



Mid-term outcomes of simultaneous mitral valve repair in patients with mitral regurgitation and concomitant annulo-aortic ectasia

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Abstract

Objective This study investigated the mid-term outcomes of simultaneous mitral valve repair in patients with mitral regurgitation (MR) and concomitant annulo-aortic ectasia.

Methods The study included 26 patients with MR and annulo-aortic ectasia [mean age 46.0 ± 19.9 (10–86) years] who underwent simultaneous mitral valve repair between January 2007 and March 2018. Of these 26 patients, 11 (42.3%) were diagnosed with Marfan syndrome and 10 (38.5%) with Barlow's disease. All patients underwent complete ring annuloplasty; a semi-rigid ring was used in 14 (53.8%) and a semi-flexible ring (anterior-flexible) in 12 patients (46.2%). All patients underwent valve-sparing root replacement using the reimplantation technique.

Results The overall 3-year survival rate was $95.7 \pm 4.3\%$. The 3-year freedom from > moderate MR rate was $94.7 \pm 5.1\%$, and the 3-year freedom from > moderate aortic regurgitation (AR) rate was $86.7 \pm 7.3\%$. The 3-year freedom from reoperation rate was 100%. The 3-year freedom from > moderate MR rate was 100% in the semi-rigid ring group and $85.7 \pm 13.2\%$ in the semi-flexible ring group (log-rank test, $p = 0.5371$). The 3-year freedom from > moderate AR rate was 100% in the semi-rigid ring group and $72.9 \pm 16.5\%$ in the semi-flexible ring group (log-rank test, $p = 0.0815$).

Conclusions Simultaneous mitral valve repair in patients with MR and concomitant annulo-aortic ectasia showed favorable mid-term outcomes.

Keywords Valve-sparing root replacement · Aortic valve repair · Mitral valve repair · Annulo-aortic ectasia

Introduction

Patients with annulo-aortic ectasia (AAE) are often diagnosed with concomitant mitral valve prolapse (MVP), particularly younger patients and those with connective tissue disorders [1, 2]. Recently, techniques for mitral valve repair have been established with excellent long-term results [3]. Notably, valve-sparing root replacement (VSRR) is widely used as the standard technique for AAE repair, particularly in younger patients [4–6]. However, few reports in the literature have described simultaneous mitral valve repair and VSRR. Moreover, which type of mitral ring (rigid vs. flexible and whole vs. partial) affects aortic root dynamics

remains unclear [7–9]. This study investigated the mid-term outcomes after simultaneous mitral valve repair in patients with mitral regurgitation (MR) and concomitant AAE. Additionally, this study investigated the effect of the type of mitral valve ring on clinical outcomes.

Patients and methods

Study population

This retrospective study was approved by the Institutional Review Board of Kobe University Hospital. Individual informed consent was waived. Between January 2007 and March 2018, among the 333 patients who underwent VSRR using the reimplantation technique at Kobe University, 28 patients (8.4%) underwent simultaneous mitral valve repair for concomitant MR. The following 2 patients were excluded from the study: a patient in whom systolic anterior motion

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was observed and turned in mitral valve repair without mitral ring, and another patient who intraoperatively required conversion to aortic valve replacement secondary to significant residual aortic regurgitation (AR). Eventually, 26 patients (total group) were enrolled in this study. These 26 patients were categorized into 2 groups: the semi-rigid ring group comprising 14 patients (Carpentier–Edwards Physio II ring, Edwards®) and the semi-flexible ring group comprising 12 patients (Colvin–Galloway Future® Annuloplasty Ring: flexible at the anterior portion, Medtronic®). With regard to the selection of type of the mitral ring, a semi-flexible ring was used after it was available. Preoperative patient characteristics are presented in Table 1. The mean age was 46.0 ± 19.9 (10–86) years, and the study included 20 men and 6 women. The mean height was 169 ± 12 (138–203) cm, mean weight was 56 ± 13 (25–84) kg, and the mean body surface area was 1.71 ± 0.15 (1.45–1.94) m². Etiology of aortic root dilatation included connective tissue disease in 12 patients (46.2%) (Marfan syndrome in 11 and Loeys–Dietz syndrome in 1 patient), hypertension in 10 patients (38.5%), bicuspid aortic valve in 2 patients (7.7%), and pseudoaneurysm in 2 patients (7.7%). In this study, Marfan syndrome included all patients with Marfanoid habitus. The incidence of Marfan syndrome was higher in the semi-rigid than in the semi-flexible ring group [9 (64.3%) vs. 3 (25.0%), $p=0.0452$]. Notably, 3 patients (11.5%) reported a history of cardiac surgery, and 10 patients (38.5%) were diagnosed with Barlow’s disease. All patients in the semi-flexible ring group underwent surgery between 2012 and 2018 [semi-rigid ring ($N=14$) vs. semi-flexible ring ($N=12$), 6 (42.9%) vs. 12 (100%), $p=0.0016$]. All patients underwent preoperative transthoracic and/or transesophageal

echocardiography. Preoperative echocardiographic data are presented in Table 2. Notably, surgery is indicated in patients with > moderate MR. However, isolated mitral annuloplasty (MAP) or MAP with concomitant mitral valve plasty is performed (based on the type of mitral valve disease) even in patients with mild MR if they meet the following criteria: high risk of progression of MR secondary to mitral valve degeneration indicated by, for example, a dilated mitral annulus, or billowing or prolapse of the mitral valve. Therefore, this study included patients with mild MR.

Outcome measures of interest

The outcomes of interest were the rates of freedom from > moderate MR and AR in the entire cohort, as well as in the semi-rigid and semi-flexible ring groups.

Statistical analysis

We obtained data from patients’ medical records. Continuous variables [presented as mean \pm standard deviation (range)] were compared using the Student’s *t* test. Categorical variables (presented as numbers and percentages of patients) were compared using the Chi-square test. Rates of freedom from > moderate MR and AR were analyzed using the Kaplan–Meier method and compared using log-rank analysis. A p value < 0.05 was considered statistically significant. All statistical analyses were performed using the IBM SPSS software, version 22.00 (IBM, Inc., Chicago, IL, USA).

Table 1 Preoperative patient characteristics

Variables	Total ($N=26$)	Semi-rigid ring ($N=14$)	Semi-flexible ring ($N=12$)	p value (semi-rigid vs semi-flexible)
Age (years)	46.0 ± 19.9 (10–86)	41.5 ± 16.3 (13–65)	51.2 ± 22.9 (10–86)	0.2366
Male (n) (%)	20 (76.9)	11 (78.6)	9 (75.0)	0.8296
Body surface area (m ²)	1.71 ± 0.15 (1.45–1.94)	1.69 ± 0.17 (1.45–1.92)	1.72 ± 0.13 (1.48–1.94)	0.6728
Etiology				
Connective tissue disease (n) (%)	12 (46.2)	9 (64.3)	3 (25.0)	0.0452*
Marfan syndrome (n) (%)	11 (42.3)	9 (64.3)	2 (16.7)	0.0117*
Loeys–Dietz syndrome (n) (%)	1 (3.85)	0	1 (8.3)	0.2069
Hypertension (n) (%)	10 (38.5)	3 (21.4)	7 (58.3)	0.0538
Bicuspid aortic valve (n) (%)	2 (7.7)	1 (7.1)	1 (8.3)	0.9096
Pseudoaneurysm (n) (%)	2 (7.7)	1 (7.1)	1 (8.3)	0.9096
Operative date				
2007–2011	8 (30.8)	8 (57.1)	0	0.0016*
2012–2018	18 (69.2)	6 (42.9)	12 (100)	0.0016*

Continuous variables are presented as mean \pm standard deviation (range)

* $p < 0.05$

Table 2 Preoperative echocardiographic data

Variables	Total (N=26)	Semi-rigid ring (N=14)	Semi-flexible ring (N=12)	p value (semi-rigid vs semi-flexible)
LVDd (mm)	56.1 ± 13.9 (31–70)	59.6 ± 8.0 (31–70)	54.6 ± 8.2 (42–65)	0.2935
LVDs (mm)	38.5 ± 10.5 (23–64)	45.8 ± 12.9 (33–64)	35.7 ± 7.3 (23–46)	0.1609
LVEF (%)	62.8 ± 16.1 (31.3–80.8)	51.8 ± 19.3 (31–72)	68.6 ± 6.8 (60–80)	0.0639
AVJ (mm)	25.3 ± 2.7 (21.4–31.0)	25.4 ± 3.0 (23–31)	24.8 ± 2.6 (21–28)	0.8562
Valsalva sinus (mm)	43.7 ± 7.3 (33.1–56.7)	42.5 ± 5.8 (37–51)	44.3 ± 9.1 (33–57)	0.6481
STJ (mm)	33.2 ± 7.3 (23.2–49.5)	32.2 ± 5.7 (24–39)	33.8 ± 8.9 (23–50)	0.6759
Preoperative grade of MR				
None (n) (%)	0	0	0	NA
Trace (n) (%)	0	0	0	NA
Mild (n) (%)	5 (19.2)	2 (14.3)	3 (25.0)	0.4896
Moderate (n) (%)	8 (30.8)	3 (21.4)	5 (41.7)	0.2644
Severe (n) (%)	15 (57.7)	10 (71.4)	5 (41.7)	0.1234
Carpentier's classification of MR				
I (n) (%)	5 (19.2)	4 (28.6)	1 (8.3)	0.1772
II (n) (%)	15 (57.7)	8 (57.1)	7 (58.3)	0.9512
IIIb (n) (%)	5 (19.2)	2 (14.3)	3 (25.0)	0.4896
I+IIIb (n) (%)	1 (3.9)	0	1 (8.3)	0.2069
Preoperative grade of AR				
None (n) (%)	1 (3.9)	1 (7.1)	0	0.2593
Trace (n) (%)	4 (15.4)	3 (21.4)	1 (8.3)	0.3448
Mild (n) (%)	9 (34.6)	5 (35.7)	4 (33.3)	0.8987
Moderate (n) (%)	6 (23.1)	1 (7.1)	5 (41.7)	0.0323*
Severe (n) (%)	6 (223.1)	4 (28.6)	2 (16.7)	0.4685

Continuous variables are presented as mean ± standard deviation (range)

LVDd Left ventricular internal dimension diastole, LVDs left ventricular internal dimension in systole, LVEF left ventricular ejection fraction, AVJ aortoventricular junction, STJ sinotubular junction, MR mitral valve regurgitation, AR aortic valve regurgitation, NA not applicable

* $p < 0.05$

Results

Perioperative data

Perioperative details of all patients are presented in Table 3. Isolated MAP was performed in 7 patients (26.9%). Concomitant techniques used for mitral valve plasty included use of artificial chordae for reconstruction of the anterior leaflet in 15 patients, use of artificial chordae for reconstruction of the posterior leaflet in 3 patients, resection and suture of the posterior leaflet in 7 patients, the folding technique of posterior leaflet reconstruction in 1 patient, and bilateral Kay's suture annuloplasty in 1 patient. All patients underwent VSRR using the reimplantation technique. Concomitant aortic cusp repair was performed using techniques such as central plication in 11 patients, cusp reinforcement in 4 patients, repair with autologous pericardial patch in 3 patients, and resuspension in 2 patients (Fig. 1). A higher incidence of aortic cusp repair was observed in the semi-flexible

vs. the semi-rigid ring group [central plication: 7 (58.3%) vs. 4 (28.6%), $p = 0.0164$; patch repair: 3 (25.0%) vs. 0, $p = 0.0239$]. Other concomitant procedures performed included the Maze procedure in 6 patients (23.1%), tricuspid annuloplasty in 6 patients (23.1%), repair of an atrial septal defect in 3 patients (11.5%), and coronary artery bypass grafting, repair of a ventricular septal defect, partial anomalous pulmonary venous return repair, and partial arch replacement in 1 patient each (3.8%). Follow-up echocardiography was performed at discharge and each subsequent year thereafter.

The mean operative time was 458.1 ± 77.7 (343–687) min. The mean cardiopulmonary bypass time was 290.1 ± 37.2 (248–384) min, and the mean cardiac ischemia time was 236.9 ± 36.9 (174–299) min. Perioperative complications included pulmonary artery injury, left atrial injury, and right coronary artery transection in 1 patient each. Post-operative intubation time, intensive care unit stay, and in-hospital stay were 9.8 ± 7.6 (3–30) h, 3.4 ± 2.2 (1–12) days, and 25.4 ± 6.7 (18–44) days, respectively.

Table 3 Perioperative details

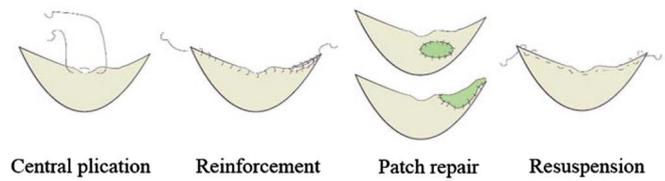
Variables	Total (N=26)	Semi-rigid ring (N=14)	Semi-flexible ring (N=12)	p value (semi-rigid vs semi-flexible)
Cross-clamp time (min)	237 ± 37 (174–299)	236 ± 42 (174–297)	237 ± 33 (196–299)	0.9665
Barlow disease	10 (38.5)	6 (42.9)	4 (33.3)	0.6180
Mean ring size (mm)	31.7 ± 3.2 (26–38)	31.5 ± 4.2 (26–38)	31.8 ± 1.6 (30–34)	0.8172
The patients with isolated MAP	7 (26.9)	4 (28.6)	3 (25.0)	0.8376
Concomitant mitral valve plasty [†]				
Reconstruction of artificial chordae (n) (%)	15 (57.7)	8 (57.1)	7 (58.3)	0.9512
For anterior leaflet (n) (%)	15 (57.7)	8 (57.1)	7 (58.3)	0.9512
For posterior leaflet (n) (%)	3 (11.5)	1 (7.1)	2 (16.7)	0.4470
Resection and suture for posterior leaflet (n) (%)	7 (26.9)	4 (28.6)	3 (25.0)	0.8376
Folding for posterior leaflet (n) (%)	1 (3.9)	1 (7.1)	0	0.2593
Kay’s annuloplasty (n) (%)	1 (3.9)	0	1 (8)	0.2319
Mean graft size (mm)	26.7 ± 1.6 (24–30)	26.0 ± 1.6 (24–28)	27.1 ± 1.5 (26–30)	0.1817
Procedure of aortic valve repair [†]				
None (n) (%)	11 (42.3)	8 (57.1)	3 (25.0)	0.0982
Central plication (n) (%)	11 (42.3)	4 (28.6)	7 (58.3)	0.0164*
Cusp reinforcement (n) (%)	4 (15.4)	1 (7.1)	3 (25.0)	0.2026
Patch repair (n) (%)	3 (11.5)	0	3 (25.0)	0.0239*
Resuspension (n) (%)	2 (7.7)	2 (14.3)	0	0.1056

Continuous variables are presented as mean ± standard deviation (range)

MAP Mitral annuloplasty

*p < 0.05. †shows including duplications

Fig. 1 Figures present schema of aortic cusp repair including central plication, reinforcement, patch repair, and resuspension



	Central plication	Reinforcement	Patch repair	Resuspension
Total (N= 26)	11 (42%)	4 (15%)	3 (12%)	2 (8%)
Semi-rigid ring (N= 14)	4 (29%)	1 (7%)	0	2 (14%)
Semi-flexible ring (N= 12)	7 (58%)	3 (25%)	3 (25%)	0

Short- and long-term outcomes

No in-hospital mortality was reported. Postoperative complications included pacemaker implantation for sick sinus syndrome in 2 patients (7.7%), complete atrioventricular block in 2 patients (7.7%), atrial fibrillation in 2 patients (7.7%), mediastinitis, and low cardiac output syndrome in 1 patient each (3.8%). The overall 3-year survival rate was 95.7 ± 4.3%. The mean follow-up period was 4.33 ± 3.27 (0.2–15) years. The 3-year freedom from > moderate MR rate was 94.7 ± 5.1% (Fig. 2). The mean follow-up period was 4.06 ± 3.72 years. During follow-up,

2 patients developed moderate MR. The 3-year freedom from > moderate AR rate was 86.6 ± 7.3% (Fig. 3). The mean follow-up period was 3.83 ± 3.84 years. During follow-up, 4 patients developed moderate AR. The 5-year freedom from reoperation rate was 100%. We performed an intergroup comparison of patients who underwent mitral valve repair using semi-rigid and semi-flexible rings. The 3-year freedom from > moderate MR rate was 100% in the semi-rigid ring group and 85.7 ± 13.2% in the semi-flexible ring group (log-rank test, p = 0.5371). The 3-year freedom from > moderate AR rate was 100% in the semi-rigid ring group and 72.9 ± 16.5% in the semi-flexible ring

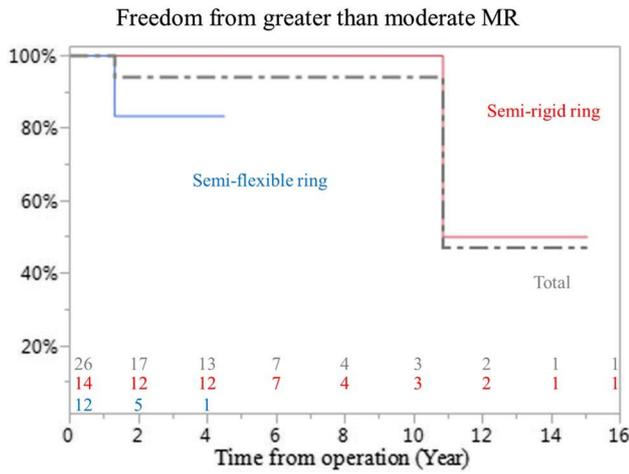


Fig. 2 Kaplan–Meier curves show freedom from greater than moderate MR in the patients underwent simultaneous repair of mitral and aortic valve (gray dot line: total, red line: semi-rigid ring group, blue line: semi-flexible ring group). MR mitral regurgitation

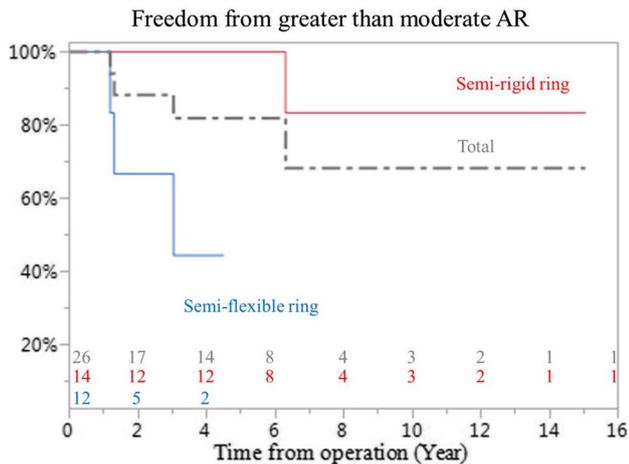


Fig. 3 Kaplan–Meier curves show freedom from greater than moderate AR in the patients underwent simultaneous repair of mitral and aortic valve (gray dot line: total, red line: semi-rigid ring group, blue line: semi-flexible ring group). AR aortic regurgitation

group (log-rank test, $p=0.0815$). No significant intergroup differences were observed in the rates of freedom from > moderate MR and AR.

The following factors were analyzed to determine their effect on freedom from > moderate MR rates. The 3-year freedom from > moderate MR rate in Barlow’s disease vs. non-Barlow’s disease was 100% vs. $88.9\% \pm 10.5\%$ (log-rank test, $p=0.9668$), MAP with mitral valve plasty vs. isolated MAP was $91.7 \pm 8.3\%$ vs. 100% at 3 years (log-rank test, $p=0.4167$), and Carpentier’s classification of MR type II vs. non-type II MR was $90.0\% \pm 9.5\%$ vs. 100% at 3 years (log-rank test, $p=0.4028$). No significant intergroup differences were observed.

We also investigated the association between reimplantation with and without aortic valve repair and freedom from > moderate AR (Fig. 4). The 3-year freedom from > moderate AR compared between the reimplantation without and with aortic valve repair groups was 100% vs. $64.6\% \pm 14.3\%$ (log-rank test, $p=0.0494$). Significant intergroup differences were observed.

To assess the learning curve, perioperative data and outcomes were compared between patients who underwent surgery between 2007 and 2011 (2007–2011 group) and those who underwent surgery between 2012 and 2018 (2012–2018 group). The rate of aortic valve repair was higher in the 2012–2018 group than in the 2007–2011 group [central plication: 10 (55.6%) vs. 1 (12.5%), $p=0.0307$, cusp reinforcement: 4 (22.2%) vs. 0, $p=0.0712$, and patch repair: 3 (16.7%) vs. 0, $p=0.1232$). The 3-year freedom from > moderate MR rates compared between the 2007–2011 and 2012–2018 groups was 100% vs. $88.9\% \pm 10.5\%$ (log-rank $p=0.3458$). The 3-year freedom from > moderate AR rates compared between the 2007–2011 and 2012–2018 groups was 100% vs. $81.5\% \pm 11.9\%$ (log-rank test, $p=0.0811$).

Discussions

Better hemodynamics and freedom from anticoagulant therapy serve as advantages of valve repair in patients undergoing the procedure [2]. However, a combined mitral valve repair and VSRR procedure is more complicated with longer cardiopulmonary bypass and cardiac ischemia times than an isolated mitral valve repair or isolated VSRR or Bentall procedure. In this study, 4 patients (15.4%) needed

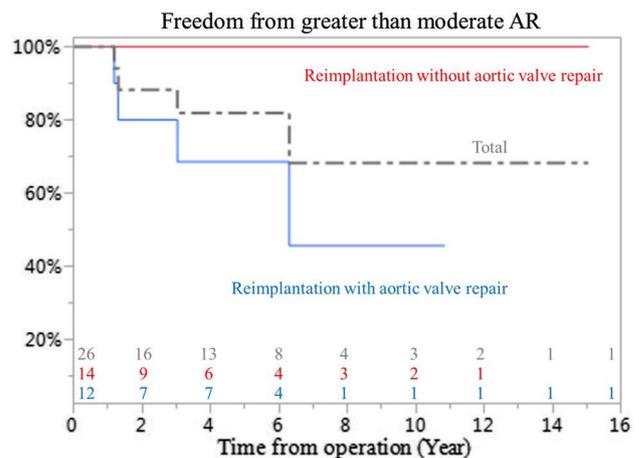


Fig. 4 Kaplan–Meier curves show freedom from greater than moderate AR in the patients underwent reimplantation with aortic valve repair and without aortic valve repair (gray dot line: total, red line: reimplantation without aortic valve repair, blue line: reimplantation with aortic valve repair). AR aortic regurgitation

postoperative pacemaker implantation. A concomitant Maze procedure was performed for chronic atrial fibrillation in 1 patient. A trans-septal approach was required in 1 patient owing to redo MVP, although the standard approach to the mitral valve used at our hospital is a left atriotomy via the inter-atrial groove. Long cross-clamp times (266 and 292 min) were required in 2 patients. These were longer than the mean cross-clamp time in this study and could have contributed to postoperative sick sinus syndrome necessitating pacemaker implantation.

Barlow's disease, Carpentier's classification of MR type II, and complex lesions usually require complicated techniques and affect the durability [10–12]. In this study, 10 patients (38.5%) were diagnosed with Barlow's disease, 15 patients (57.7%) underwent the procedure for anterior leaflet lesions, and 15 patients (57.7%) underwent reconstruction with artificial chordae. The freedom from > moderate MR rates at mid-term follow-up was excellent in the entire cohort. In contrast, the freedom from > moderate AR rate at mid-term follow-up was 86.6% in the entire cohort. The high incidence of recurrent AR could be attributed to the fact that complex procedures for aortic cusps including cusp reinforcement ($N=4$, 15.4%), patch repair ($N=3$, 11.5%), or resuspension ($N=2$, 7.7%) were more commonly performed in these patients. However, overall survival and freedom from reoperation rates were acceptable compared with previous reports [2].

The aortic and mitral valves are known to be coupled via fibrous tissue [7]. Reportedly, the entire mitral ring can affect aortic annular function in instances of altered mitral-aortic coupling [8]. In this study, no significant intergroup differences were observed between the semi-rigid and the semi-flexible ring groups with respect to freedom from moderate MR rates. The distributions of Barlow's disease, Carpentier's classification of MR, and disease lesions, which directly affect the durability, did not significantly differ between the semi-rigid and semi-flexible ring groups. The marginal difference could be attributed to differences in patients' age. Although the difference in the mean age was not statistically significant, this difference was nearly 10 years. We observed no statistically significant difference between the semi-rigid and semi-flexible ring groups in the freedom from moderate AR rates; however, the trend indicated a high incidence of residual or recurrent AR in the semi-flexible ring group. The poorer outcomes associated with aortic valve procedures could be attributed to the fact that a greater number of patients underwent reimplantation without aortic valve repair in the semi-rigid ring group, and a greater number of complicated aortic valve procedures were performed in the semi-flexible ring group owing to the progress of the learning curve. Notably, fibrous continuity measuring 5–10 mm in width is observed in the normal heart. The first row of sub-annular horizontal sutures

used during VSRR reimplantation is usually located 5 mm away from the suture line of the mitral annular ring. Future studies are warranted using more accurate and sophisticated imaging modalities, such as 3-dimensional transesophageal echocardiography or 4-dimensional computed tomography to assess aortic root dynamics.

Limitations

Following are the limitations of this study: (1) The retrospective study design serves as a drawback of the study. (2) The small sample size reduces the statistical power of the study. (3) The imaging modalities used in this study were not sophisticated enough to provide accurate and detailed information regarding aortic root dynamics. (4) The follow-up period was relatively short.

Conclusions

Simultaneous mitral valve repair in patients with MR and concomitant AAE showed favorable mid-term outcomes.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interests.

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