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

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Keywords

Valve-sparing root replacement, aortic valve-repair, Bentall

Visual abstract:

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

Key Finding: 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.

Abstract

Objectives

The study objective is to evaluate outcome of valve-sparing root replacement(VSRR) and its comparison to 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: aortic dissection, endocarditis and valvular-stenosis. Propensity score matching (3:1 ratio) was applied to compare VSRR (reimplantation 33% and remodeling 67%) and CVG-ARR.

Results

We matched 218 CVG-ARR patients to 654 VSRR patients (median age, 56.0; median follow-up was 4 years in both, IQR 1-5 years). Early mortality was 1.1% in VSRR versus 2.3% in CVG-ARR. Survival was 95.4% (95% CI 94-97%) at 5 years in VSRR versus 85.4% (95% CI 82-92%) in CVG-ARR, p = 0.002. Freedom from reintervention at 5 years was 96.8% (95% CI 95-98%) in VSRR and 95.4% (95% CI 91-99%) in CVG-ARR, p = 0.98. Additionally, there were more thromboembolism, endocarditis and bleeding events in CVG-ARR (p = 0.02).

Conclusions

This multicenter study shows excellent results after valve-sparing root replacement in patients with ascending aortic aneurysm with or without valve insufficiency. Compared to composite valve-graft aortic root replacement, survival is better and valve-related event 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 centers.

Abbreviations

VSRR = Valve-Sparing aortic Root Replacement

CVG-ARR = Composite Valve-Graft conduit Aortic Root Replacement

AI = Aortic valve Insufficiency

NYHA = New York Heart Association

LVEDD = Left Ventricular End Diastolic Diameter

LVESD = Left Ventricular End Systolic Diameter

Introduction

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

Approximately 10% of patients with aortic valve disease are diagnosed with aortic valve insufficiency (AI), due to aortic root aneurysm or other pathology, often 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 aortic root replacement (VSRR) is indicated and preferred above valve replacement, especially in younger patients and when performed in experienced centers [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 and due to efforts of expert centers there have been successful attempts of standardization of approach and technique in order to enhance the reproducibility and dissemination of valve-sparing procedures, also in less experienced centers [4-7].

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

The objective of this study is to provide large scale clinical outcome after VSRR and to compare the survival and valve-related outcome of VSRR (i.e. remodeling and reimplantation procedures) to CVG-ARR (i.e. mechanical Bentall-De Bono and biological root replacement), using the AVIATOR database. Although there are some comparative studies aiming to find differences between VSRR and CVG-

ARR [7, 10, 11], this is the first large multicenter study to present and compare outcome 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 Board of the participating centers, and a 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 centers worldwide enrolling patients undergoing surgical treatment of ascending aortic aneurysm and/or AI. Both VSRR and CVG-ARR procedures are included. This registry presents a uniform database of patients in terms of indication for surgery, which allows evaluating the outcome of valve-sparing and replacement surgery in patients with aortic root dilatation and/or severe AI. More details about the AVIATOR initiative are described elsewhere [12].

A search from the AVIATOR database revealed 2420 adult patients from 43 centers, with individual patient data and at least one (year) clinical follow-up., operated on the aortic root 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, 85% completed for echocardiographic follow-up. Exclusion criteria: aortic dissection, endocarditis and aortic stenosis. An acute indication for surgery was excluded since those patients have less predictable outcome due to other variables than the type of procedure (e.g. hemodynamic instability, organ malperfusion). This resulted in 2264 patients for analysis. Figure 1 shows the selection procedure. Ross procedures were excluded from analysis, because is a complex procedure performed by only a few centers, and normally performed for valvular stenosis as an alternative to prosthetic valve replacement. The procedure does not represent participating centers in the

AVIATOR registry.

The comparison of outcomes was based on intention-to-treat analyses. Survival and valve-related outcome were compared between VSRR and CVG-ARR. Additionally, a subgroup analysis was performed in patients with preoperatively intention to repair the valve, but who due to complex valve anatomy, underwent a valve replacement procedure. This study was approved by The Institutional Review Board of the participating centers. 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 incentive of the AVIATOR is to have annual clinical and echocardiographic follow-up from individual patients. Detailed information about the registry is published earlier [12]. Early mortality contains 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].

Operation Technique

All patients were operated through median sternotomy, using cardiopulmonary bypass and reimplantation of the coronary arteries. In VSRR, patients underwent either the aortic root remodeling or the aortic valve reimplantation procedure. In the majority of the remodeling procedures an annuloplasty was performed to stabilize the annulus, according to surgeon's preference. The operation techniques are described elsewhere [4, 14]. In valve replacing procedures

either a mechanical Bentall-de Bono procedure or a biological root replacement (stented bioprostheses sutured into a Dacron graft or a Freestyle root prosthesis) was performed. In patients with an extended (hemi)arch replacement, deep hypothermia and circulatory arrest was applied.

Statistical Methods

Continuous data are presented as mean with SD or median with IQR, Kolmogorov-Smirnov test was used for determination of the normality of the distribution. Comparison by 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, and comparison was done using the $\chi 2$ test or the Fisher exact test (low prevalence). Survival and freedom from valve reintervention were analyzed 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 outcome between VSRR and CVG-ARR. The proportional hazard assumption was met, by visual inspection (Log minus Log curves). Tests were performed 2-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 neighbor matching with a caliper width equal to 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, California USA, www.graphpad.com, were used.

Results

Clinical outcome in the Unmatched cohort

In the initial unmatched cohort of 2005 VSRR and 218 CVG-ARR patients, there were several significant differences in patient-characteristics. Table 1 displays patient characteristics in both matched and unmatched cohort. Cumulative survival at 5 years was 95.6% (95% CI 94-97%) in VSRR, and 87.6% (95% CI 82-93%) in CVG-ARR. After propensity score adjustment there were no significant differences between VSRR and CVG-ARR patients. The differences in clinical outcome in both groups remained after propensity matching. Supplemental Figures S1 and S2 show KM-curves of cumulative overall survival in VSRR and CVG-ARR and survival in a subgroup of 104 patients in the CVG-ARR cohort with preoperatively intention-to-repair the valve, respectively.

Freedom from reintervention on aortic root at 5 years was 96.9% (95% CI 95-98%) in VSRR versus 95.2% (95% CI 91-99%) in CVG-ARR. Supplemental Figure S3 shows KM-curve of freedom from reintervention on the aortic root. Freedom from AI grade >2 in VSRR was 94.9% (SE 0.01, 95%CI 92.7-96.5%) at 5 years of follow-up (Supplemental Figure 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 two groups (Supplemental Figures S5 displays the propensity score distribution). Very adequate covariate balance across the two groups was achieved. A "Love plot" of standardized differences in baseline covariate means between VSRR and CVG-ARR, before and after propensity score matching, is performed (Supplemental Figures S6).

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

Early outcome

Early death in VSRR was due to multi-organ failure in two patients, heart failure in another two, cerebrovascular event in one, respiratory failure in one, and mesenteric ischemia in one. All patients who died in CVG-ARR had received a mechanical Bentall prostheses and mortality was attributed to septic shock in three and myocardial infarction leading to death in two.

Early reintervention during hospitalization (median 9 days from initial operation; IQ range 5-47 days) was performed in 10 patients after VSRR; one due to right coronary dysfunction where a CABG procedure was performed. Hence, 9 patients underwent reintervention on the valve due to recurrent aortic valve insufficiency, detected by follow-up echocardiography during hospitalization after the initial operation: Two patients underwent an additional repair (one with fixation of a ruptured fenestration, and in another patient the plication sutures were removed leading to

desirable result). In all other reinterventions the aortic valve was replaced.

Overall survival and reintervention

During follow-up 33 patients died: 12 (1.8%) in VSRR and 21 (9.6%) in CVG-ARR group (16 in mechanical Bentall and 5 in biological root replacement). In VSRR, 51% of deaths were non-cardiac and 49% cardiac. Of the cardiac deaths, 56% was valve-related (45% sudden unexplained deaths) and 44% non-valve related. In CVG-ARR, there were 54% cardiac deaths, of which 49% valve-related deaths (80% sudden unexplained) and 51% non-valve related (cancer or unknown).
Survival was 95.4% (95% CI 94-97%) at 5 years in VSRR versus 84.4% (95% CI 82-92%) in CVG-ARR; p = 0. 002. Figure 2A shows KM-curves of cumulative survival in VSRR and CVG-ARR.
Both CVG-ARR with biological and mechanical prosthesis were associated with lower survival compared to VSRR: 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 KM-curves of survival for different procedures.

Reintervention on the aortic root/valve was performed in 15 patients in VSRR: 10 due to progressive aortic valve insufficiency, 2 aorta related ((pseudo)aneurysm), 2 stenosis of the repaired valve, and 1 endocarditis. In CVG-ARR there were 4 reinterventions: 3 aorta related and 1 valve conduit insufficiency (Freestyle). Freedom from reintervention on the aortic root at 5 years was 96.8% (95% CI 95-98%) in VSRR and 95.4% (95% CI 91-99%) in CVG-ARR, p=0.98. Figure 3 shows KM-curves of freedom from reintervention on the aortic root. Additional analysis of bicuspid aortic valves showed no association with hazard of reintervention at 5 years, in a subgroup of VSRR patients (HR 1.23, 95% CI 0.4-4.5, p=0.34).

In patients with aortic root remodeling (Yacoub), external annuloplasty shows a trend toward fewer reinterventions (HR 3.74, 95% CI 0.9-16.3, p=0.08) when compared to remodeling 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 of whom 10 were reoperated, and in 2 (0.92%) patients after CVG-ARR (biological), 1 reoperated. Freedom from AI grade >2 in VSRR was 96.1% (SE 0.01, 95%CI 93.2-96.9%) at 5 years of follow-up. The incidence of endocarditis, thromboembolism and bleeding events combined was 0.39%/patient-year in VSRR and 1.80%/patient-year in CVG-ARR (P=0.02). Details on clinical outcome are displayed in Table 2.

Additionally, since most patients were included into the registry after 2013, a subgroup analysis of patients operated before versus patients operated 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 separately 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 as thromboembolic, bleeding and endocarditis events during follow-up. Although most patients were operated in repair-oriented, experienced centers, also “low volume” centers participated in this registry. Nevertheless, when compared to valve replacement procedures in this cohort, there was a significant better survival and less valve-related events in

valve-repair procedures. Moreover, the hazard of reintervention was low and comparable to the CVG-ARR group.

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

For those patients with aortic root aneurysm, with or without AI, where 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 is outweighing the well-known "pros and cons" of the bioprosthetic and mechanical valve substitutes [15]. The lifetime hazard of thromboembolism and bleeding makes the mechanical Bentall less favorable, especially for young and active patients [16]. More than half of the patients in the CVG-ARR group in our study, were treated with a mechanical Bentall and the mortality was high (10%), possibly due to fatal bleeding events. Nevertheless, patients treated with a biological root prosthesis had a comparable mortality (9%). These data suggest worse survival after valve replacement in general, probably related to the valve prosthesis. Undoubtedly prosthetic heart valves have been, and still are, a reliable option for aortic valve replacement for decades, however, only when valve-sparing is not attainable.

While guidelines indicate that under the age of 60 mechanical valve prosthesis should be considered [17], some advocate the use of a biological prosthesis, because in the transcatheter valve (TAVI) era an valve-in-valve procedure could be performed in the future [18], however without convincing scientific evidence on the durability, especially in patients with root aneurysm. Additionally, the hazard of a reoperation due to SVD in biological valve prosthesis is substantial in young patients. 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 multicenter study evaluating the effect of prosthesis type on survival and valve-related events showed significantly worse late survival in biological prosthesis compared to mechanical prosthesis, especially in patients 45 to 54 years of age (23% more mortality in 15 years) [21]. However, these studies describe a heterogeneous cohort of patients with different indications for 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 center study by T. 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 mortality) and less valve-related complications after VSRR [7]. Importantly, the preoperative characteristics were different between the 3 groups. Moreover, reintervention on the aortic valve was significantly higher in bioprosthetic valves, while the hazard of reoperation became progressively evident after 5 years of follow-up. Although better survival and less valve-related events in VSRR were also presumptive in our study, the reintervention hazard was comparable to CVG-ARR. We found less bioprosthetic structural valve degeneration, probably because this becomes more evident after the first postoperative decade.

Another, propensity-matched, study describing data from the Japan Cardiovascular Surgery Database, compared early outcome of VSRR to CVG-ARR in elective surgery [22]. This study shows differences in preoperative patient-characteristics favorable in VSRR. Early mortality was 0.8% in VSRR and 1.8% (2.8% in solely mechanical Bentall) in CVG-ARR, comparable to our results. These excellent perioperative results are probably due to experience in aortic root surgery, since high

volume centers are associated with superior outcome [23].

In our study both reimplantation and remodeling technique, with or without (ring) annuloplasty, was used in VSRR, by preference of the surgeon. We did not find any difference in outcome, although there was a trend toward less reinterventions when annuloplasty was performed in remodeling technique. There are no large comprehensive data on this subject.

On a critical note, the inferior survival in CVG-ARR may be related to less favorable patient-related characteristics that are not included in the database (e.g. frailty) and consequently not adjusted in the analysis. Moreover, patients undergoing VSRR were selected based on assessment of the valve anatomy. It must be assumed that only in patients with a suitable valve a VSRR procedure was performed. Nevertheless, after propensity-matching there were no significant differences in patient-characteristics between VSRR and CVG-ARR, with excellent covariate balance across the groups. In the light of probable selection bias of selecting "fitter" patients for a valve-sparing procedure, we performed a subgroup analysis in 104 patients with a clear preoperative intention-to-repair the valve; based on surgeon's judgment, echocardiography and patient characteristics, in whom however, after valve analysis intraoperatively the plan changed to replacement, due to valve anatomy only and not related to patient-characteristics. Interestingly, these patients with similar preoperative characteristics as the VSRR group, have a lower survival probability compared to the VSRR group (Supplemental Figure S2). This is an important suggestion that survival may indeed be better due to VSRR. Valve-sparing procedures may have superior hemodynamics and lower risk of prosthesis-patient mismatch (although less common in larger roots), compared to prosthetic valve substitutes, which could partly explain the better survival [9].

Another issue is the age threshold of patients were VSRR is assumed to be profitable over CVG-ARR. Assumably many surgeons find valve-sparing preferable in "young" patients, and less desirable in

"elderly". A subgroup analysis of patients aged 60 years and older (supplemental Figure S7) showed the same survival benefit after VSRR, compared to CVG-ARR. There are no large data available on this subject, however, we believe that less valve-related events in VSRR will probably lead to better outcome, even in older patients, given suitable valve and patient-characteristics for repair. When life-expectancy is short and durable repair is not achievable, biological valve prosthesis remains a good alternative.

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

Limitations

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

Another issue is that VSRR was performed in 90% of the patients, and there were three types of VSRR procedures (reimplantation, remodeling with-, and remodeling without annuloplasty), compared to 2 types of valve replacing procedures (mechanical and biological). Each type of valve-sparing procedure may have different outcome, although from the limited literature the remodeling and reimplantation technique are quite similar regarding hazard of survival and reintervention. Moreover, we excluded the Ross procedures because this is a complex procedure with potential risk for reoperation, although excellent long-term outcome could be achieved [24]. Additionally, most VSRR procedures were performed in experienced centers. Hence, the excellent results may not represent average clinical practice. Another important clinical issue is the relatively short follow-up

time (4 years). The durability and hence 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 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 outcome in valve replacing procedures.

Conclusions

This study shows that valve-sparing procedures have excellent results, with low operative mortality and valve-related event rate. If the valve anatomy is feasible for repair and in case of low comorbidity and especially in younger patients, a valve-sparing strategy should be the preferred above aortic valve replacing strategy. We advocate a valve-sparing strategy even in more complex cases, when performed in experienced centers Follow-up data from the AVIATOR registry will give us clarification of potential beneficial long-term outcome after VSRR.

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The authors have nothing to disclose.

Conflict of interest: Dr Lansac is patent holder of the “Extra Aortic ring”, which is produced by Coroneo. Inc.

Data availability

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

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Figure legends

Central Image

Better survival after valve-sparing root replacement compared to aortic root replacement procedures

Figure 1. Flowchart of patient selection

Figure 2. Overall survival and survival in subgroups

A) Overall survival in VSRR and CVG-ARR, B) Survival in VSRR and CVG-ARR subdivided in biological and mechanical prosthesis. 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.

Figure 3. Freedom from reintervention on the aortic root

CVG-ARR: Composite valve-graft conduit aortic root replacement procedures; P: P-value (Log-rank); VSRR: Valve-sparing aortic root replacement. Dashed-lines indicate 95% confidence intervals.

476 **Tables**

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Table 1. Patient and Perioperative characteristics in matched and unmatched cohort

CABG: Coronary artery bypass grafting; COPD: Chronic obstructive pulmonary disease; CVA: Cerebrovascular accident; CVG-ARR: Composite valve-graft conduit aortic root replacement procedures; MAZE: surgical atrial fibrillation therapy; MVP: mitral valve plasty; PFO: Patent foramen ovale; TVP: tricuspid valve plasty; VSRR: Valve-sparing aortic root replacement. * only in remodeling procedures, ** mainly ligation of left atrial appendage; extra aortic annuloplasty; and pulmonary valve replacement in Ross

	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%	

Concomittant 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

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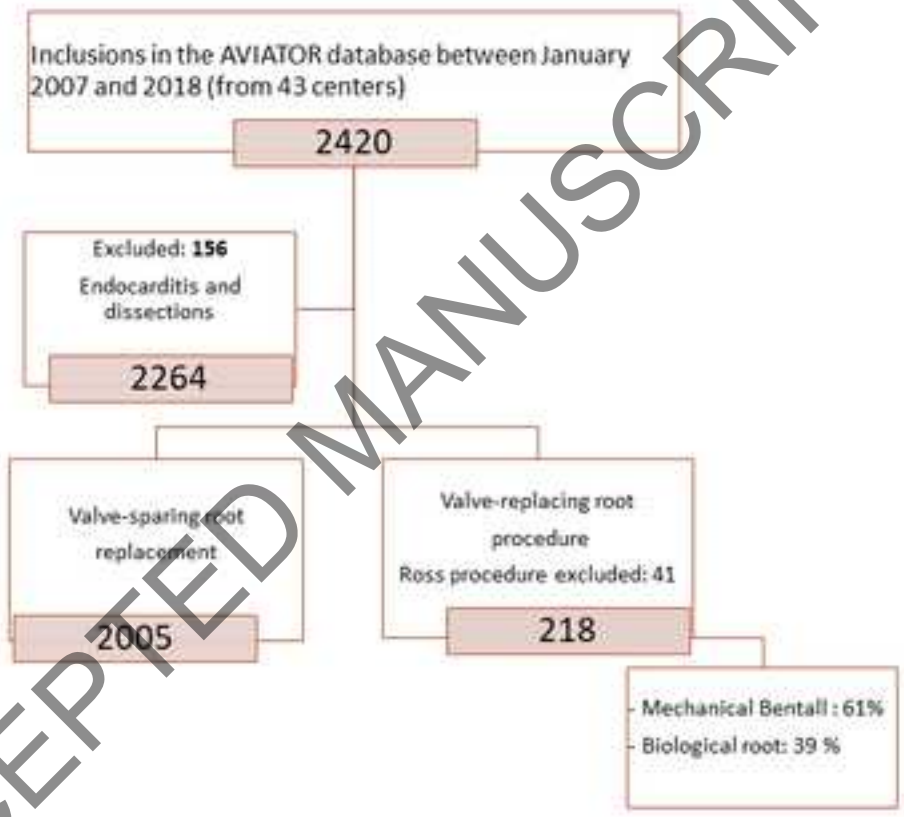
	Unmatched			Matched		
Variable	VSRR	CVG-ARR	P-value	VSRR	CVG-ARR	p-value
Total patient-years	7368	984		2576	850	
Early death, No. (%)	18 (0.89)	7 (2.7)	0.02	7 (1.1)	5 (2.3)	0.29
Late death, No. (%/y)	69 (0.94)	22 (2.24)	0.001	12 (0.47)	21 (2.47)	0.02
Reintervention, No. (%/y)	43 (0.58)	6 (0.61)	0.28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

Table 2. Valve-related events in unmatched and matched cohort

CVG-ARR: Composite valve-graft conduit aortic root replacement procedures; VSRR: Valve-sparing aortic root replacement; No.: Number; Y: Year. Data expressed as No. (%/y) is the count (linearized-occurrence-rate/y).



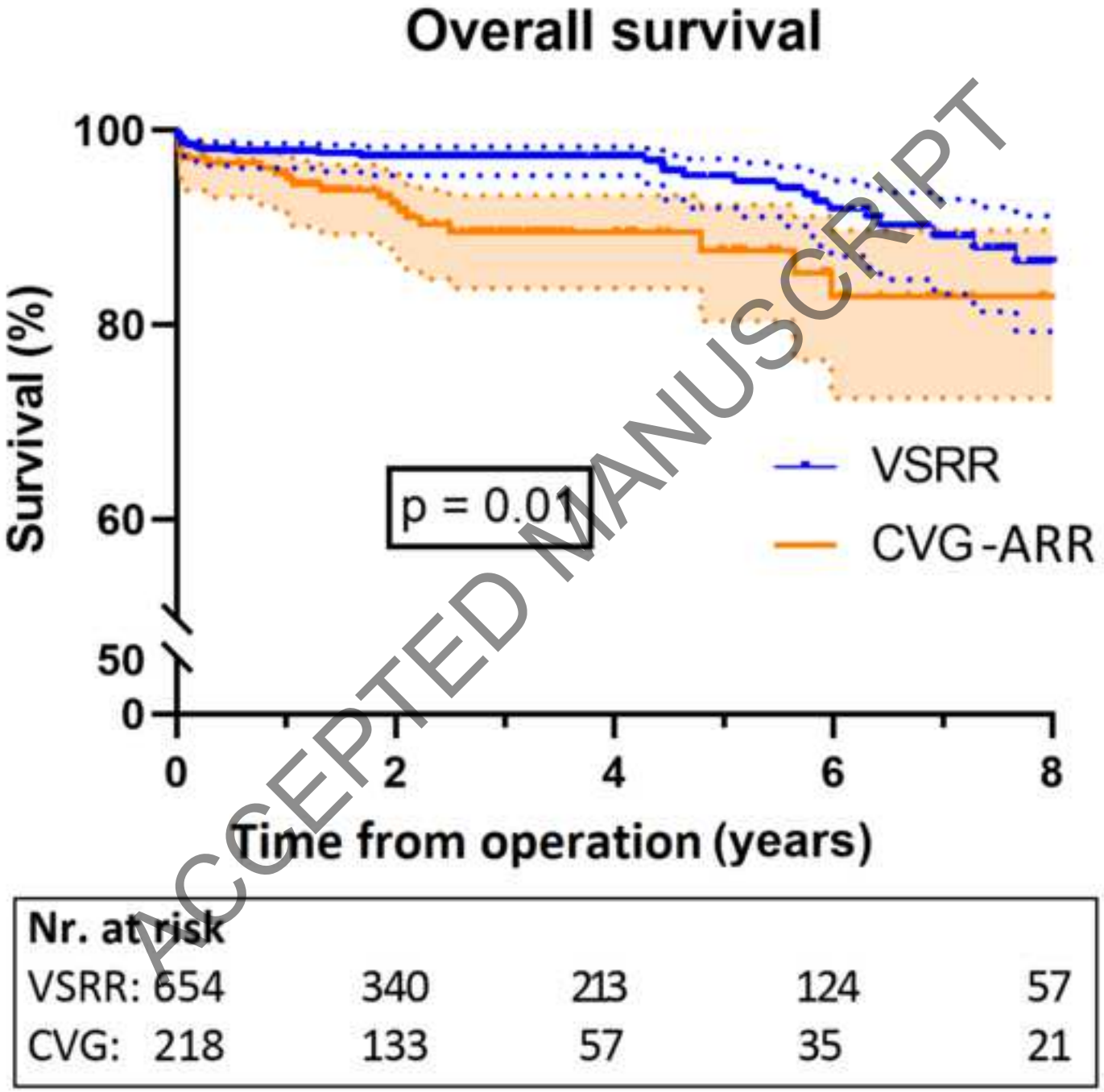
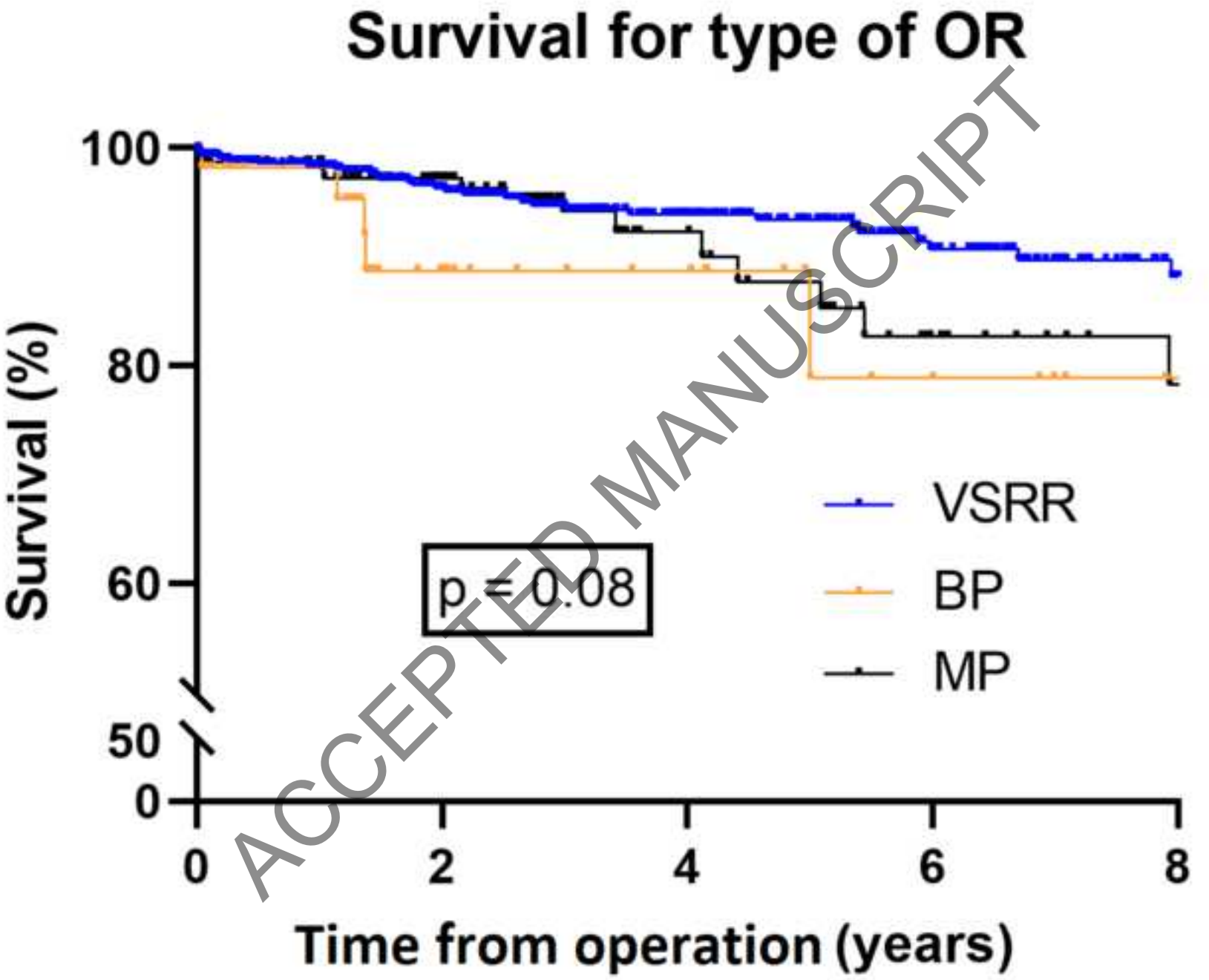
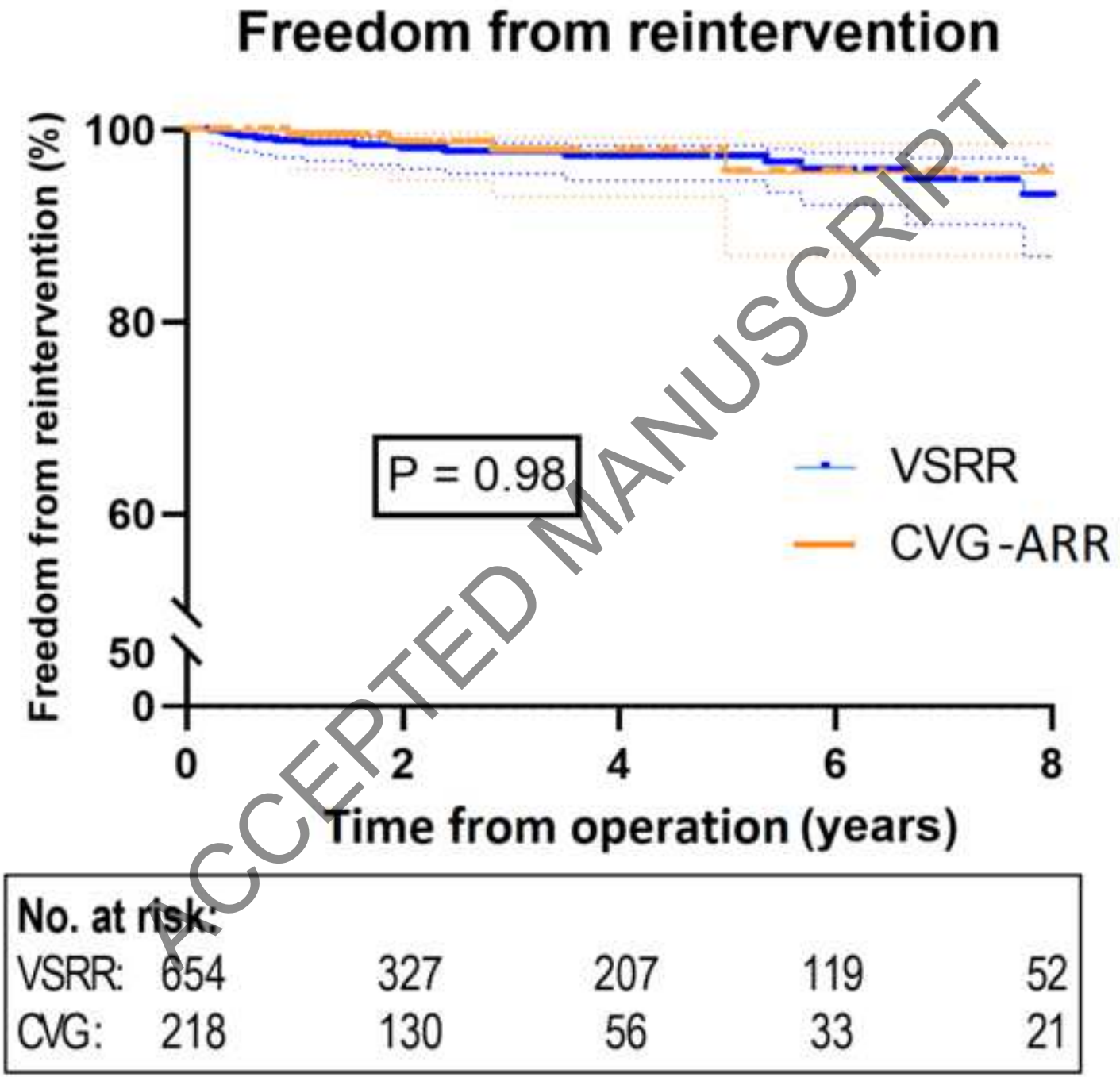
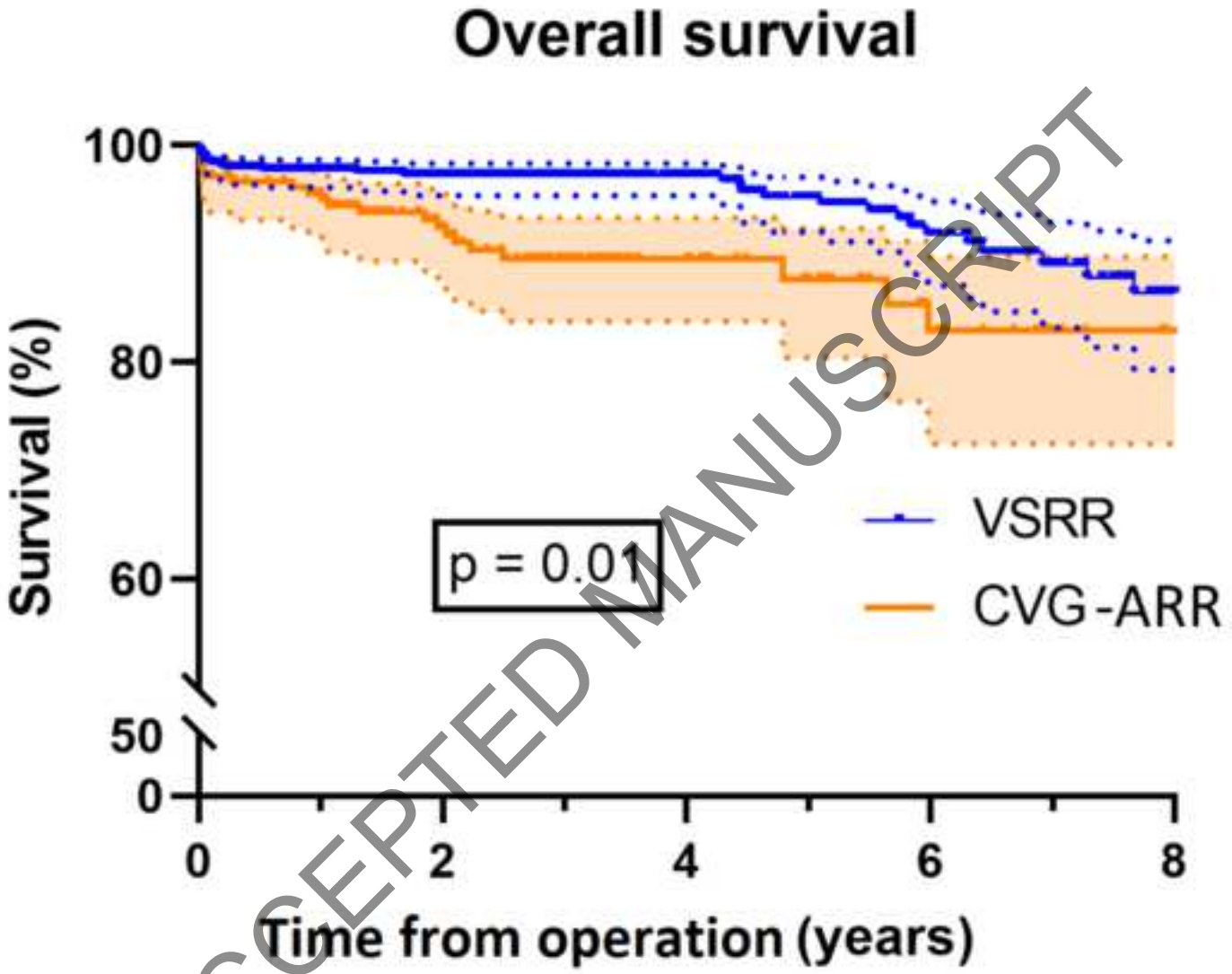


Figure 2B





central picture



pt. at risk				
VSRR: 654	340	213	124	57
CVG: 218	133	57	35	21