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Reoperation or Aortic Regurgitation Progression after Reimplantation of the Aortic Valve (David's Procedure) Using the Valsalva Graft

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Abstract

Background This study aimed to assess predictors of a composite endpoint (reoperation for aortic valve [AV] failure or aortic regurgitation [AR] grade $\geq$ 2) after reimplantation of the aortic valve (RAV) using the Valsalva graft.

Methods From 2012 to 2021, 112 patients underwent RAV in a single center. Clinical and echocardiographic data were collected retrospectively. Cox regression analysis was used to identify predictors of the composite endpoint. Kaplan–Meier methods were used for time-to-event analysis.

Results Median (interquartile range) age was 52 years (44, 62). Nineteen patients (17%) were operated for acute Type A aortic dissection, and the remainder for aortic root aneurysm, 60 mm or larger in 12/112 (11%). Thirty-day mortality was 1/112 (1%). During follow-up, four patients (3.6%) were reoperated for AV failure, and another nine patients (8.1%) developed AR grade $\geq$ 2. Overall estimated freedom from reoperation or AR grade $\geq$ 2 was 87% (95% confidence interval: 76–93%) at 5 years. Significantly lower estimated 5-year freedom from the composite endpoint was found in cases with simultaneous aortic valve repair (AVr; 77 vs. 90%, $p = 0.007$) and nearly significant for large ($\geq$ 6 cm) aortic root diameter (82 vs. 87%, $p = 0.055$). In Cox's analysis, aortic root diameter and simultaneous AVr were independent predictors for the composite endpoint.

Conclusion Outcomes (survival, reoperation, freedom from AR grade $\geq$ 2) with RAV were good up to 11-year follow-up. Larger aortic root diameter and simultaneous AVr were identified as predictors for reoperation or AR grade $\geq$ 2. Long-term follow-up remains necessary to confirm adequate AV function.

Keywords

- reimplantation of the aortic valve
- valve-sparing root replacement
- aortic valve reimplantation
- David procedure

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Introduction

Techniques for surgical repair of aortic root dilation have developed over time. Aortic root dilation with or without aortic regurgitation (AR) can be treated with remodeling or reimplantation, rather than a composite valve graft, with the advantages of lower risk of prosthesis-related complications such as thromboembolism, anticoagulation-related hemorrhage, and endocarditis.[1] Reimplantation of the aortic valve (RAV) has been successfully performed in diverse conditions such as acute or chronic dissection, connective tissue disorder (CTD), and bicuspid aortic valve (BAV).[2]

RAV was introduced in 1992 and featured stabilization of the aortic root and coronary reimplantation into a Dacron tube graft, later designated Tirone David I (TD).[2] In 1995 TD II was presented as a remodeling technique, with replacement of all three sinuses.[2] A year later an improved version, TD III, was described, with a slight modification of sutured Teflon felt used to stabilize the aortic root.[2] TD IV has similar in technique to TD I; however, this includes plication of two Dacron tube grafts at the neosinotubular junction.[2] The latest TD V includes a graft with preformed neosinus configuration.[2] The theoretical advantage of such a Valsalva graft is the recreation of a more anatomical root structure with neosinuses that can normalize vorticial blood flow into the coronary arteries as well as optimizing aortic valve (AV) leaflet motion.[3] However, TD V is more challenging surgically as there is a risk of creases and folds that can lead to distortion and dysfunction of the AV or precarious bleeding between tissue and graft.[4]

Midterm results after RAV have shown low frequency of reoperations or residual AR.[5,6] Recently, the longest follow-up data on patients with RAV presented excellent results, with a 6% reoperation rate at 20 years.[7] However, predictors for reoperation have yet to be firmly established. Aortic root diameter, CTD, BAV, simultaneous aortic valve repair (AVr), residual operative AR, and effective coaptation height are some of the variables that have been associated with reoperation or residual AR after RAV.[1,7–10]

The aim of this study, based on retrospectively collected clinical and imaging data, was to assess predictors of a composite endpoint (reoperation for AV failure or AR grade $\geq$ 2) during up to 11 years of follow-up after RAV with exclusive use of the Valsalva graft.

Materials and Methods

Study Population

From January 2012 to December 2021, all patients $\geq$ 18 years operated in a single surgical unit with RAV using the Valsalva graft were included (►**Fig. 1**). Data were collected retrospectively through electronic medical records including imaging studies with computed tomography (CT), magnetic resonance imaging (MRI), and transthoracic (TTE)/transesophageal (TEE) echocardiography. Closing date was February 20, 2022. The study was approved by the Swedish Ethical Review Authority (Dnr 2021-05562) with a waiver of individual written informed consent.

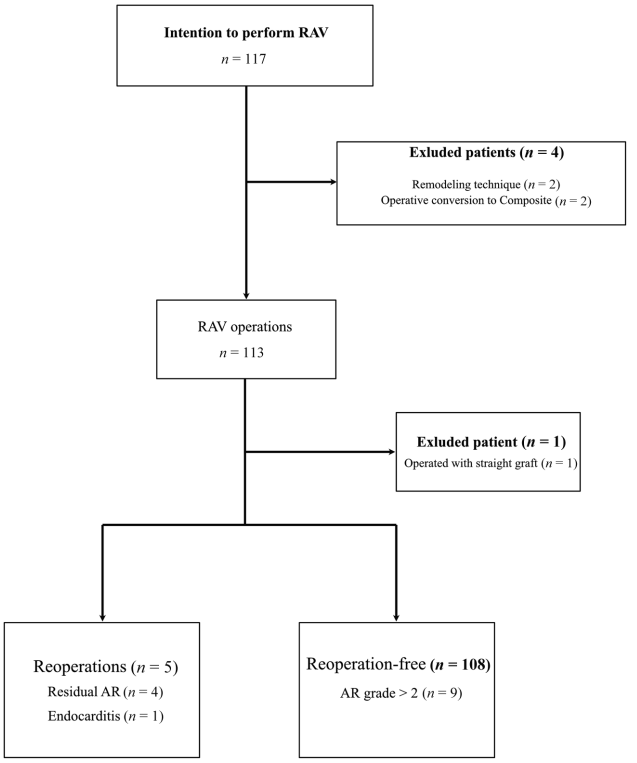

Fig. 1 Flowchart of 117 patients with intention to perform reimplantation of the aortic valve between 2012 and 2021. AR, aortic regurgitation; RAV, reimplantation of the aortic valve.

Imaging Studies and Definitions

Preoperative electrocardiogram-gated CT was used to measure aortic root and annular dimensions. Preoperative TTE or TEE was used to characterize AR and heart function. AR was graded as none (0), trivial (1), mild (2), moderate (3), or severe (4). Direction of a regurgitant jet on color doppler echocardiography was characterized as central, commissural, eccentric (mitral or septal), or any combination thereof. From TTE, TEE, or MRI, left ventricular volume was expressed as left ventricular end-diastolic diameter and left ventricular systolic function was expressed as ejection fraction (%). As evaluated from intraoperative two-dimensional x-plane and deep transgastric TEE views, as well as postoperative TTE, residual AR was defined as AR greater than grade 1. Induced AR was defined as new AR $\geq$ grade 1 appearing postoperatively in patients with grade 0 AR on preoperative examination. Definitions of clinical variables are provided in ►**Supplementary Table S1**.

Follow-up consisted of at least one postoperative TTE before discharge and approximately yearly TTE thereafter. Early mortality was defined as death occurring during the first 30 days after operation. Cardiac and noncardiac deaths were defined as per the American Association for Thoracic Surgery reporting guidelines.[11] Reoperation was defined as any reoperation for AV functional failure. Patients with combined endpoint of reoperation or AR $\geq$ 2 were defined as "failure." Date of failure for patients with AR progression was defined as the date of second consecutive echocardiography with AR grade $\geq$ 2 or last echocardiography.

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Surgical Technique

Details of the RAV procedure have been described previously.[12] A standard procedure was performed through a median sternotomy. After systemic heparinization, cardiopulmonary bypass was established, and the heart was arrested using cold blood cardioplegia, repeated intermittently in ante- and/or retrograde fashion. For operations including open distal anastomosis or arch replacement, performed first, cooling to 30°C core temperature was undertaken, followed by circulatory arrest and establishment of 20°C selective antegrade cerebral perfusion at 5 to 600 mL/min by three separate 12-French perfusion cannulae introduced directly into each head vessel ostium. The aorta was transected distal to the sinotubular junction. The aortic root was carefully dissected down to the annular plane, the coronary buttons excised, and the sinus of Valsalva aortic wall resected, leaving the AV intact with a rim of 5 to 10 mm of aortic tissue. A Valsalva graft (Terumo-Vascutek, Inchinnan, Scotland) with a diameter equal to or one size larger than the height of the commissure between the left and noncoronary cusps was implanted using 12 symmetrically placed subannular pledgeted multifilament sutures. The height of the individual commissures was accommodated by scalloping the lower end of the graft, ensuring alignment of the tip of each commissure at the upper seam of the graft bulb. The AV and the ostia of the coronary arteries were then reimplanted into the Valsalva graft.

Additional AVr was performed as needed to address cusp pathology and dysfunction. Using a caliper to ensure at least 9- to 10-mm coaptation height of each cusp, central plication with interrupted 5/0 polypropylene sutures was used most commonly. Running CV5 GoreTex-suture along the free cusp margin and pericardial patch techniques were not used. Suture line integrity and AV competence were primarily evaluated by antegrade cardioplegia given into the neoroot, and corrections performed and reevaluated accordingly.

Lastly, the distal aortic anastomosis was constructed. Cardiopulmonary bypass was weaned, intraoperative TEE performed and evaluated, and the AV reevaluated and managed (repair, rerepair, or replacement) if functioning suboptimally.

Statistical Analysis

All data were collected in a study-specific database. Categorical variables are presented as numbers and percentages. Continuous variables are presented as medians with interquartile range (IQR) or means with standard deviation. Exploratory univariate group-wise comparisons to identify variables suitable to include in multivariable analysis are made using Mann–Whitney U test for continuous variables and chi-square or Fisher's exact test for categorical variables, respectively. Multivariable analysis of independent predictors for the primary outcome is performed using Cox regression analysis. Outcomes are reported as hazard ratio (HR) with 95% confidence interval (95% CI). Kaplan–Meier methods are used to estimate follow-up freedom from primary outcome and the log-rank test used to compare survival between groups. Estimates are truncated at 8 years, as fewer than 10% of the study population remained at risk thereafter. All statistical tests were two-sided and $p < 0.05$ was considered statistically significant. Statistical data analysis was performed using Stata v16 software (Stata Corp, College Station, TX).

Results

Overall, 112 patients underwent RAV with Valsalva graft during the study period. Preoperative variables and operative data are summarized in ►**Tables 1** and **2** (►**Supplementary Fig. S1**). The median (IQR) age was 52 years (44, 62), and 79% were men. CTD patients constituted 25%. The most common disorder was Marfan syndrome (92%). Patients with acute Type A aortic dissection constituted 17%. The remainder presented with aortic root dilation as the primary indication for operation. In 12/112 (11%) the root diameter was ≥60 mm at presentation, 14/112 (13%) had BAV, and 18/112 (16%) had grade 3 to 4 AR preoperatively.

Mortality and Operative Outcomes

Early mortality occurred in one patient, a 72-year-old woman with an 8.5-cm ascending aortic aneurysm, 6-cm descending aortic aneurysm, and grade 3 to 4 AR who underwent combined total arch replacement with elephant trunk and RAV. She was reoperated for bleeding and expired on postoperative day 4 due to gastrointestinal ischemia. Late mortality was 4% (five patients), one cardiac-related, with an estimated survival at 5 years of 99% (95% CI: 93–100%, ►**Supplementary Fig. S2**). Other known causes of death were cholangiocarcinoma and splenic rupture in one case each. Postoperative outcomes are presented in ►**Table 3** and ►**Supplementary Table S2**.

Reoperation and Aortic Valve Failure

In total five patients underwent reoperation on the AV. One patient was reoperated with a composite valve graft for endocarditis within a year and was not included in univariate or multivariate analyses, which aimed to identify predictors of structural AV failure. The remaining four reoperations were due to progressive AR, one of which had combined AR and aortic stenosis. The exact mechanism for reoperation was cusp perforation in two of the cases, stenosis of cusp plication in one, and a large central coaptation defect in one. All four patients were reoperated with a mechanical AV replacement. Time to reoperation was 1.4 to 9.0 years, median of 4.5 years. In addition, another nine patients were identified with at least grade 2 AR at last follow-up echocardiography. Three patients had reported less than grade 2 AR on last echocardiography, which upon further study examination was considered moderate and, therefore, were included in the analysis (►**Fig. 2**). Time to AR grade ≥ 2 was between 0.04 and 6.9 years, median 2.6 years.

There were no independent predictors for AV reoperation as a single outcome. Variables associated with the composite endpoint were large (≥60 mm) aortic root, simultaneous AVr, subcommisural plasty, and intraoperative central regurgitant jet direction in univariate analysis (►**Table 4**). In multivariable Cox regression analysis, increasing preoperative aortic root

Table 1 Demographics and preoperative findings

Variable	$n = 112$	%
Patient characteristics:		
Age (y)	52 (44, 62)	
Male gender	88	79
Comorbidities:		
Diabetes mellitus	1	1
Smoking	53	47
Chronic obstructive pulmonary disease	0	0
Hypertension	67	60
Atrial fibrillation	9	8
New York Heart Association functional class:		
1	83	74
2	15	13
3	14	13
4	0	0
Type-A dissection	19	17
Connective tissue disorder	28	25
Laboratory findings:		
Creatinine (μmol/L)	80 (72, 89)	
Estimated glomerular filtration rate (mL/min)	109 (89, 132)	
Preoperative echocardiographic features:		
Aortic regurgitation grade:		
0	29	26
1	27	24
2	37	33
3	17	15
4	1	1
Aortic regurgitation jet direction:		
Central	35	41
Commissural[a]	5	6
Eccentric[b]	22	26
Mitral valve[a]	14	16
Septum[a]	1	1
Left ventricular end-diastolic diameter[c] (mm)	56 (52, 60)	
Left ventricular ejection fraction (%)	55 (50, 55)	
Mitral regurgitation grade > 2	7	6
Anatomical features:		
Bicuspid aortic valve:		
Type 0	2	2
Type 1	12	11
Type 2	0	0
Aortic root diameter (mm)	51 (49, 55)	
Aortic anulus diameter (mm)	29 (27, 31)	

Note: Categoric data are shown as number (%) and continuous data as median (interquartile range).
[a]Missing data, total number of patients 86.
[b]Missing data, 7 patients with eccentric jet without specified direction to mitral valve or septum.
[c]Missing data, total number of patients 105.

Table 2 Operative findings and procedures

Variable	$n = 112$	%
Aortic valve pathology:		
Fenestration	15	13
Cusp prolapse	16	14
Calcification	3	3
Aortic valve repair:		
Subcommisural plasty	3	3
Cusp plication	23	21
Graft size (mm)	30 (30, 32)	
Cardiopulmonary bypass (min)	175 (142, 199)	
Aortic cross-clamp (min)	156 (130, 177)	
Circulatory arrest time[a] (min)	23 (19, 27)	
Additional procedures:		
Coronary artery bypass grafting	2	2
Mitral valve reconstruction	5	4
Arrhythmia procedures	4	4
Atrial septal defect	2	2
Hemiarch replacement	19	17
Total arch replacement	3	3

Note: Categoric data are shown as number (%) and continuous data as median (interquartile range).
[a]Total of 25 patients were operated with circulatory arrest.

Table 3 Postoperative outcomes

Variable	$n = 112$	%
30-d mortality	1	1
Stroke	1	1
Reoperation bleeding	17	15
Respiratory insufficiency	4	4
Δ Creatinine[a] (μmol/L)	8 (−4, 37)	
Continuous renal replacement therapy	8	7
Creatine kinase-myocardial band (μg/L)	26 (17, 48)	
Atrial fibrillation	36	32
Permanent pacemaker	9	8

Note: Categoric data are shown as number (%) and continuous data as median (interquartile range).
[a]Difference between highest postoperative and preoperative creatinine.

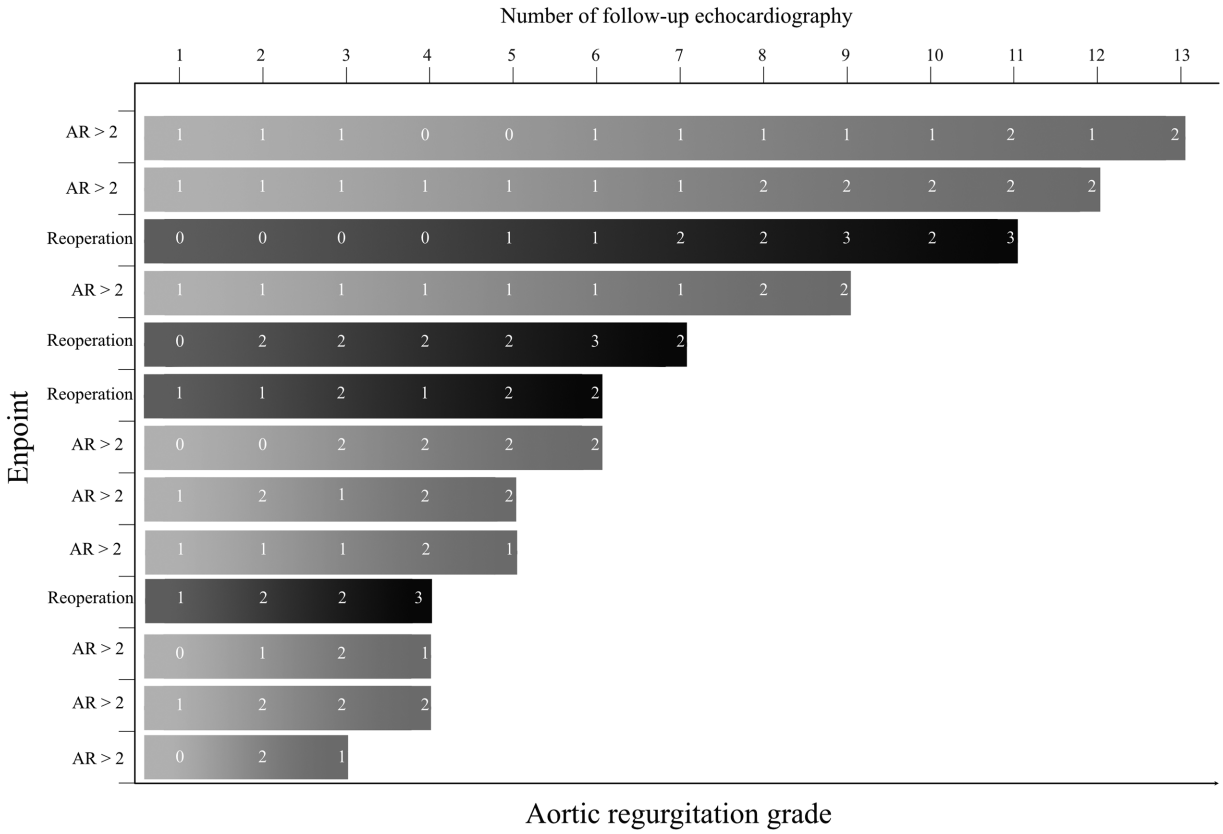

Fig. 2 Details of aortic regurgitation grade progression during follow-up from transthoracic echocardiography for 12 patients with aortic valve failure reoperation (black) or aortic regurgitation grade ≥ 2 (grey). AR, aortic regurgitation.

diameter (per mm; HR: 1.07 [95% CI: 1.01–1.13], $p = 0.02$) and AVr (HR: 3.5 [95% CI: 1.1–10.9], $p = 0.03$) were identified as predictors for the composite endpoint.

Overall estimated freedom from reoperation was 97% (95% CI: 90–99) at 5 years. Overall estimated freedom from the composite primary outcome was 87% (95% CI: 76–93) at 5 years (►**Fig. 3A** and including death in ►**Supplementary Fig. S3**). A lower estimated freedom from composite endpoint for aortic root diameter ≥ 60 mm was borderline significant at 82 (95% CI: 76–93) versus 87% (95% CI: 75–94) $p = 0.055$ at 5 years (►**Fig. 3B**). Significant lower estimated freedom from the composite endpoint at 5 years was found for simultaneous AVr as 77 (95% CI: 52–90) versus 90% (95% CI: 77–96) $p = 0.007$ (►**Fig. 3C**). Among patients without both aortic root diameter < 60 mm or AVr, 4/76 (5.2%) reached the combined endpoint, corresponding to an estimated 92% (95% CI: 77–97) freedom at 5 years.

Clinical and Echocardiographic Follow-up

Total cumulative follow-up was 515 patient-years. The median follow-up was 3.9 years and ranged from 0.01 to 10.4 years. Follow-up was 100% complete.

A total of 453 echocardiograms were collected during follow-up. The median number of echocardiograms for each patient was 4 (IQR 2, 5) over the course of their follow-up.

Overview of AR progression from pre- to first postoperative to last follow-up echocardiography to reoperation on all identified patients with intention to perform RAV is presented in ►**Fig. 4**.

During follow-up (on patients who underwent RAV) on last echocardiography, 62 (55%) patients had AR grade 0, 35 (31%) had AR grade 1, 13 (12%) had AR grade 2, and 2 patients (2%) had AR grade 3. The individual patterns of development of AR from preoperatively to the last follow-up echocardiography (or reoperation, whichever occurred first) for large (≥60 mm) aortic root, AVr, and residual AR, respectively, are depicted in ►**Supplementary Figs S4–S6**. Visually, AVr entailed the least stable condition postoperatively.

Discussion

The outcomes of RAV in 112 consecutive patients are very encouraging, with 0.9% ($n = 1$) 30-day mortality and four (3.6%) reoperations for AV failure during 515 patient-years follow-up, for an estimated freedom from reoperation of 97% at 5 years. Acknowledging the risk of progressive development of AR, a composite of reoperation or AR ≥ grade 2 constituted the primary outcome measure. Adding nine (8.1%) patients with AR grade ≥ 2, freedom from the primary outcome was 87% at 5 years. Increased aortic root diameter (HR: 1.07 per mm) and AVr (HR: 3.5) were identified in Cox analysis as independent predictors for reoperation or AR grade ≥ 2. BAV, large preoperative degree of AR, CTD, or aortic dissection were not significant predictors of the primary outcome.

RAV has proven to be a safe technique with the advantages of lower risk for prosthesis-related complications such as

Table 4 Univariate analysis of preoperative and operative variables

Variable	Nonfailure (99)	%	Failure (13)	%	*p*-Value
Preoperative variables:					
Patient characteristics:					
Age (y)	52 (44, 62)		49 (42, 63)		0.83
Male gender	78	79	10	77	0.88
Comorbidities:					
Diabetes mellitus	1	1	0	0	1.00
Smoking	45	45	8	62	0.38
Hypertension	60	61	7	54	0.64
Atrial fibrillation	9	9	0	0	0.59
New York Heart Association class >3	13	13	1	8	1.00
Type-A dissection	16	16	3	23	0.46
Connective tissue disorder	25	25	3	23	1.00
Laboratory findings:					
Creatinine (μmol/L)	80 (70, 89)		83 (77, 98)		0.42
Estimated glomerular filtration rate (mL/min)	110 (92, 132)		107 (76, 135)		0.48
Preoperative echocardiographic features:					
Aortic regurgitation grade:					
0	26	27	3	23	1.00
1	26	27	1	8	0.18
2	31	32	6	46	0.35
3	14	14	3	23	0.42
4	1	1	0	0	1.00
>2	15	15	3	23	0.46
Aortic regurgitation jet direction:					
Central	31	41	4	36	1.00
Commissural	4	5	1	9	0.50
Eccentric[a]	6	8	1	9	0.50
Mitral	11	15	3	27	0.38
Septal	1	1	0	0	1.00
Mitral regurgitation grade >2	7	7	0	0	0.59
Left ventricular end-diastolic diameter (mm)	56 (52, 60)		58 (52, 60)		0.65
Left ventricular ejection fraction (%)	55 (50, 55)		55 (50, 55)		0.99
Anatomical features:					
Bicuspid aortic valve:	11	11	3	23	0.22
Type 0	1	1	1	8	0.22
Type 1	10	10	2	15	0.63
Aortic root diameter (mm):	51 (48, 55)		54 (53, 60)		0.06
Aortic root diameter ≥ 60 mm	8	8	4	31	0.01
Aortic annulus diameter (mm):	29 (27, 31)		30 (26, 32)		0.66
Aortic annulus diameter ≥ 30 mm	40	40	7	54	0.38
Operative variables:					
Aortic valve pathology:					
Fenestration	12	12	3	23	0.28

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Table 4 (*Continued*)

Variable	Nonfailure (99)	%	Failure (13)	%	*p*-Value
Cusp prolapse	12	12	4	31	0.07
Calcification	3	3	0	0	1.00
Aortic valve repair[b]	19	19	7	54	0.005
Subannular plasty	1	1	2	15	0.04
Cusp plication	18	18	5	38	0.09
Graft size (mm)	30 (30, 32)		32 (30, 32)		0.80
Cardiopulmonary bypass (min)	175 (142, 199)		173 (161, 219)		0.50
Aortic cross-clamp (min)	155 (126, 177)		159 (143, 186)		0.42
Circulatory arrest time[c] (min)	23 (18, 27)		33 (25, 36)		0.073
Additional procedures:					
Coronary artery bypass grafting	1	1	1	8	0.22
Mitral valve reconstruction	5	5	0	0	1.00
Arrhythmia procedures	4	4	0	0	1.00
Atrial septal defect	2	2	0	0	1.00
Hemiarch replacement	18	18	5	38	0.09
Total arch replacement	2	2	1	8	0.31
Operative echocardiography					
Residual aortic regurgitation	7	7	3	23	0.09
Induced aortic regurgitation	3	3	0	0	1.00
Aortic regurgitation jet direction:					
Central	0	0	2	15	0.01
Commissural	1	1	0	0	1.00
Eccentric	1	1	1	8	0.22
Mitral	1	1	0	0	1.00
Septal	5	5	0	0	1.00

Note: Categoric data are shown as number (%) and continuous data as median (interquartile range).
[a]Missing data ($n = 7$) with eccentric jet without not specified as mitral or septal.
[b]Aortic valve repair with any technique.
[c]For patients ($n = 23$) operated using hypothermic circulatory arrest.

thromboembolism, anticoagulation-related hemorrhage in mechanical valves and endocarditis, as well as superior hemodynamic performance.[1] However, the disadvantage of RAV is the development of (premature) AV failure over time.[7] As illustrated in ►**Fig. 2**, AR often developed gradually and occurred also in patients initially free from any degree of AR.

Recently David et al[7] presented long-term experience of RAV, reporting 69% freedom from death and reoperation at 20 years. They identified BAV as the only variable significantly associated with late reoperation. In our series such association was not found for reoperation or progression to AR grade $\geq$ 2, findings in accordance with other studies.[1,5] However, the incidence of reoperations in BAV patients may increase during the second postoperative decade.[13] Moreover, it is still debated how RAV should be performed in BAV Sievers type 1, as this group is very heterogeneous.[14,15]

Large aortic root aneurysm with secondary advanced AR results in higher stress on the cusps, possibly promoting cusp fenestrations, prolapse, and increased risk for AV incompetence.[16] In our series large aortic root ($\geq$60mm), but not cusp prolapse or fenestration, was associated with the composite endpoint, even with initially satisfactory outcomes; all these patients had AR < 1 postoperatively (►**Supplementary Fig. S4**). In absence of pathology of single AV cups, a potential mechanism would be a greater risk of prolapse of all three cusps with RAV in greatly dilated aortic roots. Despite limited reports, other series have reported the same association of aortic root size with reoperation and AR progression.[9,17] Conversely, Huuskonen et al[5] did not identify aortic root dimension $\geq$ 55 mm a risk factor for reoperation. In patients without significant AR, or BAV, or CTD, guidelines quote aortic root diameter of 55 mm as an indication for prophylactic operation. Therefore, 55-mm root diameter seems counterintuitive as definition of a "large" aortic root. As performed in previous series, RAV at smaller aortic diameters were associated with excellent outcomes and should be strongly considered.[1,18] However, others maintain that surgery without aortic root dilation is too aggressive.[19] In this and other studies,

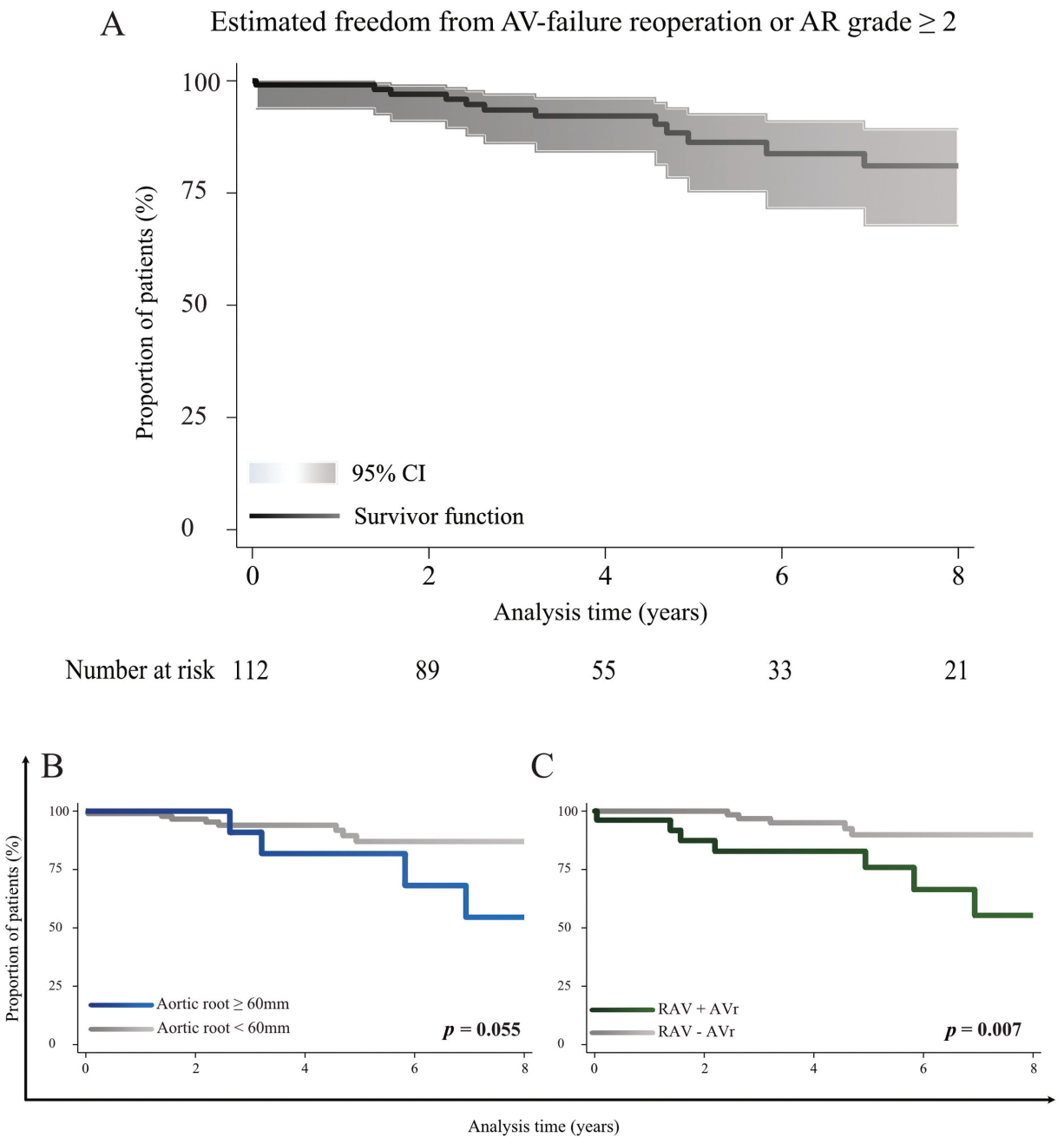

Fig. 3 (**A**) Estimated (Kaplan–Meier) freedom from reoperation or aortic regurgitation grade ≥ 2 for 112 patients undergoing reimplantation of the aortic valve. (**B**) Estimated freedom from reoperation or aortic regurgitation grade ≥ 2 using log-rank test between patients with aortic root diameter over or under 60 mm. (**C**) Estimated freedom from reoperation or aortic regurgitation grade ≥ 2 using log-rank test between patients operated with reimplantation of the aortic valve with or without aortic valve repair. AR, aortic regurgitation; AVr, aortic valve repair; CI, confidence interval; RAV, reimplantation of the aortic valve.

women usually constitute 15 to 25% of patients. Whereas aortic root aneurysm and dissection indeed may be more prevalent in men, a lower aortic diameter threshold for RAV could also result in more women undergoing the procedure, with its potential benefits compared to other strategies.

Residual (≥grade 1) AR, although undesirable, was uncommon and remained mostly stable over time (►**Supplementary Fig. S5**). No cases of AR grade 3 or reoperations occurred in this group, which will need continued close follow-up.

The strategy of simultaneous AVr with RAV differs, some having a more liberal approach and others a conservative approach to this. The same discord is reflected in the results, as some series have reported AVr associated with reoperation as well as AR progression.[9,10] In our series simultaneous AVr was identified as a predictor for AV failure and AR progression, with a pattern of degeneration of AV function over time (►**Supplementary Fig. S6**). In contrast, some other reports have not identified the same association between AVr and reoperation or AR progression.[15,20] Long-term experiences with RAV from Mastrobuoni et al[1] and David et al[7] present two sides of the same coin, the former with a liberal approach to AVr and the latter with a conservative.

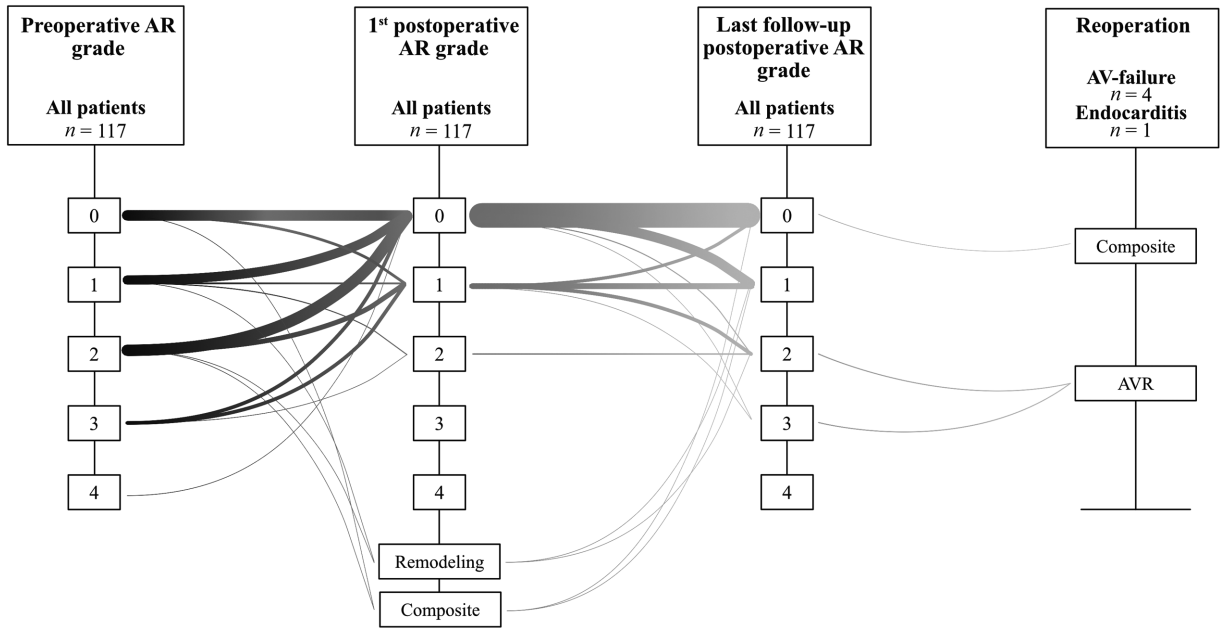

Fig. 4 Aortic regurgitation progression on echocardiography from preoperative to first postoperative to last follow-up echocardiography to reoperation on all 117 patients with intention to perform reimplantation of the aortic valve. Line thickness correlates to number of patients. AR, aortic regurgitation; AV, aortic valve; AVR, aortic valve replacement.

Mastrobuoni et al[1] reported freedom from reoperation of 89.6% at 10 years, despite AVr in 72.7% and pericardial patch in 4.5%. David et al[7] presented freedom from reoperation of 95% at 10 years, despite AVr in 64% without any use of pericardial patch. Both teams present excellent results, but inevitably there might be a slightly higher risk for reoperation in case of a liberal approach to valve repair. To be safe and effective in the long-term AVr must achieve a nearly perfect result, in turn obtained with extensive experience. In our center AVr procedures are generally employed in a very limited number of patients with or without simultaneous RAV, a possible mechanistic explanation for the finding of AVr as an independent predictor for the composite outcome.

RAV in aortic dissection has often proved successful, with good early outcomes in a highly select patient population.[21] In the current study, 4/15 (27%) patients with aortic dissection experienced an adverse late outcome: one reoperation after 9 years, one death after 9 years, and two AR grade 2 after 2.4 and 2.6 years, respectively. Survivors after aortic dissection continue to require very long-term surveillance, regardless of type of index operation.

The Valsalva graft, resembling native aortic root anatomy, may simplify the type TD-V RAV and make more reproducible. In the current study, only including Valsalva grafts, the technical success rate was high, and the overall outcomes in the medium term very favorable. The Valsalva configuration holds promise of natural sinus vortices to optimize coronary blood flow, and physiological hemodynamics, including full cusp excursion without impediment.[22]

Head-on comparison between straight and Valsalva grafts are scarce, but the Lübeck group reported significantly fewer reoperations (0.9 vs. 10%) and better follow-up survival ($p = 0.035$) in 108 patients with Valsalva graft compared with 159 with straight graft.[23] David's group, however, reported excellent long-term outcomes using almost exclusively straight grafts.[7] Other variables besides graft type may well be more important predictors of late outcomes.

Study Limitations

Several limitations need to be considered. Foremost, the rate of reoperation was too low to allow intelligible statistical analysis. Therefore, patients with AR grade ≥ 2 were included in the composite endpoint. Furthermore, even though cumulative follow-up was 515 patient-years, median follow-up was a moderate 3.9 years and 14% of the population had only one postoperative echocardiogram. Arguably, more endpoints would accrue during longer follow-up, and therefore, long-term follow-up remains crucial to fully evaluate surgical outcomes. As echocardiographic findings are to some degree examiner dependent for measurement of AR grade and AR jet direction, these potentially may not be fully accurate. Further, as this is a single-center study with all operations carried out by a small number of surgeons, our results might not be generalizable. Finally, the retrospective nature of the study includes its own limitations. A comprehensive multicenter study with longer follow-up is needed for assessment of reoperation risk factors, particularly in subgroups such as patients with BAV Sievers type 1.

Conclusion

RAV using a Valsalva graft produced favorable results in terms of survival, reoperation rate, and AR progression with medium term (up to 11 y) follow-up in a mixed population including patients with BAV, acute Type A aortic dissection, and CTD. Aortic root diameter and simultaneous AVr were identified

as predictors for AV failure reoperation or AR grade ≥ 2. These findings help inform decision-making for RAV, with possible incentive to perform the procedure at smaller aortic root dimensions and careful selection of cases in which to repair the AV.

Authors Contributions

Concept/design: E.C., A.F-C., C.O.; data collection: K.M., C.O.; data analysis/interpretation: K.M., E.C., A.F-C., C.O.; Statistics: K.M., C.O.; drafting article: K.M., C.O.; critical revision: K.M., E.C., A.F-C., C.O.; approval: KM, E.C., A.F-C., CO; funding: A.F-C., C.O.

Ethics and Integrity Policies Statements

All procedures performed in studies involving human participants were in accordance with 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Institutional Review Board Approval or Waiver

This study was approved by the institutional review board (no. 2021-05562)

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Conflict of Interest

The authors declare no conflict of interest related to this article.

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