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# Two decades of valve-sparing root reimplantation in tricuspid aortic valve: impact of aortic regurgitation and cusp repair

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**Key question**

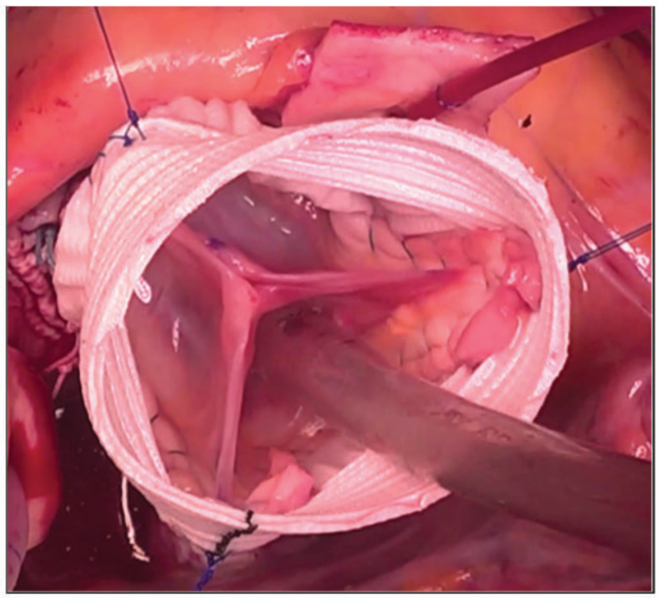
Do aortic regurgitation (AR) and cusp repair impact outcomes after valve-sparing procedures in tricuspid aortic valves?

**Key finding(s)**

No impact was noted on survival and reoperation, but severe AR and multiple cusp repair favour recurrence of moderate to severe AR.

**Take-home message**

Severe AR increases risk of valve-sparing failure, but cusp repair can attenuate that risk for at least the first decade.



## Abstract

**OBJECTIVES:** Our goal was to analyse the influence of preoperative aortic regurgitation (AR) on the necessity of cusp repair during valve-sparing reimplantation (VSR). We focused on patients with tricuspid aortic valves (TAV) and evaluated the impact of AR and cusp repair on long-term outcomes.

**METHODS:** From March 1998 to December 2018, a total of 512 consecutive patients underwent VSR at our institution; of these, 303 had a TAV. The mean age was 53 ± 15 years, and the median follow-up was 6.12 years. The rate and type of cusp repair were analysed based on preoperative AR. Time-to-event analysis was performed, as well as risk of death, reoperation and AR recurrence.

**RESULTS:** Cusp repair was necessary in 168 (55.4%) patients; the rate rose significantly as AR grade increased ($P < 0.001$). In-hospital mortality was 1% ($n = 3$). At 5 and 10 years, overall survival was 92 ± 2% and 75 ± 5%, respectively. Freedom from valve reoperation was 95 ± 2%

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CONVENTIONAL VALVE OPERATIONS

and 90 ± 3%. Freedom from AR >2+ and AR >1+ at 10 years was 88 ± 4% and 70.4 ± 4.6%, respectively. Independent predictors of death included age, New York Heart Association functional class and type-A aortic dissection. Predictors of AR greater than mild included previous cardiac surgery and severe preoperative AR.

**CONCLUSION:** In patients with TAV receiving VSR, the necessity of cusp repair increased with the degree of preoperative AR. Preoperative AR and cusp repair do not impact long-term survival and aortic valve reoperation, but severe preoperative AR and multiple cusp repair increase the risk of recurrent moderate-to-severe AR. Overall, cusp repair seems to attenuate the negative impact of preoperative AR for at least 1 decade in a majority of patients.

**Keywords:** Aortic valve repair • Aortic valve-sparing surgery • Tricuspid aortic valve • Cusp repair

**ABBREVIATIONS**

| | |
|---|---|
| AR | Aortic regurgitation |
| AV | Aortic valve |
| BAV | Bicuspid aortic valve |
| eH | Effective height |
| HR | Hazard ratio |
| NYHA | New York Heart Association |
| TAAD | Type-A aortic dissection |
| TAV | Tricuspid aortic valve |
| VSR | Valve-sparing reimplantation |
| VSRR | Valve-sparing root replacement |

## INTRODUCTION

Valve-sparing root replacement (VSRR) techniques have proven to be a durable strategy in treating patients with aortic root aneurysm and favourable cusp morphology [1]. Over the years, VSRR techniques not only underwent technical modifications (e.g. annuloplasty, artificial sinuses) but also indications were extended to patients with more complex disease than isolated root aneurysm [e.g. root dilatation plus aortic insufficiency, bicuspid aortic valve (BAV), acute aortic dissections)] [2, 3].

While the use of VSRR is nowadays widely adopted in patients with root aneurysm and a functional aortic valve (AV), VSRR is much less frequently performed when aortic regurgitation (AR) is present. This is mainly due to a lack of surgeon's expertise in cusp repair, and the fear of jeopardizing long-term outcomes. Few studies thus far have analysed the relationship between preoperative AR and cusp repair in VSRR; and the impact of these factors on long-term outcomes [3–5].

The aim of this study was to analyse how preoperative AR influenced cusp repair during valve-sparing reimplantation (VSR) procedure, in patients with tricuspid aortic valves (TAV) in a large unicentric series. We also sought to analyse the impact of cusp repair on long-term outcomes, in the setting of preoperative AR.

## MATERIALS AND METHODS

### Patient population

From March 1998 to December 2018, 512 consecutive patients underwent VSR at our institution; of these 303 had TAV and accordingly constitute our study cohort.

Indications for VSR included aortic root aneurysm with or without significant AR [6], acute aortic dissection or AR with annuloectasia (Table 1). The latter defines patients who underwent surgery for severe AR, having large aortic annulus and moderately dilated roots (40–45 mm). In these patients, VSR was also chosen to provide additional annuloplasty, thus stabilizing the functional aortic annulus [7].

This study was approved by the Review Ethics Board of Université Catholique de Louvain, and patient informed consent was obtained (ID Brussels: 2013/03JUI/356).

### Operative techniques

All patients underwent surgery via full sternotomy, under cardiopulmonary bypass. Details of VSR have previously been described, and an accompanying video details the technique (Video 1) [8]. From 1998 to 2001, VSR was performed using standard tubular graft (Gelweave, Vascutek Ltd, Terumo Company, Renfrewshire, Scotland), sized according to best STJ diameter for valve coaptation plus 4–5 mm. Since 2001, Gelweave Valsalva graft (Vascutek Ltd, Terumo Company, Renfrewshire, Scotland) was exclusively used. Sizing of Valsalva graft is done by measuring the height of non-to-left commissure [9]. In patients with valvular lesions such as cusp prolapse, thickening, large fenestrations or perforation, the valve was repaired before VSR using respectively central cusp plication, shaving or pericardial patch. After VSR, the valve was systematically (re-)assessed for any residual or induced cusp prolapse, which was mainly treated with central plication or, less often, with free margin resuspension utilizing running suture of Gore-Tex 7-0 (W.L. Gore and Associates, Inc, Newark, DE, USA) [10]. Cusp coaptation was evaluated via visual inspection, and since December 2014, effective height (eH) is measured intraoperatively using Schäfers' calliper in addition to visual inspection [11]. Central plication was applied until free margin reached an eH of 8–10 mm and all 3 free margins achieved same level at visual inspection.

Additional Cabrol stitch (subcommissural annuloplasty) was applied when judged necessary to further reduce annulus size and improve cusp coaptation in 1 or 2 of the commissures [7]. Cabrol was also used during second run where it served as a beneficial adjunct technique to treat residual AR.

### Echocardiographic assessment and follow-up

Preoperative AR characteristics and aorta dimensions were obtained from intraoperative transoesophageal echocardiography, performed before and after every repair to assess degree of residual AR and orientation of its jet. Prerequisites for successful repair included coaptation length of at least 5 mm at the mid-portion of the free margin and eH of 8–10 mm. Signs of residual moderate or mild eccentric AR almost always led to re-exploration of the AV [12, 13].

**Table 1:** Patient demographics

| | n = 303 |
|---|---|
| Age (years), mean ± SD | 52.9 ± 15.3 |
| Male gender, n (%) | 268 (88.4) |
| BSA, mean ± SD | 2.0 ± 0.2 |
| Connective tissues disease, n (%) | 42 (13.9) |
| Marfan | 34 (11.2) |
| Others (Loeys-Dietz, Ehler-Danlos, ACTA2) | 8 (2.6) |
| Indication for surgery[a], n (%) | |
| Root dilatation without AR (AR 0–1+) | 111 (36.6) |
| Root dilatation with AR (AR ≥2+) | 154 (50.8) |
| AR with annuloectasia (AR ≥3+, aorta <45 mm) | 25 (8.3) |
| Type-A acute dissection | 13 (4.3) |
| Clinical characteristics | |
| NYHA functional class, n (%) | |
| NYHA I | 179 (59.1) |
| NYHA II | 91 (30) |
| NYHA III | 31 (10.2) |
| NYHA IV | 2 (0.7) |
| Previous cardiac surgery, n (%) | 49 (16.2) |
| Ross | 31 (10.2) |
| Others (AV repair, mitral, congenital) | 18 (5.9) |
| Echocardiographic data | |
| Aortic regurgitation grade, n (%) | |
| AR grade 0–1 | 102 (33.7) |
| AR grade 2 | 72 (23.8) |
| AR grade 3 | 88 (29) |
| AR grade 4 | 41 (13.5) |
| LV ejection fraction, n (%) | |
| ≥50% | 255 (84.2) |
| 31–49% | 44 (14.5) |
| ≤30% | 4 (1.3) |
| VAJ diameter (mm), mean ± SD | 26.9 ± 3.6 |
| Root diameter (mm), mean ± SD | 48.0 ± 7.5 |
| STJ diameter (mm), mean ± SD | 42.1 ± 8.3 |
| Ascending aorta diameter (mm), mean ± SD | 42.7 ± 10.2 |
| Maximal aortic diameter (mm), mean ± SD | 50.3 ± 8.1 |

AR: aortic regurgitation; BSA: body surface area; LV: left ventricle; NYHA: New York heart association; SD: standard deviation; STJ: sinotubular junction; VAJ: ventriculo-aortic junction.

[a]Root dilatation defined as aortic root diameter ≥45mm.

Clinical follow-up data were obtained by direct phone contact, either with the patient or with the referring physician. Data from hospitalization and outpatient visits were collected from hospital records and cardiologists' reports.

Transthoracic echocardiography was performed routinely at discharge and at regular intervals of follow-up. The median follow-up was 6.12 years (interquartile range: 2.8–10.2 years), and 14 patients (4.6%) were lost to follow-up following discharge. Total cumulative follow-up was 1855 patient-years.

Early mortality was defined as any death occurring during hospital stay or during the first 30 days after operation, while any other deaths were considered as late mortality. Cardiac and non-cardiac deaths were defined as per the American Association for Thoracic Surgery (AATS) reporting guidelines [14, 15]. Outcomes of interest included survival status, AV reoperation, residual AR over time, incidence of systemic embolism, major bleeding events and endocarditis.

## Statistical analysis

Categorical variables are presented as numbers and percentages. Continuous variables are presented as mean ± SD. Time-to-event analysis was performed with Kaplan–Meier method. Univariable comparison of survival curves was estimated with the log-rank test. A $P < 0.05$ was considered statistically significant. All P-values are two-sided. Statistical analyses were performed using Stata IC version 16.1 (StataCorp LP, College Station, TX, USA).

Between-group comparison was made with chi-square or Fisher's exact test as appropriate for categorical variables or using binary logistic regression analysis, when comparing continuous to dichotomous variables.

Univariable cox-regression analysis was used to identify significant predictors of late mortality, AV reoperation and risk of moderate-to-severe AR (AR ≥2+). Covariates are listed in the Supplementary Material. The choice of prognostic variables that were identified and analysed in a multivariable model was based on both clinical knowledge and statistical analysis from the univariable model.

The Schoenfeld residuals test was used to check proportional hazard assumption for all categorical covariates and was met for all reported covariates.

We corrected for multiple comparisons using Benjamini–Hochberg false discovery rate correction with a cut-off for false discovery rate at 5% or less.

# RESULTS

## Preoperative and perioperative data

Patient characteristics and preoperative echocardiographic data are summarized in Table 1. The patient mean age was 52.9 ± 15.3 years, ranging between 11 and 85 years, of which 88.4% were male. Marfan patients constituted 11% ($n = 34$) of the cohort of which half (53%) were without AR (AR grade ≤1+). Indication for surgery included aneurysm without AR (AR 0–1+, $n = 111$, 36.6%), aneurysm with significant AR (AR ≥2+, $n = 154$, 50.8%), severe AR with annuloectasia [AR ≥3+, aorta (40–44 mm $n = 20$), aorta (35–39 mm $n = 5$), 8.3%] and type-A aortic dissection (TAAD) ($n = 13$, 4.3%). Out of 49 patients who previously underwent surgery, 31 (10.2%) previously had a Ross procedure and underwent VSR due to pulmonary autograft dilatation with AR >1+ ($n = 23$) or without AR ($n = 8$). The yearly rates of patients with severe AR (>2+) and patients necessitating cusp repair remained relatively stable over the study period (Supplementary Material, Fig. S1).

## Cusp repair

Cusp repair techniques were used in 168 (55.4%) patients in total, often including >1 cusp (Tables 2 and 3). The most common techniques of cusp prolapse repair were central cusp plication ($n = 147$), followed by free margin resuspension with Gore-Tex ($n = 44$). Pericardial patch was only used in 4 (1.3%) patients, mainly for closing fenestrations.

Cusp repair rate in the different groups (aneurysm without AR, aneurysm with AR and dystrophic AR) was 36%, 64.3% and 92% respectively ($P < 0.001$). Cusp repair increased aortic cross-clamp time in average by 7.1 ± 5.2 min ($P = 0.03$). Second run was required in 5.9% of patients without cusp repair versus 8.9% of patients with cusp repair ($P = 0.39$).

The rate of cusp repair increased significantly as AR grade increased ($P < 0.001$) from one-third of patients without AR to almost 80% of patients with AR grade 4 (Table 3). For most preoperative AR grades, cusp repair was more frequent on the right coronary cusp followed by the left coronary and then the non-coronary cusp. Cusp repair was also more frequently performed on 1 cusp than on 2 or 3 cusps (Table 3).

In patients with root dilatation (≥45 mm), aortic size was not a predictor of cusp repair ($P = 0.87$). However, when considering only those with none-to-moderate AR (grade ≤2+), sinotubular junction size predicted the need for cusp repair (OR = 1.064; $P = 0.009$).

**Table 2:** Surgical techniques and perioperative outcomes

| | *n* = 303 |
|---|---|
| Cusp repair techniques, *n* (%) | 168 (55.4) |
| Central plication | 147 (48.5) |
| Gore-Tex free-margin resuspension | 44 (14.5) |
| Patch cusp repair | 4 (1.3) |
| Graft size (mm), median | 30 |
| Straight Graft, *n* (%), [median] | 55 (18), [30] |
| Valsalva® Sinus Graft, *n* (%), [median] | 248 (82), [30] |
| Additional cabrol annuloplasty,[a] *n* (%) | 28 (9.2) |
| 1 stitch | 15 (5) |
| 2 stitches | 10 (3.3) |
| 3 stitches | 3 (1) |
| Additional procedures, *n* (%) | 100 (33) |
| CABG | 33 (10.9) |
| Hemi-arch | 14 (4.6) |
| Mitral valve repair | 27 (8.9) |
| Others | 26 (8.6) |
| CPB time (min), mean ± SD | 155.3 ± 39.9 |
| ACC time (min), mean ± SD | 127.2 ± 29.4 |
| Second run, *n* (%) | 23 (7.6) |

ACC: aortic cross-clamp; AR: aortic regurgitation; CABG: coronary artery bypass grafting; CPB: cardiopulmonary bypass; SD: standard deviation.
[a]Cabrol annuloplasty in 18 patients (1° CPB) run and in 10 (2° run).

## Survival

Hospital mortality was 1% (3 patients including 2 TAAD). Late mortality included 15 (5%) cardiac-related deaths and 34 (11.2%) non-cardiac deaths. Overall survival rate was 92 ± 2% at 5 years and 75 ± 5% at 10 years. Compared to a gender- and age-matched general population, our series that includes a substantial number of patients with TAAD and connective tissue disorder shows an inferior survival rate after 5 years of follow-up. Freedom from cardiac death was 97.4 ± 1.2% and 96.6 ± 1.4% at 5 and 10 years, respectively (Fig. 1).

Univariable cox-regression analysis showed that predictors of death were TAAD (HR [hazard ratio]: 6.68; $P = 0.001$), New York heart association (NYHA) class (HR: 1.67; $P = 0.020$), age (HR:

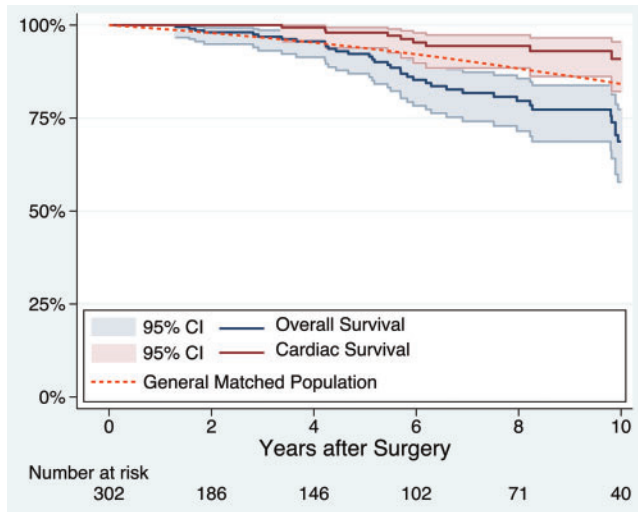


**Figure 1:** Time-to-event Kaplan–Meier survival graph. Overall and cardiac survival in valve-sparing reimplantation at 10 years was 75 ± 5% and 96.6 ± 1.4%, respectively. Overall survival was inferior compared to a gender- and age-matched general population, after 5 years of follow-up. CI: confidence interval.

**Table 3:** Cusp repair techniques

| *n* (%) | Total | AR 0–1 (*n* = 102) | AR 2 (*n* = 72) | AR 3 (*n* = 88) | AR 4 (*n* = 41) | $\chi^2$ |
|---|---|---|---|---|---|---|
| Any cusp repair | 168 (55.4) | 34 (33.3) | 40 (55.6) | 62 (70.5) | 32 (78.0) | *<0.001* |
| Cusp repair technique | | | | | | |
| Central plication | 147 (48.5) | 30 (29.4) | 35 (48.6) | 52 (59.1) | 30 (73.2) | *<0.001* |
| Free margin resuspension | 44 (14.5) | 4 (3.9) | 8 (11.1) | 20 (22.7) | 12 (29.3) | *<0.001* |
| Patch repair | 4 (1.3) | 0 | 1 (1.4) | 3 (3.4) | 0 | *0.32* |
| Number of cusp repaired[a] | | | | | | |
| 1 cusp | 83 (27.4) | 18 (17.6) | 25 (34.7) | 27 (30.7) | 13 (31.7) | *0.091* |
| 2 cusps | 56 (18.5) | 10 (9.8) | 11 (15.3) | 24 (27.3) | 11 (26.8) | *0.021* |
| 3 cusps | 29 (9.6) | 6 (5.9) | 4 (5.6) | 11 (12.5) | 8 (19.5) | *0.032* |
| Cusp repair localization | | | | | | |
| RCC | 137 (45.2) | 27 (26.5) | 32 (44.4) | 50 (56.8) | 28 (68.3) | <0.001 |
| LCC | 83 (27.4) | 14 (13.7) | 15 (20.8) | 35 (39.8) | 19 (46.3) | <0.001 |
| NCC | 62 (20.5) | 15 (14.7) | 12 (16.7) | 23 (26.1) | 12 (29.3) | 0.17 |
| Cochran *Q* test | <0.001 | 0.014 | <0.001 | <0.001 | <0.001 | |

Numbers between brackets are percentage. $\chi^2$: compares the rate of cusp repair or techniques between different grades of preoperative AR. Cochran *Q* test: compares localization (RCC, LCC or NCC) of cusp repair in the different grade of preoperative AR.
AR: aortic regurgitation;LCC: left coronary cusp; NCC: non-coronary cusp; RCC: right coronary cusp.
[a]$\chi^2$ comparing the proportion of 1, 2 or 3 cusps repaired in each AR grade category ($P = 0.42$).

**Table 4:** Cox-regression analysis

| | Univariable | | Multivariable | |
|---|---|---|---|---|
| | *P*-value | HR [95% CI] | *P*-value | HR [95% CI] |
| Death | | | | |
| Age | 0.003 | 1.04 [1.01, 1.07] | 0.002 | 1.05 [1.02, 1.07]* |
| TAAD | 0.001 | 6.68 [2.28, 19.5] | 0.012 | 5.28 [1.49, 18.66]* |
| NYHA | 0.020 | 1.67 [1.08, 2.58] | 0.040 | 1.62 [1.02, 2.56]* |
| CPB | 0.008 | 1.01 [1.01, 1.02] | | |
| ACC | 0.008 | 1.02 [1.01, 1.03] | | |
| Cusp repair | 0.14 | 0.61 [0.32, 1.18] | | |
| AR >2+ | | | | |
| LVEDD | 0.011 | 1.06 [1.01, 1.10] | 0.13 | 1.04 [0.99, 1.1] |
| Preoperative AR >2+ | 0.032 | 3.7 [1.17, 11.84] | 0.21 | 2.30 [0.63, 8.43] |
| NYHA | 0.032 | 2.11 [1.09, 4.08] | | |
| Cusp repair | 0.47 | 1.46 [0.52, 4.12] | | |
| AR >1+ | | | | |
| Redo | 0.021 | 2.19 [1.15, 4.15] | 0.023 | 2.22 [1.15, 4.26]* |
| Preoperative AR >2+ | <0.001 | 2.93 [1.65, 5.23] | 0.030 | 2.29 [1.10, 4.75]* |
| Indication for surgery | <0.01 | 1.6 [1.14, 2.26] | | |
| NYHA | 0.011 | 1.6 [1.11, 2.24] | | |
| Number of cusps repaired | 0.005 | 1.45 [1.11, 1.87] | | |
| LVEDD | 0.032 | 1.03 [1.01, 1.07] | | |
| Cusp repair | 0.050 | 1.80 [1.00, 3.25] | | |

AR: aortic regurgitation; ACC: aortic cross-clamp; CI: confidence interval; CPB: cardiopulmonary bypass time; HR: hazard ratio; LVEDD: left-ventricular end-diastolic diameter; NYHA: New York heart association; TAAD: type-a aortic dissection.

*P-values are significant after applying the Benjamini–Hochberg procedure specified with a false discovery rate of 0.05.

1.04; $P = 0.003$), cardiopulmonary bypass time (HR: 1.01; $P = 0.008$) and aortic cross-clamp time (HR: 1.02; $P = 0.008$), of which only TAAD and age remained significant in a multivariable model (Table 4). Note that neither preoperative AR grade ($P = 0.43$ HR = 1.14) nor cusp repair ($P = 0.14$ HR = 0.61) had significant impact on mortality. Overall survival for patients with cusp repair was 93.4 ± 2% and 77.6 ± 5% at 5 and 10 years, respectively, vs 95 ± 2% and 66.7 ± 7% in patients without cusp repair ($P = 0.34$).

## Reoperations

None of the patients required early reoperation for repair failure. Eighteen patients (5.94%) required AV reoperation during the follow-up period, with a linearized rate of AV reoperation at 0.97% patient-years. The median interval to reoperation was at 4.9 years (interquartile range: 2.6–9.6 years). Out of 10 patients who were reoperated for recurrent severe AR, 5 underwent AV re-repair, while all other AV reoperated patients underwent replacement. Other indications for AV reoperation included endocarditis in 5 (1.7%), stenosis in 2 (0.7%) and mixed AV disease in 1 patient (0.3%) and all those patients received a replacement.

Freedom from AV reoperation was 100%, 95 ± 2% and 90 ± 3% at 1, 5 and 10 years, respectively (Fig. 2A).

Freedom from AV reoperation was similar in patients with or without cusp repair (90 ± 4% with vs 89.3 ± 4.1% without repair at 10 years; $P = 0.71$). In patients with preoperative AR >2+, freedom from reoperation was slightly, yet non-significantly, lower compared to those with preoperative AR ≤2+ (84 ± 5% vs 93.2 ± 3.4%, respectively, at 10 years; $P = 0.09$) (Fig. 3A and B).

Univariable cox-regression analysis of AV reoperation identified no significant predictors.

## Echocardiographic outcomes

At discharge, transthoracic echocardiography showed no AR in 118 patients (39%), AR grade 1+ in 180 (59%) and grade 2+ in 3 (1%).

Upon follow-up, freedom from recurrent AR >2+ was 100%, 93.7 ± 2% and 88.3 ± 4% at 1, 5 and 10 years, respectively, while freedom from AR >1+ was 93.7 ± 1.5%, 81.2 ± 2.8% and 70.4 ± 4.6% (Fig. 2B).

Freedom from recurrent AR >2+ was similar between patients with or without cusp repair (91.1 ± 3.3% vs 88.9 ± 5.6% at 10 years, $P = 0.47$) but was significantly lower in patients with preoperative AR >2+ compared to those with preoperative AR ≤2+ (89 ± 5.8% vs 85.5 ± 4.6% at 10 years, $P = 0.017$) (Fig. 4A and B). Freedom from recurrent AR >1+ significantly decreased as the number of cusps repaired increased ($P = 0.02$) (Fig. 4C).

In univariable cox-regression analysis, predictors of recurrent AR >2+ were preoperative AR >2+ (HR: 3.7; $P = 0.026$), NYHA class (HR: 2.1; $P = 0.026$) and preoperative left-ventricular end-diastolic diameter (HR: 1.057; $P = 0.013$). None remained significant in a multivariable model.

Univariable predictors of recurrent AR >1+ were indication for surgery (specifically aneurysm with AR and TAAD, HR 1.6; $P = 0.012$), NYHA class (HR: 1.6; $P = 0.023$), previous cardiac surgery (HR: 2.3; $P = 0.011$), preoperative left-ventricular end-diastolic diameter (HR: 1.04; $P = 0.033$), number of cusps repaired (HR: 1.45; $P = 0.005$) and preoperative AR >2+ (HR: 2.94; $P < 0.001$). In multivariable analysis, only previous cardiac surgery and presence of preoperative AR >2+ remained significant predictors of recurrent AR >1+ (Table 4).

## Valve-related events

Thrombo-embolic events occurred in 8 (2.64%) patients, with a linearized rate of 0.43% patient-year. Freedom from thrombo-

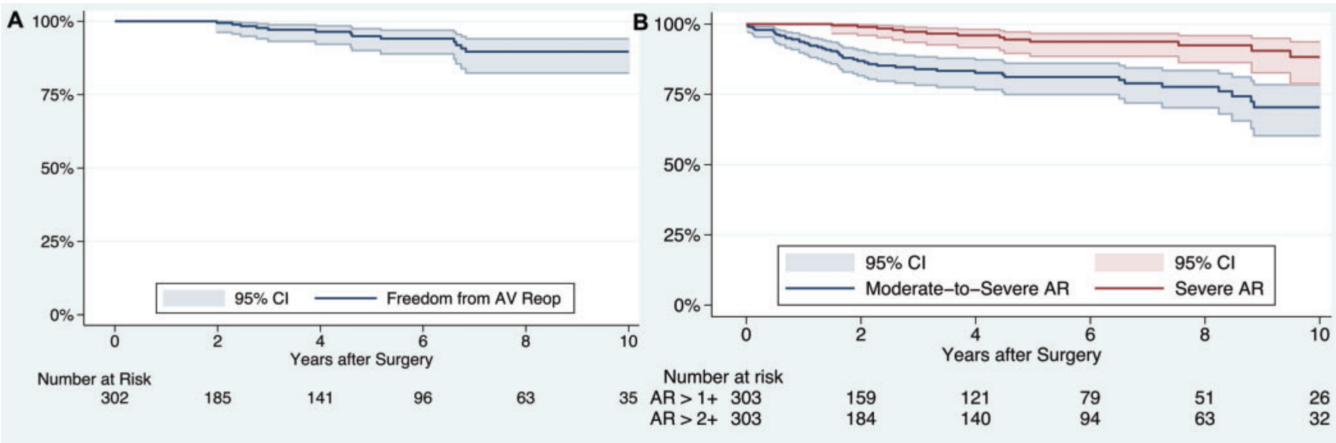


Figure 2: (**A**) Freedom from reoperation on the aortic valve. (**B**) Freedom from aortic regurgitation >1+ and aortic regurgitation >2+ recurrence. AR: aortic regurgitation; AV: aortic valve; CI: confidence interval.

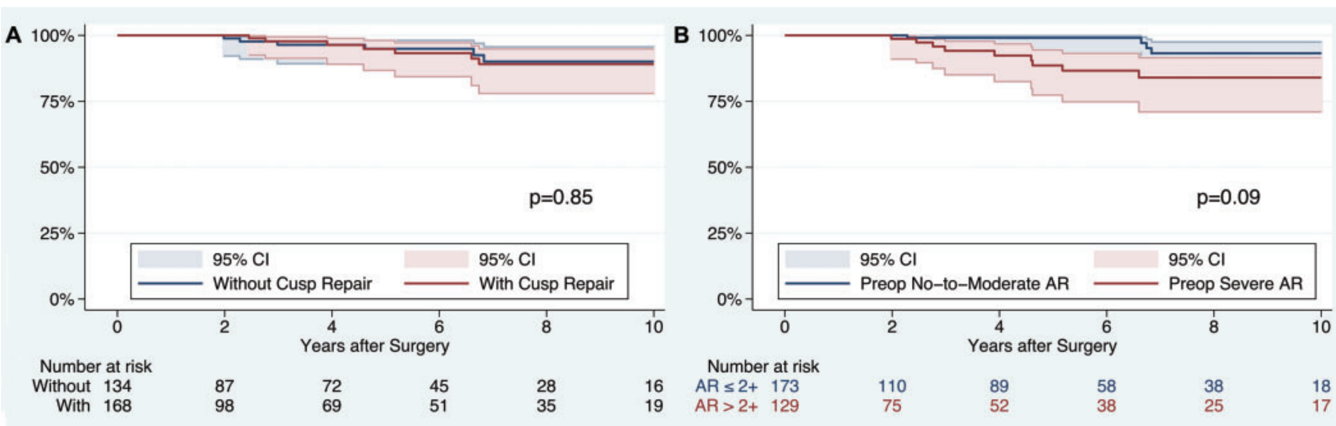


Figure 3: Freedom from aortic valve reoperation (**A**) compared between patients who benefitted from cusp repair or not (**B**) by preoperative aortic regurgitation grade (aortic regurgitation ≤2+ versus aortic regurgitation >2+). AR: aortic regurgitation; CI: confidence interval.

embolic events was 99.7 ± 0.3%, 98.9 ± 0.7% and 96 ± 1.8% at 1, 5 and 10 years, respectively. Freedom from major bleeding events was 98 ± 1%, 96.7 ± 1% and 95.8 ± 1% at 1, 5 and 10 years respectively, with a linearized rate of 0.59% patient-year. Infective endocarditis occurred in 6 patients with a linearized rate of 0.32% patient-year. Of these patients, 5 were reoperated, as reported earlier, and 1 was treated with antibiotics alone.

## DISCUSSION

Over the last 2 decades, we learned to expand the indications for valve-sparing techniques to include patients with AR. Our experience from repair failures in the early era has highlighted the need to assess valve pathologies in all AV-sparing procedures and to perform cusp repair when appropriate [12–14]. In addition to pre-existing valve lesions (e.g. cusp prolapse), that require cusp repair, we learned that by reducing aortic root dimensions, VSR leads to increased cusp mobility. This alone can result in potential cusp prolapse. The risk of inducing prolapse is further accentuated in these patients by elongation of the cusps' free margin due to chronic overstretching of the valve in dilated aortic roots [16, 17]. Visual inspection and measurement of cusp eH after VSRR is therefore crucial, to correct induced cusp prolapse and low coaptation height, when needed [3, 11, 13].

Gaining experience with VSR, we aimed to apply it in young patients with severe AR, large annulus and moderately dilated root (38–45 mm). In those patients, the rationale to perform VSR is essentially performing strong stable circumferential prosthetic-based annuloplasty. In addition, VSR normalizes and stabilizes the entire functional AV annulus comprising ventriculo-aortic junction, root and STJ. We have already shown that this complete root stabilization improves the durability of BAV repair compared to Cabrol annuloplasty [18]. Other experts have decreased, like us, their threshold for root replacement in the context of AV repair with the similar objective of stabilizing the entire aortic root [19].

In our cohort of patients with TAV undergoing VSR, rate of cusp repair was 55.4% and varied significantly from 33% in patients with none-to-mild AR up to 78% in patients with severe AR. The right coronary cusp was twice as frequently repaired compared to left or non-coronary cusps. In the literature, cusp repair rate in TAV is usually lower than in BAV during VSRR and varied extensively from 6% to 50% [20–23]. No study, however, demonstrated any factors influencing cusp repair, except for 1 group who found, like us, but in BAV, an increased incidence of cusp repair with higher grade of preoperative AR [24]. Kari *et al.* [25] showed that probability of cusp repair was not influenced by VSRR technique (Yacoub versus reimplantation).

This study also analysed in-depth the impact of preoperative AR and cusp repair on patient outcomes. As previously published

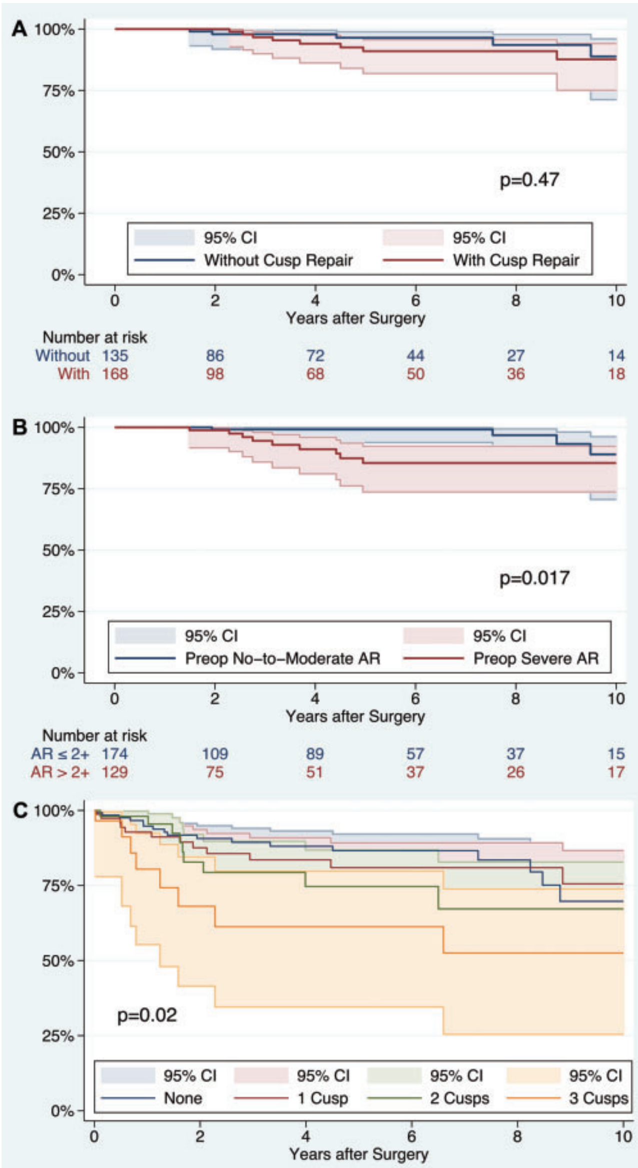


**Figure 4:** (**A**) Freedom from aortic regurgitation >2+ with or without cusp repair. (**B**) Freedom from aortic regurgitation >2+ in patients by preoperative aortic regurgitation grade (aortic regurgitation ≤2+ versus aortic regurgitation >2+). (**C**) Freedom from aortic regurgitation >1+ by the number of cusps repaired. AR: aortic regurgitation; CI: confidence interval.

in 2009, in a mixed cohort of TAV and BAV patients, we found that these parameters did not significantly influence the patient's clinical outcomes, such as survival or AV reoperation [4]. Here, however, we found that preoperative AR grade 3+/4+ and 3-cusp repair increased the risk of recurrence of moderate-to-severe AR during follow-up. Those results show that indications of VSRR can be broadened to patients with AR; however, they also show the limitation of the repair's techniques in patients with severe AR necessitating multiple cusp repair. On the other hand, knowing that preoperative AR increases risk of AR recurrence; results suggest that cusp repair can attenuate that risk in a majority of patients at least during the first decade after surgery. This interpretation of the results is based on experience and literature data demonstrating that cusp prolapse left untreated after VSRR represents high risk to develop early AR recurrence [5, 14]. Thus, just like in other studies, if cusp repair had no or poor efficiency to correct prolapse, the repair durability of patients with cusp repair would be definitely worse, and not comparable to patients without cusp repair. Adjacently, outcomes of patients with preoperative AR would be much worse compared to patients without.

Comparing our results to literature, several other studies have shown no significant impact of preoperative AR on either of the 3 outcomes (survival, AV reoperation or recurrent AR) [2, 23, 26, 27]. However, another study has similarly found a negative impact of preoperative moderate-to-severe AR on AR recurrence [2]. Finally, Escobar Kvitting *et al.* [28] have shown an impact of severe preoperative AR on a composite end-point regrouping survival, AV reop and TE events with a hazard ratio of 6.

Regarding the impact of cusp repair, no studies demonstrated any impact on survival [25, 27–29], neither on AV reoperation [2, 3, 25, 29]. These studies included either entirely or in their majority, TAV patients. Even though we admit that cusp repair and AR are obviously closely related and thus constitute confounding factors influencing long-term outcomes, the conclusion drawn from current literature encourages cusp repair in VSRR. Settepani *et al.* [29] also emphasized the need for cusp repair in VSRR since most of their reoperations were for prolapse in patients that had not benefitted from cusp repair during the initial procedure. Finally, AR recurrence also saw no influence from cusp repair in most studies [2, 20, 27, 30]. On the other hand, cusp technique showed controversial results, specifically free margin resuspension with running suture of PTFE. Where Tanaka showed positive impact of free margin resuspension on severe AR recurrence [30], David *et al.* [27] found a negative impact of that technique (HR 3.25). As for the effect of number of cusps repaired, which impacted AR recurrence in our case, only 1 study from Settepani *et al.* [29] found a similar effect. Overall, we found that the literature supported our findings that, in general, cusp repair has no negative impact on long-term outcomes. In other words, cusp repair is efficient in improving valve configuration and durability in case of preoperative AR and residual prolapse after VSRR; however, this efficiency is limited when multiple cusps are involved.

## Limitations

This is a retrospective study and therefore carries all the limitations of such an analysis. We have evaluated a single-center historical cohort of patients, where learning curve is observed utilizing VSR and cusp repair techniques. With additional experience, better results were likely achieved and our technique of prolapse repair gradually shifted to preferentially using central cusp plication and eH measurement.

Some other criteria that potentially impact necessity of cusp repair or outcomes may be missing from our analysis (e.g. eccentric AR jet or asymmetrical root dilatation).

## CONCLUSION

In patients with TAV receiving VSR, the necessity of cusp repair increases with degree of preoperative AR. Right coronary cusp repair is twice more frequent than left or non-coronary cusp repair. Preoperative AR and cusp repair do not impact long-term survival and AV reoperation. However, severe AR and multiple cusp repair predict the recurrence of moderate-to-severe AR during the first decade of follow-up. Based on these findings, it is reasonable to consider that severe AR increases the risk of valve-sparing failure,

CONVENTIONAL VALVE OPERATIONS

while cusp repair attenuates that risk at least for the majority of the patients during the first decade. Cusp repair expertise is recommended in VSRR especially in the presence of AR.

## SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

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## Author contributions

**Saadallah Tamer:** Data curation; Formal analysis; Writing—original draft. **Stefano Mastrobuoni:** Methodology; Software. **Guillaume Lemaire:** Investigation. **Jama Jahanyar:** Writing—review & editing. **Emiliano Navarra:** Methodology; Software. **Alain Poncelet:** Conceptualization. **Parla Astarci:** Conceptualization. **Gebrine El Khoury:** Validation. **Laurent de Kerchove:** Supervision; Writing—review & editing.

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