Surgical Repair of a Sinus of Valsalva Aneurysm: A 22-Year Single-Center Experience

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Abstract

Background Several reports described the repair of sinus of Valsalva aneurysms (SVAs); however, there is still debate regarding the optimal method of operation. We investigated the determinants of the development of significant aortic regurgitation (AR) and long-term survival after surgical repair.

Methods Between January 1995 and December 2016, 71 patients (31 females; median age: 33.3 years) underwent surgical SVA repair with ($n = 60$) or without ($n = 11$) rupture. Aortic valvuloplasty (AVP) was performed using Trusler's technique in 28 patients (39.4%), and 11 patients (15.5%) underwent aortic valve replacement during the first operation.

Results There was no early mortality, and three deaths occurred during follow-up (median: 65.4 months). Patients with grade II preoperative AR who underwent AVP tended to develop significant postoperative AR, but freedom from significant AR did not differ statistically ($p = 0.387$). Among patients who underwent AVP, freedom from significant AR did not differ statistically between those with grades I and II and those with grades III and IV ($p = 0.460$).

Conclusion Surgical repair of SVA with or without rupture can be performed safely using the dual approach technique. Concomitant aortic valve repair can be performed without difficulty and should be recommended not only for patients with moderate or severe preoperative AR (grades III and IV) but also for those with minimal or mild preoperative AR (grades I and II), whose aortic valve geometry needs correction.

Keywords
- aortic regurgitation
- aneurysm
- aorta/aortic

Introduction

Sinus of Valsalva aneurysm (SVA) is a rare cardiac anomaly, primarily caused by the congenital absence of elastic and muscular tissue in the aortic wall of the sinus of Valsalva.[1] It may also be acquired, with infective endocarditis of the aortic valve as the most common cause.[2] The incidence of SVA is higher in Eastern populations than in Western ones,[1] and 65 to 80% of SVA patients are male.[3] SVA was first described by Hope in 1839.[4] The first report of successful surgical repair was reported by Lillehei et al in 1957.[5] Since then, several reports have described SVA repair techniques, and at present, there is still debate regarding the optimal method of surgical repair.

At Samsung Medical Center, we recently established a prudent repair technique based on a dual approach. In this

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study, we reviewed our 22-year experience with SVAs to investigate the determinants of the development of significant aortic regurgitation (AR) and long-term survival after surgical repair.

Materials and Methods

Study Patients

During the 22-year period from January 1995 to December 2016, 71 patients (31 females and 40 males) underwent surgical repair of SVA with ($n = 60$, 84.5%) or without rupture ($n = 11$, 15.5%). Patients with aortic root or ascending aortic dilatation or connective tissue disease were excluded. The median age at the time of operation was 33.3 years (range: 11.8–62.7 years). Our Institutional Review Board approved this study, and the need for patient consent was waived (IRB number; SMC 2019-02-020).

At the time of admission, 57 patients (80.3%) were symptomatic. Major symptoms were dyspnea on exertion in 41 patients (57.7%, most common), followed by chest discomfort or pain, palpitation, fever, chills, and fatigue. In total, 14 patients (19.7%) were asymptomatic and diagnosed incidentally during routine examinations.

The origins of the SVAs and the exit site of ruptured SVAs are summarized in ►**Table 1**. The right coronary sinus was the most common site of origin of the aneurysm ($n = 59$, 83.1%). The aneurysms ruptured into the right ventricle (RV) in 42 patients and into the right atrium (RA) in 18 patients. No patients experienced the formation of a fistula into the pulmonary trunk or the pericardial sac.

Ventricular septal defect (VSD) was the most common coexisting cardiac lesion. There were 48 patients (67.6%) with VSDs, including the subarterial type in 41 patients, the perimembranous type in 3, the muscular outlet type in 1, and the total conal defect type in 3. AR (≥ grade I) was the second most common cardiac malformation ($n = 45$, 63.4%), followed by right ventricular outflow tract (RVOT) obstruction in 10 patients (14.1%), infective endocarditis in 9 (12.7%), and bicuspid aortic valve in 5 (7.0%). The AR severity was grade I in 14 patients, grade II in 13, grade III in 7, and grade IV in 11.

Operative Procedures

Surgical repair was performed under cardiopulmonary bypass (CPB) with moderate hypothermia. Median sternotomy was used in all patients. The left ventricle was vented. After the ascending aorta was cross-clamped, the RA or the main pulmonary artery was opened to clamp the fistula opening and antegrade cardioplegia was infused through the root cannula. If there was AR (≥ grade I), the ascending aorta was opened obliquely and cardioplegia was delivered either directly via the coronary ostia or in a retrograde manner via the coronary sinus, depending on the surgeon's preference. Cold crystalloid cardioplegia ($n = 5$), Custodiol histidine-tryptophan-ketoglutarate solution ($n = 15$), and cold blood cardioplegia ($n = 51$) were used for myocardial protection.

Surgery was performed through an aortotomy in 15 patients (21.1%), the chamber of termination (RA or RV) in 5 (7.0%), and the dual approach (both RA/RV and aortic sides) in 51 (72.8%). The aortotomy group was defined as patients who underwent surgical repair of SVA through aortotomy only. The exit site group was defined as patients who underwent surgical repair of SVA through the chamber of termination only. The dual approach group was defined as patients who underwent surgical repair of SVA through the dual approach (both the RA/RV and aortic sides). Excluding 11 patients who underwent aortic valve replacement (AVR) during the first SVA repair operation, the surgical approaches involved an aortotomy in 9 patients (aortotomy group; 9/60, 15.0%), the chamber of termination (RA or RV) in 5 (exit site group; 5/60, 8.3%), and the dual approach (both RA/RV and aortic side) in 46 (dual approach group; 46/60, 76.7%). Several methods for the surgical repair of SVA including primary or patch closure with a glutaraldehyde-fixed autologous pericardial patch, a bovine pericardial patch or a Dacron patch (DuPont, Wilmington, Delaware, United States) are summarized in ►**Table 2**.

An illustration depicting the underlying pathology (with or without VSD) as well as the types of repair is summarized in ►**Table 3**. VSD closure was performed primarily ($n = 4$) or by patching ($n = 44$) through the RA, the RV, or the main pulmonary artery (►**Table 4**).

Over the 22-year study period, our institution has used several methods for the surgical repair of SVA through aortotomy only, through the chamber of termination only, or via a dual approach (both the RA/RV and aorta sides). In the past 3 years, we have established a prudent repair technique using a dual approach that is based on a transaortic procedure. Our anatomic correction comprises (1) resection of the ruptured or unruptured aneurysmal sac, (2) patch closure of the defect in the sinus of origin through the aortotomy, (3) direct suture closure of the distal end of the remaining sac margin through the chamber of termination, and (4) correction of coexisting

Table 1 Sinus of origin and exit site of the ruptured SVA in all patients ($n = 71$)

Sinus of origin	Patients (*n*)	Unruptured	Ruptured	Chamber of rupture		
				RA	RV	LV
Right coronary sinus	59	9	50	10	40	0
Noncoronary sinus	10	2	8	8	0	0
Left coronary sinus	2	0	2	0	2	0
Total	71	11	60	18	42	0

Abbreviations: LV, left ventricle; RA, right atrium; RV, right ventricle; SVA, sinus of Valsalva aneurysm.

Table 2 Surgical repair of SVA (patients who underwent aortic valve replacement during the first operation were excluded) ($n = 60$; 9 in the aortotomy group, 5 in the exit site group, and 46 in the dual approach group)

	Primary	Autologous pericardial patch	Bovine	Dacron	Total
Aorta side	9	29	14	3	55
Aortotomy group	2	4	3	0	9
Dual approach group	7	25	11	3	46
Exit side	45	3	1	2	51
Exit site group	5	0	0	0	5
Dual approach group	40	3	1	2	46

Abbreviation: SVA, sinus of Valsalva aneurysm.

Table 3 Surgical repair of SVA (patients who underwent aortic valve replacement during the first operation were excluded) ($n = 60$; with or without VSD)

VSD type	Dual approach group	Aortotomy group	Exit site group	Total
Subarterial	26	7	3	36
Perimembranous	1	1	0	2
Muscular outlet	1	0	0	1
Total conal defect	2	0	0	2
No VSD	16	1	2	19

Abbreviations: SVA, sinus of Valsalva aneurysm; VSD, ventricular septal defect.

Table 4 Profile of patients with VSD ($n = 48$)

VSD type	Patch closure			Primary closure	Total
	Dacron	Bovine	Autologous pericardial patch		
Subarterial	35	3	0	3	41
Perimembranous	2	0	0	1	3
Muscular outlet	1	0	0	0	1
Total conal defect	1	1	1	0	3
Total	39	4	1	4	48

Abbreviation: VSD, ventricular septal defect.

cardiac lesions, such as VSD closure using the patch or direct suture technique.

Aortic valvuloplasty (AVP) was performed using Trusler's technique in 28 patients (39.4%), and AVR was performed at the first operation in 11 patients (15.5%) with mechanical valves ($n = 9$) or tissue valves ($n = 2$). The most common abnormality of the aortic valve in patients who underwent AVP or AVR was prolapse of the right coronary or noncoronary sinus. The overall profile of the patients with or without aortic valve procedures is summarized in ►**Table 5**.

Ten patients (14.1%) required RVOT reconstruction for RVOT obstruction, while nine patients (12.7%) with infective endocarditis required vegetation removal with aortic valve intervention.

The mean aortic cross-clamp time was 109.9 ± 54.4 minutes (median: 104, range: 25–351 minutes), and the mean CPB time was 144.8 ± 65.3 minutes (median: 134, range: 45–469 minutes). Patients who did not undergo aortic valve procedures were given aspirin for 3 months postoperatively.

End Points, Definitions, and Follow-up

The primary end point of this study was freedom from significant AR. The secondary end point was overall survival. Significant AR was defined as moderate or severe postoperative AR ($\geq$ grade III/IV) based on echocardiographic follow-up. The AVP group was defined as patients who underwent surgical repair of SVA with AVP. The no-AVP group was defined as patients who underwent surgical repair of SVA without AVP or AVR. The AR group was defined as patients diagnosed with significant AR postoperatively. The no-AR group was defined as patients who did not have significant AR postoperatively.

Baseline clinical data were collected from medical records and databases. The echocardiographic follow-up was performed at our outpatient department. Follow-up clinical data

Table 5 Profile of all patients, with or without aortic valve procedures ($n = 71$)

Preoperative AR	Aortic valve procedure (No.)	Aortic valvuloplasty (No.)	Aortic valve replacement (No.)	Total
No (grade 0)	22	2	2	26
Minimal (grade I)	9	4	1	14
Mild (grade II)	1	12	0	13
Moderate (grade III)	0	5	2	7
Severe (grade IV)	0	5	6	11
Total	32	28	11	71

Abbreviation: AR, aortic regurgitation.

were acquired through telephone interviews and medical records reviews. To obtain complete follow-up data, including mortality, information was collected from the National Registry of Births and Deaths using each patient's unique personal identification number.

Statistical Analysis

This retrospective study was designed to investigate the determinants contributing to the development of significant AR and long-term survival after surgical repair.

For each of the baseline characteristics, we obtained the hazard ratio (HR) and its 95% confidence interval (CI) using a univariate Cox's regression. The Kaplan–Meier's survival method was used to draw survival curves for various survival outcomes along with 5-, 10-, and 15-year survival probabilities for freedom from AR. A log-rank test was used to test the differences in survival curves among groups. All tests were two tailed.

A p-value of less than 0.05 was considered statistically significant. The statistical analysis was performed using SPSS, version 22.0 (SPSS, Chicago, Illinois, United States) and the R programming language, version 3.3.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline Characteristics

The baseline characteristics of the patients in the two groups (the AR group and the no-AR group) are summarized in ►**Table 6**. Patients with bicuspid aortic valves had a tendency to develop significant postoperative AR, and after adjustments, the incidence of bicuspid aortic valves was noted to be significantly higher in the AR group than in the no-AR group (HR for the AR group: 5.119; 95% CI: 1.029–25.471; $p = 0.046$). There were no patients with infective endocarditis in the AR group.

Overall Clinical Outcomes

There was no early mortality. Postoperative complications included postoperative bleeding ($n = 1$), neurologic complications ($n = 2$; seizure on the first postoperative day in one patient, new-onset subdural hemorrhage on the 13th postoperative day in one), and wound infection ($n = 1$). The median mechanical ventilator support time was 9.0 hours (range: 0.8–135.5 hours), the median intensive care unit stay was 1 day (range: 0.3–10.3 days), and the median postoperative hospital stay was 7 days (range: 4–58 days).

Table 6 Baseline characteristics of patients ($n = 71$)

Variables	p-Value	HR	Lower 95% CI	Upper 95% CI
Age	0.722	1.290	0.319	5.221
Female gender	0.411	1.706	0.478	6.094
Infective endocarditis	0.435	–	–	–
VSD	0.366	2.047	0.434	9.661
Preoperative AR	0.114	3.507	0.741	16.600
RVOT obstruction	0.994	0.993	0.125	7.891
Bicuspid aortic valve	0.046	5.119	1.029	25.471
Ruptured SVA	0.720	0.750	0.155	3.626

Abbreviations: AR, aortic regurgitation; CI, confidence interval; HR, hazard ratio; RVOT, right ventricle outflow tract; SVA, sinus of Valsalva aneurysm; VSD, ventricular septal defect.

During the follow-up period (median: 65.4 months, range: 0.3–237.9 months), there were three late deaths. The causes of late deaths were underlying disease (gastric cancer) in one case (5.5 years after operation with the dual approach) and unknown in two cases (14.2 years after operation with the dual approach and 16.7 years after operation with AVR). The overall survival is summarized in ►**Fig. 1A**.

When 11 patients with AVR during the first SVA repair operation were excluded, 10 patients (10/60, 16.7%) had recurrent or newly developed significant AR. Among these 10, 1 patient underwent reoperation for AVR during the follow-up period (after 9 months).

Freedom from significant AR of the patients is summarized in ►**Fig. 1B–D**. In the AVP and no-AVP groups, freedom from significant AR according to the severity of preoperative AR is summarized in ►**Fig. 1E**. When the patients with preoperative AR were reclassified into two groups (no preoperative AR, grades I and II vs. grades III and IV preoperative AR), freedom from significant AR in the patients with low-grade preoperative AR ($\leq$ grade II) was significantly higher than those with high-grade preoperative AR ($\geq$ grade III) ($p = 0.014$; ►**Fig. 1F**).

Among the 26 patients with low-grade preoperative AR (grade I or II) when the patients with no preoperative AR were

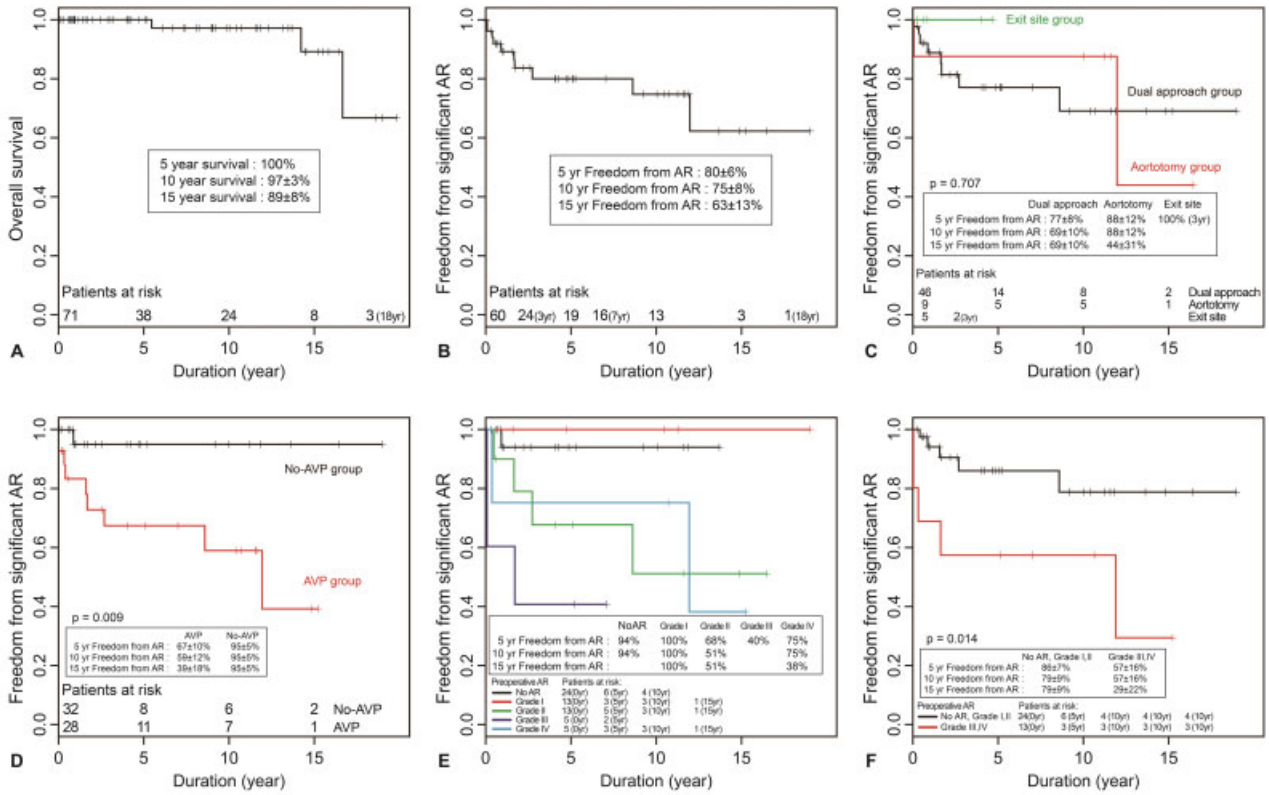

Fig. 1 (A) Overall survival ($n = 71$). (B) Freedom from significant AR (excluding 11 patients who underwent AVR during the first operation) ($n = 60$). (C) Freedom from significant AR in the aortotomy group, the exit site group, and the dual approach group ($n = 60$). (D) Freedom from significant AR in the AVP group and the no-AVP group ($n = 60$). (E) Freedom from significant AR according to the severity of preoperative AR ($n = 60$). (F) Freedom from significant AR according to the severity of preoperative AR, divided into two groups ($\leq$ grades II vs. $\geq$ grades III) ($n = 60$). AR, aortic regurgitation; AVP, aortic valvuloplasty; AVR, aortic valve replacement.

excluded, the patients in the AVP group had a tendency to develop significant postoperative AR, but freedom from significant AR did not differ statistically ($p = 0.125$; ►**Fig. 2A**). Among the 13 patients with grade II preoperative AR, those in the AVP group had a tendency to develop postoperative significant AR, but their freedom from significant AR did not differ statistically from that of the patients in the no-AVP group ($p = 0.387$; ►**Fig. 2B**). Among the 26 patients who underwent AVP (omitting 2 patients without preoperative AR), freedom from significant AR did not differ statistically between the two severity groups (grades I and II vs. grades III and IV, $p = 0.460$; ►**Fig. 3**).

Discussion

SVA is a rare cardiac anomaly responsible for ~0.15 to 1.5% of congenital cardiac surgeries involving CPB.[6] Moustafa et al reported that the site of origin of the SVA was the right coronary sinus in 69.8% of patients, the noncoronary sinus in 25.6%, and the left coronary sinus in 4.7%.[2] In this study, the right coronary sinus was the most common site of origin of the aneurysm ($n = 59$, 83.1%), followed by the noncoronary sinus ($n = 10$, 14.1%) and the left coronary sinus ($n = 2$, 2.8%).

Patients with unruptured SVAs are usually asymptomatic.[3] If patients with unruptured SVAs do not have any complications, such as RVOT obstruction, compression of the ostia of coronary arteries, abnormal cardiac rhythms, embolic events, or infection, SVAs are usually diagnosed only incidentally.[7,8] In our study, 14 patients (19.7%) were asymptomatic, and they were diagnosed incidentally during routine examinations.

Coexisting cardiac abnormalities are common in patients with congenital and ruptured or unruptured SVAs. VSD is the most common associated lesion, occurring in 12 to 53% of SVA patients.[2,9] In our study, 48 patients (67.6%) had a VSD. AR is also commonly associated disorder with VSD,[1] and it is more common in patients with ruptured SVA.[2] In our study, AR ($\geq$ grade I) was the second most common cardiac malformation ($n = 45$, 63.4%).

Surgery for anatomic correction is the mainstay of treatment for SVA.[1,3,9,10] The primary goals of surgical repair of SVAs are to close the SVAs without distorting the aortic sinus, remove the aneurysmal sac, correct any associated intracardiac abnormalities, and prevent residual AR. Previous reports have described various methods for the surgical repair of SVAs,[10,11] and several publications have demonstrated that SVAs can be surgically repaired with low-risk and excellent long-term outcomes.[11–16] Yacoub et al used the transaortic technique with a series of interrupted sutures through the crest of the ventricular septum and the annulus of the aortic cusp to plicate the dilated sinus of Valsalva.[10] Another study

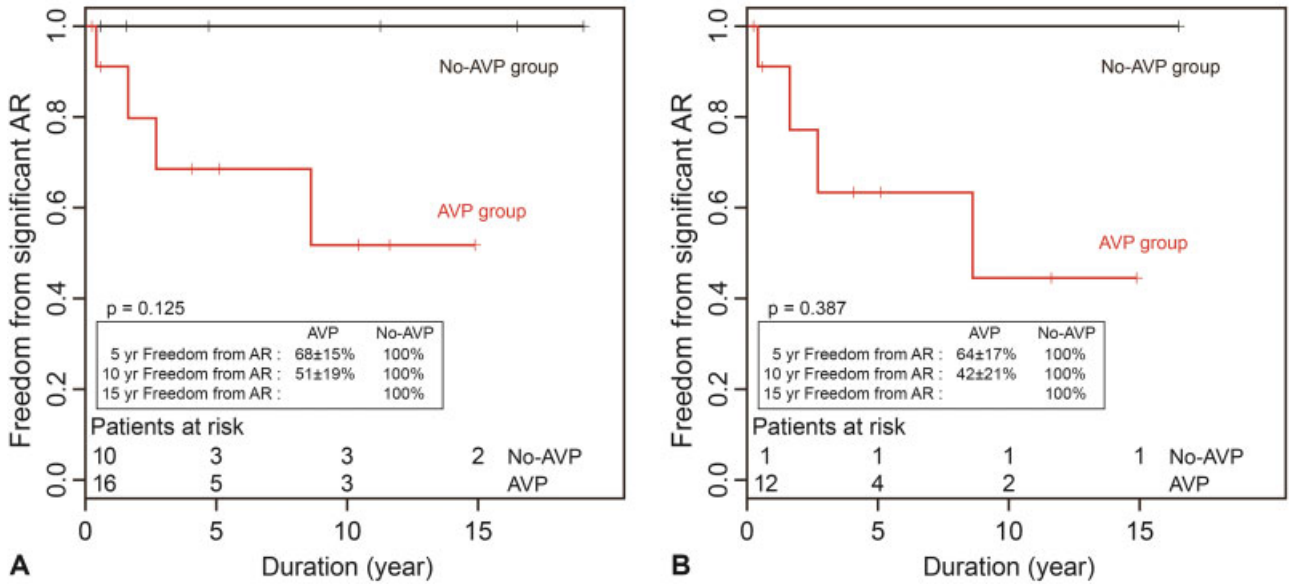

Fig. 2 (A) Freedom from significant AR in patients (AVP group vs. no-AVP group) with low-grade preoperative AR (grade I or II) ($n = 26$). (B) Freedom from significant AR in patients (AVP group vs. no-AVP group) with mild preoperative AR (grade II) ($n = 13$). AR, aortic regurgitation; AVP, aortic valvuloplasty.

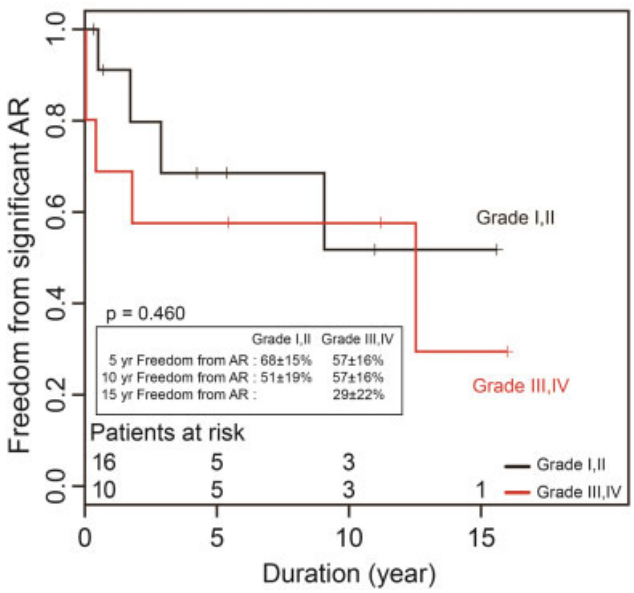

Fig. 3 Freedom from significant AR in patients with AVP classified according to the severity of preoperative AR, divided into two groups (grades I and II vs. grades III and IV) ($n = 26$). AR, aortic regurgitation; AVP, aortic valvuloplasty.

found that transaortic repair of SVAs with an optimal geometric design of the sinus of Valsalva could reduce the incidence of postoperative AR.[14] In contrast, Jung et al demonstrated that the transaortic approach may cause a high risk of postoperative AR by distorting the aortic sinus geometry.[11] Thus, the optimal surgical correction method remains a controversial issue because of the rarity of SVAs. Controversies regarding strategies for the surgical procedure persist, particularly regarding the operative approach (transaortic or nontransaortic) and the surgical technique (primary closure or patch closure)[11] and the decision to undergo concomitant surgical procedures, such as aortic valve repair or replacement.

The advantages of the nontransaortic approach include minimizing the risk of aortic sinus distortion by preserving the geometry of the sinus of Valsalva and avoiding the use of foreign materials in the aortic sinus.[11] However, this technique cannot reach the origin of the SVA, and it is impossible to perform before the onset of the SVA in the cusp.[10] Careful inspection of the coronary ostia to determine the optimal position, patency, and the anatomy of the aortic root complex and aortic valve status is possible using the transaortic approach, and an aortic valve intervention, such as AVP or AVR, can be performed only through an aortotomy.[3,11] Postoperative AR, either residual or progressive, is an important risk factor that affects a patient's prognosis,[1,12] and it can have a critical influence on postoperative cardiac function.[1] Although there is a minor risk of VSD or recurrent fistula,[11,17] AR either new or recurrent can result in a risk of early or late complications after surgical correction.[11] Therefore, careful inspection to determine whether to perform aortic valve intervention is a very important step in the surgical repair of SVA. The key point of our surgical strategy is resolving the lack or defect of the aortic media in the sinus of Valsalva, which is the major pathological cause of ruptured or unruptured SVA.

AVP was performed in patients with preoperative AR diagnosed as grade III (moderate) or IV (severe), based on the surgeon's preference. AVR was performed during the first operation when it was impossible to repair the aortic valve via AVP, as in cases of infective endocarditis. The most common abnormality of the aortic valve among the patients who underwent AVP or AVR was prolapse of the right coronary sinus or noncoronary sinus.

According to previous reports, surgical outcomes for SVA are excellent and satisfactory.[2,10,11] Our survival rates at 5,

10, and 15 years were 100, 97, and 89%, respectively, which are not inferior to that of previous reports.

The baseline characteristics of the patients in the AR group and the no-AR group did not differ significantly, except for the incidence of bicuspid aortic valve, which was significantly higher in the AR group than in the no-AR group. The combination of bicuspid aortic valve and SVA is rare and could be explained by the abnormal flow pattern of the dysplastic valve against the aortic wall,[18] and it is believed to be related to significant postoperative AR.

Freedom from significant AR did not differ significantly among the three surgical technique groups. There was no correlation between the degree of postoperative AR and the SVA repair method. Thus, the transaortic approach including aortotomy could be a risk factor for significant postoperative AR, but the risk is not statistically higher. ►**Fig. 1C** shows that the Kaplan–Meier's curve was reversed after 10 years between the dual approach group and the aortotomy group. However, a limited number of patients were at risk during the period, and the data could not be statistically significant. In a recently published article, Luo et al demonstrated that routine aortotomy for simple ruptured SVAs has been remained a controversial issue, and the variable approaches such as aortotomy, right atriotomy, and pulmonary arteriotomy could be viable options.[19]

The important finding in this study is that patients with low-grade preoperative AR (grade I or II; those with no preoperative AR were excluded) who underwent AVP had a tendency to develop significant postoperative AR, but freedom from significant AR did not differ statistically. Another impressive result is that patients with grade II preoperative AR who underwent AVP had a tendency to develop significant postoperative AR, but their freedom from significant AR did not differ statistically from that of patients who did not undergo AVP. This finding indicates that aortic valve intervention, such as AVP, in patients with low-grade preoperative AR can improve the outcome of postoperative AR, and AVP can be recommended for those patients.

Additionally, among the 26 patients who underwent AVP (omitting 2 patients with no preoperative AR), freedom from significant AR did not differ statistically between the two groups (grades I and II vs. grades III and IV). This reflects the possibility of improving the outcome by performing AVP to reduce AR in patients with high-grade preoperative AR.

Therefore, concomitant aortic valve repair should be recommended not only for patients with moderate or severe preoperative AR (grades III and IV) but also for those with minimal or mild preoperative AR (grades I and II), whose aortic valve geometry needs correction.

This study has several limitations. First, freedom from significant AR was significantly higher in the no-AVP group than in the AVP group. This difference may have occurred because the patients in the AVP group had a tendency to have more severe preoperative AR than those in the no-AVP group. Second, the follow-up period might not have been long enough to permit an investigation of the long-term clinical outcomes of overall survival and freedom from AR. Third, this was a small retrospective study with only 71 patients, and its statistical power may be limited. One goal of future research should be to perform a prospective multicenter large study with long-term close follow-up of the development of significant AR.

Conclusion

Surgical repair of SVA with or without rupture can be performed safely using the dual approach technique. Concomitant aortic valve repair can be performed without difficulty and should be recommended not only for patients with moderate or severe preoperative AR (grades III and IV) but also for those with minimal or mild preoperative AR (grades I and II), whose aortic valve geometry needs correction. Long-term close follow-up for the development of significant AR is mandatory.

Note

This article was presented by Jun Ho Lee (lead author) at the 19th Annual Meeting of the Japanese Society for Adult Congenital Heart Disease, January 14–15, 2017.

Conflict of Interest

The authors declare no conflict of interest.

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