

# Ascending Aorta Aneurysm: What is the Risk of Replacing the Aortic Root?

## *Aneurisma de aorta ascendente: ¿cuál es el riesgo de reemplazar la raíz?*

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### ABSTRACT

**Background:** In mildly dilated aortic root, the cost-benefit of replacing the sinuses of Valsalva with the resulting reimplantation of the coronary arteries compared with the alternative of preserving them is still a matter of debate.

**Objective:** The goal of this study was to analyze the postoperative and long-term morbidity and mortality of patients undergoing aortic root replacement versus aortic root surgery with sinus of Valsalva preservation.

**Methods:** Between 2002 and 2016, 426 patients underwent replacement of the ascending aorta. After excluding patients undergoing urgent procedures, genetic aortic diseases (except for bicuspid aortic valve), reoperations and surgery of the aortic arch, the study cohort was made up of 259 patients. The ascending aorta was replaced preserving the aortic root in 99 (38.2%) of these patients, and they were compared with the remaining 160 (61.8%) patients who underwent replacement of the sinuses of Valsalva.

**Results:** Patients with preservation of the aortic root were older, had higher percentage of female sex, higher EuroSCORE and with greater incidence of bicuspid aortic valve and coronary artery disease. Cardiopulmonary bypass time was longer in the group undergoing aortic root replacement. There were no significant differences in in-hospital mortality between both groups (1% in the group with preservation of the aortic root vs. 3.1% in the group with replacement of the sinuses of Valsalva,  $p=0.272$ ). Multivariate analysis showed that cardiopulmonary bypass time was a predictor of in-hospital mortality. Survival at 8 years was similar in both groups. There were no new operations due to complications in the aorta during follow-up. At multivariate analysis, age and mitral valve disease were identified as predictors of long-term mortality.

**Conclusion:** Replacement of the ascending aorta, either replacing the aortic root or preserving the sinuses of Valsalva, is a safe procedure, with low in-hospital morbidity and mortality. Preservation of the sinuses of Valsalva is not associated with greater long-term rate of events or mortality.

**Key words:** Aorta – Aortic Aneurysm – Sinus of Valsalva

### RESUMEN

**Introducción:** El riesgo-beneficio del reemplazo de los senos de Valsalva con el consiguiente reimplante coronario frente a la alternativa de mantenerlos, cuando hay dilataciones moderadas de la raíz, es un tópico que se debe definir.

**Objetivo:** Analizar la morbimortalidad posoperatoria y a largo plazo en pacientes sometidos a reemplazo de la raíz aórtica comparados con aquellos en los que se han respetado los senos de Valsalva.

**Material y métodos:** Entre 2002 y 2016, a 426 pacientes se les realizó reemplazo de aorta ascendente. Tras excluir de esa población las cirugías de urgencia, las aortopatías genéticas (excepto bicúspide), las reoperaciones y las cirugías del arco, se conformó una población de 259 pacientes. En 99 de ellos (38,2%) se reemplazó la aorta ascendente conservando la raíz; estos pacientes fueron comparados con los 160 (61,8%) pacientes restantes, en quienes se reemplazaron los senos de Valsalva.

**Resultados:** El grupo en el que se preservó la raíz fue más añoso, con más mujeres, con un Euroscore mayor, con mayor incidencia de válvula bicúspide y enfermedad coronaria. El tiempo de circulación extracorpórea fue mayor en el grupo en el que se reemplazó la raíz. La mortalidad hospitalaria no fue diferente (1% para la conservación de raíz vs. 3,1% para el reemplazo de los senos de Valsalva ( $p = 0,272$ )). En el análisis multivariado, el tiempo de circulación extracorpórea fue predictor de mortalidad posoperatoria. La sobrevida a 8 años no mostró diferencias significativas entre grupos. En el seguimiento, ningún paciente requirió reoperación debido a complicaciones de la aorta. En el análisis multivariado, la edad y la presencia de enfermedad valvular mitral fueron predictores de mortalidad alejada.

**Conclusión:** El reemplazo de la aorta ascendente, ya sea reemplazando la raíz o respetando los senos de Valsalva, es una cirugía segura, con baja morbimortalidad hospitalaria. A largo plazo, la preservación de los senos de Valsalva no se asocia con más eventos ni con mayor mortalidad.

**Palabras clave:** Aorta - Aneurisma de Aorta – Senos de Valsalva

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## INTRODUCTION

When evaluating if a patient should undergo a surgical procedure, the risk of the intervention must be assessed against the risk of the disease. In the case of patients with ascending aortic aneurysm, assessment should include the aortic root, the tubular segment of the aorta and the presence or absence of aortic valve involvement (Figure 1A).

Clinical practice guidelines are very clear about when to replace the aorta, but in some patients the risk of performing reimplantation of the coronary arteries during the procedure should be evaluated considering the patient's age and the presence of comorbidities. (1-5) The risk of replacing the aortic root with reimplantation of the coronary arteries seems to be higher, but the actual impact of this technique compared with replacing only the tubular segment (preserving the sinuses of Valsalva) is not clearly defined in terms of perioperative risk and long-term follow-up. The primary objective of this study was to evaluate perioperative morbidity and mortality of aortic root replacement with reimplantation of the coronary arteries compared with preservation of the sinuses of Valsalva during replacement of the ascending aorta. The secondary objective was to compare the rate of aortic complications and survival of patients undergoing such procedures.

## METHODS

### Study design and patient population

From May 2002 to May 2016, 426 consecutive patients underwent ascending aorta replacement. This analysis excluded non-elective procedures, genetic aortic diseases (except for bicuspid aortic valve), cardiac reoperations and concomitant surgery of the aortic arch. Thus, 259 patients undergoing elective surgery of the ascending aorta were analyzed. Among these patients, 99 (38.2%) underwent replacement of the ascending aorta preserving the aortic root (Figure 1B, left panel), while in the remaining 160 patients (61.8%) replacement of the ascending aorta included aortic root replacement with reimplantation of the coronary arteries (valve-sparing aortic root replacement or composite valve-graft procedure) (Figure 1B, right panel). These two groups of patients represent the core of the study. A total of 60 pairs

were matched using propensity scores. The demographic and clinical characteristics of the patients are presented in Table 1.

All the patients' data were prospectively collected from our database (Microsoft Access; Microsoft Corp, Redmond, WA), which is used daily for clinical data management.

### Endpoint analysis

The following early results were analyzed: in-hospital mortality, postoperative stroke, deep sternal wound infection, acute kidney failure requiring dialysis, postoperative pacemaker implantation and reintervention due to bleeding. Multivariate analysis was performed in order to identify independent predictors of in-hospital mortality.

Long-term survival was evaluated by direct communication with the patients, their family or attending physicians, and also through medical records. Multivariate analysis was performed in order to identify independent predictors of long-term mortality.

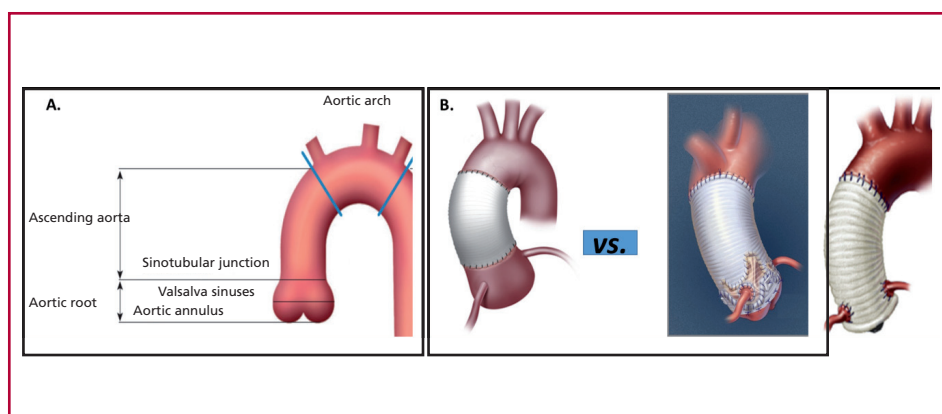
During follow-up, the aortic diameter was evaluated at the level of the sinuses of Valsalva with Doppler echocardiography in the patients who did not undergo aortic root replacement.

### Surgical procedure and indication

An aortic diameter of 50 mm or greater in the ascending aorta or aortic root was indication for aortic replacement. When the diameter or the aortic root was <50 mm, the indication was left at the discretion of the surgeon. All patients were operated on through a median sternotomy. In patients with preservation of the aortic root, the ascending aorta was resected above the sinotubular junction, and either aortic valve replacement or aortic valve repair were performed in case the aortic valve was involved. In the group of patients with reimplantation of the coronary arteries, replacement of the aortic root and ascending aorta was performed with a composite valve graft (with a biologic or mechanical prosthesis) or patients underwent a valve-sparing procedure (remodeling technique—Yacoub procedure— or reimplantation technique—Tirone David procedure) (Figure 1B, right panel). A closed distal anastomosis was performed in all cases and in both groups.

### Statistical analysis

Preoperative patient characteristics were expressed as mean  $\pm$  standard deviation, median and interquartile range (IQR), or prevalence (in percentage), as appropriate. Student's t test for independent samples or the Mann-Whitney U test



**Fig. 1. A.** Anatomy of the aortic root and ascending aorta. **B.** Schematic diagram of the study comparing ascending aorta replacement preserving the aortic root (left panel) compared with ascending aorta and aortic root replacement with reimplantation of the coronary arteries in the graft (right panel), using either valve-sparing aortic root replacement (Tirone David procedure) or composite valve-graft procedures.

**Table 1.** Demographic data and clinical characteristics of the patients included in the study

	General population			Group adjusted by risk score		
	Aortic root preservation N=99	Coronary artery reimplantation N=160	p	Aortic root preservation N=69	Coronary artery reimplantation N=69	p
Women	35.4%	13.8%	0.0001	23.2%	17.4%	0.397
Age (years)	66.3 ± 11.4	57.6 ± 14	0.0001	64.3 ± 12.3	62.4 ± 11.4	0.338
Logistic EuroSCORE	5.8 ± 2.2	4.7 ± 1.6	0.0001	5.4 ± 2.1	5.1 ± 1.8	0.291
History of myocardial infarction	5.1%	1.3%	0.067	2.9%	2.9%	1.00
History of percutaneous coronary intervention	6.1%	1.9%	0.074	4.3%	4.3%	1.00
Peripheral vascular disease	1.0%	0.0%	0.203	0.0%	0.0%	1.00
Chronic kidney failure	4.0%	2.5%	0.486	5.8%	1.4%	0.172
Hypertension	69.7%	62.5%	0.237	69.6%	72.5%	0.707
Dyslipidemia	48.5%	34.4%	0.024	44.9%	36.2%	0.298
Former smoker	56.6%	42.5%	0.028	56.5%	50.7%	0.495
Diabetes	8.1%	1.9%	0.016	5.8%	2.9%	0.404
Bicuspid aortic valve	33.3%	18.8%	0.008	29.0%	26.1%	0.703
Aortic valve disease	89.9%	96.3%	0.039	97.1%	92.8%	0.245
Aortic stenosis	47.2%	73.4%	0.0001	49.3%	75%	0.002
Aortic regurgitation	52.8%	26.6%	0.0001	50.7%	25.0%	0.002
Aortic diameter						
Aortic root (mm)	37.2 ± 7.7	49.2 ± 9.3	0.0001	37.0 ± 9.1	49.9 ± 10.2	0.001
Ascending aorta (mm)	53.5 ± 7.8	55.9 ± 7.4	0.066	54.8 ± 8.5	55.2 ± 7.7	0.803
Aortic dissection	4.0%	6%	0.052	1.4%	1.4%	1.00
Mitral valve disease	4.0%	4.4%	0.897	4.3%	4.3%	1.00
Coronary artery disease	26.3%	13.5%	0.008	19.4%	25.0%	0.547
Single-vessel disease	12.1%	6.9%	0.033	13.0%	13.0%	0.642
Two-vessel disease	4.0%	3.1%		2.9%	5.8%	
Three-vessel disease	8.1%	1.9%		8.7%	4.3%	
Left main coronary artery disease	2.0%	1.3%	0.625	0%	1.4%	0.316
Endocarditis	1.0%	0.6%	0.731	-	-	-
Ejection fraction <35%	11.1%	16.3%	0.251	8.7%	15.9%	0.195

for continuous variables and the chi square test for categorical variables were applied to examine differences between groups. A propensity score of undergoing coronary artery implantation was calculated for each patient using a logistic regression model that included all the preoperative variables listed in Table 1.

Patients were matched by propensity score in a 1:1 ratio using the greedy matching technique without replacement. A nearest neighbor-matching algorithm was used with caliper of 0.0001. The outcomes of interest between the matched groups were compared using the paired t test for continuous variables and the McNemar test for categorical variables. Event-free survival curves were estimated with the Kaplan-Meier method and the log-rank test was used to assess differences in survival between both groups. Univariate and multivariate Cox proportional hazard analyses were performed to investigate the significant predictors of long-term mortality. The clinical variables detailed in Tables 1 and 2 were used for the univariate analysis. The variables with  $p < 0.2$  on univariate analysis were included in the multivariate model. The level of statistical significance was established as  $p < 0.05$ .

### Ethical considerations

The institutional Ethics Committee approved the study and surgical consent was obtained from each patient regarding the surgical method and postoperative evaluations

## RESULTS

### Baseline characteristics

The preoperative clinical profile of the study population is presented in Table 1. Patients undergoing preservation of the aortic root were older and had higher percentage of women. Logistic EuroSCORE was higher in this group of patients and the prevalence of dyslipidemia, diabetes, smoking habits and bicuspid aortic valve was greater. In addition, this group presented higher prevalence of aortic regurgitation and coronary artery disease. The group undergoing aortic root replacement had more prevalence of asymptomatic patients, higher rate of aortic stenosis, and as expected by the study design, the diameter of the aortic root was greater ( $37.2 \pm 7.7$  vs.  $49.2 \pm 9.3$

mm,  $p < 0.0001$ ). On the contrary, the diameter of the ascending aorta was similar in both groups (preservation of the aortic root  $53.5 \pm 7.8$  mm vs. aortic root replacement  $55.9 \pm 7.4$  mm;  $p < 0.066$ ).

### Surgical data

Cardiopulmonary bypass time was longer in the group undergoing aortic root replacement, both in the general population ( $151 \pm 45$  vs.  $109 \pm 35$  minutes;  $p < 0.0001$ ) as in the population adjusted for risk score ( $155 \pm 37$  vs.  $111 \pm 36$  minutes;  $p < 0.001$ ). The group with preservation of the aortic root received a higher percentage of biological valve implantation (77.9% vs. 39.6%;  $p = 0.0001$ ) and the number of combined coronary artery bypass graft surgeries was greater (26.3% vs. 13.1%;  $p = 0.008$ ) though the latter showed no significant difference in the population adjusted by risk score. The remaining surgical data are summarized in Table 2.

### Postoperative results

There were no significant differences in in-hospital

mortality between both groups in the general population (1% in the group with preservation of the aortic root vs. 3.1% in the group undergoing aortic root replacement  $p = 0.272$ ) or in the population adjusted by risk score (1.4% vs. 4.3%;  $p = 0.310$ ). Postoperative stroke was more common in the group with preservation of the aortic root (3% vs. 0%;  $p = 0.027$ ) but did not present significant differences in the population adjusted by risk score. Postoperative vasoplegic syndrome was more common in the group with aortic root replacement (16.3% vs. 7.1%;  $p = 0.031$ ), but did not present significant differences in the population adjusted by risk score. Other postoperative complications as bleeding-related re-exploration, low cardiac output syndrome, atrial fibrillation, pacemaker implantation and need for dialysis was similar in the two groups, both in the general population as in the population adjusted by risk score.

Multivariate analysis showed that only cardiopulmonary bypass time was a predictor of in-hospital mortality (HR: 1.022; 95% CI: 1.007-1.037;  $p = 0.003$ ).

**Table 1.** Operative data and immediate postoperative results

	General population			Group adjusted by risk score		
	Aortic root preservation (RP) N=99	Coronary artery reimplantation N=160	p	Aortic root preservation N=69	Coronary artery reimplantation N=69	p
Cardiopulmonary bypass time (min)	109 ± 35	151 ± 45	0.0001	111 ± 36	155 ± 37	0.0001
Aortic cross-clamping time (min)	88 ± 31	127 ± 39	0.0001	89 ± 31	129 ± 35	0.0001
Mechanical prosthesis (n)	15.2% (15)	60.4% (67)	0.0001	17.4% (12)	34.8% (24)	0.02
Biological prosthesis (n)	53.5% (53)	39.6% (44)		56.5% (39)	34.8% (24)	
Aortic valve repair + RP (n)	1% (1)	.	.	1.4% (1)	.	.
Aortic valve resuspension +RP (n)	30.3% (30)	.	.	24.6% (17)	.	.
Valved graft with Bentall procedure (n)	.	66.9% (107)	.	.	66.7% (46)	.
Valved graft with Cabrol procedure (n)	.	2.5% (4)	.	.	2.9% (2)	.
Aortic root replacement with Tirone David procedure (n)	.	25.6% (41)	.	.	24.6% (17)	.
Aortic root replacement with Yacoub procedure (n)	.	5.0% (8)	.	.	5.8% (4)	.
Combined procedure with coronary artery bypass graft	26.3%	13.1%	0.008	26.1%	23.2%	0.693
Combined procedure with mitral valve surgery	4.0%	4.4%	0.897	4.3%	4.3%	1.000
In-hospital mortality	1.0%	3.1%	0.272	1.4%	4.3%	0.310
1-year survival	98 ± 1.4%	97.5 ± 1.2%	0.804	98.6 ± 1.4%	95.7 ± 2.5%	0.318
5-year survival	94.6 ± 2.8%	92.2 ± 2.4%	0.474	94.1 ± 3.4%	87.7 ± 4.5%	0.210
Reoperation for bleeding	7.1%	8.1%	0.757	8.7%	7.2%	0.753
Low cardiac output syndrome	3.0%	4.4%	0.585	2.9%	7.2%	0.245
Vasoplegic syndrome	7.1%	16.3%	0.031	7.2%	17.4%	0.070
Atrial fibrillation	17.2%	15.6%	0.743	15.9%	20.3%	0.507
Need for pacemaker	1.0%	3.8%	0.186	0.0%	1.4%	0.316
Dialysis	0.0%	1.3%	0.264	0.0%	2.6%	0.155
Stroke	3.0%	0.0%	0.027	4.3%	0.0%	0.080
Mediastinitis	0.0%	0.6%	0.431	0.0%	1.4%	0.316

**Follow-up and survival**

Follow-up time was  $5.4 \pm 3.4$  years (IQR: 2.7-8 years). The Kaplan-Meier curve showed that survival at 8 years was similar in the two groups, both in the general population ( $p=0.474$ ) as in the population adjusted by risk score ( $p=0.210$ ) (Figure 2). Overall survival in the group with preservation of the aortic root at 1, 5 and 8 years was  $98\% \pm 2\%$ ,  $95\% \pm 3\%$  and  $91\% \pm 4\%$ , respectively. In turn, in the group of patients undergoing aortic root replacement, overall survival was  $96\% \pm 1\%$ ,  $92\% \pm 3\%$  and  $88\% \pm 3\%$  at 1, 5 and 8 years, respectively.

During follow-up, none of the patients with preservation of the aortic root required a reoperation due to a complication associated to its preservation. The diameter of the sinuses of Valsalva that were not replaced remained stable at  $35 \pm 5.2$  mm over time and did not exceed 50 mm in any of the patients. Only one patient in the aortic root replacement group required a re-operation 6 years after the first surgery due to endocarditis of the valved graft.

At multivariate analysis, age (HR: 1.064; IQR: 1.008-1.123;  $p=0.011$ ) and mitral valve disease (HR: 7.763; IQR: 1.963-30.726;  $p=0.001$ ) were identified as predictors of long-term mortality.

**DISCUSSION**

In patients with ascending aortic aneurysms, the surgeon and the attending cardiologist should decide whether to indicate replacement of the aortic root with valved conduits or with preservation of the sinuses of Valsalva in moderate dilations of the aortic root. Such decision implies assuming the risk of re-implantation of the coronary arteries if the sinuses of Valsalva are not preserved or the risk of sinus dilation if they are preserved. (6)

The primary objective of this study was to evaluate the risks and benefits in terms of perioperative morbidity and mortality of aortic root replacement with reimplantation of the coronary arteries versus preservation of the sinuses of Valsalva during replacement

of the ascending aorta. Although in-hospital mortality was statistically similar in both groups, it was three times greater, expressed in percentage, in the group with aortic root replacement (3.1% vs. 1%,  $p=0.272$ ). This indicates that aortic root replacement is a more complex procedure and involves a certain risk. Moreover, the lack of statistical significance after comparing both groups may be due to the number of patients evaluated.

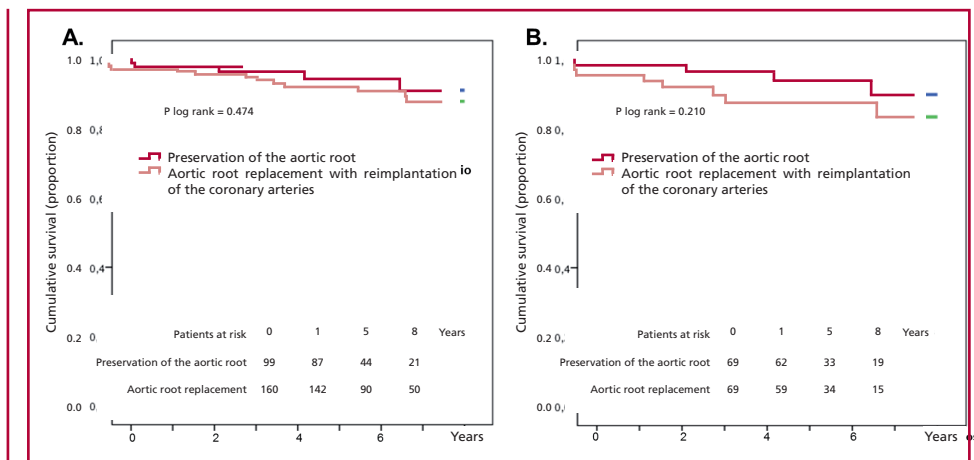
Interestingly, the rate of stroke was higher in patients with preserved aortic root (with a non-significant difference in the population adjusted by risk score), which may be attributed to the fact that this was an older group, with a higher EuroSCORE and higher prevalence of cardiovascular risk factors.

The multivariate analysis confirmed the importance of cardiopulmonary bypass time as a predictor of in-hospital mortality. The secondary objective was to compare the aortic complications and survival of patients undergoing these procedures. During follow-up, mortality was similar in both groups and none of the patients with preservation of the aortic root required a reoperation due to progressive dilation of the root. Age and mitral valve disease were predictors of long-term mortality. The presence of mitral valve disease as a predictor of mortality at follow-up is noteworthy and has not been reported in other series, probably because aortic root replacement combined with mitral valve surgery is a complex procedure and could have a negative impact during follow-up. (7)

We used a cut-off value of 50 mm diameter to decide the replacement of the sinuses of Valsalva. This cut-off value does not strictly follow the recommendations of the practice guidelines which recommend resection of the aortic root when the diameter is  $> 45$  mm. (1-5) We point out that the recommendation of the guidelines is based on studies describing the natural history of aortic aneurysms rather than on comparative studies or clinical trials with different treatment options. (8-11)

Milewski et al. evaluated 428 patients undergo-

**Fig. 2.** Kaplan-Meier curves with estimated survival at 8 years in the general population (A) and in a sub-population adjusted by risk score (B) according to the type of surgery: preservation of the aortic root vs. aortic root replacement.



ing aortic valve replacement with supracoronary ascending aorta replacement preserving the sinuses of Valsalva. (12) Patients were stratified on the basis of valve morphology (tricuspid aortic valve vs. bicuspid aortic valve), valvular pathology (aortic stenosis vs. aortic regurgitation) and preoperative aortic root dimensions (<40 mm vs. 40-45 mm vs. >45 mm). The sinus of Valsalva dimensions remained stable in all the groups over a mean follow-up of 43.5 months. In the few cases requiring re-operation, the indication was not due to progressive dilation of the sinuses of Valsalva.

In a recent study, Hui et al. evaluated 426 patients undergoing aortic valve replacement without replacement of the aortic root during a mean follow-up of 8.1 years, and reported that the aorta remained stable over time and only one patient required re-operation due to aneurysmal dilation. They concluded that if the aortic root is not dilated at the time of surgery, the risk of enlargement over time is minimal, and rules out the need for prophylactic root replacement. (13) Such findings are similar to those of the present study, suggesting that the remnant sinuses of Valsalva will probably remain stable over time.

Our study has the limitations inherent to its retrospective design and the size of the cohorts included is limited. Nevertheless, it offers information about the daily practice in a single center, with uniform approach in decision-making and treatment, which can mitigate the above-mentioned shortcomings. Another limitation of this study is the follow-up period, though it is similar to the one of other publications, as that of Peterss et al. from the University of Yale. In that study, the authors reported a slow growth of the aortic root in 102 patients over 6 years, regardless of concomitant valve replacement, (14) and estimated that preoperative root dimensions <45 mm would need 29 years to reach 50 mm, a time frame that would only be of importance in young patients.

The in-hospital and long-term results of our study are similar to those reported by other series. Using the information about replacement of the ascending aorta retrieved from the Society of Thoracic Surgeons (STS) database with 45,894 patients analyzed, Williams et al. reported an operative mortality of 3.41% for elective cases of isolated replacement of the ascending aorta with preservation of the sinuses of Valsalva. (15) In the same sense, Di Marco et al. reported a 4.4% mortality rate for elective procedures in 1,045 patients undergoing replacement of the sinuses of Valsalva with valved graft. Both results are similar to those of the present study, with a mortality rate of 1% with preservation of the sinuses of Valsalva and 3.1% with aortic root replacement. (16)

Are these results enough to convince surgeons and cardiologists that they do not need to worry about the sinuses of Valsalva in patients with moderate dilation of the aortic root (<50 mm)? (17) A randomized study or a large observational study including patients with

aortic root diameters <50 mm would be necessary to answer this question, and should include several co-factors (such as age, height, family history of dissection or rupture, connective tissue disorders, valve morphology, and others). The study should also be multicenter, as surgeries of the aortic root and ascending aorta are not commonly performed in all institutions. For example, in the United States, the median of aortic root surgeries is 2, and only 5% of the participating institutions in the STS database perform 16% of these surgeries per year. (18)

## CONCLUSION

In this study, replacement of the ascending aorta, either replacing the aortic root or preserving the sinuses of Valsalva, is a safe procedure, with low in-hospital morbidity and mortality. Preservation of the sinuses of Valsalva is not associated with higher long-term rates of events or mortality.

## Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material)

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