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ORIGINAL ARTICLE

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Long-term durability of bicuspid aortic valve repair: a comparison of 2 annuloplasty techniques

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Key question

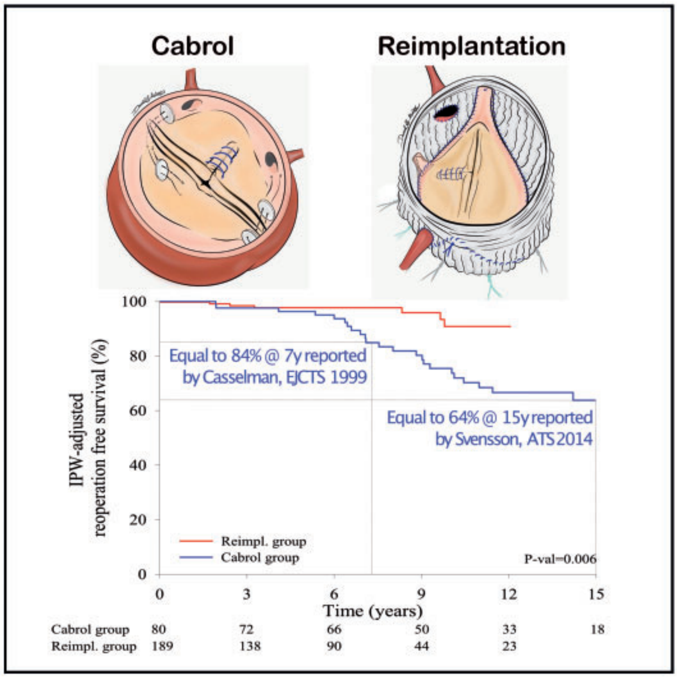
What is the impact on long-term durability of Cabrol annuloplasty versus the reimplantation technique in bicuspid aortic valve repair?

Key finding(s)

Reimplantation offers superior durability with equivalent survival; recurrence of AR is rare after reimplantation.

Take-home message

In bicuspid valve repair, Cabrol annuloplasty is obsolete. The 180° reimplantation technique is safe and effective in achieving the best long-term results.



Abstract

OBJECTIVES: To compare long-term outcomes after bicuspid aortic valve (BAV) repair utilizing the Cabrol annuloplasty versus valve sparing Reimplantation technique.

METHODS: From 1996 to 2018, 340 consecutive patients underwent BAV repair. Eighty underwent Cabrol annuloplasty and 189 underwent Reimplantation. Exclusion criteria were re-repairs ($n = 6$), active endocarditis ($n = 4$), no annuloplasty ($n = 41$) and ring or suture annuloplasty ($n = 20$). We compared both groups for survival, reoperations, valve related events and recurrent severe aortic regurgitation

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(AR > 2+). Inverse probability weighting (IPW) was used to balance the 2 groups. Cox regression analysis was used to identify outcome predictors.

RESULTS: After weighting, pre- and intraoperative characteristics were similar between groups, except for aorta replacement techniques and operative time, which was longer in the Reimplantation group ($P < 0.001$). At 12 years, overall survival was similar between groups (IPW: Cabrol 97 ± 2% vs Reimplantation 94 ± 3%, $P = 0.52$). Freedom from reoperation and freedom from AR > 2+ were significantly lower in the Cabrol group (reoperation IPW: 69 ± 9% vs 91 ± 4%, $P = 0.004$ and AR > 2+ IPW: 71 ± 8% vs 97 ± 2%, $P < 0.001$). The Reimplantation technique was the only independent predictor of reoperation (hazard ratio 0.31; confidence interval 0.19–0.7; $P = 0.005$).

CONCLUSIONS: In this study, comparing 2 annuloplasty strategies for BAV repair, we found statistically significant differences in long-term durability favouring the Reimplantation technique, and no differences in overall survival. The results support our current strategy of Reimplantation technique and repair of AR in patients with BAV. Cabrol annuloplasty is obsolete and should be generally abandoned in patients undergoing BAV repair for AR.

Keywords: Valve repair • Bicuspid • Valve sparing • Annuloplasty

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ABBREVIATIONS

AV	Aortic valve
AR	Aortic regurgitation
BAV	Bicuspid aortic valve
IPW	Inverse probability weighting
IQR	Interquartile range

INTRODUCTION

Sixty years ago, Cabrol described the plication of the aortic valve (AV) interleaflet triangles to achieve a reduction of root base circumference [1]. This original technique was later referred to as commissural or sub-commissural annuloplasty, and gained widespread popularity during the late 80s and 90s, due to the works of Duran and Cosgrove [2, 3], who published the first large series of patients undergoing AV repair. Many surgeons, including our group, have then adopted this simple means as the main annuloplasty technique for patients with aortic regurgitation (AR) in the setting of a non-dilated aortic root. In the interim, the development of valve sparing root replacement procedures (David and Yacoub techniques) have extended the indications for AV repair and stimulated the emergence of new concept for AV annuloplasty [4–7]. Effectively, the circumferential annuloplasty carried out in the David—Reimplantation technique, rather than in the Yacoub—Remodelling, seemed to be an advantage for long-term valve function in patients with a large aortic annulus [8, 9].

While several studies have shown encouraging initial and mid-term results with Cabrol annuloplasty, studies on long-term outcomes are scarce [2, 10–12]. Ten years ago, we showed that recurrent AR and reoperations were more frequent after Cabrol annuloplasty compared to the Reimplantation technique in patients undergoing bicuspid aortic valve (BAV) repair [13]. Currently, we have gained additional experience, and thus almost doubled our patient numbers and respective follow-up period. Particularly at our institution, the modified Reimplantation technique for BAV (El Khoury technique) has clearly evolved to the new standard of care for the repair of BAV with AR. In this study, we report the very long-term outcomes of our initial BAV repair approach using Cabrol annuloplasty; and utilizing an advanced matching technique for analysis, these results were compared to the more recent Reimplantation technique.

METHODS

Ethical statement

This study was approved by the ethics review board at our institution (ID Brussels: 2013/03JUI/356).

Study population

Between 1996 and 2018, 340 consecutive patients underwent surgery for BAV repair at our institution. Inclusion criteria were BAV repair with Cabrol annuloplasty or Reimplantation technique. Exclusion criteria were BAV repair without annuloplasty, repair with ring or suture annuloplasty, BAV re-repair and active endocarditis (Supplementary Material, Fig. S1: Study flow chart). Patients without annuloplasty were excluded because 'no annuloplasty' has never been our standard approach to repair BAV with AR. Ring and suture annuloplasty were excluded because these techniques were performed more recently in a relatively small group of patients. Patients' data were extracted from the institutional prospective database on AV repair.

Surgical techniques

Since the beginning of our AV repair programme in 1995, Cabrol annuloplasty was mainly used in patients without root dilatation (<45 mm) and occasionally in patients with root dilatation as an adjunct to partial or complete root Remodelling techniques. As of 1999, we progressively switched from Remodelling to Reimplantation technique, because of the intrinsic annuloplasty with Reimplantation. During the first decade of our practice, we observed several patients returning with recurrent AR following an initially successful Cabrol repair. For this reason, and due to our increased confidence in the long-term stability of the Reimplantation technique, we decided since 2009 to favour this technique to repair BAV with AR, even in patients with no or only moderate root dilatation (<45 mm). The proportion of Cabrol annuloplasty and Reimplantation over the study period is illustrated in Supplementary Material, Fig. S2.

The technical details of Cabrol annuloplasty, Reimplantation technique and cusp repair have been reported previously [13]. Briefly, Cabrol annuloplasty sutures (2–0 Ticron with pledgets) were placed in the middle one-third of the interleaflet triangle on both commissures. The Reimplantation technique was initially performed with a straight tube, which was progressively replaced with the Gelweave^{TM} Valsalva graft (Vascutek Ltd., Terumo Group, Renfrewshire, Scotland, UK) as of 2002. During the study period, along with the change of graft type, our Reimplantation technique evolved with deeper external root dissection and with a systematic reimplantation of the commissure at 180° [14]. Regarding cusp repair techniques, we progressively abandoned the technique of free margin resuspension with Gore-Tex in favour of the central plication technique to repair cusp prolapse.

Echocardiography

All patients underwent a comprehensive preoperative transthoracic and transoesophageal examination. The degree of AR, left ventricular dimension and ejection fraction and aortic root dimensions were measured as per active guidelines [15]. After repair, intraoperative transoesophageal echocardiography was performed in all patients to assess the degree of residual AR, orientation of the regurgitant jet (if present), and the coaptation length and height [16]. Coaptation length of at least 5 mm at the midportion of the free margin or a coaptation height above the AV annulus were prerequisites for a successful repair. The presence of residual AR more than mild was an indication for re-exploration of the AV, especially if the AR jet was eccentric. Transthoracic echocardiography was performed in all patients before discharge and at regular intervals during follow-up.

Follow-up and outcome

Patients in our AV repair database have systematic follow-up every 2–3 years by a dedicated research nurse. For the present study, follow-up events were updated between January and April 2019, via phone contact with physicians, cardiologists or patients themselves. Morbidity and mortality were reported according to the 2008 Society of Thoracic Surgeons (STS)/American Association for Thoracic Surgery (AATS)/European Association for Cardio-Thoracic Surgery (EACTS) guidelines [17]. Clinical events of interest included the incidence of reoperation on the AV, endocarditis, systemic embolism and major bleeding events.

The overall median follow-up time was 7.0 years [interquartile range (IQR) 3.6–12.1]. In the Cabrol group, the median follow-up was 12.4 years (IQR 9.5–15.8) and in the Reimplantation group, it was 5.7 years (IQR 2.7–8.7). Fourteen (5%) patients were lost to follow-up, 1 (1.2%) in the Cabrol group and 13 (6.9%) in the Reimplantation group.

Statistical analysis

All statistical analyses were performed using R software (version 3.4.0). Continuous variables were expressed as means ± 1 SD, categorical variables as counts and percentages. To compare groups, independent sample *t*-tests were used for continuous variables and or χ^2 tests were used for categorical variables. A *P*-value of <0.05 was considered indicative of a statistically significant difference. Follow-up times were calculated using the inverse Kaplan–Meier method and were expressed as median and IQR. Cox's proportional-hazards survival analysis was used to determine factors independently associated with outcome and reoperation. For this, the univariable analysis was performed with all the clinical and surgical variables. After that, the variables with a *P*-value <0.10 were proposed for inclusion in the multivariable model. Variable selection was performed using a backward stepwise selection procedure using the maximum partial likelihood ratio chi-square statistic. Overall survival was computed using the Kaplan–Meier method, and 2 groups were compared using the log-rank test. For each patient enrolled in the study, the corresponding average age- and gender-specific annual mortality rates of the Belgian general population were obtained. Based on these mortality data, the probability of cumulative expected survival was determined, and an expected survival curve was constructed.

Inverse probability weighting. To predict the inverse probability of undergoing reimplantation, 10 covariables were used to estimate the patient's case-weight. These covariables were age, smoking, hypertension, degree of AR (none or mild, moderate and severe), presence of aortic root or tubular aorta dilatation (≥45 mm), cusp repair with a patch, cusp resection/shaving, cusp resuspension with Gore-Tex, concomitant mitral valve repair and presence of cusp calcifications. A single propensity score was generated for each patient.

Weighted *t*-tests and weighted χ^2 tests were used in the inverse probability weighting (IPW)-adjusted cohort to compare continuous or categorical variables in the 2 groups. Standardized differences were calculated to compare baseline characteristics in the 2 groups for the original and the IPW-adjusted cohort [18]. A Cox proportional hazard regression model was adjusted for inverse probability weights [19], assessed with Schoenfeld residuals.

RESULTS

Baseline characteristics

The study cohort consisted of 269 patients who met the inclusion criteria; of these, 80 patients underwent Cabrol annuloplasty (Cabrol group) and 189 underwent Reimplantation procedure (Reimplantation group).

Before matching, the 2 groups were similar for most baseline clinical parameters except for creatinine level ($P = 0.039$), left ventricular diameters ($P = 0.007$), left ventricular dysfunction ($P = 0.03$) and aortic dilatation ≥45 mm ($P < 0.001$) (Table 1).

Cusp resuspension with Gore-Tex 7-0, cusp resection or shaving and cusp repair with the pericardial patch was more frequent in the Cabrol group ($P < 0.001$) (Table 2). As expected, root and ascending aorta replacement was more frequent in Reimplantation group ($P < 0.001$). Clamp time and cardiopulmonary bypass time was shorter in the Cabrol group ($P < 0.001$) despite the more frequent second run in this group ($P = 0.02$).

After IPW adjustment, no significant differences were observed anymore between the groups regarding all baseline and intraoperative parameters.

Survival

There were no hospital mortalities. After follow-up, 12 patients had died; 6 in each group. The causes of death are non-cardiovascular in 6 and cardiovascular in 6 (3 cardiovascular deaths in each group). Overall survival of the entire study cohort was 96 ± 2% at 12 years, respectively. Long-term survival was

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Table 1: Baseline patients' characteristics

	Total (*n* = 269)	Initial population			IPW population		
		Reimplantation (*n* = 189)	Cabrol (*n* = 80)	*P*-value	Reimplantation (*n* = 189)	Cabrol (*n* = 80)	*P*-value
Age (years), mean ± SD	43 ± 12	43 ± 12	45 ± 12	0.19	44 ± 12	46 ± 12	0.35
Male, *n* (%)	249 (93)	176 (93)	73 (91)	0.59	94	88	0.15
Weight (kg), mean ± SD	84 ± 16	85 ± 16	82 ± 16	0.21	86 ± 16	82 ± 15	0.056
Height (m), mean ± SD	1.78 ± 0.09	1.78 ± 0.08	1.77 ± 0.09	0.12	1.79 ± 0.08	1.77 ± 0.10	0.14
NYHA class >II, *n* (%)	17 (6)	9 (5)	8 (10)	0.11	6	6	0.92
Atrial fibrillation, *n* (%)	4 (1)	2 (1)	2 (3)	0.37	1	2	0.66
Smoking, *n* (%)	84 (31)	54 (29)	30 (38)	0.15	30	31	0.88
Hypertension, *n* (%)	93 (35)	61 (32)	32 (40)	0.22	36	49	0.057
Diabetes mellitus, *n* (%)	6 (2)	3 (2)	3 (4)	0.27	1	2	0.61
Dyslipidaemia, *n* (%)	47 (17)	30 (16)	17 (21)	0.29	19	27	0.14
Family history, *n* (%)	41 (15)	26 (14)	15 (19)	0.3	16	17	0.77
Creatinine (mg/dl), mean ± SD	0.98 ± 0.37	0.95 ± 0.20	1.05 ± 0.60	0.039	0.96 ± 0.20	1.05 ± 0.50	0.13
COPD, *n* (%)	5 (2)	3 (2)	2 (3)	0.61	2	1	0.47
History of cardiac surgery, *n* (%)	3 (1)	2 (1)	1 (1)	0.892	1	4	0.21
EF ≥50%, *n* (%)	248 (92)	178 (94)	70 (88)	0.06	94	93	0.72
EF <50% to ≥30%, *n* (%)	19 (7)	11 (6)	8 (10)	0.22	6	5	0.64
EF <30%, *n* (%)	2 (1)	0 (0)	2 (3)	0.03	0	3	0.15
No or mild AR, *n* (%)	69 (26)	54 (29)	15 (19)	0.09	29	37	0.26
Moderate AR, *n* (%)	28 (10)	18 (10)	10 (13)	0.47	10	14	0.40
Severe AR, *n* (%)	172 (64)	117 (62)	55 (69)	0.29	60	49	0.10
LVEDD (mm), mean ± SD	60 ± 8	59 ± 8	62 ± 9	0.006	59 ± 8	59 ± 9	0.92
LVEDS (mm), mean ± SD	40 ± 8	39 ± 7	42 ± 9	0.007	39 ± 7	38 ± 9	0.78
Aortic root or tubular aorta dilatation ≥45 mm, *n* (%)	142 (53)	113 (60)	29 (36)	<0.001	56	61	0.45

AR: aortic regurgitation; COPD: chronic obstructive pulmonary disease; EF: ejection fraction; IPW: inverse probability weighting; LVEDD: left ventricular end-diastolic diameter; LVEDS, left ventricular end-systolic diameter; NYHA, New York Heart Association; SD: standard deviation.

Table 2: Intraoperative techniques

	Total (*n* = 269)	Initial population			IPW population		
		Reimplantation (*n* = 189)	Cabrol (*n* = 80)	*P*-value	Reimplantation (*n* = 189)	Cabrol (*n* = 80)	*P*-value
Cusp lesion, *n* (%)							
Prolapse	217 (81)	153 (81)	64 (80)	0.86	83	74	0.11
Calcification	68 (25)	42 (22)	26 (33)	0.077	27	30	0.59
Cusp repair, *n* (%)							
Central plication	236 (88)	170 (90)	66 (83)	0.09	88	80	0.11
Resuspension with Goretex	80 (30)	35 (19)	45 (56)	<0.001	30	31	0.90
Resection/shaving	171 (64)	105 (56)	66 (83)	<0.001	64	66	0.77
Patch	31 (12)	15 (8)	16 (20)	<0.001	10	11	0.74
Aorta repair, *n* (%)							
Reimplantation	189 (70)	189 (100)	0 (0)		100	0	
Remodelling	2 (1)	0 (0)	2 (3)	0.03	0	5	0.058
Tubular aorta replacement	21 (8)	0 (0)	21 (26)	<0.001	0	33	<0.001
Tubular aorta replacement +one sinus	8 (3)	0 (0)	8 (10)	<0.001	0	25	<0.001
None	49 (18)	0 (0)	49 (61)	<0.001	0	38	<0.001
Associated procedures, *n* (%)							
(Hemi-)arch replacement	8 (3)	5 (3)	3 (4)	0.63	2	10	0.036
CABG	11 (4)	6 (3)	5 (6)	0.25	5	6	0.69
Mitral repair	10 (4)	5 (3)	5 (6)	0.15	4	3	0.90
Tricuspid repair	3 (1)	1 (1)	2 (3)	0.16	1	2	0.72
Second run	16 (6)	7 (4)	9 (11)	0.02	4	11	0.074
Cardiopulmonary bypass time (min), mean ± SD	129 ± 37	144 ± 25	94 ± 38	<0.001	146 ± 27	94 ± 38	<0.001
Clamp time (min), mean ± SD	108 ± 33	123 ± 22	72 ± 26	<0.001	125 ± 24	70 ± 22	<0.001

CABG: coronary artery bypass grafting; IPW: inverse probability weighting; SD: standard deviation.

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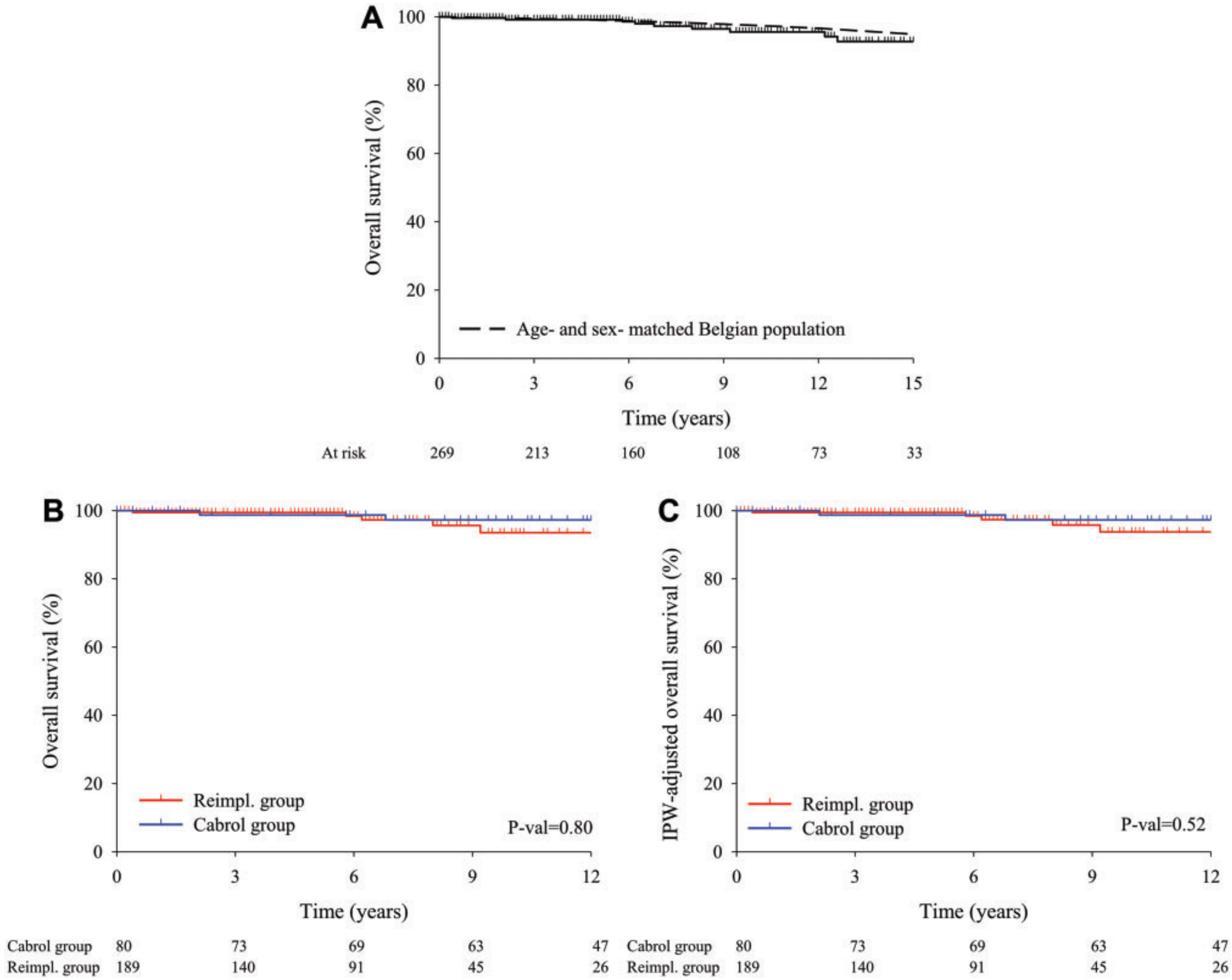

Figure 1: Kaplan–Meier estimates of overall survival. (**A**) Overall survival of entire cohort and survival of Belgian population matched for age and gender, (**B**) unmatched comparison between Cabrol and Reimplantation group ($P = 0.8$) and (**C**) inverse probability weighting-adjusted comparison ($P = 0.52$).

Table 3: Multivariable cox analysis

Reoperation-free survival	Unmatched		IPW adjusted	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Smoking, *n* (%)	1.91 (1.24–3.9)	0.075	1.94 (1.25–3.96)	0.069
Central plication, *n* (%)	0.53 (0.33–1.15)	0.11	0.56 (0.35–1.22)	0.14
Reimplantation technique, *n* (%)	0.33 (0.2–0.74)	0.007	0.31 (0.19–0.7)	0.005

CI: confidence interval; HR: hazard ratio; IPW: inverse probability weighting.

similar to the survival of the Belgian population matched for age and sex (Fig. 1A). Overall survival was similar between Cabrol and Reimplantation group in unmatched and IPW-adjusted cohort (Fig. 1B and C).

In univariable analysis, age, smoking history, presence of moderate AR, diabetes mellitus and chronic obstructive pulmonary disease were found as predictors of death (Supplementary Material, Table S1). No independent predictors were found in multivariable Cox analysis, due to the small number of deaths (Table 3).

Aortic valve reoperation

AV reoperation was necessary for 33 (12.3%) patients during the follow-up; 25 (31%) in the Cabrol group and 8 (4%) in the Reimplantation group. In the Cabrol group, the reason for reoperation was pure AR in 11, stenosis or mixed AV disease in 12 and endocarditis in 2. In patients with pure AR, the mechanisms of failure were annulus dilatation and prolapse of the fused cusp. In the Reimplantation group, the reason for reoperation was

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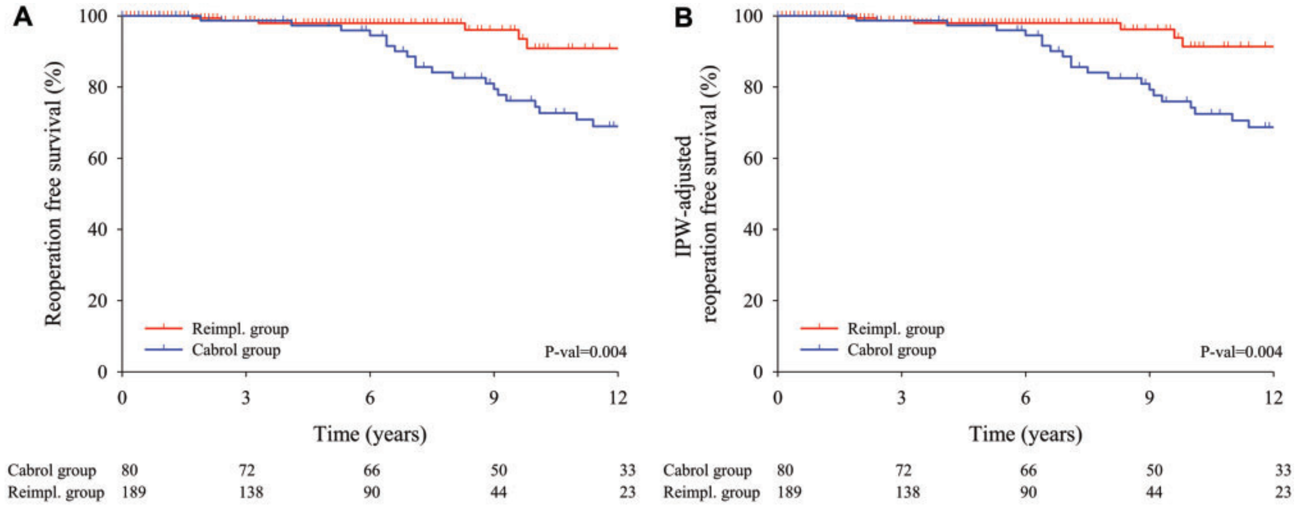

Figure 2: Kaplan–Meier estimates of aortic valve reoperation free survival. (**A**) Unmatched comparison between the Cabrol and Reimplantation group ($P = 0.004$) and (B) IPW-adjusted comparison ($P = 0.004$). IPW: inverse probability weighting.

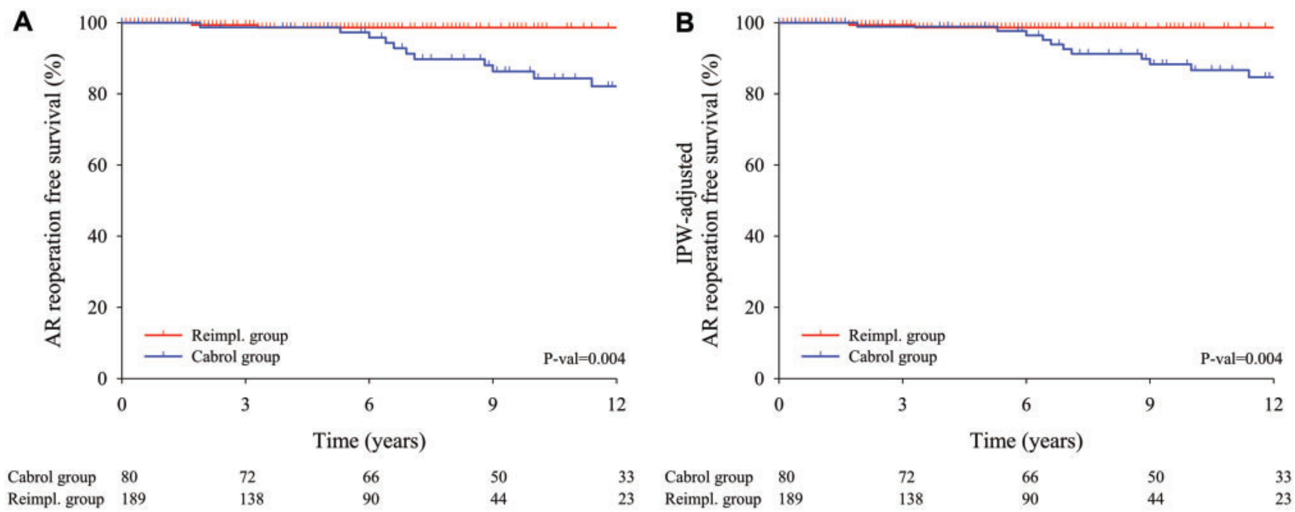

Figure 3: Kaplan–Meier estimates of reoperation for aortic regurgitation free survival. (**A**) Unmatched comparison between the Cabrol and Reimplantation group ($P = 0.004$) and (**B**) IPW-adjusted comparison ($P = 0.004$). AR: aortic regurgitation; IPW: inverse probability weighting.

pure AR in 2 (1.1%), stenosis or mixed AV disease in 5 (2.6%) and endocarditis in 1 (0.5%). Mechanisms of pure AR after reimplantation were suture dehiscence and commissure disruption.

Twelve-year freedom from AV reoperation was 69 ± 8% in Cabrol and 91 ± 5% in the Reimplantation group ($P = 0.004$) (Fig. 2A). The difference between groups was significant in the IPW-adjusted cohort ($P = 0.004$) (Fig. 2B). In multivariable Cox analysis, the Reimplantation technique was the only independent protector from reoperation (Table 3).

Freedom from reoperation for pure AR at 12 years was 82 ± 6% in Cabrol and 99 ± 1% in the Reimplantation group ($P = 0.004$) (Fig. 3A). The difference between groups was significant in the IPW-adjusted cohort ($P = 0.004$) (Fig. 3B).

Freedom from reoperation for AV stenosis or disease at 12 years was 85 ± 6% in Cabrol and 93 ± 4% in the Reimplantation group ($P = 0.23$) (Fig. 4A). The difference between groups was not significant in the IPW-adjusted cohort ($P = 0.058$) (Fig. 4B).

Recurrence of severe aortic regurgitation

Freedom from recurrent AR greater than 2+ at 12 years was 71 ± 8% in Cabrol and 97 ± 2% in the Reimplantation group ($P < 0.001$) (Fig. 5A). The difference between groups was significant in the IPW-adjusted cohort ($P < 0.001$) (Fig. 5B).

Other valve related events

During the follow-up, 10 thromboembolic events occurred, 5 in the Reimplantation group (4 strokes, 1 transient ischaemic attack) and 5 in the Cabrol group (4 strokes, 1 transient ischaemic attack). Five major bleeding events occurred, 3 in the Reimplantation group and 2 in the Cabrol group. Freedom from thromboembolic and bleeding events were similar between Cabrol and Reimplantation group in unmatched and IPW-adjusted cohorts (IPW-adjusted comparison, at 12 years: 93 ± 3% vs 90 ± 5% $P = 0.36$, Supplementary Material, Fig. S3).

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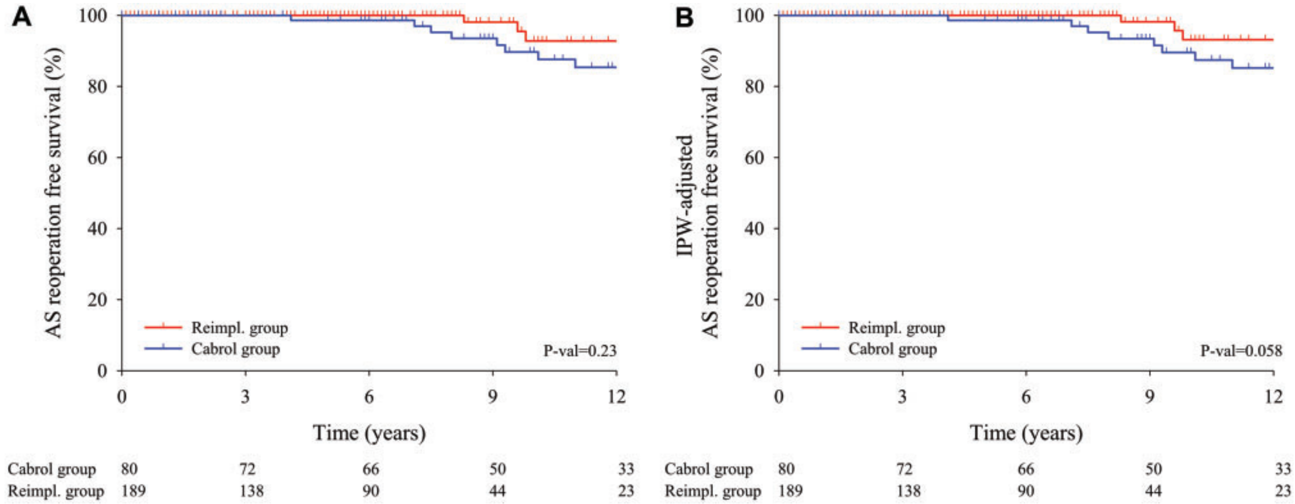

Figure 4: Kaplan–Meier estimates of reoperation for aortic stenosis free survival. (**A**) Unmatched comparison between the Cabrol and Reimplantation group (*P* = 0.23) and (**B**) IPW-adjusted comparison (*P* = 0.058). AS: aortic stenosis; IPW: inverse probability weighting.

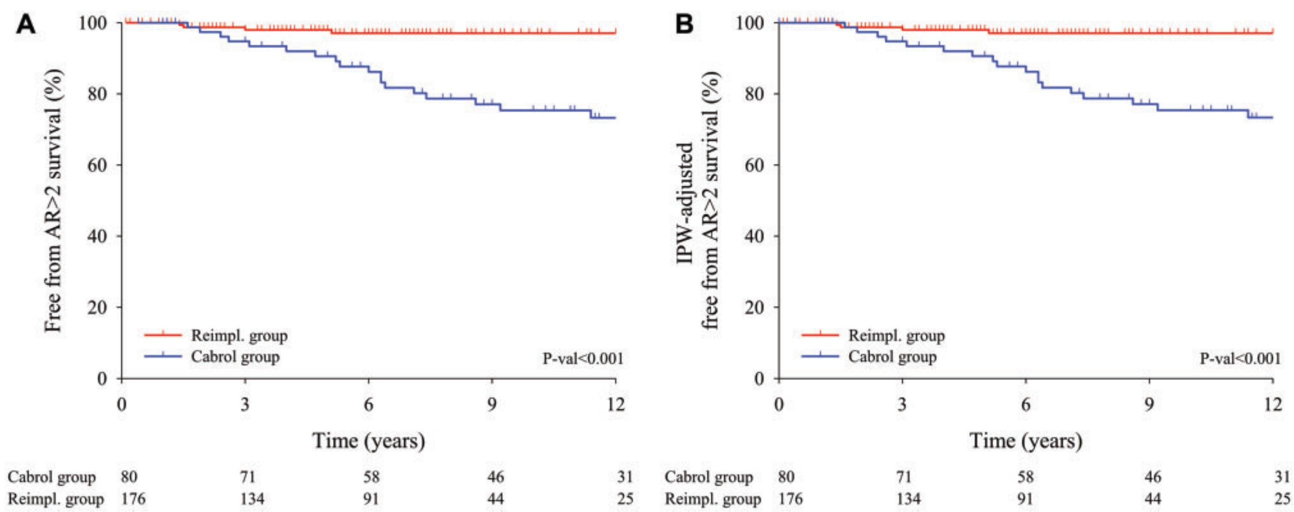

Figure 5: Kaplan–Meier estimates of severe aortic regurgitation free survival. (**A**) Unmatched comparison between the Cabrol and Reimplantation group (*P* < 0.001) and (**B**) IPW-adjusted comparison (*P* < 0.001). AR: aortic regurgitation; IPW: inverse probability weighting.

DISCUSSION

This study gathers our experience with BAV repair over 3 decades and represents the largest experience with the Reimplantation technique in BAVs in the world to date. We demonstrated that BAV repair overall offers survival, which equals the survival of a sex/age-matched cohort of the general Belgian population. We found also improved long-term durability of BAV repair with our new approach using the Reimplantation technique compared to the previous Cabrol annuloplasty. In more detail, the main benefit is highlighted by the gain in freedom from reoperation of 20% at 12 years with the Reimplantation technique, which is in general due to a lower recurrence rate for AR. In addition, we showed that the Reimplantation technique, certainly a more invasive technique compared to Cabrol annuloplasty, is safe and does not increase hospital or late mortality.

Several studies have shown that an untreated large annulus is an independent risk factor for AV repair failure [9, 20]. In this study, we showed that all annuloplasties are not equivalent in their ability to prevent repair failure. The better results obtained with the Reimplantation technique are likely secondary to several factors, including a more reliable and extensive stabilization of the aortic annulus afforded by the Dacron graft. The annuloplasty gained through the Cabrol sutures is limited to the commissural areas and therefore incomplete, and thus appears to become ineffective over time, especially in a patient with larger aortic annulus as in BAV with AR [21, 22]. In this study, long-term results with the Cabrol technique were overall unsatisfactory with half of the failures due to recurrent AR and freedom from reoperation of 74% and 66% at 10 and 15 years, respectively. Only 2 other studies report similar long-term follow-up after Cabrol annuloplasty. Svensson *et al.* [11] reported the cohort of BAV repairs from the Cleveland Clinic with 728 patients, where Cabrol annuloplasty was used as the principal annuloplasty technique. In this study, freedom from reoperation was 78% and 64% at 10 and 15 years, respectively and recurrent AR was the cause of failure in 40% of the reoperations, followed by stenosis in 27%, mixed AV disease in 17% and root aneurysm in 15% [11, 12]. In the second

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study, Sharma *et al.* [12] report the results of 331 patients who underwent AV repair for isolated AR at the Mayo Clinic. In this study, which enrolled 40% of BAV and 60% of tricuspid aortic valve patients, Cabrol annuloplasty was utilized in 81% of patients as the only annuloplasty technique. At 10 and 15 years, the authors reported freedom from AV reoperation of 79% and 72% and freedom from severe AR of 75% and 58%, respectively. They identified recurrent aortic dilatation and recurrent prolapse as a mechanism of failure in almost half of the reoperations. In a previous study, we described that recurrent AR in the Cabrol group was mainly caused by annulus dilatation and cusp prolapse [13]. In that study and another on tricuspid aortic valve repair, we found that in the majority of patients receiving Cabrol annuloplasty, the annulus returns almost to its native size within a few years after surgery [13, 22].

A decrease of recurrent AR observed with the Reimplantation technique compared to the Cabrol technique can certainly be related to the better stabilization of the aortic annulus provided by the circumferential annuloplasty, but other technical aspects of the Reimplantation technique can also have played a significant role. First, the Reimplantation technique grants not only stabilization to the aortic annulus but also to the entire aortic root, from the basal ring to the sino-tubular junction. One study supporting that theory shows that in addition to ventriculo-aortic junction annuloplasty, the additional stabilization of sino-tubular junction with a ring can further improve repair durability [23]. Another advantage of the Reimplantation technique is the ability to modify the valve geometry by placing the commissure at 180°, to achieve a symmetric BAV. It has been suggested that naturally symmetric valves or the ones that were made more symmetric (>160°) during valve repair would achieve a better function and durability [24]. Across the spectrum of BAV phenotypes, commissure orientation varies from 180° to 120°, and the valve morphology varies in parallel and in accordance with that geometrical configuration [25]. Valve symmetrization is thus particularly interesting in asymmetric phenotypes (with commissure orientation <160°) to improve haemodynamics across the valve and reduce postoperative gradients in comparison to repairs where valve geometry was not modified [13, 26]. The combination of annuloplasty, root replacement and commissural positioning at 180°, allows to treat fused cusp prolapse by plication–direct closure, avoiding the need for patch extension and the risk of repair failure due to patch degeneration [27].

Next to the Reimplantation technique, other techniques exist to repair BAV with an approach that is similar to ours regarding stabilization and symmetrization. The external aortic ring and the suture annuloplasty are 2 techniques that provide circumferential annuloplasty [28, 29]. The root Remodelling and sinus plication are 2 techniques that can make BAV more symmetric [26, 27]. These techniques have shown encouraging results in BAV repair for isolated AR, especially with the adjunct of sinus plication in asymmetric BAV and sino-tubular junction stabilization with a second ring [23, 26].

Finally, while we demonstrated that the Reimplantation technique can reduce overall reoperation rates, thanks to less recurrent AR compared to Cabrol annuloplasty, it seems that the development of late stenosis is independent of the annuloplasty technique. Reasons for late stenosis are likely multifactorial and approximate 10% at 12–15 years. In a large series of BAV repair with the Remodelling technique, factors inducing late stenosis were pre-existing valve calcifications and the used patch as cusp augmentation [27]. Potentially, this mode of failure could be alleviated by better patient selection and more restrictive use of patches.

Limitations

This is a retrospective study that carries the limitations of such an analysis. We have evaluated our historical cohort of patients and there was certainly a learning curve in utilizing the different techniques and our overall care standards have likely also improved over time. The enrolment into each respective treatment arm has varied throughout this exceptionally long study period and therefore could have inadvertently introduced a bias into the analysis. To address this issue, we analysed the outcomes of patients enrolled in the first part of the recruitment period (before 2008) separately from the second part (from 2008 on). Although the follow-up is shorter for the 2008–2018 period, the survival benefits derived from the Reimplantation technique were found to be similar between the periods 1996–2007 and 2008–2018 (data shown in Supplementary Material).

During the second half of the study period, we increased our recruitment of foreign patients; accordingly, this has resulted in a higher percentage of patients lost to follow-up in the Reimplantation cohort compared to the Cabrol group (6.9% vs 1.2%). This also may have introduced a slight bias in the study.

Our statistical analysis also carries the limitations of IPW. Although observed baseline covariates are balanced between techniques, it does not include unmeasured characteristics or confounders (e.g. physiopathology of AR vs aneurysmal disease, valve tissue quality and quantity) that could remain different between groups.

CONCLUSIONS

In this study, comparing 2 annuloplasty strategies in BAV repair, we found statistically significant differences for long-term durability in favour of the Reimplantation technique and no significant difference for overall survival. The results support our current strategy of the Reimplantation technique and repair of AR in patients with BAV. Cabrol annuloplasty is obsolete and should be generally abandoned in patients undergoing BAV repair for AR.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

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Author contributions

Christophe de Meester: Formal analysis; Writing—original draft; Writing—review & editing. **Jean-Louis Vanoverschelde:** Conceptualization; Methodology;

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Supervision. **Jama Jahanyar:** Visualization; Writing—review & editing. **Saadallah Tamer:** Software; Visualization. **Stefano Mastrobuoni:** Formal analysis; Methodology. **Michel Van Dyck:** Investigation. **Emiliano Navarra:** Validation; Writing—review & editing. **Alain Poncelet:** Validation; Writing—review & editing. **Parla Astarci:** Project administration; Resources. **Gebrine el Khoury:** Investigation; Supervision; Validation; Writing—review & editing. **Laurent de Kerchove:** Conceptualization; Investigation; Methodology; Writing—original draft.

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REFERENCES

[1] Cabrol C, Cabrol A, Guiraudon G, Bertrand M. [Treatment of aortic insufficiency by means of aortic annuloplasty]. Arch Mal Coeur Vaiss 1966;59:1305–12.

[2] Duran C, Kumar N, Gometza B, Al Halees Z. Indications and limitations of aortic valve reconstruction. Ann Thorac Surg 1991;52:447–53; discussion 53–4.

[3] Cosgrove DM 3rd. Aortic valve repair. Ann Thorac Surg 1992;54:1014–5.

[4] David TE, Feindel CM. An aortic valve-sparing operation for patients with aortic incompetence and aneurysm of the ascending aorta. J Thorac Cardiovasc Surg 1992;103:617–21; discussion 22.

[5] Sarsam MA, Yacoub M. Remodeling of the aortic valve anulus. J Thorac Cardiovasc Surg 1993;105:435–8.

[6] David TE. An anatomic and physiologic approach to acquired heart disease. 8th annual meeting of the European Cardio-thoracic Association, The Hague, Netherlands, September 25-28, 1994. Eur J Cardiothorac Surg 1995;9:175–80.

[7] Lansac E, Di Centa I, Varnous S, Rama A, Jault F, Duran CM *et al.* External aortic annuloplasty ring for valve-sparing procedures. Ann Thorac Surg 2005;79:356–8.

[8] Leyh RG, Fischer S, Kallenbach K, Kofidis T, Pethig K, Harringer W *et al.* High failure rate after valve-sparing aortic root replacement using the "remodeling technique" in acute type A aortic dissection. Circulation 2002;106:I229–33.

[9] Hanke T, Charitos EI, Stierle U, Robinson D, Gorski A, Sievers HH *et al.* Factors associated with the development of aortic valve regurgitation over time after two different techniques of valve-sparing aortic root surgery. J Thorac Cardiovasc Surg 2009;137:314–19.

[10] Casselman FP, Gillinov AM, Akhrass R, Kasirajan V, Blackstone EH, Cosgrove DM. Intermediate-term durability of bicuspid aortic valve repair for prolapsing leaflet. Eur J Cardiothorac Surg 1999;15:302–8.

[11] Svensson LG, Al Kindi AH, Vivacqua A, Pettersson GB, Gillinov AM, Mihaljevic T *et al.* Long-term durability of bicuspid aortic valve repair. Ann Thorac Surg 2014;97:1539–47; discussion 48.

[12] Sharma V, Suri RM, Dearani JA, Burkhart HM, Park SJ, Joyce LD *et al.* Expanding relevance of aortic valve repair-is earlier operation indicated? J Thorac Cardiovasc Surg 2014;147:100–7.

[13] de Kerchove L, Boodhwani M, Glineur D, Vandyck M, Vanoverschelde JL, Noirhomme P *et al.* Valve sparing-root replacement with the reimplantation technique to increase the durability of bicuspid aortic valve repair. J Thorac Cardiovasc Surg 2011;142:1430–8.

[14] Nawaytou O, Mastrobuoni S, de Kerchove L, Baert J, Boodhwani M, El Khoury G. Deep circumferential annuloplasty as an adjunct to repair regurgitant bicuspid aortic valves with a dilated annulus. J Thorac Cardiovasc Surg 2018;156:590–7.

[15] Zoghbi WA, Enriquez-Sarano M, Foster E, Grayburn PA, Kraft CD, Levine RA *et al.* Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. J Am Soc Echocardiogr 2003;16:777–802.

[16] Le Polain de Waroux JB, Pouleur AC, Goffinet C, Vancraeynest D, Van Dyck M, Robert A *et al.* Functional anatomy of aortic regurgitation: accuracy, prediction of surgical repairability, and outcome implications of transesophageal echocardiography. Circulation 2007;116:I264–9.

[17] Akins CW, Miller DC, Turina MI, Kouchoukos NT, Blackstone EH, Grunkemeier GL *et al.* Guidelines for reporting mortality and morbidity after cardiac valve interventions. J Thorac Cardiovasc Surg 2008;135:732–8.

[18] Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. Stat Med 2009;28:3083–107.

[19] Hernan MBB, Robins JM. Marginal structural models to estimate the joint causal effect of non randomized treatments. J Am Stat Assoc 2011;96:440–8.

[20] Schafers HJ, Raddatz A, Schmied W, Takahashi H, Miura Y, Kunihara T *et al.* Reexamining remodeling. J Thorac Cardiovasc Surg 2015;149:S30–6.

[21] Navarra E, El Khoury G, Glineur D, Boodhwani M, Van Dyck M, Vanoverschelde JL *et al.* Effect of annulus dimension and annuloplasty on bicuspid aortic valve repair. Eur J Cardiothorac Surg 2013;44:316–22; discussion 22–3.

[22] de Kerchove L, Mastrobuoni S, Boodhwani M, Astarci P, Rubay J, Poncelet A *et al.* The role of annular dimension and annuloplasty in tricuspid aortic valve repair. Eur J Cardiothorac Surg 2016;49:428–37; discussion 37–8.

[23] Zakkar M, Youssefi P, Di Centa I, Khelil N, Debauchez M, Lansac E. Isolated aortic valve repair-how to do it and long-term results: external ring annuloplasty. Ann Cardiothorac Surg 2019;8:418–21.

[24] Aicher D, Kunihara T, Abou Issa O, Brittner B, Gräber S, Schäfers H-J. Valve configuration determines long-term results after repair of the bicuspid aortic valve. Circulation 2011;123:178–85.

[25] De Kerchove L, Mastrobuoni S, Froede L, Tamer S, Boodhwani M, Van Dyck M *et al.*. Variability of repairable bicuspid aortic valve phenotypes: towards an anatomical and repair-oriented classification†. Eur J Cardiothorac Surg2019;56:351–9.

[26] Schneider U, Schmied W, Aicher D, Giebels C, Winter L, Schafers HJ. Sinus plication to improve valve configuration in bicuspid aortic valve repair-early results. Ann Thorac Surg 2017;103:580–5.

[27] Schneider U, Feldner SK, Hofmann C, Schope J, Wagenpfeil S, Giebels C *et al.* Two decades of experience with root remodeling and valve repair for bicuspid aortic valves. J Thorac Cardiovasc Surg 2017;153:S65–71.

[28] Schneider U, Hofmann C, Aicher D, Takahashi H, Miura Y, Schafers HJ. Suture annuloplasty significantly improves the durability of bicuspid aortic valve repair. Ann Thorac Surg 2017;103:504–10.

[29] Lansac E, Di Centa I, Sleilaty G, Lejeune S, Khelil N, Berrebi A *et al.* Long-term results of external aortic ring annuloplasty for aortic valve repair. Eur J Cardiothorac Surg 2016;50:350–60.

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