European Journal of Cardio-Thoracic Surgery 00 (2022) 1–8
https://doi.org/10.1093/ejcts/ezac149

ORIGINAL ARTICLE

Cite this article as: Forteza Gil A, Martinez-Lopez D, Centeno J, Rivas Oyarzabal J, García Suarez J, de Villarreal Soto JE *et al.* Aortic valve reimplantation in patients with connective tissue syndromes: A 15-year follow-up. Eur J Cardiothorac Surg 2022; doi:10.1093/ejcts/ezac149.

Aortic valve reimplantation in patients with connective tissue syndromes: A 15-year follow-up

Alberto Forteza Gil [a,b,†], Daniel Martinez-Lopez [a,†], Jorge Centeno[b], Jorge Rivas Oyarzabal[b], Jessica García Suarez [c], Juan Esteban de Villarreal Soto [a], Elsa Carolina Ríos Rosado [a], Beatriz Vera Puente[a], Susana Villar García[a], Victor Manuel Ospina Mosquera[a], Susana Mingo [d], Vanesa Moñivas[d], Santiago Serrano-Fiz[a] and Daniel Martínez López[a,b,*]

[a] Cardiac Surgery Department, Hospital Universitario Puerta de Hierro, Majadahonda, Madrid, Spain
[b] Cardiac Surgery Department, Hospital Universitario Quiron-Madrid, Madrid, Spain
[c] Anesthesiology Department, Hospital Universitario Puerta de Hierro, Majadahonda, Madrid, Spain
[d] Cardiology Department, Hospital Universitario Puerta de Hierro, Majadahonda, Madrid, Spain

* Corresponding author. Hospital Universitario Puerta de Hierro Majadahonda, Manuel de Falla 1, Majadahonda, 28222, Spain. Tel: +34 675 016 591; e-mail: dani.martinezlop@gmail.com (D. Martínez López)

Received 20 September 2021; received in revised form 7 February 2022; accepted 21 February 2022

Key question

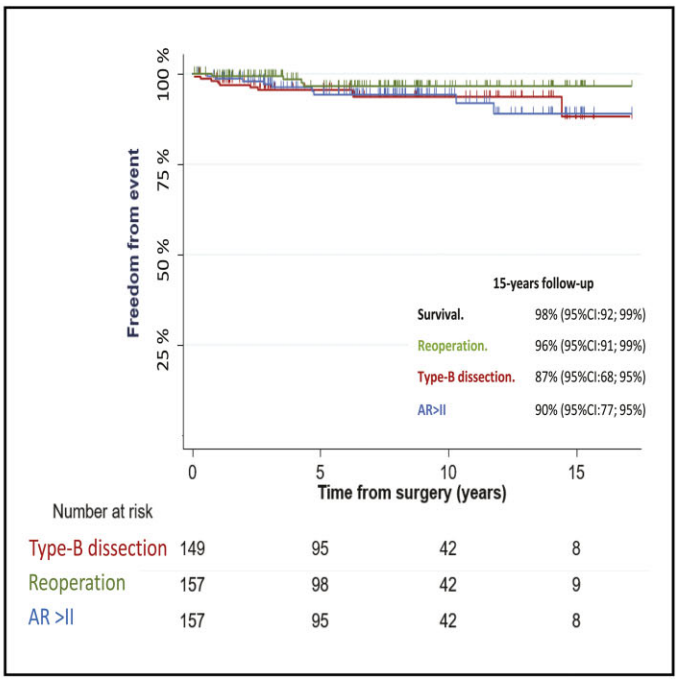
What are the long-term results of aortic valve reimplantation technique in patients with heritable thoracic aortic disease?

Key finding(s)

David operation shows excellent long-term results and no differences in survival compared to the general population.

Take-home message

David operation is a safe and durable option for treatment of aortic root aneurysms in young patients with heritable thoracic aortic disease.



†The first two authors contributed equally to this work.
Manuscript was presented at the 35th Annual Meeting of the European Association of Cardio-Thoracic surgery (13-16 October 2021, Barcelona, Spain).

Abstract

OBJECTIVES: The goal of this study was to analyse early- and long-term outcomes of aortic valve reimplantation (David operation) in patients with heritable thoracic aortic disease.

METHODS: This is a retrospective observational analysis using data from a prospectively maintained surgical database from March 2004 to April 2021. Patients with heritable thoracic aortic disease were included in the study.

RESULTS: A total of 157 patients with aortic root aneurysm with the diagnosis of heritable thoracic aortic disease received the David procedure. Marfan syndrome was found in 143 (91.1%) patients, Loeys-Dietz in 13 and Ehler-Danlos in 1 patient. The median age was 35.0 (IQR: 17.5) years and the median ascending aorta diameter in the Valsalva sinuses was 48 mm (IQR: 4). A Valsalva graft was used in 8 patients; the David V technique was performed in the rest of the cases. The median follow-up time was 7.3 years [standard deviation: 0.58, 95% confidence interval (CI): 6.12–8.05]. Only 2 patients died during the follow-up period. The overall survival was 99% (95% CI: 95%; 99%); 98% (95% CI: 92%; 99%); and 98% (95% CI: 92%; 99%) at 5, 10 and 15 years. Freedom from significant aortic regurgitation (AR> II), reintervention and postoperative type-B dissection was 90% (95% CI: 77%; 95%), 96% (95% CI: 91%; 99%) and 87% (95% CI: 68%; 95%) at 15 years, respectively. No differences were found in any outcome between Marfan syndrome and Loeys-Dietz syndrome. No statistically significant differences in survival were found when we compared expected gender- and age-specific population survival values.

CONCLUSIONS: The David operation is an excellent option for the treatment of patients with heritable thoracic aortic disease and dilatated aortic root. Surgical expertise in referral centres is essential to achieve the best long-term results.

Keywords: Valve-sparing • aortic root • David operation • Aortic valve reimplantation • Marfan

ABBREVIATION

AR	Aortic regurgitation
LDS	Loeys-Dietz syndrome
MS	Marfan's syndrome
SMR	Standardized mortality ratio
VS	Valsalva sinuses

INTRODUCTION

Connective tissue syndromes are genetic disorders that frequently involve musculoskeletal, cardiovascular and ocular manifestations. Mutations in the extracellular matrix protein fibrillin-1 are responsible for Marfan syndrome (MS), which is the most common connective tissue syndrome, with an incidence of 2–3 per 10 000 individuals [1]. MS manifestations are not unique, and several disorders should be included in the differential diagnosis of MS, including Loeys-Dietz syndrome (LDS) or Ehler-Danlos type IV syndrome, which are known for the aggressive behaviour of the vascular manifestations. Ascending aortic aneurysms and type-A aortic dissection are the main life-threatening manifestations in these syndromes that, untreated, frequently lead to death in young adulthood [1].

However, survival has changed dramatically since the introduction of the Bentall-de Bono technique [2], allowing surgeons to safely perform prophylactic surgery on the ascending aorta in these patients. Nevertheless, many patients with connective tissue syndromes present for surgery at a very young age. Thus, mechanical prosthesis are chosen over biological prostheses.

Valve-sparing techniques were developed more than 20 years ago in response to the potential complications related to a mechanical prosthesis and long-term anticoagulation. Aortic valve-sparing techniques not only improve the quality of life of these young patients, but they also make the inevitable need for future interventions safer [3].

Current guidelines recommend aortic valve reimplantation or aortic root remodelling with annuloplasty in young patients with an aortic root aneurysm [4], but in patients with MS and other connective tissue syndromes, the long-term durability of remodelling has been questioned [5]. We describe our experience with the reimplantation techniques [6, 7] in patients with connective tissue syndromes and aortic root aneurysms, analysing valve-related complications and long-term outcomes.

MATERIAL AND METHODS

Ethical statement

This study was approved by our institutional ethics review board (ID: 57/490633.9/21).

Patient selection. This is a retrospective observational study. We collected data from our prospectively maintained connective tissue syndromes surgical database from March 2004 to April 2021. Patients with aortic root aneurysm with the diagnosis of any kind of connective tissue syndrome were included in this study. Ghent diagnostic criteria and/or genetic tests were used for the diagnosis [8]. Only patients with connective tissue syndromes who received a valve-sparing intervention were included in this analysis. Patients with intraoperative failure of the valve-sparing procedure in whom a prosthetic valve was implanted were not included in the analysis. All the patients underwent surgery by the same cardiac surgery team in 2 different hospitals. All patients are being followed by the "Marfan and heritable thoracic aortic syndromes" department at the Hospital Puerta de Hierro in a national referral unit.

Surgical technique. The David I technique was performed in the first 8 patients using the manufactured Valsalva graft designed by De Paulis *et al.* [9]. The David V technique was performed according to the technique previously published by Miller *et al.* [6, 7] in the following 149 patients. The aortic valve is reimplanted by removing the ascending aorta and detaching the coronary ostia from the aortic sinuses. The diameter of a 32- to 34 -mm tubular Dacron graft prosthesis is reduced by plication stitches at 3 symmetrical points; then, the graft is sutured to the left ventricular outflow tract by passing 6 to 9 interrupted

mattress sutures of polyethylene terephthalate with a polytetrafluoroethylene pledget (Ti-cron Coviden) below the aortic anulus. The remnants of the aortic sinuses are then sutured inside the Dacron graft with continuous 4/0 polypropylene suture. Later, coronary arteries are reattached to the graft. To recreate the physiological shape of the Valsava sinuses (VS) and the sinotubular junction, a slightly smaller graft was sutured to the first one.

Follow-up and data retrieval. All patients were followed up annually at our institution's dedicated connective tissue syndromes and heritable aortic thoracic diseases unit. Echocardiographic studies were performed every year, and computed tomography or magnetic resonance images were requested to analyse the remaining segments of the aorta. Follow-up was completed in all patients. For the type-B dissection analysis, only those patients with new onset of this event were included in the analysis. We excluded the patients with prior type-B dissection or residual type-B dissection after acute type-A dissection. Aortic regurgitation (AR) is described as AR I for none or trace, AR II for mild, AR III for moderate and AR IV for severe regurgitation.

Effective height (measured from the basal plane to the central coaptation level), residual prolapse and coaptation below the aortic annulus were measured intraoperatively with transoesophageal echocardiography . These variables have been measured since 2011. Complete data for these variables were available for 78 patients (49.7%)

Statistical analyses. Descriptive statistics are presented as median and interquartile range (for numerical variables) or absolute and relative frequencies (categorical variables). Overall survival was defined as the time from surgery to death from any cause and estimated using the Kaplan–Meier curve. Time to aortic regurgitation was defined as the time from the operation to the next echocardiographic follow-up with an aortic regurgitation greater than II. Time to aortic type-B dissection was defined as the time from the operation to the first image test with the diagnosis of type-B dissection. Time to reoperation was defined as the time from the operation to the reoperation over the aortic valve. All these variables were analysed according to a competing risk method and considering death from any cause as a competing event. In these outcomes, cumulative incidence function was estimated along with their corresponding 95% confidence intervals.

Median follow-up was estimated by the reverse Kaplan-Meier methods; the log-rank test was used to find differences between connective tissue syndromes regarding survival, significant AR and type-B dissection. The standardized mortality ratio (SMR) was defined as the ratio of the observed number of deaths (our cohort) to the expected number of deaths, with the rates observed in the general population taken as reference from the life tables from the Spanish Health Ministry from 2004 to 2018. SMRs and 95% confidence intervals (CIs) were calculated under the assumption of a Poisson distribution for deaths observed in the follow-up period. We performed a complete case analysis, because we assumed a completely at random pattern of missingness.

Univariable Fine and Gray regression models were performed to identify factors associated with aortic valve regurgitation, and subhazard ratios are shown with their corresponding 95% CI. Statistical significance was declared at the two-sided 5% alpha level. For standardized mortality rates, the statistical package Stata/IC v.15.1 (StataCorp. 2017, Stata Statistical Software: Release 15. StataCorp, College Station, TX, USA) was used. The rest of the analysis was performed using SPSS 2.7 (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY, USA).

RESULTS

Preoperative patient characteristics and surgical data

From March 2004 to April 2021, a total of 157 patients with any connective tissue syndromes and aortic root aneurysms received aortic valve reimplants. MS was found in 143 patients (91.1%), Loeys-Dietz syndrome was diagnosed in 13 (8.3%) patients and Ehler-Danlos type IV was the genetic syndrome detected in only 1 (0.6%) patient. Baseline data of the patients are summarized in Table 1.

The David V technique was performed in 149 (94.9%) patients. The minimal diameter of the VS Dacron graft was 28 mm and the maximal diameter was 34 mm. For the ascending aorta, the minimal and maximal diameters of the Dacron graft were 24 mm and 32 mm each. In 8 (5.1%) patients, aortic valve reimplantation was performed using a manufactured Valsalva graft following the David I technique. Surgical characteristics are specified in Table 2.

Postoperative results

There were no 30-day or in-hospital deaths, and no strokes were reported. Two patients (1.3%) presented a non-complicated perioperative myocardial infarction. Seven patients (4.5%) required reoperation for surgical bleeding. Atrial fibrillation was found in 9 patients (5.7%).

A permanent atrioventricular blockade was observed in 1 patient, and a pacemaker was implanted.

Late survival

Follow-up was completed for all patients. The median follow-up time was 7.3 years (SD: 0.58, 95% CI: 6.12–8.05). Overall survival was 99% (95% CI: 95%; 99%); 98% (95% CI: 92%; 99%); and 98% (95% CI: 92%; 99%) at 5, 10 and 15 years (Fig. 1) Only 2 patients died during the follow-up period. The first case was a 55 -year-old man who died of an acute type-B dissection. The other patient was a 30 -year-old woman who suffered an acute rupture of an intracranial aneurysm 6 years after the valve-sparing technique. There were no differences in survival regarding the connective tissue syndrome (log-rank: $P = 0.7$) (Fig. 2).

We analysed the number of deaths among our patients and those among the general population of Spain for the same age and gender. The 2 observed deaths in the cohort were compared to the 0.22 expected mortality for the Spanish general population; we found no statistically significant differences between the 2 groups (SMR 9.3, 95% CI: -3.6; 22.1) (Fig. 1).

Table 1. Baseline characteristics of the patients with connective tissue syndromes

	Connective tissue syndromes N = 157
Age (years)	35.0 (17.5)
Gender	
Female	51 (32.5 %)
Male	106 (67.5 %)
BSA (m^2)	1.9 (0.4)
EuroSCORE II (%)	1.6 (1.8)
Hypertension	12 (7.6%)
Diabetes	6 (3.8%)
Dyslipidemia	9 (5.7%)
Connective tissue disease	
Marfan syndrome	143 (91.1%)
Loeys-Dietz syndrome	13 (8.3%)
Ehler-Danlos type IV syndrome	1 (0.6%)
LVEF	
>55%	149 (94.9%)
35-55%	8 (5.1%)
Aortic regurgitation	
Grades I–II	133 (84.7%)
Grades III-IV	24 (15.3%)
NYHA functional class	
I	147 (93.7%)
II	9 (5.7%)
III	1 (0.6%)
Aortic type-A dissection	7 (4.5%)
Ascending aorta diameter in the Valsalva sinuses (mm)	48.0 (4)

Data are presented as n (%), median and interquartile range (IQR).
AR: aortic regurgitation; BSA: body surface area, LVEF: left ventricular ejection fraction; NYHA: New York Heart Association dyspnoea grading scale.

Table 2. Surgical characteristics of the analysed patients

	Connective tissue syndromes N = 157
Valve-sparring procedure	
David V	149 (94.9%)
David I Valsalva graft	8 (5.1%)
Aortic leaflet valve repair (central plication)	47 (29,7%)
Valsalva graft (mm)**	32 (28-34)
Ascending aorta graft (mm)**	26 (24-32)
Associated surgery	
Atrial septal defect	21 (26.6%)
Mitral valve repair	30 (38%)
Tricuspid valve repair	7 (8.9%)
Combined mitral and tricuspid valve repair	9 (11.4%)
Aortic arch surgery	12 (15.2%)
CPBP time (min)	120 (40)
Cross-clamping time (min)	106 (33)
Intraoperative echocardiographic results	
Effective height (mm)*	1.0 (0.2)
Residual prolapse*	8 (5.1%)
Low coaptation*	1 (0.6%)
Residual aortic regurgitation	
AR 0-I (none-trace)	153 (97.5%)
AR II (mild)	4 (2.5%)

Data are presented as n (%) or median and interquartile range (IQR).
*Results of over 78 records available.
**For the grafts, data are presented as median and minimal and maximum graft sizes.
AR: aortic regurgitation; CPBP: cardiopulmonary bypass perfusion.

Aortic valve regurgitation during follow-up

Intraoperative residual prolapse was found in 8 patients. All of them remained with no or mild AR, and none of them required reoperation of the aortic valve. The patient who presented a leaflet coaptation below the aortic annulus remained stable and asymptomatic with an AR grade II after a 3-year follow-up.

Only 4 patients (2.5%) presented residual AR grade II as viewed on intraoperative transoesophageal echocardiography. Three of them developed severe AR. Therefore, aortic valve replacement was needed at 1 year and 4 years postoperatively for 2 of them. No data are available regarding effective height, residual prolapse and coaptation below the aortic annulus for these 4 patients. Only 1 patient remained with an AR II after 14 years. There were no differences in late significant aortic regurgitation regarding the connective tissue syndrome (log-rank $P = 0.39$) (Supplementary Fig. 1). We have registered 14 patients with AR>II. Freedom from AR > II was 91.8% (95% CI: 86.9%; 96.7%), 89.6% (95% CI: 83.1%; 96.1%) and 73.3% (95% CI: 58.6%; 88%) at 5, 10 and 15 years.

AR grade III-IV appeared in 9 patients during follow-up. Freedom from AR grade III-IV was 95% (95% CI: 88%; 97%), 92% (95% CI: 88%; 97%) and 90% (95% CI: 77%; 95%) at 5, 10 and 15 years (Fig. 3). The univariable analysis identified an AR 0-I after the operation as a protective factor for the development of AR grade III-IV during follow-up (0.05; CI 95%: 0.01– 0.2 $P < 0.001$) (Table 3). Permanent anticoagulation only was needed in the 4 patients who required an aortic valve replacement during follow-up.

Four patients (2.5%) needed surgery on the aortic valve during the follow-up period. One patient had infective endocarditis over the reimplanted aortic valve and required aortic valve replacement 4 years after the surgery. No other infective endocarditis episodes are registered. The remaining 3 patients needed surgery for severe AR as explained previously. Freedom from reintervention was 96% (95% CI: 91%; 99%) at 5, 10 and 15 years (Fig. 3).

Type-B acute aortic dissection during follow-up

Freedom from Stanford type-B dissection was 96% (95% CI: 90%; 98%); 94% (95% CI: 87%; 97%) and 87% (95% CI: 68%; 95%) at 5, 10 and 15 years (Fig. 3). A total of 92.4% of the patients were given antihypertensive treatment during follow-up. Type-B acute aortic dissection occurred in 8 patients. One patient had a pregnancy-related type-B dissection. Five patients underwent thoracic aorta surgical replacement, and 2 patients received a thoracic endoprosthesis. There were no differences in late type-B dissection regarding the connective tissue syndrome (log-rank $P = 0.532$). More information about these patients is provided in Supplementary Table 1.

DISCUSSION

Aortic valve-sparing procedures have been established as a standard treatment for patients with aortic root aneurysms [10]. However, there has always been uncertainty about the long-term

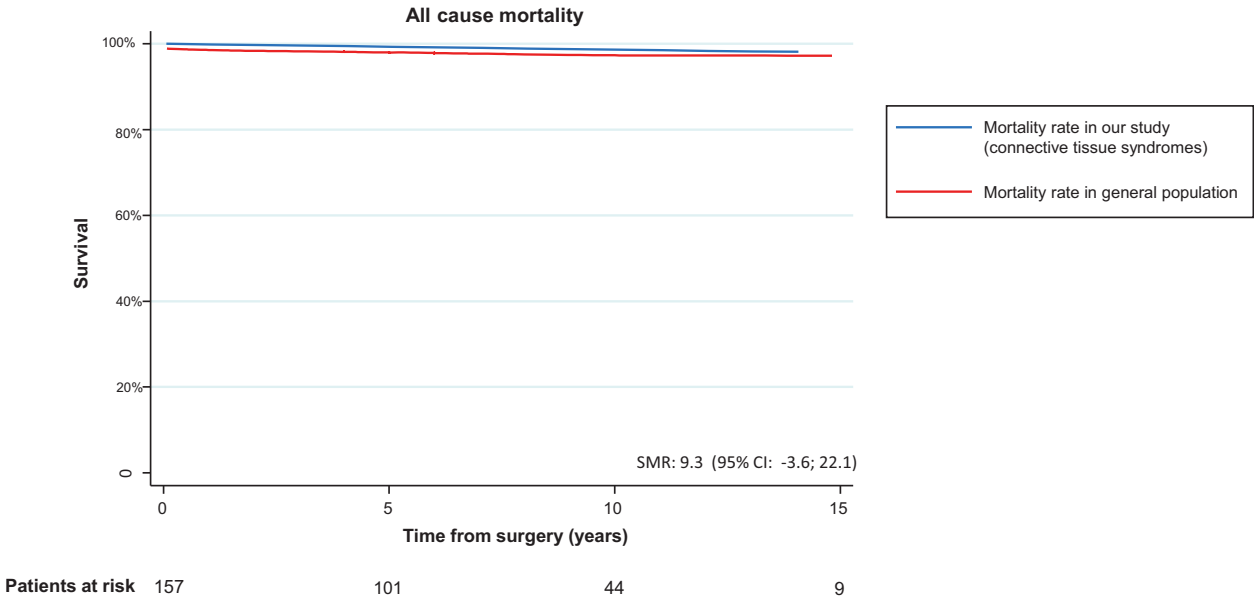


Figure 1: The ratio of the observed number of deaths in our cohort is compared to the mortality rates expected in the general population (life tables from the Spanish Health Ministry between 2004 and 2018 matched for age and gender). No statistically significant differences between the 2 groups were found (SMR 9.3; 95% CI: -3.6; 22.1).

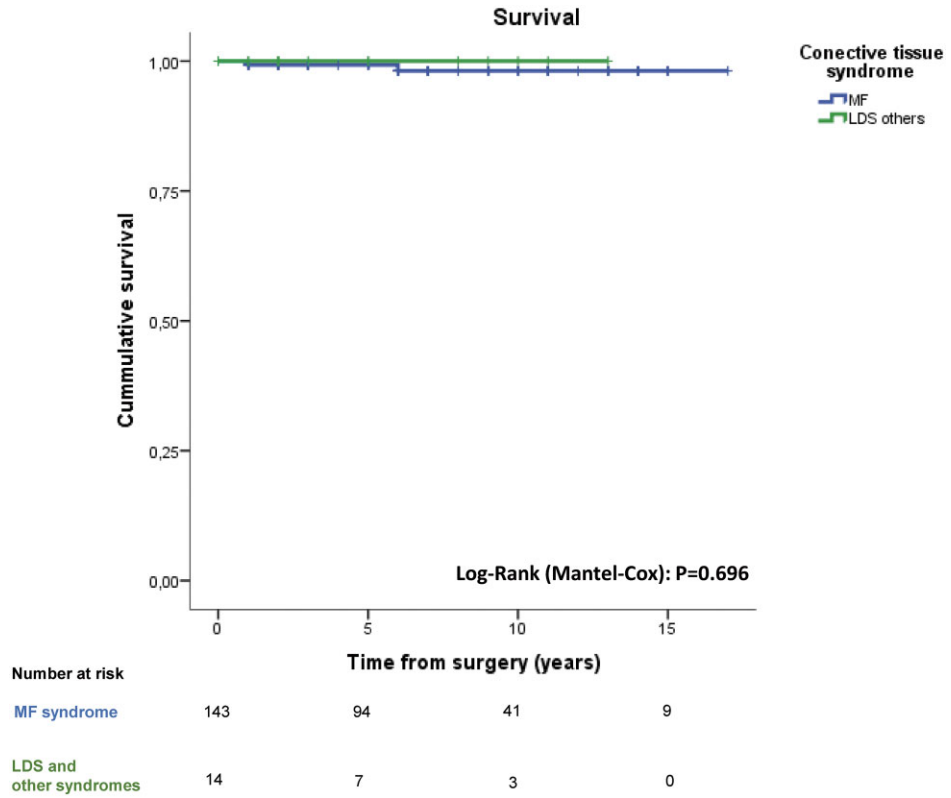


Figure 2: Kaplan-Meier estimates for survival after valve-sparring intervention. The log-rank test is used to compare survival of patients with MS and other connective tissue syndromes. There were no differences in survival regarding the connective tissue syndrome (log-rank: $P = 0.696$).

outcomes of these procedures in patients with MS and other connective tissue syndromes have always been uncertain. We present our 15 years of experience with the David technique in 157 patients with MS and other connective tissue syndromes. Our outcomes at 15 years after the operations, with survival rates and freedom from reintervention above 95%, support the safety and effectiveness of this technique in patients with connective tissue syndromes (Central image).

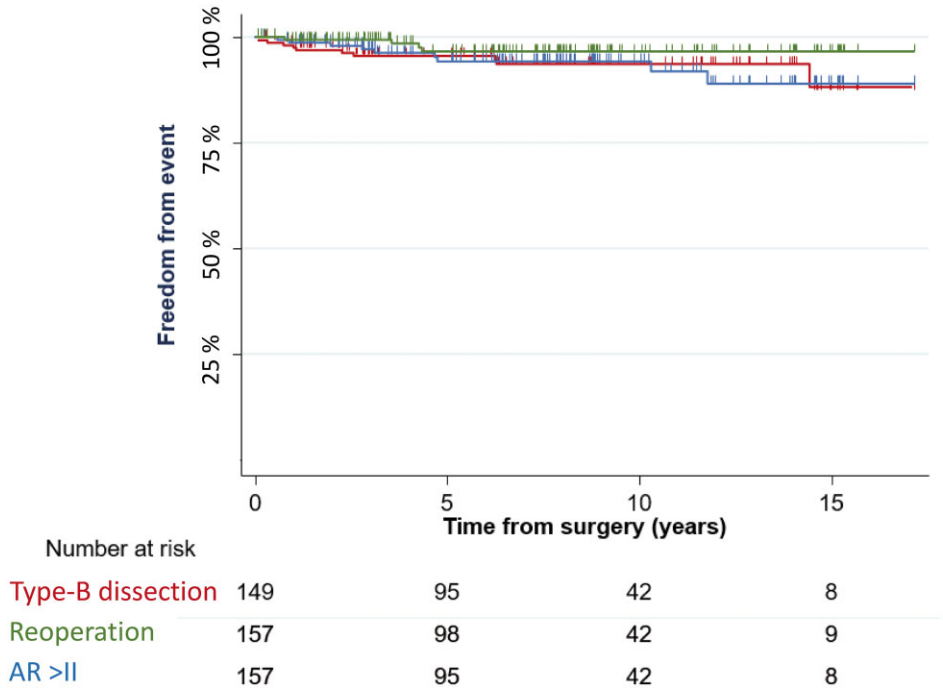


Figure 3: Cumulative incidence curves for freedom from reoperation of the aortic valve, postoperative type-B dissection and significant aortic regurgitation. AR: aortic regurgitation.

Table 3. Univariable Fine and Gray competing risk regression analyses for aortic regurgitation >II during follow-up

	SHR	95% CI	*P*-value
Age	0.99	0.94–1.04	0.782
Cusps plasty (yes)	1.65	0.36–7.52	0.519
Preoperative aortic ring >27 mm	1.01	0.23–4.32	0.995
Preoperative AR>II	2.16	0.47–9.91	0.320
No or trace AR after surgery (AR 0 or I)	0.046	0.010-0.209	< 0.001

AR: aortic regurgitation; CI: confidence interval; SHR: subhazard ratios.

Patients with MS and LDS have a reduced life expectancy due to aortic dissection or aortic aneurysms [1, 11]. Since the introduction of the Bentall procedure, prophylactic surgery of the aortic root could be safely performed, increasing the survival of these patients. However, composite valve grafts have shown more thromboembolic and haemorrhagic events than valve-sparing techniques [12]. In our studied cohort, no thromboembolic events are registered. These findings support the idea previously published by Schoenhoff *et al.* [3] that if the risk of reintervention after the reimplantation procedure is low, the patient will benefit from the David technique even if redo surgery becomes necessary during the follow-up period.

Our results show that long-term survival in patients with MS and LDS after the reimplantation technique is excellent, with survival rates of 98% at 15 years. Moreover, we can assume similar life-expectancy rates after the David technique in patients with MS and LDS compared to the general population. These findings are particularly relevant in patients with LDS, in whom, due to its more aggressive behaviour, we could expect a higher rate of deaths and acute aortic dissections. We believe that these results are enhanced by the closer follow-up in our "Marfan and heritable thoracic aortic syndromes" department. These mortality rates are in line with those published by other experienced groups using different techniques [3, 9, 13–16], and they indicate the importance of lifelong surveillance with imaging techniques such as echocardiography and tomography to assess the aortic valve function and closely monitor the diameters of the aortas. At our institution, patients are followed up annually, and a transthoracic echocardiogram is performed to assess valve function and motion. Aortic diameters are assessed every 2 to 3 years, depending on the pathology or risks factors of each patient.

Since valve-sparing procedures were first described, several technical modifications and new grafts conforming to the VS have been developed [7, 9–14]. Some authors have hypothesized that removing the VS may have negative consequences for aortic valve function [17–19]. However, experienced groups have reported good results using a straight graft [5, 15]. Along these lines, the Hanover group recently published their experience with the David I technique in 104 patients with MS with freedom from aortic-valve reoperation of 86% and 80% at 10 and 20 years, respectively [5].

Although we tried to conform to the VS, only in vitro and imaging studies have described these advantages, and no clinical correlation has been proved. Therefore, other variables may play a more important role in the durability of aortic valves. A standardized technical approach by experienced surgeons and the creation of reference centres might be the key to success. We found that freedom from AR III-IV and reintervention was 90% (95% CI: 77%; 95%) and 96% (95% CI: 91%; 99%) at 15 years, respectively. Similar rates are published by other groups using different aortic valve reimplantation [5, 20–22] or remodelling [13, 23, 24] techniques.

In this analysis, a correlation between residual AR after surgery and failure of the repair is exposed. Because we were aware of this correlation since the first cases appeared, we became more aggressive with leaflet plication and the correction of any residual prolapse to secure a better coaptation that assures a mild or absent AR before leaving the operating room.

Furthermore, our group recently analysed the risk of suffering an aortic event in 397 patients with MS. We found that the risk of suffering any aortic event increases with aortic root diameters of 45 mm or greater [25]. Considering that the elective surgical mortality is lower than 1% in experienced centres, we believe that it is reasonable to perform the operation early and not to wait until the aorta reaches a diameter of 50 mm or more. In addition, a moderate aortic root dilatation would not affect the quality of the cusps, and only minor structural abnormalities might be found [15]. The results of this study support this idea. The median maximum diameter of the patients included in this series is 48 mm, under the 50 -mm threshold. Current recommendations for surgical treatment are mostly based on cohort studies with thoracic aneurysms of many different aetiologies [26, 27], and patients with MS do not exceed 10% of the total [25]. We hope that these good results might encourage a change in the prophylactic operative threshold for future guidelines.

To our knowledge, this is the largest series reported of using the David V technique in patients with MS and other connective tissue syndromes and one of the major series regarding any kind of valve-sparing technique in these patients. We hope that these good results, added to the experience from other groups, will encourage surgeons to learn and perform this ground-breaking technique for the treatment of aortic root aneurysms in these patients.

Study limitations

Notwithstanding the prospective maintenance of this database, we performed a retrospective analysis of the data, and thus the data are affected by the limitations of this kind of study. The number of adverse events was scarce, which has limited the value of the statistical analysis. Moreover, we did not have echocardiographic data regarding the coaptation length, effective height or cusps prolapse for all patients; therefore we are probably missing the predictive factors for AR during follow-up. However, these limitations also confirm the safety and efficacy of the technique performed. Also, only 14 patients who received a valve-sparing intervention had other connective tissue syndromes. Therefore, more studies are needed to assess the long-term results of these procedures in LDS and other heritable thoracic aortic syndromes. Finally, most of the interventions were performed by the same surgeon (AFG; therefore, the results may not be generalized.

CONCLUSIONS

Aortic valve reimplantation is an excellent option for the treatment of patients with connective tissue syndromes and dilatated aortic root. To achieve the best surgical results, these patients should be treated in referral centres by experienced surgeons. In addition, considering the excellent results shared in this and other papers, the threshold for prophylactic surgery in connective tissue syndromes should be reviewed and lowered. Lifelong surveillance is mandatory and will guarantee the best long-term outcomes.

ACKNOWLEDGEMENTS

We thank Ana Royuela-Vicente for the statistical analysis and review of the data presented in this paper.

Funding

There was no financial support for this work neither any relationship with industry that could have influenced its outcome.

Conflict of interest: The authors have no conflicts of interest to declare.

Data Availability Statement

The data that support the findings of this study are available on request to the first author (A. Forteza Gil). The data are not openly available to preserve the privacy of the participants included in this study.

REFERENCES

[1] Judge DP, Dietz HC. Marfan's syndrome. Lancet (London, England) 2005; 366:1965–76.
[2] Bentall H, Bono A. D. A technique for complete replacement of the ascending aorta. Thorax 1968;23:338–9.
[3] Schoenhoff FS, Langhammer B, Wustmann K, Reineke D, Kadner A, Carrel T. Decision-making in aortic root surgery in Marfan syndrome: bleeding, thromboembolism and risk of reintervention after valve-sparing or mechanical aortic root replacement. Eur J Cardiothorac Surg 2015;48:931–5. discussion 935–6.
[4] Beyersdorf F, Vahanian A, Milojevic M, Praz F, Baldus S, Bauersachs J, ESC/EACTS Scientific Document Group *et al.* 2021 ESC/EACTS Guidelines for the management of valvular heart disease. Eur J Cardiothorac Surg 2021;60:727–800.
[5] Martens A, Beckmann E, Kaufeld T, Fleissner F, Neuser J, Korte W *et al.* Valve-sparing aortic root replacement (David I procedure) in Marfan disease: single-centre 20-year experience in more than 100 patients†. Eur J Cardiothorac Surg 2019;55:476–83.
[6] 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 622.
[7] Miller DC. Valve-sparing aortic root replacement in patients with the Marfan syndrome. J Thorac Cardiovasc Surg 2003;125:773–8.
[8] Paepe AD. Devereux RB, Dietz HC, Hennekam RC, Pyeritz RE. Revised diagnostic criteria for the Marfan syndrome. Am J Med Genet 1996;62: 417–26.
[9] Paulis RD. Scaffa R. Nardella S, Maselli D, Weltert L Bertoldo F *et al.* Use of the Valsalva graft and long-term follow-up. J Thorac Cardiovasc Surg 2010;140:S23–7. discussion S45-51.
[10] David TE, Feindel CM, David CM, Manlhiot C. A quarter of a century of experience with aortic valve-sparing operations. J Thorac Cardiovasc Surg 2014;148:872–9. discussion 879–80.
[11] Murdoch JL, Walker BA, Halpern BL, Kuzma JW, McKusick VA. Life expectancy and causes of death in the Marfan syndrome. N Engl J Med 1972;286:804–8.
[12] Price J, Magruder JT, Young A, Grimm JC, Patel ND, Alejo D *et al.* Long-term outcomes of aortic root operations for Marfan syndrome: a comparison of Bentall versus aortic valve-sparing procedures. The Journal of Thoracic and Cardiovascular Surgery 2016;151:330–6.
[13] Schneider U, Ehrlich T, Karliova I, Giebels C, Schäfers H-J. Valve-sparing aortic root replacement in patients with Marfan syndrome—the Homburg experience. Ann Cardiothorac Surg 2017;6:697–703.
[14] Ando M, Yamauchi H, Morota T, Taketani T, Shimada S, Nawata K *et al.* Long-term outcome after the original and simple modified technique of valve-sparing aortic root reimplantation in Marfan-based population, David V University of Tokyo modification. J Cardiol 2016;67:86–91.

[15] David TE, David CM, Manlhiot C, Colman J, Crean AM, Bradley T. Outcomes of Aortic Valve-Sparing Operations in Marfan Syndrome. J Am Coll Cardiol 2015;66:1445–53.
[16] David TE, David CM, Feindel CM, Manlhiot C. Reimplantation of the aortic valve at 20 years. The Journal of Thoracic and Cardiovascular Surgery 2017;153:232–8.
[17] Galea N, Piatti F, Sturla F, Weinsaft JW, Lau C, Chirichilli I, Cornell International Consortium for Aortic Surgery (CICAS) *et al.* Novel insights by 4D Flow imaging on aortic flow physiology after valve-sparing root replacement with or without neosinuses. Interact CardioVasc Thorac Surg 2018;26:957–64.
[18] Galea N, Piatti F, Lau C, Sturla F, Weltert L, Carbone I, Cornell International Consortium for Aortic Surgery (CICAS) *et al.* 4D flow characterization of aortic blood flow after valve sparing root reimplantation procedure. J Vis Surg 2018;4:95.
[19] Oechtering TH, Frydrychowicz A, Sievers H-H. Malrotated sinus vortices in straight graft valve-sparing aortic root treatment: a matter of concern? J Thorac Cardiovasc Surg 2017;154:794–7.
[20] Coselli JS, Volguina IV, LeMaire SA, Sundt TM, Connolly HM, Stephens EH, Aortic Valve Operative Outcomes in Marfan Patients Study Group *et al.* Early and 1-year outcomes of aortic root surgery in patients with Marfan syndrome: a prospective, multicenter, comparative study. J Thorac Cardiovasc Surg 2014;147:1758–66. 1767.e1-4.
[21] Beckmann E, Martens A, Krüger H, Korte W, Kaufeld T, Stettinger A *et al.* Aortic valve-sparing root replacement with Tirone E. David's reimplantation technique: single-centre 25-year experience. Eur J Cardiothorac Surg 2021;60:642–8.
[22] David TE, David CM, Ouzounian M, Feindel CM, Lafreniere-Roula M, A progress report on reimplantation of the aortic valve. J Thorac Cardiovasc Surg 2021;161(3):890–99. doi: 10.1016/j.jtcvs.2020.07.121
[23] Bilkhu R, Tome M, Marciniak A, Edsell M, Jahangiri M. Does the Aortic Annulus Dilate After Aortic Root Remodeling? Ann Thorac Surg 2020; 110:943–7.
[24] Lansac E, Centa I. D, Sleilaty G, Lejeune S, Berrebi A, Zacek P *et al.* Remodeling root repair with an external aortic ring annuloplasty. J Thorac Cardiovasc Surg 2017;153:1033–42.
[25] Martín C, Evangelista A, Serrano-Fiz S, Villar S, Ospina V, Martínez D *et al*. Aortic Complications in Marfan Syndrome: should We Anticipate Preventive Aortic Root Surgery? Ann Thorac Surg 2020; 109:1850–7.
[26] Vahanian A, Alfieri O, Andreotti F, Antunes MJ, Barón-Esquivias G, Baumgartner H, Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC), European Association for Cardio-Thoracic Surgery (EACTS) *et al.* Guidelines on the management of valvular heart disease (version 2012). Eur Heart J 2012;33: 2451–96.
[27] Baumgartner H, Bonhoeffer P, Groot N. D, Haan F. D, Deanfield JE, Galie N, ESC Committee for Practice Guidelines (CPG) *et al.* ESC Guidelines for the management of grown-up congenital heart disease (new version 2010). Eur Heart J 2010;31:2915–57.