A multicentre, propensity score matched analysis comparing a valve-sparing approach to valve replacement in aortic root aneurysm: insight from the AVIATOR database

Arabkhani, B.; Klautz, R.J.M.; Heer, F. de; Kerchove, L. de; Khoury, G. el; Lansac, E.; ... ; Brakel, T.J. van

European Journal of Cardio-Thoracic Surgery 2023, 63(2), ezac514
https://doi.org/10.1093/ejcts/ezac514 Advance Access publication 29 October 2022

ORIGINAL ARTICLE

Cite this article as: Arabkhani B, Klautz RJM, de Heer F, De Kerchove L, El Khoury G, Lansac E *et al.* A multicentre, propensity score matched analysis comparing a valve-sparing approach to valve replacement in aortic root aneurysm: Insight from the AVIATOR database. Eur J Cardiothorac Surg 2023; doi:10.1093/ejcts/ezac514.

A multicentre, propensity score matched analysis comparing a valve-sparing approach to valve replacement in aortic root aneurysm: Insight from the AVIATOR database

Bardia Arabkhani [a,*], Robert J.M. Klautz [a], Frederiek de Heer [b], Laurent De Kerchove [c], Gebrine El Khoury [c], Emmanuel Lansac [d], Hans-Joachim Schäfers [e], Ismail El-Hamamsy[f], Marien Lenoir[f], José I. Aramendi [g], Bart Meuris [h], Peter Verbrugghe [h], Jolanda Kluin [i], Dave R. Koolbergen[i], Olivier Bouchot [j], Igor Rudez[k], Adrian Kolesar [l] and Thomas J. van Brakel [a]

[a] Leiden University Medical Center (LUMC), Leiden, The Netherlands
[b] AVIATOR registry, Heart Valve Society, The Netherlands
[c] Cliniques universitaires Saint-Luc, Bruxelles, Belgium
[d] Institut Mutualiste Montsouris, Paris, France
[e] Homburg-Saarland University Medical Center, Homburg, Germany
[f] Montréal Heart Institute, Montréal, Quebec, Canada
[g] Hospital de Cruces, Bilbao, Spain
[h] University Hospitals Leuven, Leuven, Belgium
[i] Amsterdam UMC, Amsterdam, Netherlands
[j] CHU le Bocage, Dijon, France
[k] University Hospital Dubrava, Zagreb, Croatia
[l] Regional Hospital "Ca Foncello", Treviso, Italy
[m] East Slovakian Institute for Cardiac and Vascular Diseases, Kosice, Slovakia

* Corresponding author. Leiden University Medical Center (LUMC), Leiden, The Netherlands. Tel: 0031649310032: e-mail: b.arabkhani@lumc.nl

Received 28 January 2022; received in revised form 15 October 2022; accepted 24 October 2022

Key question

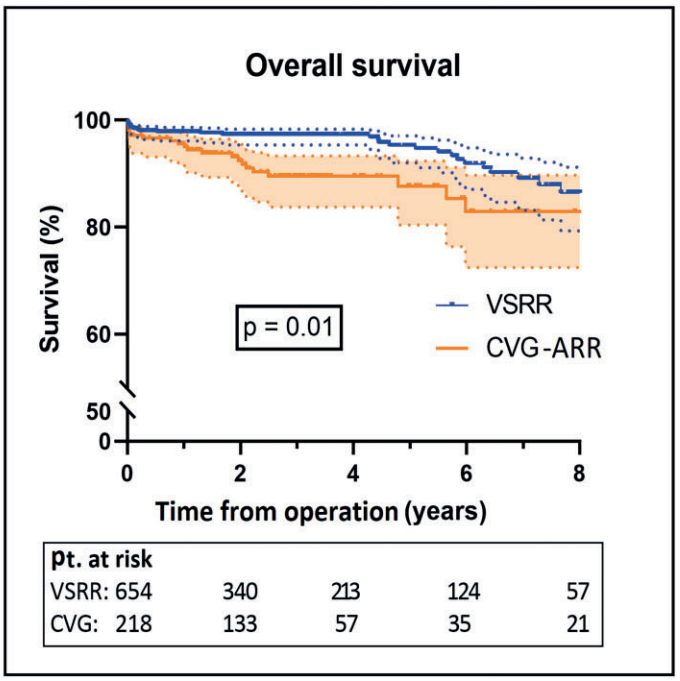
Is valve-sparing aortic root replacement better, in terms of clinical outcome, compared to valve replacement procedures?

Key finding(s)

This multicenter study shows superior clinical outcome in valve-sparing procedures compared to valve replacement.

Take-home message

In patients with aortic root aneurysms with or without aortic valve insufficiency and non-stenotic valve disease, valve-sparing procedures have excellent midterm results, and should be considered as a valuable treatment option.



Aortic Valve Repair Research Network Investigators from the Heart Valve Society, Collaborators.

Abstract

OBJECTIVES: Our goal was to evaluate the outcome of valve-sparing root replacement (VSRR) and to compare the outcomes to those of patients having composite valve–graft conduit aortic root replacement (CVG-ARR) in a cohort of patients with aortic root aneurysm ± valve insufficiency, without valvular stenosis. Although valve-sparing procedures are preferable in young patients, there is a lack of comparative data in comparable patients.

METHODS: The VSRR procedures were performed in 2005 patients, and 218 patients underwent a CVG-ARR procedure. Exclusion criteria included aortic dissection, endocarditis and valvular stenosis. Propensity score matching (3:1 ratio) was applied to compare VSRR (reimplantation 33% and remodelling 67%) and CVG-ARR.

RESULTS: We matched 218 patients with CVG-ARR to 654 patients with VSRR (median age, 56.0; median follow-up was 4 years in both groups; interquartile range 1–5 years). Early mortality was 1.1% of those who had VSRR versus 2.3% in those who had CVG-ARR. Survival was 95.4% [95% confidence interval (CI) 94–97%] at 5 years in patients who had VSRR versus 85.4% (95% CI 82–92%) in those who had CVG-ARR; $P = 0.002$. Freedom from reintervention at 5 years was 96.8% (95% CI 95–98%) with VSRR and 95.4% (95% CI 91–99%) with CVG-ARR ($P = 0.98$). Additionally, there were more thromboembolic, endocarditis and bleeding events in the patients who had CVG-ARR ($P = 0.02$).

CONCLUSIONS: This multicentre study shows excellent results after valve-sparing root replacement in patients with an ascending aortic aneurysm with or without valve insufficiency. Compared to composite valve-graft aortic root replacement, survival is better and valve-related events are fewer. Consequently, valve-sparing procedures should be considered whenever a durable repair is feasible. We advocate a valve-sparing strategy even in more complex cases when performed in experienced centres.

Keywords: Valve-sparing root replacement • aortic valve-repair • Bentall

ABBREVIATIONS

AI	aortic valve insufficiency
AVIATOR	Aortic Valve Insufficiency and ascending aorta Aneurysm InternATiOnal Registry
CI	confidence interval
CVG-ARR	composite valve-graft conduit aortic root replacement
VSRR	HR hazard ratio valve-sparing aortic root replacement

INTRODUCTION

Valve-sparing aortic root surgery is the alternative to valve replacement in patients with aortic root dilatation with or without aortic insufficiency. However, the clinical and valve-related data comparing outcomes from aortic valve-sparing surgery to those from surgical replacement in patients with comparable characteristics are limited.

Approximately 10% of patients with aortic valve disease are diagnosed with aortic valve insufficiency (AI) due to an aortic root aneurysm or other pathology; often they are young patients [1]. According to the latest European Society of Cardiology and European Association for Cardio-Thoracic Surgery (ESC/EACTS) guidelines on valvular heart disease, valve-sparing root replacement (VSRR) is indicated and preferred above valve replacement, especially in younger patients and when performed in experienced centres [2].

An analysis of the Society of Thoracic Surgeons database reported that only 14% of patients with AI are treated with a valve-sparing procedure whereas the majority of valves are replaced [3]. However, valve-sparing procedures have gained popularity in the last decade. Due to the efforts of expert centres, some attempts to standardize the approach and technique in order to enhance the reproducibility and dissemination of valve-sparing procedures have been successful, also in less experienced centres [4–7].

Moreover, there is evidence that valve-sparing procedures are associated with superior results in terms of valve-related outcomes and haemodynamics, although the patient cohorts in these studies are small and not homogeneous [8, 9].

The objective of this study was to provide large-scale clinical outcomes after VSRR and to compare the survival and valve-related outcomes of patients having VSRR (i.e. remodelling and reimplantation procedures) compared to the outcomes of patients having composite valve-graft conduit aortic root replacement (CVG-ARR) (i.e. mechanical Bentall-De Bono and biological root replacement), using the Aortic Valve Insufficiency and ascending aorta Aneurysm InternATiOnal Registry (AVIATOR) database. Although some comparative studies have tried to find differences between VSRR and CVG-ARR [7, 10, 11], this is the first large multicentre study to present and compare outcomes between these procedures in a cohort of patients with comparable valve pathology.

MATERIALS AND METHODS

Ethics statement

This study was approved by the institutional review boards of the participating centres. Written informed consent was obtained from all individual patients (14072013).

The AVIATOR database is an international, observational cohort study initiated by a workgroup within the Heart Valve Society, with 58 centres worldwide enrolling patients undergoing surgical treatment of ascending aortic aneurysm and/or AI. Both the VSRR and the CVG-ARR procedures are included. This registry presents a uniform database of patients in terms of indication for surgery, which allows us to evaluate the outcome of valve-sparing and replacement operations in patients with aortic root dilatation and/or severe AI. More details about the AVIATOR initiative are described elsewhere [12].

A search of the AVIATOR database revealed 2420 adult patients from 43 centres, with individual patient data and at least

1 (year) clinical follow-up, whose aortic root was operated on because of AI with or without aortic root dilatation, between 2007 and 2018. All patient characteristics and preoperative echocardiography data were available. Follow-up was 99% completed for clinical outcome and 85% completed for echocardiographic follow-up. Exclusion criteria included aortic dissection, endocarditis and aortic stenosis. Patients with an acute indication for surgery were excluded because they have less predictable outcomes due to variables other than the type of procedure (e.g. haemodynamic instability, organ malperfusion). This process resulted in 2264 patients for analysis. Figure 1 shows the selection procedure. Patients who had Ross procedures were excluded from the analysis because it is a complex procedure performed in only a few centres, normally for valvular stenosis as an alternative to prosthetic valve replacement. The procedure does not represent participating centres in the AVIATOR registry.

The comparison of outcomes was based on intention-to-treat analyses. Survival and valve-related outcomes were compared between the VSRR and the CVG-ARR groups. Additionally, a subgroup analysis was performed of patients for whom our preoperative intention was to repair the valve but who, due to complex valve anatomy, underwent a valve replacement procedure. This study was approved by the institutional review boards of the participating centres. Informed consent was waived.

Follow-up

Patients were followed up prospectively through out-patient clinical visits. Additionally, all available echocardiographic follow-up data were entered into the database. The majority of patients were included in the AVIATOR registry from 2013 onward. The goal of the AVIATOR registry is to have annual clinical and echocardiographic follow-up from individual patients. Detailed information about the registry was published previously [12]. Early mortality includes operative, in-hospital and/or 30-day mortality. Valve-related events were registered according to the 2008 American Association for Thoracic Surgery/Society of Thoracic Surgeons/European Association for Cardiothoracic Surgery guidelines for reporting mortality and morbidity after cardiac valve interventions [13].

Operative technique

All patients were operated on through a median sternotomy using cardiopulmonary bypass and reimplantation of the coronary arteries. Patients having VSRR underwent either the aortic root remodelling or the aortic valve reimplantation procedure. In the majority of the remodelling procedures, an annuloplasty was performed to stabilize the annulus, according to the surgeon's preference. The operative techniques are described elsewhere [4, 14]. In valve-replacing procedures, either a mechanical Bentall-de Bono procedure or a biological root replacement (stented bioprosthesis sutured into a Dacron graft or a Freestyle root prosthesis (Medtronic, Minneapolis, MN, USA) was performed. In patients with an extended (hemi)arch replacement, deep hypothermia and circulatory arrest were applied.

Statistical methods

Continuous data are presented as the mean with standard deviation or the median with interquartile range. The Kolmogorov-Smirnov test was used to determine the normality of the distribution. The data were compared using the Student *t*-test unless the data were not normally distributed; in these instances, the Mann–Whitney U-test was used. Categorical data are presented as proportions. A comparison was done using the χ^2 test or the Fisher exact test (low prevalence). Survival and freedom from

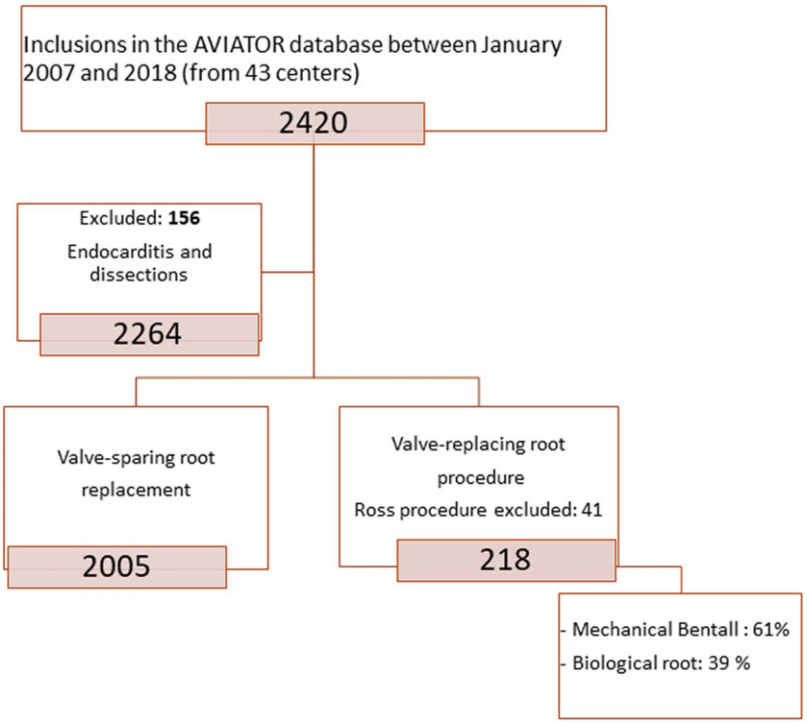


Figure 1: Flow chart for patient selection.

valve reintervention were analysed with the Kaplan–Meier method and the log-rank test. The Cox proportional hazard model was used for analyses of time-related events and to compare time-related outcomes between the VSRR and CVG-ARR groups. The proportional hazard assumption was met by visual inspection (log minus log curves). Tests were performed two-sided, and a *P*-value of 0.05 was considered statistically significant.

Propensity score matching

The propensity scores were constructed using a "nonparsimonious" multivariable logistic regression model with the treatment variable (VSRR vs CVG-ARR) as the dependent variable. Moreover, all baseline characteristics were included as covariates in the propensity model (Supplemental Table S1). Matching was done between patients who underwent VSRR with those who underwent CVG-ARR replacement in a 3:1 ratio using nearest neighbour matching with a caliper width equal to a 0.25 standard deviation of the propensity score. For the analyses mentioned previously, R (version 3.1.3, available at www.r-project.org) and GraphPad Prism version 9.3.1 for Windows (GraphPad Software, San Diego, CA USA) (www.graphpad.com), were used.

RESULTS

Clinical outcome in the unmatched cohort

In the initial unmatched cohort of 2005 patients having VSRR and 218 patients having CVG-ARR, several significant differences were noted in patient characteristics. Table 1 displays patient characteristics in both the matched and unmatched cohorts. Cumulative survival at 5 years was 95.6% [95% confidence interval (CI) 94–97%] in the VSRR group, and 87.6% (95% CI 82–93%) in the CVG-ARR group. After the propensity score adjustment, there were no significant differences in patients having VSRR and those having CVG-ARR. The differences in clinical outcomes in both groups remained after propensity matching. Supplemental Figs. S1 and S2 show Kaplan–Meier curves of cumulative overall survival in the VSRR and CVG-ARR groups and survival in a subgroup of 104 patients in the CVG-ARR cohort with a preoperative intention to repair the valve, respectively.

Freedom from reintervention on the aortic root at 5 years was 96.9% (95% CI 95–98%) for patients having VSRR versus 95.2% (95% CI 91–99%) for those having CVG-ARR. Supplemental Fig. S3 shows a Kaplan–Meier curve for freedom from reintervention on the aortic root. Freedom from AI grade >2 in the VSRR group was 94.9% (standard error 0.01, 95% CI 92.7–96.5%) at 5 years of follow-up (Supplemental Fig. S4).

Clinical outcome in the matched cohort

The propensity score was used to match 218 patients in the CVG-ARR group to 654 patients in the VSRR group in a 1:3 ratio. After propensity matching, there were no significant differences in baseline characteristics between the 2 groups (Supplemental Fig. S5 displays the propensity score distribution). An adequate covariate balance across the 2 groups was achieved. A love.plot of standardized differences in baseline covariate means between the VSRR and CVG-ARR cohorts, before and after propensity score matching, was performed (Supplemental Fig. S6).

The median follow-up time was 4.3 years in the unmatched and 4.2 years in the matched cohort (interquartile range 1–5; range: 0–12 years in both cohorts). In the VSRR group, 1343 patients (67%) underwent the remodelling procedure; 662 (33%) underwent the reimplantation procedure. In 59% of the remodelling procedures, an annuloplasty was performed to stabilize the annulus. Table 2 presents survival and valve-related outcome events in the unmatched and matched cohorts.

Early outcome

Early death in the VSRR group was due to multiorgan failure in 2 patients, heart failure in another 2, a cerebrovascular event in 1, respiratory failure in 1 and mesenteric ischaemia in 1. All patients from the CVG-ARR group who died had received a mechanical Bentall prosthesis; 3 patients died of septic shock and 2 died of myocardial infarction.

Early reintervention during hospitalization (median 9 days from initial operation; interquartile range, 5–47 days) was performed in 10 patients after VSRR; 1 was due to right coronary dysfunction where a CABG procedure was performed. Hence, 9 patients underwent reintervention on the valve due to recurrent AI that was detected by follow-up echocardiography during hospitalization after the initial operation: Two patients underwent an additional repair (1 with fixation of a ruptured fenestration and 1 in whom the plication sutures were removed, which led to a desirable result). In all other reinterventions, the aortic valve was replaced.

Overall survival and reintervention

During the follow-up period, 33 patients died: 12 (1.8%) in the VSRR cohort and 21 (9.6%) in the CVG-ARR cohort (16 who had a mechanical Bentall and 5 who had biological root replacements). In the VSRR group, 51% of deaths were non-cardiac and 49% were cardiac. Of the cardiac deaths, 56% were valve-related (45% sudden unexplained deaths) and 44% were non-valve related. In the CVG-ARR cohort, there were 54% cardiac deaths, 49% of which were valve-related (80% sudden unexplained) and 51% were non-valve related (cancer or unknown).

Survival was 95.4% (95% CI 94–97%) at 5 years in the VSRR group versus 84.4% (95% CI 82–92%) in the CVG-ARR group (*P* = 0. 002). Figure 2A shows Kaplan–Meier curves of cumulative survival in the VSRR and CVG-ARR groups.

CVG-ARR with both biological and mechanical prosthesis was associated with lower survival compared to VSRR: hazard ratio (HR) 1.81, 95% CI 1.41–2.25 (*P* = 0.004); and HR 3.96, 95% CI 1.58–9.91 (*P* = 0.003), respectively. Figure 2B shows Kaplan–Meier curves of survival for the different procedures.

Reintervention on the aortic root/valve was performed in 15 patients in the VSRR group: 10 due to progressive AI; 2 due to aorta-related issues [(pseudo)aneurysm]; 2 due to stenosis of the repaired valve; and 1 due to endocarditis. In the CVG-ARR group, there were 4 reinterventions: 3 were related to the aorta and 1 due to valve conduit insufficiency (Freestyle valve). Freedom from reintervention on the aortic root at 5 years was 96.8% (95% CI 95–98%) in the VSRR group and 95.4% (95% CI 91–99%) in the CVG-ARR group (*P* = 0.98). Figure 3 shows Kaplan–Meier curves of freedom from reintervention on the aortic root. Additional

Table 1: Patient and perioperative characteristics in matched and unmatched cohorts

	Unmatched			Matched		
	VSRR (n = 2005)	CVG-ARR (n = 218)	*P*-value	VSRR (n = 654)	CVG-ARR (n = 218)	*P*-value
Age, years (range, SD)	51.3 (18 -83, 13.9)	56.0(20-84, 12.6)	0.04	56.1 (19-83, 12.8)	56.0 (20-84, 12.6)	0.95
Male (%)	85	86	0.88	86	86	1.0
Connective tissue disease (%)	21	19	0.42	18	19	0.52
Insulin-dependent diabetes mellitus, %	1.4	1	0.35	1	1	1.0
COPD, %	3.9	3	0.28	3	3	1.0
Impaired renal function, %	0.1	0	0.88	0	0	1.0
Pulmonary hypertension, %	4.5	3	0.46	3	3	0.92
Previous cardiac surgery, %	7%	4	0.07	5	4	0.84
Recent myocardial infarction, %	1.1	1	0.90	1	1	0.88
No. of cusps			0.10			0.78
Tricuspid, %	58	57		59	57	
Bicuspid, %	39	33		31	33	
Other (unicuspid, undefined) , %	3	10		10	10	
Rhythm			0.41			0.92
Sinus, %	93	92		92	92	
Atrial fibrillation, %	6	7		7	7	
Pacemaker, %	1	1		1	1	
NYHA			0.03			0.70
I+II, %	69	79		80	79	
III+IV, %	31	21		20	21	
Preoperative LVF			0.34			0.70
Good to moderate, %	99	98		98	98	
Less than moderate, %	1	2		2	2	
Preop annulus diameter, mm (SD)	27.0 (5.7)	26.8 (4.2)	0.34	26.9 (3.8)	26.8 (4.2)	0.72
Preop LVEDD, mm (SD)	44.4 (3.9)	41.5 (4.2)	0.67	41.8 (4.0)	41.5 (4.2)	0.62
Preop LVESD, mm (SD)	28.4 (2.5)	24.0 (2.8)	0.03	24.3 (2.4)	24.0 (2.8)	0.55
Preop AI grade			0.06			0.61
Trivial/none, %	29	20		22	20	
Moderate, %	54	59		59	59	
Severe, %	17	21		19	21	
Concomitant procedures						
CABG, %	8	9	0.68	9	9	1.0
MVP, %	4	4	0.88	5	4	0.55
Maze, %	1	1	0.49	1	1	0.84
(Hemi)Arch replacement, %	12	1	0.001	3	1	0.40
TVP, %	0	1	0.006	1	1	0.70
PFO closure, %	3	2	0.08	2	2	0.65
Aortic cross-clamp time, min (SD)	118 (16)	112 (12)	0.48	118 (17)	112 (12)	0.42
Bleeding requiring reoperation, %	5	5	0.42	5	5	0.82
Permanent pacemaker, %	2.0	2	0.90	2	2	0.64

[a]Only in remodelling procedures.

[b]Mainly ligation of the left atrial appendage; extra aortic annuloplasty; and pulmonary valve replacement in Ross.

AI: aortic valve insufficiency; CABG: coronary artery bypass grafting; COPD: chronic obstructive pulmonary disease; CVG-ARR: composite valve-graft conduit aortic root replacement; maze: surgical atrial fibrillation therapy; LVEDD: left ventricular end diastolic diameter; LVESD: left ventricular end systolic diameter; LVF: left ventricular failure; MVP: mitral valve plasty; NYHA: New York Heart Association; PFO: patent foramen ovale; Preop: preoperative; SD: standard deviation; TVP: tricuspid valve plasty; VSRR: valve-sparing aortic root replacement.

analysis of bicuspid aortic valves showed no association with a hazard of reintervention at 5 years in a subgroup of patients having VSRR (HR 1.23, 95% CI 0.4–4.5, $P = 0.34$).

In patients with aortic root remodelling (Yacoub), external annuloplasty shows a trend towards fewer reinterventions (HR 3.74, 95% CI 0.9–16.3, $P = 0.08$) compared to remodelling without external annuloplasty.

Valve-related outcome

There was no documented valve thrombosis at follow-up. Aortic insufficiency grade > 2 occurred in 12 (1.8%) patients after VSRR, 10 of whom were reoperated on and in 2 (0.92%) patients after CVG-ARR (biological), 1 of whom had a reoperation. Freedom from AI grade >2 in the VSRR group was 96.1% (standard error 0.01, 95% CI 93.2–96.9%) at the 5-year follow-up. The incidence of endocarditis, thromboembolism and bleeding events combined was 0.39%/patient-year in the VSRR group and 1.80%/patient-year in the CVG-ARR ($P = 0.02$) group. Details on clinical outcome are displayed in Table 2.

Additionally, because most patients were included in the registry after 2013, a subgroup analysis of patients operated on before versus patients operated on after 2013 was performed. There was no difference in survival in the matched group: HR 0.89 (95% CI 0.44–1.78). Also in the VSRR and CVG-ARR groups separately,

Table 2: Valve-related events in unmatched and matched cohorts

Variable	Unmatched			Matched		
	VSRR	CVG-ARR	*P*-value	VSRR	CVG-ARR	*P*-value
Total patient-years	7368	984		2576	850	
Early death, no. (%)	18 (0.89)	7 (2.7)	0.02	7 (1.1)	5 (2.3)	0.29
Late death, no. (%/year)	69 (0.94)	22 (2.24)	0.001	12 (0.47)	21 (2.47)	0.02
Reintervention, no. (%/year)	43 (0.58)	6 (0.61)	0.28	15 (0.58)	4 (0.47)	0.42
Thromboembolism, no. (%/year)	6 (0.08)	4 (0.41)	0.002	1 (0.04)	4 (0.47)	0.01
Bleeding, no. (%/year)	14 (0.19)	9 (0.91)	0.001	8 (0.31)	8 (0.94)	0.01
Endocarditis, no. (%/ear)	2 (0.03)	3 (0.30)	0.001	1 (0.04)	3 (0.35)	0.03

Data expressed as no. (%/year) is the count (linearized-occurrence-rate/year).

CVG-ARR: composite valve-graft conduit aortic root replacement; no.: number; VSRR: valve-sparing aortic root replacement.

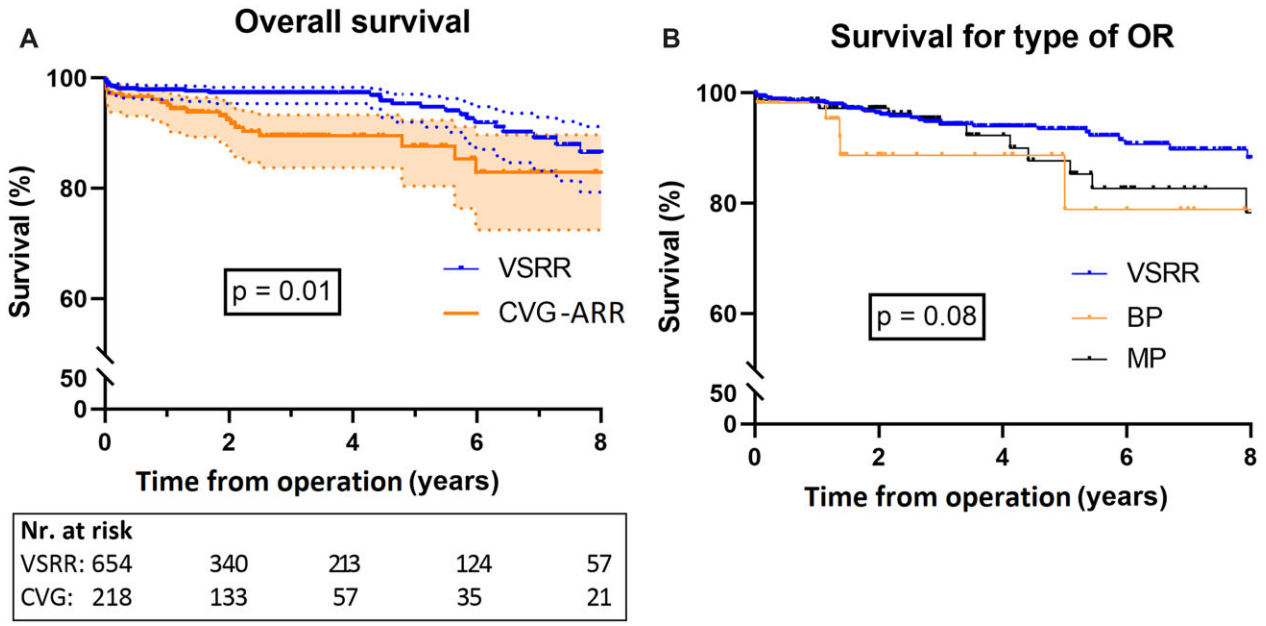


Figure 2: Overall survival and survival in subgroups. (**A**) Overall survival in VSRR and CVG-ARR cohorts. (**B**) Survival in VSRR and CVG-ARR cohorts subdivided by biological and mechanical prostheses. Dashed lines indicate 95% confidence intervals. CVG-ARR: composite valve-graft conduit aortic root replacement procedures; *P*: *P*-value (log-rank); VSRR: valve-sparing aortic root replacement.

there were no differences in survival: HR 0.60 (95% CI 0.2–1.73) and HR 1.97 (95% CI 0.75–5.14), respectively. The distribution of the years of surgery between groups is displayed in Supplemental Table S2.

DISCUSSION

This study presents the largest prospective cohort of patients with a valve-sparing root replacement procedure. Early mortality was low, and overall survival was excellent. Additionally, there were few cases of valve-related complications such as thromboembolic, bleeding and endocarditis events during the follow-up period. Although most patients were operated on in repair-oriented, experienced centres, "low volume" centres also participated in this registry. Nevertheless, when compared to VSRR procedures in this cohort, there was significantly better survival and fewer valve-related events associated with the valve-repair procedures. Moreover, the HR of reintervention was low and comparable to that of the CVG-ARR group.

These excellent results are in line with those reported in a meta-analysis on clinical outcome in the VSRR group, including 4777 patients with 21716 patient-years, which showed low early (2%) mortality and few valve-related events [8]. The slightly lower early mortality in our study might be explained by the more experienced centres participating, as well as the improvements in perioperative care in general during the last decade.

For those patients with an aortic root aneurysm, with or without AI, in whom a repair is not feasible, CVG-ARR is the alternative. Unfortunately, there is no ideal heart valve prosthesis for patients with aortic valve disease. The dilemma outweighs the well-known "pros and cons" of the bioprosthetic and mechanical valve substitutes [15]. The lifetime hazards of thromboembolism and bleeding make the mechanical Bentall less favourable, especially for young, active patients [16]. More than half of the patients in the CVG-ARR group in our study were treated with a

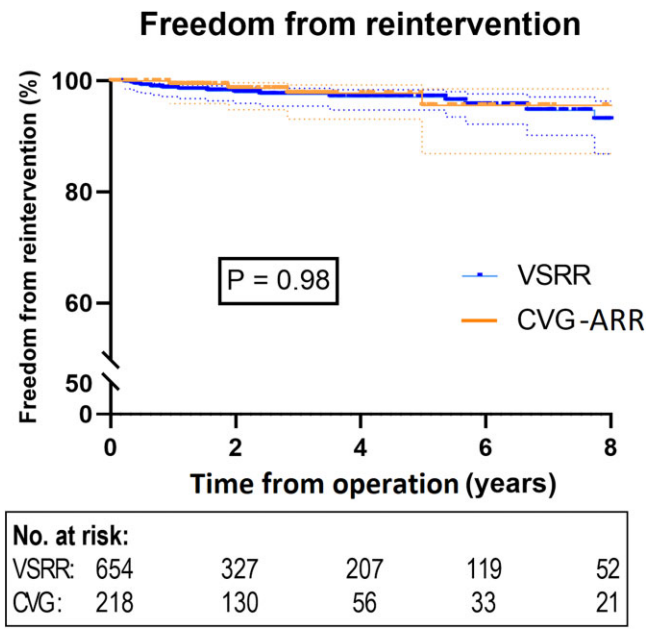


Figure 3: Freedom from reintervention on the aortic root. Dashed lines indicate 95% confidence intervals. CVG-ARR: composite valve-graft conduit aortic root replacement; *P*: *P*-value (log-rank); VSRR: valve-sparing aortic root replacement.

mechanical Bentall, and the mortality was high (10%), possibly due to fatal bleeding events. Nevertheless, a comparable number of patients treated with a biological root prosthesis died (9%). These data suggest worse survival after valve replacement in general, probably related to the valve prosthesis. Prosthetic heart valves have been for decades, and still are, a reliable option for aortic valve replacement; however, this observation is true only when valve sparing is not attainable.

Although guidelines indicate that a mechanical valve prosthesis should be considered only in patients under the age of 60 [17], some advocate the use of a biological prosthesis because, in the transcatheter valve era, a valve-in-valve procedure could be performed in the future [18]. The procedure would have to be done, however, without convincing scientific evidence on the durability of the prosthesis, especially in patients with a root aneurysm. Additionally, the hazard of a reoperation due to structural valve deterioration (SVD) in a biological valve prosthesis is substantial in young patients. In a meta-analysis including 2685 patients, the risk of lifetime reoperation due to SVD was almost 45% in 50-year-olds, and the risk of thromboembolic events was 1.4%/patient-year [19], which is considerable. The Mayo Clinic has already investigated the association between bioprosthetic valves and valve thrombosis and, consequently, SVD [20]. A multicentre study evaluating the effect of prosthesis type on survival and valve-related events showed significantly worse late survival in patients with a biological prosthesis compared to those with a mechanical prosthesis, especially in patients 45 to 54 years of age (23% more deaths in 15 years) [21]. However, these studies describe a heterogeneous cohort of patients with different indications for an operation, and the difference in outcome may be due to selection bias. Nevertheless, these data show the imperfectness of both prosthetic valves and the substantial lifetime hazard of valve-related events after aortic valve replacement.

A single-centre study by David *et al.* comparing 253 VSRR procedures to 183 mechanical and 180 biological valve substitutes, showed better survival (hazard ratio 7 times higher for cardiac-related deaths) and fewer valve-related complications after VSRR [7]. Importantly, the preoperative characteristics were different among the 3 groups. Moreover, reintervention on the aortic valve was significantly higher in patients with bioprosthetic valves, whereas the hazard of reoperation became progressively evident after 5 years of follow-up. Although better survival and fewer valve-related events in the VSRR group were also presumptive in our study, the reintervention hazard was comparable to that in the CVG-ARR group. We found less bioprosthetic structural valve degeneration, probably because it becomes more evident after the first postoperative decade.

Another propensity matched study describing data from the Japan Cardiovascular Surgery Database compared the early outcome following VSRR to that following CVG-ARR in elective surgery [22]. This study shows differences in preoperative patient characteristics favourable for VSRR. Early mortality was 0.8% in the VSRR group and 1.8% (2.8% in patients having solely a mechanical Bentall) in the CVG-ARR group, comparable to our results. These excellent perioperative results are probably due to experience in aortic root surgery, because high-volume centres are associated with superior outcomes [23].

In our study, both reimplantation and remodelling techniques, with or without (ring) annuloplasty, were used in the VSRR group according to the preference of the surgeon. We did not find any difference in outcomes, although there was a trend towards fewer reinterventions when annuloplasty was performed as part of the remodelling technique. There are no comprehensive data on this subject.

On a critical note, the inferior survival in the CVG-ARR group may be related to less favourable patient-related characteristics that are not included in the database (e.g. frailty) and consequently not adjusted for in the analysis. Moreover, patients undergoing VSRR were selected based on assessment of the valve anatomy. It must be assumed that a VSRR procedure was performed only in patients with a suitable valve. Nevertheless, after propensity matching, there were no significant differences in patient characteristics between the VSRR and the CVG-ARR groups, with excellent covariate balance across the groups.

In light of the probable selection bias of selecting "fitter" patients for a valve-sparing procedure, we performed a subgroup analysis of 104 patients. Initially, based on the judgement of the surgeon, echocardiographic evidence and patient characteristics, the preoperative plan was to repair the valve. However, after analysing the valve intraoperatively, the plan changed to replacement because of the anatomy of the valve rather than any patient-related characteristics. Interestingly, patients with preoperative characteristics similar to those in the VSRR group have a lower probability of survival compared to those in the VSRR group (Supplemental Fig. S2). The suggestion that survival may be better due to VSRR is important. Valve-sparing procedures may have superior haemodynamics and a lower risk of prosthesis-patient mismatch (although this situation in less common with larger roots), compared to prosthetic valve substitutes, which could partly explain the better survival [9].

Another issue is the fact that the age threshold of patients in the VSRR group is assumed to be beneficial compared to that in the CVG-ARR group. It is assumed that many surgeons find valve sparing preferable in "young" patients, and less desirable in "older" patients. A subgroup analysis of patients aged 60 years and older (Supplemental Fig. S7) showed the same survival benefit in the VSRR group compared to that in the CVG-ARR group.

Minimal data are available on this subject; however, we believe that fewer valve-related events in the VSRR group will probably lead to better outcomes, even in older patients, given that the valves and the patient characteristics are suitable for repair. When life expectancy is short and durable repair is not achievable, the biological valve prosthesis remains a good alternative.

Based on this multicentre, international collaborative study, overall outcome is superior following VSRR compared to CVG-ARR. Consequently, the first surgical choice should be a valve-sparing procedure in patients with an aortic root aneurysm, especially in those without severe comorbidities and when a durable repair is desired. We advocate referral to more experienced centres when there is a lack of specific expertise onsite.

Limitations

Although this study contains data from a prospective cohort, there may still be some information bias because the data collected from different sites may not be complete for every patient.

Another issue is that VSRR was performed in 90% of the patients using 3 types of VSRR procedures (reimplantation, remodelling with and remodelling without annuloplasty) compared to 2 types of valve-replacing procedures (mechanical and biological). Each type of valve-sparing procedure may have a different outcome, although from the limited information available in the literature, the remodelling and reimplantation techniques are similar regarding the hazards of survival and of reintervention. Moreover, we excluded the Ross procedure because it is a complex procedure with a potential risk for reoperation, although excellent long-term outcomes could be achieved [24]. Additionally, most VSRR procedures were performed in experienced centres. Hence, the excellent results may not represent results possible in an average clinical practice. Another important clinical issue is the relatively short follow-up time (4 years). The durability and hence the hazard of reoperation due to valve failure, especially in valve-sparing procedures and valve replacement with biological prostheses, are probably more prevalent after the first postoperative decade. Longer follow-up of these patients is warranted to evaluate the long-term results. Finally, the choice of valve replacement may have been due to characteristics that are not entered into the database and not adjusted for in the analysis (e.g. frailty), which may have led to worse outcomes in valve-replacing procedures.

CONCLUSIONS

This study shows that valve-sparing procedures have excellent results, with low operative mortality and valve-related event rates. If the valve anatomy is feasible for repair and if the patients are younger with fewer comorbidities, a valve-sparing strategy should be preferred over a valve-replacing strategy. We advocate a valve-sparing strategy even in more complex cases when performed in experienced centres. Follow-up data from the AVIATOR registry will help us clarify the potential beneficial long-term outcome after VSRR.

Funding

This study received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Conflict of interest: Dr Lansac holds the patent for the EXTRA-AORTIC Ring, which is produced by Coroneo, Montreal, Quebec, Canada. The other authors have nothing to disclose.

Data availability

The data underlying this article were provided by the Heart Valve Society workgroup "AVIATOR". Data will be shared on request to the corresponding author with permission of HVS.

REFERENCES

[1] Iung B, Baron G, Butchart EG, Delahaye F, Gohlke-Barwolf C, Levang OW *et al.* A prospective survey of patients with valvular heart disease in Europe: the Euro Heart Survey on Valvular Heart Disease. Eur Heart J 2003;24:1231–43.

[2] Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J et al 2021 ESC/EACTS Guidelines for the management of valvular heart disease: developed by the Task Force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). European Heart Journal 2021;43:561–632.

[3] Stamou SC, Williams ML, Gunn TM, Hagberg RC, Lobdell KW, Kouchoukos NT. Aortic root surgery in the United States: a report from the Society of Thoracic Surgeons database. J Thorac Cardiovasc Surg 2015;149:116–22 e4.

[4] Lansac E, Di Centa I, Sleilaty G, Crozat EA, Bouchot O, Hacini R *et al.* An aortic ring: from physiologic reconstruction of the root to a standardized approach for aortic valve repair. J Thorac Cardiovasc Surg 2010;140: S28–35. discussion S45-51.

[5] Schafers HJ, Bierbach B, Aicher D. A new approach to the assessment of aortic cusp geometry. J Thorac Cardiovasc Surg 2006;132:436–8.

[6] Boodhwani M, de Kerchove L, Glineur D, Poncelet A, Rubay J, Astarci P *et al.* Repair-oriented classification of aortic insufficiency: impact on surgical techniques and clinical outcomes. J Thorac Cardiovasc Surg 2009; 137:286–94.

[7] Ouzounian M, Rao V, Manlhiot C, Abraham N, David C, Feindel CM et al Valve-Sparing Root Replacement Compared With Composite Valve Graft Procedures in Patients With Aortic Root Dilation. J Am Coll Cardiol 2016;68:1838–47.

[8] Arabkhani B, Mookhoek A, Di Centa I, Lansac E, Bekkers JA, De Lind Van Wijngaarden R *et al.* Reported Outcome After Valve-Sparing Aortic Root Replacement for Aortic Root Aneurysm: a Systematic Review and Meta-Analysis. Ann Thorac Surg 2015;100:1126–31.

[9] Collins JD, Semaan E, Barker A, McCarthy PM, Carr JC, Markl M *et al.* Comparison of Hemodynamics After Aortic Root Replacement Using Valve-Sparing or Bioprosthetic Valved Conduit. Ann Thorac Surg 2015; 100:1556–62.

[10] Esaki J, Leshnower BG, Binongo JN, Lasanajak Y, McPherson L, Halkos ME *et al.* Clinical Outcomes of the David V Valve-Sparing Root Replacement Compared With Bioprosthetic Valve-Conduits for Aortic Root Aneurysms. Ann Thorac Surg 2017;103:1824–32.

[11] Yamabe T, Zhao Y, Kurlansky PA, Nitta S, Borger MA, George I *et al.* Assessment of long-term outcomes: aortic valve reimplantation versus aortic valve and root replacement with biological valved conduit in aortic root aneurysm with tricuspid valve. Eur J Cardiothorac Surg 2021;59: 658–65.

[12] de Heer F, Kluin J, Elkhoury G, Jondeau G, Enriquez-Sarano M, Schafers HJ, Aortic Valve Repair Research Network Investigators *et al.* AVIATOR: an open international registry to evaluate medical and surgical outcomes of aortic valve insufficiency and ascending aorta aneurysm. J Thorac Cardiovasc Surg 2019;157:2202–11.e7. e7.

[13] Akins CW, Miller DC, Turina MI, Kouchoukos NT, Blackstone EH, Grunkemeier GL *et al.* Guidelines for reporting mortality and morbidity after cardiac valve interventions. Eur J Cardiothorac Surg 2008;33:523–8.

[14] David TE, Maganti M, Armstrong S. Aortic root aneurysm: principles of repair and long-term follow-up. J Thorac Cardiovasc Surg 2010;140: S14–9. discussion S45-51.

[15] Rahimtoola SH. Choice of prosthetic heart valve in adults an update. J Am Coll Cardiol 2010;55:2413–26.
[16] Mookhoek A, Korteland NM, Arabkhani B, Di Centa I, Lansac E, Bekkers JA *et al.* Bentall Procedure: A Systematic Review and Meta-Analysis. Ann Thorac Surg 2016;101:1684–9.
[17] Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, ESC Scientific Document Group *et al.* 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J 2017;38:2739–91.
[18] Etz CD, Girrbach FF, von Aspern K, Battellini R, Dohmen P, Hoyer A *et al.* Longevity after aortic root replacement: is the mechanically valved conduit really the gold standard for quinquagenarians? Circulation 2013; 128:S253–62.
[19] Puvimanasinghe JP, Takkenberg JJ, Eijkemans MJ, van Herwerden LA, Jamieson WR, Grunkemeier GL *et al.* Comparison of Carpentier-Edwards pericardial and supraannular bioprostheses in aortic valve replacement. Eur J Cardiothorac Surg 2006;29:374–9.
[20] Egbe AC, Pislaru SV, Pellikka PA, Poterucha JT, Schaff HV, Maleszewski JJ *et al.* Bioprosthetic Valve Thrombosis Versus Structural Failure: clinical and Echocardiographic Predictors. J Am Coll Cardiol 2015;66: 2285–94.
[21] Goldstone AB, Chiu P, Baiocchi M, Lingala B, Patrick WL, Fischbein MP *et al.* Mechanical or Biologic Prostheses for Aortic-Valve and Mitral-Valve Replacement. N Engl J Med 2017;377:1847–57.
[22] Kunihara T, Ichihara N, Miyata H, Motomura N, Sasaki K, Matsuhama M, Japan Cardiovascular Surgery Database *et al.* Valve-sparing root replacement and composite valve graft replacement in patients with aortic regurgitation: from the Japan Cardiovascular Surgery Database. J Thorac Cardiovasc Surg 2019;158:1501–11 e6.
[23] Hughes GC, Zhao Y, Rankin JS, Scarborough JE, O'Brien S, Bavaria JE *et al.* Effects of institutional volumes on operative outcomes for aortic root replacement in North America. J Thorac Cardiovasc Surg 2013;145: 166–70.
[24] Skillington PD, Mokhles MM, Takkenberg JJ, O'Keefe M, Grigg L, Wilson W *et al.* Twenty-year analysis of autologous support of the pulmonary autograft in the Ross procedure. Ann Thorac Surg 2013;96:823–9.