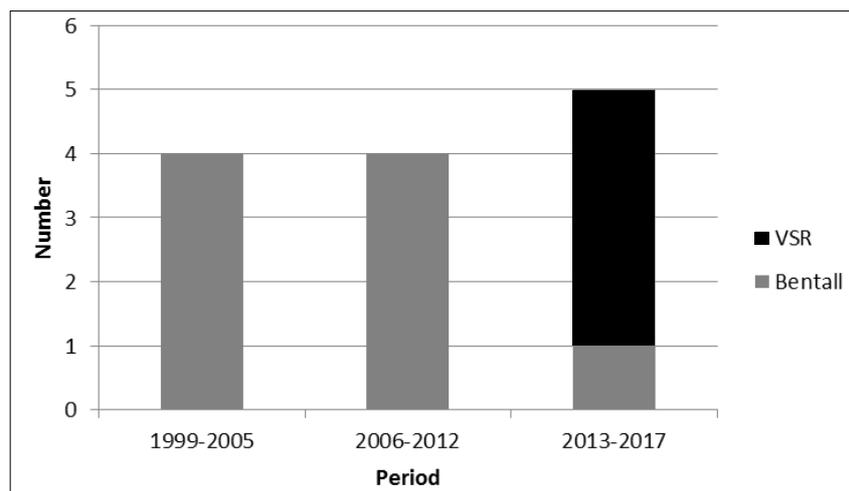

Figure. 1 The number of Bentall procedure and valve-sparing root replacement according to the surgical period. VSR: valve-sparing root replacement

Table 2. Operative data and concomitant procedures

Variables	Bentall (n = 9)	VSR (n = 4)	p-value
Operation time (min.)	385.1 ± 94.4	505.3 ± 59.2	0.031
CPB time (min.)	217.1 ± 69.2	295.8 ± 49.9	0.045
ACC time (min.)	139.9 ± 57.3	227.8 ± 43.1	0.021
Graft size (mm)	25.1 ± 1.4	25.5 ± 0.9	0.276
Prosthetic valve size (mm)	22 ± 1.5		
Concomitant procedures	6 (66.7%)	3 (75%)	0.773
Total or Hemiarch replacement	4 (44.4%)	3 (75%)	
MVR/MP	1 (11.1%)	0	
AVP	0	1 (25%)	
CABG	1 (11.1%)	0	
ASD closure	1 (11.1%)	0	

CPB: Cardio-pulmonary bypass
ACC: Aortic cross clamp
MVR: mitral valve replacement
MP: mitral valve plasty
AVP: aortic valve plasty
CABG: coronary artery bypass graft
ASD: atrial septal defect
VSR: valve-sparing root replacement

Early results

There was no early death in the both groups. Reoperation for bleeding was performed in one patient in the Bentall group. There was no stroke or thromboembolism in the both groups during hospital stay. The mean duration of intensive care unit (ICU) stay and hospital stay after surgery in the total study patients were 3.3 ± 2.6 days and 28.2 ± 7.5 days, respectively. ICU stay and hospital stay after operation were not significantly different between the 2 groups (Table 3).

Late results

There was one late death with unknown cause in the Bentall group 6 years after surgery, while no death in the VSR group. No statistical difference in late death between two groups was observed (P=0.50). In the Bentall group, subarachnoid hemorrhage occurred in one patient 4 years after surgery, and cerebral hemorrhage in one 14 years after surgery. On the other hand, there were no hemorrhagic and thromboembolic complications in the VSR group. There was no endocarditis or permanent pacemaker insertion in the both groups. Echocardiography showed improvement of the grade of AR (2.9 ± 1.4 at pre-operation and 0.5 ± 0.4 at post-operation, P = 0.03) and there was no reoperation for the post-operative aortic valve dysfunction in the VSR group.

Discussion

The major surgical procedures for aortic root aneurysm or dissection are Bentall procedure and VSR. Since the first description in 1968 by Bentall and De Bono,[1] Bentall procedure has been considered the standard procedure for aortic

Table 3. Early results

Variables	Bentall (n = 9)	VSR (n = 4)	p-value
ICU stay (days)	3.8 ± 3.0	2.3 ± 0.8	0.284
hospital stay (days)	30.8 ± 7.5	22.5 ± 3.4	0.064
early death	0	0	
reoperation for bleeding	1 (11.1%)	0	0.501
stroke	0	0	
thromboembolism	0	0	
endocarditis	0	0	
pacemaker insertion	0	0	

VSR: valve-sparing root replacement
ICU: intensive care unit

Table 4. Late results

Variables	Bentall (n = 9)	VSR (n = 4)	p-value
late death (> 30 days)	1 (11.1%)	0	0.501
reoperation for aortic valve	0	0	
stroke	2 (22.2%)	0	0.325
thromboembolism	0	0	
endocarditis	0	0	
pacemaker insertion	0	0	

VSR: valve-sparing root replacement

root replacement.[2] However, as implantation of a mechanical valve needs life-long anticoagulation, patients are exposed to the risk of thromboembolic and hemorrhagic complications.[2]

VSR procedures were described by David and Feindel in 1992[5], and Sarsam and Yacoub in 1993.[6] Because of the preservation of the native aortic valve in VSR, complications associated with prosthetic valve can be avoided.[2] David and colleagues reported that reimplantation of the aortic root, which is one of the types of VSR, was associated with excellent long-term survival and low rates of valve-related complications.[13] Lee and colleagues evaluated the outcomes of VSR procedure compared with Bentall procedure.[2] In their study, although the patients with both Marfan and non-Marfan were included, VSR showed comparable or better outcomes than Bentall procedure.

In patients with Marfan syndrome, because of the presence of abnormal fibrillin in the aortic valve, indication for VSR was initially questioned.[3] Long-term durability and the future requirement for reoperation for aortic valve dysfunction may be another concern. Benedotto and colleagues found that the probability of reoperation was 4 times higher after VSR than after Bentall procedure.[14] In contrast, David and colleagues showed VSR, particularly the reimplantation procedure for patients with Marfan syndrome were associated with low rates of valve-related complications in long-term follow up.[4] Several reports have shown that the 2 procedures had similar long-term survival, freedom from reoperation, and VSR resulted in fewer thromboembolic and hemorrhagic complications than Bentall in patients with Marfan syndrome.[4, 5, 6, 7]

In our study, 9 patients underwent Bentall procedure and 4 underwent VSR. The concern with the use of VSR may be its time-consuming nature because of the long suture line. The operation time, CPB and ACC times in VSR were significantly longer than those in Bentall procedure. However, no early mortality and morbidity were recorded in the VSR group. We experienced one conversion case from VSR to Bentall. That was an emergency case with ascending aorta dissection and therefore root remodeling technique which requires shorter suture line compared to reimplantation technique, was applied to reduce the ACC time. As a result, AR could not be controlled. In the emergency case, the procedure time for valve repair should be limited and we eventually decided the case to convert to valve replacement. Thus, possibility of repair failure may be another concern about VSR because of its technically demanding aspect. There was no significant statistical difference in early outcomes between the 2 groups. But, there were one late death and 2 stroke events in the Bentall group. On the other hand there was no overall death and no complication associated with anticoag-

ulation in the VSR group. If those are taking into consideration, VSR can be considered to be an alternative or possibly preferable to Bentall procedure in patients with Marfan syndrome.

The small number of study patients, and the difference in the follow-up period between the 2 groups are the limitations of our study. Further study with large number and long-term follow up is needed.

Conclusion

No statistical difference in early and late outcome between VSR and Bentall procedure was demonstrated. The number of study patients is not large enough to conclude, however, anticoagulation-related complications were avoided in all patients with VSR. Thus, our result suggests VSR as a preferable alternative to Bentall operation in Marfan syndrome patients with aortic root pathology.

Conflict of Interest

The authors declare no conflict of interest.

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