Aortic annulus does not dilate over time after aortic root remodeling with or without annuloplasty

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ABSTRACT

Objective: The lack of annular stabilization is the drawback of aortic root remodeling, and recently the addition of annuloplasty has been proposed. Limited data, however, exist on late annular size after remodeling. We studied annular size over time.

Methods: In 241 patients (53 ± 16 years) annular size was determined preoperatively (T0), before discharge (T1), and at least 2 years after remodeling (T2, 54 ± 27 months) with ($n = 52$) or without external suture annuloplasty. Seventeen patients had Marfan syndrome (7%), 100 a bicuspid valve (41%), and 22 acute dissection (9%). Mean graft size was 25.2 ± 1.3 mm, and annuloplasty size 24.3 ± 1.4 mm.

Results: Annular size was significantly reduced after repair and remained stable over time (T0: 27.4 ± 3.0 mm, T1: 24.2 ± 2.5 mm, T2: 24.2 ± 2.6 mm). After propensity-score matching ($n = 33$ each), baseline annular size was similar (with annuloplasty vs without: 28.7 ± 4.1 mm vs 27.8 ± 2.8 mm). Annular reduction was less effective without annuloplasty (23.9 ± 2.0 mm vs 25.6 ± 2.2 mm, $P < .01$); size was identical at follow-up (23.8 ± 2.2 mm vs 25.1 ± 2.5 mm, $P = .03$). After matching, freedom from annular size increase $>10\%$ at 4 years was $93 \pm 5\%$ without annuloplasty and $91 \pm 9\%$ with annuloplasty ($P = .92$). A linear mixed-effects model identified no significant effect of annuloplasty on annulus diameter change at T2 ($P = .48$). Era after 2004, Marfan syndrome, and smaller annulus diameter at discharge were the independent predictors for late annular expansion.

Conclusions: Aortic annulus rarely dilates over time after remodeling. In the case of annular dilatation, annuloplasty normalizes annular size and may prevent further dilatation by enhancing cusp coaptation. Even without annuloplasty, the aortic annulus becomes smaller compared with preoperative dimensions when aortic valve remains competent. (J Thorac Cardiovasc Surg 2018;155:885-94)

Aortoventricular junction diameter in patients with or without annuloplasty.

Central Message

The aortic annulus rarely dilates over time after remodeling with annuloplasty in cases with annular dilatation. Even without annuloplasty, it becomes smaller, which may be due to annular reverse remodeling.

Perspective

The aortic annulus rarely dilates over time after remodeling, at least in cases without marked annular dilatation at the time of surgery. If annular dilatation is present, external suture annuloplasty normalizes annular size and prevents further dilatation. Even without annuloplasty, aortic annulus becomes smaller over time when aortic valve remains competent, which may be due to annular reverse remodeling.

See Editorial Commentary page 895.

Two types of valve-preserving root replacement have been performed to treat aortic root dilatation with or without aortic valve regurgitation (AR) in the last 2 decades.^{1,2}

Aortic root remodeling is one of these alternatives and has been established as a simple, physiological, and effective procedure. We have reported favorable long-term outcomes with sufficient caseload over 15 years.³ The major advantage of remodeling technique is the preservation of interleaflet triangles, which is believed to play a key role in optimal root hemodynamic physiology.⁴

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Scanning this QR code will take you to the supplemental video, appendix, figures, and table for the article.

Abbreviation and Acronyms

AR = aortic valve regurgitation
 AVJ = aortoventricular junction
 BAV = bicuspid aortic valve
 TAV = tricuspid aortic valve

However, most surgeons are still reluctant to apply remodeling because one of the drawbacks of this technique is the assumed lack of annular stabilization and the resultant risk of late aortic regurgitation, especially in cases with connective tissue disease⁵ or large annulus.^{3,6}

Therefore, different modifications of aortic annuloplasty have been proposed: external suture annuloplasty,⁷ external ring annuloplasty,⁸ and internal ring annuloplasty.⁹ Each has both advantages and disadvantages, and the superiority of one alternative over others remains unclear because of the lack of long-term data. We have consistently applied external suture annuloplasty in cases with pre-existing annular dilatation regardless of root replacement because it is simple and effective.^{3,7} With satisfactory mid-term results and low invasiveness, we have now applied annuloplasty for all patients undergoing aortic valve/root repair routinely to enhance cusp coaptation and to prevent late annular dilatation. It is, however, unclear whether the annuloplasty contributes to valve stability, and, if so, in which patients. In a retrospective analysis, we studied annular size over time after remodeling with or without annuloplasty to confirm our hypothesis that annuloplasty can normalize the large annulus and stabilize over time.

MATERIAL AND METHODS**Patients**

Between October 1995 and December 2013, 798 patients underwent valve-preserving root replacement by a single surgeon (H.J.S.). Of these, 29 patients who underwent aortic valve reimplantation and 6 patients treated with external ring annuloplasty were excluded. Among the remaining 763 patients, external suture annuloplasty was performed in 310 patients (41%) since January 2009. Echocardiography was scheduled at 3 and 12 months postoperatively, then annually or every 2 years. The majority of patients were followed by referral cardiologists, who sent their echo studies for follow-up analysis. In-house echocardiography with measurement of aortoventricular junction (AVJ) diameter at least more than 2 years after the operation was performed in 241 patients, who were further analyzed in this study (Figure 1). Follow-up was complete in these individuals. Annual number of cases using each technique including additional technical modifications is illustrated in the Figure E1. The institutional ethical committee approved the anonymous use of patient data.

Their mean age was 53 ± 16 years, and the majority were male ($n = 184$, 76%). Eight patients (3%) had undergone previous cardiac/aortic surgery through a median sternotomy. Aortic valve repair had been performed in 4, mitral valve repair in 1, coronary artery bypass grafting in 1, replacement of the ascending aorta due to acute aortic dissection in 1, and Ross operation in 1. Seventeen patients (7%) suffered from Marfan syndrome, and 100 patients (41%) had bicuspid aortic valve (BAV) anatomy. Twenty-two patients (9%) were operated in the emergent setting due to type A acute aortic dissection. Preoperative mean AR grade was 2.5 ± 0.8 (Table 1).

FIGURE 1. A Consolidated Standards of Reporting Trials–type diagram of all patients who underwent aortic root remodeling with or without external suture annuloplasty. AVJ, Aortoventricular junction.

Indication and Operative Technique

Our routine technique of remodeling and anesthesia has been described in detail previously.⁶ Preoperatively, all patients underwent transesophageal echocardiography (ATL HDI-3000 [Philips Ultrasound, Bothell, Wash] or Sequoia 256 [Acuson Corp, Mountain View, Calif]). The diameter of sinuses of Valsalva, AVJ, and sinotubular junction as well as AR grade were measured as shown in Table 1. When the aortic root was dilated (≥ 43 –45 mm depending on patient size), valve-sparing root replacement was performed if the cusps were pliable and not retracted. For BAV anatomy, this threshold was slightly lower than tricuspid aortic valve (TAV), although a decision-making was really subjective. The degree of AR, the presence of cusp prolapse or fenestrations, and size of aortic root were not considered as exclusion criteria for valve preservation. Initially, we performed remodeling in cases with AVJ ≤ 29 mm and reimplantation with larger AVJ. Since January 2008, we have only applied root remodeling.

For TAV, 3 sinuses were excised, and a Dacron graft was chosen with similar diameter of the native AVJ, also taking the size of the patient into consideration. We used a 26-mm graft most frequently ($n = 146$) followed by a 24-mm graft ($n = 79$) (Table E1). Three tongues were created equally and the graft sutured into the aortic root close to the cusp insertion lines. Care was taken to create maximum height of the commissures. In cases with BAV, 2 symmetrical tongues were created and 2 commissures were repositioned in the 180° angle.

In 52 patients since January 2009, an external circular suture annuloplasty using a CV-0 expanded polytetrafluoroethylene suture (W. L. Gore & Associates, Inc, Flagstaff, Ariz) was added⁷ (the annuloplasty group; the other 189 patients were the no-annuloplasty group). The suture was circularly passed around the outside of the root at

TABLE 1. Baseline characteristics, root geometry, and operative procedures of the 2 groups

Variable	Before matching			After matching		
	Annuloplasty		P value	Annuloplasty		P value
	(−)	(+)		(−)	(+)	
	(n = 189)	(n = 52)		(n = 33)	(n = 33)	
Baseline characteristics						
Sex, male	139 (74%)	45 (87%)	.07	26 (79%)	27 (82%)	.76
Age, y	55 ± 15	45 ± 16	<.01	48 ± 15	49 ± 15	.72
Body height, cm	175 ± 10	182 ± 9	<.01	180 ± 8	179 ± 7	.56
Body weight, kg	81 ± 16	86 ± 13	.06	85 ± 16	85 ± 14	.81
Body surface area, m ²	2.0 ± 0.2	2.0 ± 0.3	.41	2.1 ± 0.2	2.0 ± 0.2	
Bicuspid aortic valve	79 (42%)	21 (40%)	.86	14 (42%)	10 (30%)	.31
Marfan syndrome	11 (6%)	6 (12%)	.13	4 (12%)	4 (12%)	NA
Acute aortic dissection	20 (11%)	2 (4%)	.16	1 (3%)	1 (3%)	NA
Previous cardiac/aortic operation	7 (4%)	1 (2%)	.47	3 (9%)	1 (3%)	.30
Aortic valve regurgitation grade	2.5 ± 0.7	2.4 ± 0.9	.45	2.4 ± 1.0	2.4 ± 0.9	.95
Root geometry						
AVJ diameter, mm	27 ± 2	30 ± 4	<.01	28 ± 3	29 ± 4	.35
Valsalva sinus diameter, mm	55 ± 7	47 ± 7	<.01	49 ± 5	48 ± 7	.57
STJ diameter, mm	45 ± 7	43 ± 10	.47	43 ± 11	43 ± 9	.98
Postoperative effective height, mm	9.7 ± 1.5	9.5 ± 1.2	.99	9.8 ± 1.5	9.9 ± 1.2	.77
Operative procedures						
Central cusp plication	135 (71%)	47 (94%)	<.01	30 (91%)	30 (91%)	NA
Concomitant CABG	36 (19%)	0	<.01	3 (9%)	0	.08
Partial/total arch replacement	65 (34%)	7 (15%)	<.01	5 (15%)	6 (18%)	.74
Duration of CPB, min	111 ± 30	94 ± 22	<.01	104 ± 22	95 ± 22	.11
Duration of AXC, min	82 ± 17	74 ± 15	<.01	77 ± 15	75 ± 17	.57
Prosthesis, mm	25 ± 1	25 ± 1	.22	25 ± 1	25 ± 1	.30

NA, Not applicable; AVJ, aortoventricular junction; STJ, sinotubular junction; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; AXC, aortic crossclamping.

the level of the basal ring and tied around a Hegar dilator (Aesculap, Tuttingen, Germany), which was usually 1 mm smaller than the size of the prosthesis used (Video 1). When geometric cusp height¹⁰ was less than 20 mm, a Hegar dilator was used with a diameter 2 mm smaller. The mean diameter of a Hegar dilator was thus 24.3 ± 1.4 mm (23 or 25 mm most frequently) (Table E1). Care was taken not to interfere with the circumflex coronary artery and not to disturb the heart conduction system.

After completion of root replacement, aortic cusp configuration was evaluated carefully. Initially, the presence of prolapse was determined by visual inspection. Since 2004, the height difference between the central

VIDEO 1. External suture annuloplasty combined with aortic root remodeling operation using a CV-0 expanded polytetrafluoroethylene suture (W. L. Gore). Video available at: [http://www.jtcvsonline.org/article/S0022-5223\(17\)32404-2/fulltext](http://www.jtcvsonline.org/article/S0022-5223(17)32404-2/fulltext).

free cusp margin and the nadir of aortic insertion (effective height) was measured routinely.¹¹ An effective height less than 9 mm was considered as prolapse and corrected to 9 to 10 mm in each cusp.¹² Cusp prolapse was present in two thirds of patients (n = 182, 76%) and corrected by central plication of the free margin using a single 5-0 or 6-0 polypropylene suture (PROLENE; Ethicon, Inc, Hamburg, Germany).¹³ The coronary ostia were reimplemented via the button technique. Intraoperative transesophageal echocardiography was performed after discontinuation of cardiopulmonary bypass to confirm valve configuration and function.

In cases with aortic arch dilatation, partial (n = 61) or total (n = 11) arch replacement with short period of circulatory arrest with a nasopharyngeal temperature of 18 ± 1°C was performed. In cases with acute aortic dissection, the dissected aortic arch layers were readapted with either gelatin–resorcin–formalin glue (Cardial, Technopole, Sainte-Etienne, France) in the early series or BioGlue (CryoLife International Inc, Kennesaw, Ga) in the recent series. For proximal lesion (ie, detached commissures), no biological glue was used in the majority of patients. Teflon (DuPont Pharmaceuticals, Wilmington, Del) felt was only used to reinforce the suture line to the descending aorta in cases with total arch replacement due to acute aortic dissection.

Propensity Score Matching Analysis

Using multivariable logistic regression analysis, we calculated the probability of being assigned to annuloplasty over no annuloplasty from baseline characteristics as shown in Appendix E1. The linearity of all continuous covariates in the logistic regression was confirmed. A P value less than .20 was defined for selecting variables for entry into the final model (indicated as characters in bold in Appendix E1). Using selected covariables, we calculated a propensity score for each patient. A propensity

score could not be calculated in 2 patients in the annuloplasty group and 23 patients in the no-annuloplasty group due to missing data; thus, a multiple imputation technique was used to impute missing values of these 25 patients. Each patient with annuloplasty was matched to 1 patient without annuloplasty via greedy (nearest neighbor) matching.¹⁴ The tolerance for matching (a predicted probability difference) was set at 0.1. The mean difference of propensity score for a matching was less than 0.5 standard deviations (mean 0.068 ± 0.056 , 0.001-0.144). C-statistic of the propensity score model was .918 ($P < .01$; 95% confidence interval, 0.879-0.958). Using this technique, we identified comparable patient cohorts (33 patients from each group) for the final analysis. A mirror histogram before and after matching of the propensity scores in each group is shown in Figure E2.

Clinical Endpoints

Primary endpoint was freedom from reoperation. Secondary endpoint was freedom from annular expansion $>10\%$, which was set according to the previous report.⁴

Statistical Analysis

Statistical analysis was performed with the StatView 5.0 program (SAS Institute Inc, Cary, NC) or Statistical Program for Social Sciences for Windows, version 22.0 (IBM Corp, Armonk, NY). All values are expressed as mean $\pm$ standard deviation, except data from the Kaplan–Meier curve, expressed as Kaplan–Meier estimate $\pm$ standard error. Kaplan–Meier curves were transected at 6 or 4 years because of small number of patients at risk thereafter and compared between groups via the log-rank test. The Student *t* test was used for comparison of the continuous variables, and the χ^2 test was used for comparison of frequencies between the groups. A *P* value of less than .05 was considered statistically significant. The factors listed in the Appendix E1 influencing late annular stability were analyzed with the Cox proportional hazard model. A *P* value $< .1$ in the univariate analysis was defined for selecting variables for entry into the multivariate one.

To minimize the major drawback of this retrospective study design converting a longitudinal data into time-to-event data, a linear mixed effects model was performed to test the effect of annuloplasty on late annular expansion. In addition, propensity score was also used as a covariable to test the effect of annuloplasty on reoperation and late annular expansion.

RESULTS

Baseline Characteristics

In the entire population, patients in the no-annuloplasty group were significantly older and shorter in height compared with those in the annuloplasty group. They had a significantly smaller AVJ diameter but larger sinus diameter. Central cusp plication was carried out more frequently for the annuloplasty group. Coronary artery bypass grafting and aortic arch replacement were more frequently necessary in the no-annuloplasty group; they required longer duration of cardiopulmonary bypass and aortic crossclamping. Characteristics of propensity score-matched pairs were almost similar, including baseline variables and root geometry (Table 1). A standardized difference plot to show the bias reduction after matching is demonstrated in Figure E3.

Follow-up

All patients were followed clinically with mean follow-up time of 118 ± 51 months. Follow-up was significantly shorter in patients with annuloplasty (55 ± 17 months) than without (136 ± 43 months, $P < .01$). Transthoracic

echocardiography was performed at admission (T0), discharge (T1), and later than 2 years postoperatively (T2), and AVJ diameter was measured in addition to a routine assessment. Follow-up was 100% complete. Mean duration between T0 and T2 was 54 ± 27 months (24-165 months) and significantly shorter in patients with annuloplasty (37 ± 11 months) than without (59 ± 28 months, $P < .01$). In the matched cohort, the difference became shorter but was still significant (38 ± 12 months vs 50 ± 19 months, $P < .01$). Long-term outcomes with regard to reoperation on the aortic valve were analyzed.

After the last echocardiography measurement, 18 of 189 patients in the no-annuloplasty group died at 99 ± 34 months postoperatively. Freedom from death was $99 \pm 1\%$ at 5 years and $84 \pm 4\%$ at 10 years after the surgery. No patients in the annuloplasty group died.

AR and Reoperation

In unmatched patients, AR at T1 and T2 were 0.5 ± 0.8 , 0.7 ± 0.6 in the no-annuloplasty group and 0.2 ± 0.4 , 0.7 ± 0.7 in the annuloplasty group, respectively ($P < .01$ at T1, $P = .64$ at T2 in comparison between groups). In matched patients, ARs at T1 and T2 were 0.5 ± 0.7 and 0.8 ± 0.6 in the no-annuloplasty group and 0.1 ± 0.3 and 0.6 ± 0.6 in the annuloplasty group, respectively ($P = .07$ at T1, $P = .33$ at T2 in comparison between groups).

In the entire cohort, 12 patients in the no-annuloplasty group required reoperation on the aortic valve and/or aortic root due to cusp prolapse ($n = 6$) or cusp calcification/restriction ($n = 6$) at 101 ± 43 (27-182) months after the initial operation. All of the initial operations of these patients were performed before 2004, when effective height was not measured routinely. Five patients underwent re-repair, whereas another 7 patients were treated by replacement. Three patients in the annuloplasty group underwent reoperation due to cusp calcification/restriction ($n = 2$, aortitis = 1) or patch dehiscence ($n = 1$) at 12, 19, and 63 months postoperatively. Two patients underwent replacement, the other re-repair. After matching, only 1 patient in the annuloplasty group underwent reoperation due to cusp restriction, whereas 3 in the no-annuloplasty group due to cusp prolapse ($n = 1$) or cusp calcification/restriction ($n = 2$).

In 15 patients who underwent reoperation, AVJ diameter at the time of reoperation was $3.9 \pm 6.6\%$ larger than that at discharge (24.1 ± 3.1 mm to 25.2 ± 4.0 mm). In the other 226 patients, AVJ diameter at the last follow-up was identical to the size at discharge (24.2 ± 2.5 mm to 24.2 ± 2.6 mm). AR grade of these 226 patients was 0.3 ± 0.5 at T1 and 0.7 ± 0.6 at T2.

In the patients before matching, freedom from reoperation at 5 years was $98 \pm 1\%$; $99 \pm 1\%$ for the no-annuloplasty group and $96 \pm 3\%$ for the annuloplasty group ($P = .03$) (Figure 2). In the matched patients, freedom

Freedom from reoperation

FIGURE 2. Freedom from reoperation on the aortic valve or root in patients with (blue line) or without (red line) annuloplasty before (left) and after (right) propensity score matching.

from reoperation at 5 years was $99 \pm 2\%$; $97 \pm 3\%$ for the no-annuloplasty group and 100% for the annuloplasty group ($P = .72$) (Figure 2).

Using the Cox proportional hazards model within entire population, we identified no variable as a significant risk factor for reoperation. When the propensity score was used as a covariate, use of annuloplasty was also not a risk factor for reoperation (annuloplasty: $P = .33$, hazard ratio, 2.631; 95% confidence interval, 0.373-18.54 and propensity score: $P = .43$; hazard ratio, 2.700; 95% confidence interval, 0.235-30.978).

Annular Size

Before matching, AVJ size of all patients was significantly reduced after repair and remained stable over time (T0: 27.4 ± 3.0 mm T1: 24.2 ± 2.5 mm, T2: 24.2 ± 2.6 mm, $P < .01$ compared with T0 and T1, T2). Baseline AVJ diameter was significantly larger in the annuloplasty group compared with the no-annuloplasty group ($P < .01$) (Figure 3, left). However, they became similar postoperatively ($P = .79$) and remained stable over time ($P = .97$). AVJ diameter of the annuloplasty group was 29.6 ± 3.9 , 24.1 ± 2.2 , and 24.2 ± 2.4 mm, that of the no-annuloplasty group was 26.7 ± 2.3 , 24.2 ± 2.6 , and 24.2 ± 2.6 mm at T0, T1, and T2, respectively ($P < .01$ compared with T0 and T1, T2 for both groups).

After matching, baseline AVJ size was similar between groups ($P = .35$ at T0) (Figure 3, right). Annular reduction was less effective without annuloplasty than with annuloplasty both at discharge ($P < .01$ at T1) and

follow-up ($P = .03$ at T2). AVJ diameter of the annuloplasty group was 28.7 ± 4.1 , 23.9 ± 2.0 , and 23.8 ± 2.2 mm and that of the no-annuloplasty group was 27.8 ± 2.8 , 25.6 ± 2.2 , and 25.1 ± 2.5 mm at T0, T1, and T2, respectively. ($P < .01$ compared with T0 and T1, T2 for both groups).

Left Ventricular Size

Before matching, left ventricular end-diastolic diameter at T0, T1, and T2 was 59 ± 8 mm, 54 ± 6 mm, and 52 ± 6 mm in the no-annuloplasty group ($P < .01$ between T0 and T1, T2) and 57 ± 10 mm, 53 ± 6 mm, and 52 ± 6 mm in the annuloplasty group ($P < .01$ between T0 and T1, T2). There was no significant difference in left ventricular end-diastolic diameter between groups (Figure 4, left).

After matching, left ventricular end-diastolic diameter at T0, T1, and T2 was 59 ± 8 mm, 56 ± 6 mm, and 53 ± 7 mm in the no-annuloplasty group ($P < .01$ between T0 and T2 and $P < .05$ between T0 and T1 or T1 and T2) and 56 ± 8 mm, 52 ± 6 mm, and 52 ± 5 mm in the annuloplasty group ($P < .01$ between T0 and T1 and $P = .01$ between T0 and T2) (Figure 4, right). There was significant difference in left ventricular end-diastolic diameter at T1 between groups ($P = .02$).

Factors Affecting Annular Size

In a linear mixed effects model for repeated measures, use of annuloplasty, and repeated measures for AVJ diameter at T0-T2, adjusted to duration between T0 and

FIGURE 3. Time course of AVJ diameter in patients with (blue line) or without (red line) annuloplasty before (left) and after (right) propensity score matching. See text for each time point. AVJ, Aortoventricular junction.

T2, there were significant effects of annuloplasty, repeated time, and their interaction (each $P < .01$). After stratification by repeated measures for AVJ diameter, a linear mixed effects model identified no significant effect of annuloplasty

on annulus diameter change at T2 ($P = .48$). There were significant differences in AVJ diameter between T0 and T1 or T2, whereas there was no significant difference between T1 and T2.

FIGURE 4. Time course of LVEDd in patients with (blue line) or without (red line) annuloplasty before (left) and after (right) propensity score matching. See text for each time point. LVEDd, Left ventricle end-diastolic diameter.

Freedom from annular expansion >10%

FIGURE 5. Freedom from annular expansion >10% in patients with (blue line) or without (red line) annuloplasty before (left) and after (right) propensity score matching.

Before matching, annular size increase >10% occurred in 14 patients of the no-annuloplasty group and 3 of the annuloplasty group. Among these 14 patients of the no-annuloplasty group, only 2 patients underwent reoperation on the aortic valve due to cusp prolapse ($n = 1$) and cusp calcification ($n = 1$). After matching, it occurred in 3 patients of the no-annuloplasty group and 2 of the annuloplasty group without the incidence of reoperation on the aortic valve. Freedom from annular size increase >10% was $96 \pm 1\%$ at 4 years in overall patients, which was slightly greater in the no-annuloplasty group ($97 \pm 1\%$) compared with the annuloplasty group ($92 \pm 5\%$), without statistical significance ($P = .10$). After matching, it was $92 \pm 4\%$ and similar between groups ($93 \pm 5\%$ in the no-annuloplasty group, $91 \pm 9\%$ in the annuloplasty group, $P = .92$) (Figure 5).

Using the Cox proportional hazards model within entire population, we identified era after 2004, larger body surface area, Marfan syndrome, TAV, previous cardiac/aortic operation, use of cusp plication, and smaller AVJ diameter at discharge as significant risk factors for late annular expansion more than 10%. However, stepwise forward selection method identified only era after 2004, Marfan syndrome, and smaller AVJ diameter at discharge as independent risk factors (Table 2). Freedom from late annular expansion >10% at 4 years was $99 \pm 1\%$ in patients operated before 2004 and $94 \pm 3\%$ after 2004 ($P < .01$). Freedom from late annular expansion >10% at 4 years in patients with or without Marfan syndrome was $83 \pm 11\%$ and $97 \pm 1\%$, respectively ($P < .01$). When

the propensity score was used as a covariate, use of annuloplasty was no more risk factor for late annular expansion >10% (annuloplasty: $P = .94$; hazard ratio, 1.084; 95% confidence interval, 0.147-7.969 and propensity score: $P = .04$; hazard ratio, 15.618; 95% confidence interval, 1.159-210.411).

DISCUSSION

Annular stabilization plays a key role in success of mitral repair. It thus appears logical to assume that similar conditions also apply to the aortic valve. The majority of patients with AR have a large aortic annulus, which may prevent securing sufficient coaptation of each cusp. Very impressive results have been obtained in isolated repair of BAV.¹⁵ According to the law of Laplace, the larger the annulus expands, the greater the stress will be.

The concept can also be assumed to be important in cases with annular enlargement undergoing valve-preserving root replacement. In this scenario, remodeling has a drawback with regard to annular stabilization compared with reimplantation. Thus additional annuloplasty has been assumed to be essential for better early and late valve durability after remodeling.⁸ Actually, aortic root dilatation has emerged as a risk factor for recurrence of AR in the era beyond refinement of annuloplasty.^{6,16} With aggressive application of annuloplasty, preoperative root dilatation has proved to be no longer a risk factor for recurrence of AR, although routine measurement of effective height has contributed to the outcome together.⁸ Different approaches

TABLE 2. Predictors of late annular expansion >10%

Variable	Univariate	Multivariate		
	P value	P value	HR	95% CI
Era after 2004	<.01	<.01	5.934	1.661-21.195
Marfan syndrome	<.01	.03	3.856	1.171-12.698
Smaller AVJ diameter at discharge	.03	.05	0.788	0.623-0.998
Redo operation	<.01	.30		
Tricuspid aortic valve	.02	.27		
Use of cusp plication	.04	.16		
Larger body surface area	.04	.12		
Taller height	.05	.14		
Greater body weight	.07	.16		
Larger preoperative diameter of sinus of Valsalva	.09	.25		

HR, Hazard ratio; CI, confidence interval; AVJ, aortoventricular junction.

to aortic annuloplasty have been advocated.¹⁷ Their clinical advantages and disadvantages have not clearly been proven.¹⁸

The most popular and simple annuloplasty is subcommissural annuloplasty, which was first performed by Cabrol and colleagues¹⁹ in 1966. In the meantime, it has been shown to be associated with a high risk of recurrence of annular dilatation and AR.¹⁵ David reinforced the fibrous portion of the aortic root partially for remodeling operation as the “David-III operation.”²⁰ The results were apparently suboptimal.^{20,21} Thus, a circumferential stabilization may be superior.⁷ The most common circumferential annular supports currently used are the suture annuloplasty,⁷ the implantation of an expansible ring,⁸ and the insertion of an internal rigid device.⁹

The internal ring annuloplasty has an apparent advantage of annular reduction at the basal plane without root dissection. There are, however, no mid-term data, and the proximity of the device to the cusps has been subject of concern. Reoperations were necessary in 7 of 65 (10.8%) after implantation of this ring during mean follow-up of 2 years.⁹

External ring annuloplasty can stabilize the annulus at the same level as the first suture line of the aortic valve reimplantation operation. Remodeling with the expansible ring may preserve root distensibility, which is an advantage compared with reimplantation. However, this ring requires deep dissection to the basal ring, which is difficult in cases with ventricular muscle within the right sinus.^{22,23}

The advantage of external suture annuloplasty is its simplicity. It requires less root dissection and reduces the annular diameter evenly. Thus, the addition of external suture annuloplasty did not prolong the myocardial

ischemia time in our cohort, as shown in Table 1. Postoperative annular size can be predicted exactly according to the size of Hegar dilator used. In fact, postoperative AVJ diameter was 24.1 ± 2.2 mm after remodeling plus annuloplasty with the mean diameter of a Hegar dilator of 24.3 ± 1.4 mm in this study. It could not be predicted exactly after external ring or reimplantation technique because human root base thickness varies from 3.3 to 6.2 mm at the right coronary sinus.^{22,23}

Nonetheless, these approaches are still not standardized but controversial because of lack of long-term fate of the annular geometry and physiology. Wuliya and colleagues⁴ found that annular diameter remained stable and some systolic annular expansibility was maintained after external expansible ring annuloplasty during a median 19-month follow-up. Interleaflet triangles can be preserved after remodeling; thus, root distensibility can also be preserved regardless of the use of annuloplasty or not, which seems the most advantage of remodeling over reimplantation.

Our current findings showed that annular diameter remained stable after remodeling for mean follow-up time of 54 months, interestingly with or without external suture annuloplasty. Annuloplasty could effectively reduce the annular size up to near normal level shortly after the surgery for patients with larger annulus, which proved to be a risk factor for recurrence of AR.^{3,6,16} For larger annulus, remodeling alone was not enough for annular size normalization; however, the annular size further decreased over time when aortic valve remained competent, maybe as a consequence of annular remodeling. This was the most striking finding in the current study.^{24,25} Indeed, left ventricular reverse remodeling between T1 and T2 was more evident in the no-annuloplasty group compared with the annuloplasty group. There have been many reports of left ventricular reverse remodeling after aortic valve replacement for patients with AR,^{24,25} but no evidence of annular reverse remodeling after aortic valve repair has been found up to now.

In contrast, when aortic valve did not remain competent, the results could be different from our current findings. After matching, AVJ diameter and left ventricular end-diastolic diameter at discharge were significantly larger in the no-annuloplasty group than the annuloplasty group. As a result, AR at discharge tended to be more in the no-annuloplasty group (0.5 ± 0.7) than the annuloplasty group (0.1 ± 0.3 , $P = .07$). Our patients without annuloplasty were thus jeopardized during the early period. As we had discussed in our previous study,³ annuloplasty might facilitate improvement of the coaptation depth between each cusp and increase the proportion of completely competent valves. Therefore, annuloplasty might play an important role in eliminating the risk of failure due to residual AR, especially in cases with large annulus. Indeed, all causes of reoperation were not annular

expansion but cusp-related. Further investigations are mandatory to confirm the role of annuloplasty on long-term valve durability.

Interestingly, the number of patients who developed late annular expansion more than 10% was similar between the era before 2004 (4/97, 4.1%) and after 2004 (11/144, 7.6%, $P = .27$). However, the follow-up duration was significantly longer in patients before 2004 (73 ± 27 months) than after 2004 (42 ± 18 months, $P < .01$). Therefore, freedom from late annular expansion $>10\%$ at 4 years was 5% greater in patients before 2004. Mean annular diameter was quite similar at discharge and follow-up between cases before 2004 (24.4 ± 2.9 mm to 24.5 ± 2.8 mm) and after 2004 (23.9 ± 2.2 mm to 24.0 ± 2.4 mm). It is thus unclear whether the era after 2004 being a predictor for dilatation was a statistical artifact. A possible explanation may be expanded indication for aortic remodeling in our recent series as our results become improved and steady.

Limitations

There were some limitations inherent in the current study. First, the sample size of studied groups seems relatively small. This is a retrospective study with consecutive patients. Therefore, we performed propensity score matching to compare 2 homogenous groups, which reduced the sample size greatly. It was impossible to perform 1:2 or 1:3 matching because of great discrepancy of propensity score between groups, as shown in [Figure E2](#). We set the tolerance for matching (a predicted probability difference) at 0.1, because 0.1 or less is considered to be eligible match. Indeed, the 2 groups became inhomogeneous with the tolerance for matching at 0.2 or more. Indeed, standardized difference after matching ([Figure E3](#)) suggests the expected bias reduction ($<\pm 10\%$) could not sufficiently be achieved. Therefore, we abandoned further increases of the sample size. Another reason is that an external suture annuloplasty was introduced in January 2009. Therefore, the number of patients who underwent both annuloplasty and a follow-up echocardiography was less than those without annuloplasty. When we used echocardiography data from referral local cardiologists, the total number of patients increased. However, the anatomical location and time phase during the cardiac cycle of their annular measurement was highly variable. Therefore, we decided to use in-house echocardiography data alone to confirm the accuracy and reproducibility of assessment. Therefore, we could study only 32% of entire patients who underwent remodeling (241/763) and 8.7% after matching ([Figure 1](#)).

Second, differential follow-up of the 2 groups and time-to-event analysis are important concerns in this study. Annulus diameter might reach a specific size before echocardiographic measurement. However, our institution is referral center, and many patients were referred from a distant place. Serial echocardiographic measurements are

relatively frequent in the first 2 years; however, they become very sporadic afterward. The inherent nature of the current retrospective study design focusing measurements beyond 2 years after the surgical intervention alone might prevent the detection of the exact period of annular expansion. To overcome this drawback, we analyzed a linear mixed effects model adjusted to follow-up duration and used the propensity score as a covariate in a Cox proportional hazard model. Further long-term and frequent observations with sufficient case volume, ideally with prospective study design, are mandatory to confirm our findings.

Third, some technical details were modified over time (ie, effective height since 2004). Also baseline characteristics, root dimension, and surgical technique were significantly different between groups. We believe that our sophisticated statistical arrangement could resolve this concern. A randomized study with or without annuloplasty for larger annulus may be ideal to estimate the real effect of annuloplasty. We suppose that the constant participation of a single surgeon (H.J.S) might minimize differences in surgical technique between groups.

Fourth, all measurements were performed with 2-dimensional echocardiography. It has well been known that aortic annulus is elliptical. Thus, a more precise evaluation should be performed by 3-dimensional echocardiography or computed tomography. This is impossible in a retrospective study; however, the longitudinal comparison with consistent measurement with in-house echocardiography alone might minimize this limitation.

Fifth, there might be criticism that our patients had been operated in their early phase. Our indication for operation was strictly decided within our heart team. Patients with small aortic root might have more AR and those with less AR might have large aortic root. Nearly 40% of our patients had BAV anatomy; thus, the threshold of indication for these patients was obviously lower than others. Previous reports have already indicated that AVJ diameter >28 mm is a risk factor for late failure.^{3,6} Unfortunately, most of the other articles reporting remodeling technique with sufficient case volume had not disclosed the annulus diameter. Lansac and colleagues⁸ only clarified preoperative mean annulus diameter of 28.0 ± 2.4 mm in patients who underwent remodeling, which seems similar to ours. In addition, the group from Brussels disclosed a preoperative diameter of the Valsalva sinus of 48 ± 7 mm in patients assigned to reimplantation, which seems quite similar to ours.²⁶ Therefore, we believe that our patients were not at early stage but at risk of failure.

In conclusion, the aortic annulus does not appear dilated over time after remodeling, at least in those instances in which marked annular dilatation was absent at the time of surgery. If annular dilatation is present, we can confirm our hypothesis that external suture

annuloplasty normalizes annular size just postoperatively and prevents further dilatation. Even without annuloplasty, the aortic annulus becomes smaller over time when the aortic valve remains competent, which may be due to annular reverse remodeling. Annuloplasty may be advantageous to enhance cusp coaptation in the early phase and prevent subsequent failure.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: aortic root remodeling, annuloplasty, aortic annulus, annular reverse remodeling, propensity-score matching

APPENDIX E1. FACTORS ENTERED INTO THE PROPENSITY-SCORE MATCHING ANALYSIS TO ASSIGN PATIENTS WITH ANNULOPLASTY OVER WITHOUT ANNULOPLASTY OR THE ANALYSIS OF PREDICTORS FOR REOPERATION OR LATE ANNULAR EXPANSION USING THE COX PROPORTIONAL HAZARD MODEL

Baseline characteristics

- Age
- Sex
- Body height
- Body weight
- Body surface area
- Bicuspid aortic valve
- Marfan syndrome
- Acute aortic dissection
- Previous cardiac/aortic operation
- Aortic valve insufficiency grade

- Operated period since 2004
- Root geometry
 - Aortoventricular junction diameter
 - Valsalva sinus diameter
 - Sinotubular junction diameter
 - Postoperative effective height
- Operative procedures
 - Central cusp plication
 - Concomitant coronary artery bypass grafting
 - Partial/total arch replacement
 - Duration of cardiopulmonary bypass
 - Duration of aortic crossclamping
 - Prosthesis size

Factors from operative procedures were used for the latter alone. Factors in bold indicate selected variable for entry into the final model for the propensity-score matching.

FIGURE E1. Annual number of cases using each technique including additional technical modifications. AVJ, Aortoventricular junction.

FIGURE E2. A mirror histogram of distribution of the propensity scores for patients who underwent annuloplasty (bars above zero line) or not (bars below zero line) before and after matching. Darkened area represents matched patient pairs, showing that they cover the complete spectrum of cases.

FIGURE E3. Covariable balance plot before (red circle) and after (blue square) propensity-score matching on selected covariables to show the bias reduction after matching. Symbols depict standardized differences for covariables between patients who underwent annuloplasty or not. AVJ, Aortoventricular junction; STJ, sinotubular junction.

TABLE E1. Size of prosthesis used and intended annuloplasty size

Size	Before matching		After matching	
	Annuloplasty	Annuloplasty	Annuloplasty	Annuloplasty
	(-) (n = 189)	(+) (n = 52)	(-) (n = 33)	(+) (n = 33)
Prosthesis, mm				
18	1	0	0	0
20	0	1	0	0
22	7	2	1	2
24	69	10	12	6
26	108	38	20	24
28	4	1	0	1
Annuloplasty, mm				
19		1		0
21		2		2
23		13		9
25		35		21
27		1		1