Featured Article

Outcomes of aortic root replacement in patients with Marfan syndrome: the role of valve-sparing and valve-replacing approaches

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Background: Marfan syndrome (MFS) is a heritable thoracic aortic disease with pervasive cardiovascular effects, including commonly, a dilated aortic root. Traditionally, the root is replaced using a mechanical composite valve graft (CVG); however, this valve-replacing (VR) approach necessitates a lifelong regimen of anticoagulation with a potential for late bleeding complications. In time, valve-sparing (VS) approaches were developed. Today, several options for aortic root replacement (ARR) exist; each has advantages and disadvantages that helps inform choice. The Aortic Valve Operative Outcomes in Marfan Patients (AVOMP) is a multi-center international registry to analyze clinical outcomes of ARR in MFS patients using either VR or VS techniques to better elucidate choice. We summarize outcomes of AVOMP and present our own experience.

Methods: We performed 223 consecutive elective ARR [1991–2023] in patients with MFS; 15 such repairs were included in AVOMP. Repairs included 113 (51%) using a mechanical CVG, 62 (28%) using a VS approach, and 48 (22%) using a bioprosthetic root. Many patients underwent aortic arch repair (30% to 54% by type).

Results: The median patient age was 38 [29–52] years. In comparing VS and VR groups, patients were similar in age and rates of major comorbidities and symptoms. Patients with VR repair had a more complex aortic history. The rate of redo sternotomy was 24% (n=54). Operative death was uncommon [4% overall (10/223); ranging from 2% to 8% by type], and stroke was rare [1/223 (<1%)]. Late survival and reoperation differed by operative approach; survival was improved in patients who underwent VS repair.

Conclusions: We found that repair in patients with MFS undergoing ARR resulted in low operative risk. Our late results were similar to those of AVOMP in that patients undergoing VS repair tended to experience greater rates of valvular-structural deterioration, although this did not appear to impact survival.

Keywords: Marfan syndrome (MFS); aortic aneurysm; aortic root; valve-sparing aortic root replacement (ARR); heritable thoracic aortic disease

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Introduction

Marfan syndrome (MFS) is a heritable disease that results from autosomal dominant mutations in the gene that encodes fibrillin-1 (*FBN1*). It has far-reaching effects on the skeletal, ocular, and cardiovascular systems (1). The signature manifestation of cardiovascular pathology in patients with MFS is a dilated aortic root (*Figure 1*), which commonly results in aneurysm, aortic valve regurgitation, and an increased risk of aortic dissection, rupture, and related death. Historically, this and other cardiovascular involvement resulted in a greatly reduced lifespan (2). The original approach for aortic root replacement (ARR) was introduced by Bentall and De Bono (3) in 1968 using a Teflon graft and Starr valve in a 33-year-old male with presumed MFS. Mechanical valve-replacing (VR) ARR, such as the Bentall procedure, typically necessitates a life-long regimen of anticoagulation to mitigate the risk of thromboembolism, exposing young MFS patients to substantial limitations due to the potential for bleeding complications. To conserve the native aortic valve, Yacoub (4) introduced the sinus remodeling approach to ARR, and several iterations by David and others that relied on sinus reimplantation soon followed (5-8). At the end of the 20th century, Gott and others (9) published a landmark multi-center report describing nearly the entirety of surgical experience in ARR in patients with MFS at the time. Although this work demonstrated the clear benefit of elective ARR in such patients, the role of valve-sparing (VS) approaches remained unclear.

In contemporary repair, there remain two basic competing approaches to ARR in patients with MFS, VR and VS. In both of these broad approaches, several options have emerged over the last 40 years to reduce the risk of late complications and to capitalize on the development of new replacement materials (e.g., synthetic grafts with prefabricated sinuses and porcine aortic roots). Each option has advantages and disadvantages that help inform which approach to use in a given patient. An international multi-center prospective registry [Aortic Valve Operative Outcomes in Marfan Patients (AVOMP)] was initiated in 2005 to analyze clinical outcomes of ARR in MFS patients using either VR or VS techniques in hopes of better elucidating this choice of approach.

Overview of AVOMP

The AVOMP international observational study enrolled 316 participants from 19 surgical centers and followed them clinically, relying on echocardiographic surveillance by a core imaging center. Several publications have been released from this study, highlighting key findings and comparisons between the VR and VS groups. The initial publication in 2009 showed that early enrollment reflected the pervasive clinical trend towards using VS approaches and found no significant differences in valve-related or cardiac complications between the two groups (10). Additionally, an analysis in 2011 described intraoperative conversion from a VS to a VR procedure during the index surgery; importantly, intraoperative echocardiographic results may necessitate an unanticipated change in approach (11).

By 2014, initial follow-up was completed and analysis of early and 1-year results were presented. The VR group had older and sicker patients compared to the VS group. While there were no significant differences in survival, valve-related morbidity, or major adverse valve-related events (MAVRE) at 1 year, more bleeding events occurred after VR and more valve dysfunction after VS (12). In 2018, 3-year data were reported showing a higher incidence of aortic regurgitation ≥2+ (mild or greater) in the VS group compared to the VR group. Weighted Cox models revealed a higher risk of developing composite outcomes—MAVRE, valve-related morbidity, and structural valve deterioration/nonstructural valve dysfunction—in the VS group at 3 years (13). Notably, preoperative mitral regurgitation and urgent operations were identified as significant predictors of adverse outcomes. In 2023, the latest AVOMP publication presented 5-year results and continued to show that aortic regurgitation ≥2+ was more prevalent in the VS group (*Figure 2*) and contributed weighted Cox models to the evaluation of differences in composite events (namely, MAVRE, valve-related morbidity, and structural valve deterioration/nonstructural valve dysfunction) (14). Overall, the AVOMP study provides valuable insight into the outcomes of VR and VS procedures in patients with Marfan syndrome across several international centers. While both techniques are associated with low early complication rates, there are key differences in late outcomes, which should be considered when making clinical decisions. Because further long-term follow-up and analysis are necessary to fully understand the implications of these findings, the patients enrolled in the AVOMP study will be followed through 20 years.

Single-practice experience

Although we serve as the coordinating center for the

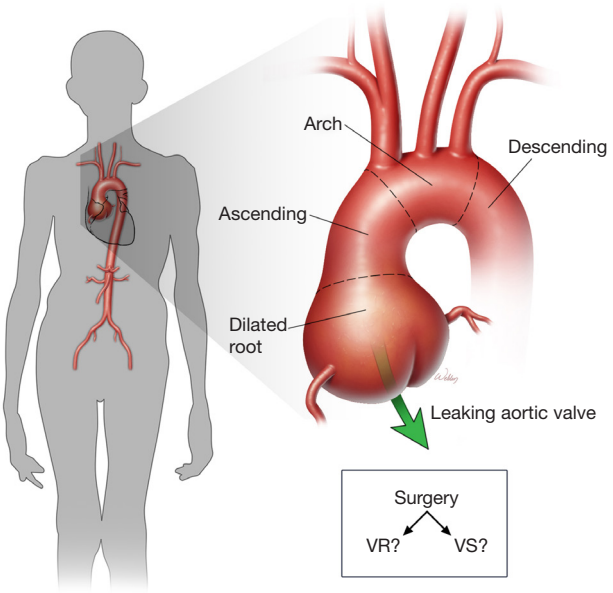

Figure 1 Patients with Marfan syndrome commonly have a dilated aortic root and often develop aortic valve regurgitation, with blood flow leaking back through the valve. When surgery to replace the aortic root becomes necessary, a choice is made between VR and VS approaches. Printed with permission of Baylor College of Medicine. VS, valve-sparing; VR, valve-replacing.

AVOMP study, our experience with ARR in patients with MFS predates this study and extends across four decades. Therefore, we present our related data stratified by the selection of a composite valve graft (CVG) using a mechanical valve, a VS approach, or the use of a bioprosthetic root (i.e., a homograft root, a porcine bioroot, or a specially prepared CVG using a tissue-based valve) (*Figure 3*).

Study protocol and patient cohort

Baylor College of Medicine's institutional review board approved our clinical research protocol (#18095) in 2006. For patients who underwent operation after protocol approval, clinical data were collected prospectively, and informed consent was obtained whenever possible. A waiver of consent was approved for patients whose illness prevented them from providing consent and who had no family members available to provide consent for them. For patients who underwent surgery before the protocol was approved, waiver of consent was approved, and data were collected retrospectively from medical records. As necessary, medical records were reviewed to clarify abstracted data. From February 1991 to March 2023, 223 consecutive,

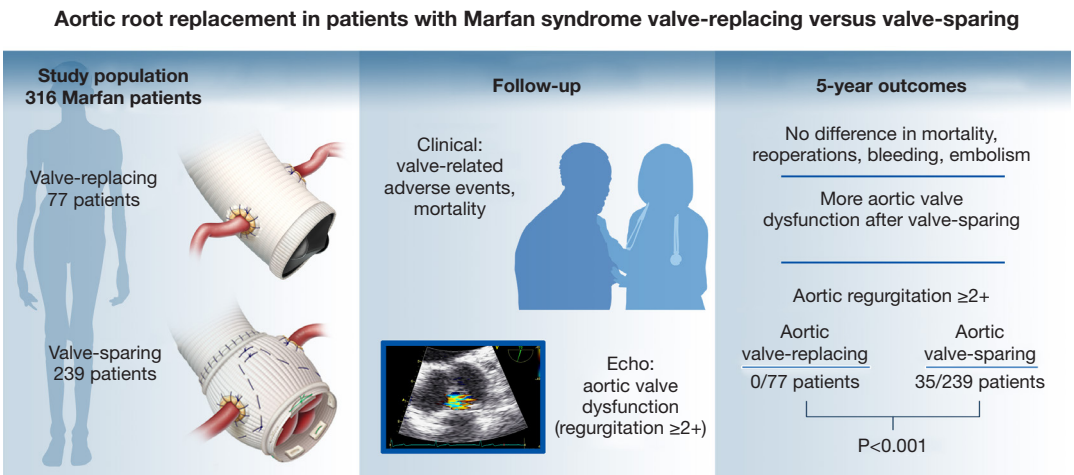

Figure 2 Graphical representation of 5-year outcomes for the AVOMP registry. Of 316 patients with Marfan syndrome, 77 underwent aortic valve-replacing root replacement surgery and 239 underwent aortic valve-sparing root replacement surgery between 2005 and 2010. Median follow-up was 64 months. At five years postoperatively, major adverse valve-related events and valve-related morbidity were more frequent after aortic valve-sparing root replacement than after aortic valve-replacing root replacement, primarily because of more frequent aortic valve dysfunction in the valve-sparing group. Notably, overall mortality and reintervention rates were similar between the groups. Printed with permission of Baylor College of Medicine. AVOMP, Aortic Valve Operative Outcomes in Marfan Patients.

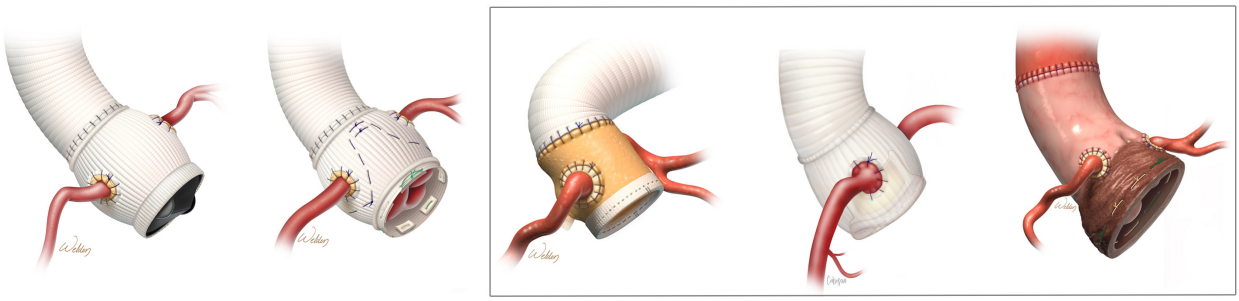

Figure 3 Aortic root replacement necessitates a patient-specific approach to repair. Traditionally, patients with Marfan syndrome received composite valve grafts with mechanical valves. However, contemporary repair in such patients often centers on valve-sparing approaches. Less commonly discussed, other tissue-based approaches—including the use of stentless porcine bioroots, composite valve grafts with tissue valves, and homograft roots—may be useful in select patients that would benefit from a tissue-based approach but whose native leaflets are unsuitable for a valve-sparing ARR. Printed with permission of Baylor College of Medicine. ARR, aortic root replacement.

elective ARRs in patients with MFS were performed by our practice at Baylor College of Medicine. Repairs included 113 (51%) using a mechanical CVG, 62 (28%) using a VS approach, and 48 (22%) using a bioprosthetic root. Fifteen of the 223 repairs we describe were included in the AVOMP registry.

Study definitions and follow-up

All data were collected by using standard definitions (15). All patients who were referred to our practice with the diagnosis of MFS and had elective ARR operations were included in the analysis (16). The proximal aorta included the aortic root, the ascending aorta, and the aortic arch. Aortic interventions included open and endovascular procedures performed on any aortic segment. We defined operative death as death within 30 days of surgery or before final discharge from our hospital or any other hospital or long-term acute care facility to which patients might have been transferred. Postoperative follow-up information was obtained through clinic visit, telephone interview, written correspondence, medical records, and surveillance imaging reports. Late adverse event was defined as experiencing a repair failure or aortic valve structural deterioration with or without related reintervention. Repair failure was defined as failure directly involving the index repair (including any concomitant repair), namely pseudoaneurysm, fistula, endocarditis, or graft infection, and did not include subsequent repair necessitated by progression of aortic disease adjacent to the repair; some patients had more than one type of failure. Valvular-structural deterioration was defined as greater than mild aortic valve regurgitation or stenosis; both may occur simultaneously. The Social Security Death Index (up to 2011) and internet obituary searches were used to identify deaths among patients who were lost to follow-up.

Surgical techniques

We have described our techniques for ARR in detail elsewhere (16-21). Briefly, all patients underwent repair via median sternotomy using cardiopulmonary bypass. Patients underwent one of three basic approaches to ARR, and many types of ARR have been used over our lengthy experience. Although our approach to mechanical CVG has remained relatively constant over our larger surgical experience, the choice of tissue options has varied substantially; initially, patients were offered homografts to treat aneurysms when there was a need to avoid anticoagulation, shifting to bioprosthetic porcine roots, and later to VS approaches where possible. Additionally, we aimed to isolate the coronary arteries with minimal aortic tissue as part of a button reattachment strategy; in case of reoperation or other complicating factors, an alternate strategy of reattachment (e.g., Cabrol approach) was used. Poor quality leaflets may preclude the use of VS approaches, and a variety of techniques may be needed in these complex patients. When repairs extended into the aortic arch, a period of hypothermic circulatory arrest was used. We often used finer sutures when performing repairs in patients with

Marfan syndrome. Importantly, in selecting the operative approach, we strived to facilitate subsequent aortic repair whenever possible, especially when aortic dissection is present.

Statistical analysis

Statistical analyses were performed with IBM SPSS Statistics 28 (IBM Corp., Armonk, NY, USA), and R version 4.2.2 from The R Project for Statistical Computing. Continuous data was tested for assumptions of normality using the Shapiro-Wilk test, determined to be abnormally distributed, and presented as median [Quartile 1–Quartile 3]. Categorical data was presented as count (percentage). Univariate comparisons across the three groups were conducted with the Pearson chi-square test, Fisher exact test, or nonparametric Kruskal-Wallis test, as appropriate. Late events were analyzed by the Kaplan-Meier and competing risk methods. A P value less than 0.05 was considered statistically significant.

Results

Preoperative characteristics

The overall median patient age was 38 [29–52] years. In comparing VS and VR groups, patients were similar in age and rates of major comorbidities and symptoms (*Table 1*). However, patients undergoing VS repair were less likely to have chronic proximal aortic dissection or a prior proximal aortic repair. Many patients undergoing mechanical CVG repair had a complex aortic history, with 1 in 5 experiencing a failure of a prior proximal aortic repair, and many patients have multiple prior aortic interventions at the time of ARR.

Operative details

The overall rate of redo sternotomy was 24% (n=54); however, this rate differed by type of repair, ranging from 2% to 37%. There was no difference in the duration of cardiopulmonary bypass (*Table 2*). Although the duration of aortic clamp and cardiac ischemic times statistically differed, these were not considered clinically significant, varying less than 15 minutes. Many patients underwent aortic arch repair—this ranged from 30% to 54% depending on the type of ARR.

Early outcomes

Operative death was uncommon [4% overall (10/223)] and ranged from 2% to 8% depending on the type of repair (*Table 3*). Notably, death appeared increased for patients undergoing reoperation [5/47 (11%) compared to those without prior repair 5/176 (3%); P=0.04; *Table 4*]. Overall, stroke was rare [1/223 (<1%)], and persistent renal failure necessitating dialysis was uncommon [5/223 (2%)]. However, cardiac complications were relatively frequent,

Table 1 Preoperative characteristics stratified by type of aortic root replacement

Variable	Mechanical CVG (n=113)	Valve sparing (n=62)	Bioprosthetic root (n=48)	P value
Age, years	36 [30–47]	38 [28–51]	43 [33–57]	0.3
Male	72 (64%)	38 (61%)	27 (56%)	0.7
Proximal aneurysm without dissection	83 (73%)	62 (100%)	39 (81%)	<0.001
Any aortic dissection	37 (33%)	10 (16%)	17 (35%)	0.046
Aortic dissection (proximal aortal)	30 (27%)	0	9 (19%)	<0.001
Chronic DeBakey type I	25 (22%)	0	9 (19%)	<0.001
Prior DeBakey type II	5 (4%)	0	0	0.08
Chronic DeBakey type III (distal aorta)	7 (6%)	10 (16%)	8 (17%)	0.08
Aortic root diameter, mm	55 [50–60]	50 [47–53]	52 [50–56]	<0.001
Coronary artery disease	12 (11%)	4 (7%)	9 (19%)	0.1
Cerebrovascular disease	14 (12%)	2 (3%)	4 (8%)	0.1

Table 1 (*continued*)

Table 1 (*continued*)

Variable	Mechanical CVG (n=113)	Valve sparing (n=62)	Bioprosthetic root (n=48)	P value
Chronic kidney disease	5 (4%)	2 (3%)	4 (8%)	0.5
COPD	4 (4%)	1 (2%)	3 (6%)	0.4
Current tobacco use	36 (32%)	19 (31%)	21 (44%)	0.3
Rupture	0	0	0	–
Symptomatic	56 (40%)	38 (61%)	23 (48%)	0.3
Acute	7 (6%)	0	3 (6%)	0.1
Chronic	48 (43%)	37 (60%)	20 (42%)	0.07
Peripheral vascular disease	1 (1%)	3 (5%)	6 (13%)	0.005
Bicuspid aortic valve[1]	11 (10%)	1 (2%)	5 (10%)	0.1
Normal LV ejection fraction (≥55%)	62 (55%)	45 (73%)	31 (65%)	0.06
Aortic valve regurgitation				
None	17 (15%)	23 (37%)	11 (23%)	0.004
Mild	26 (23%)	18 (29%)	8 (17%)	0.3
Moderate	38 (34%)	15 (24%)	15 (31%)	0.4
Severe	30 (27%)	6 (10%)	14 (29%)	0.02
Unknown	2 (2%)	0	0	0.4
Aortic valve stenosis				
None	106 (94%)	62 (100%)	47 (98%)	0.09
Mild	0	0	0	–
Moderate	1 (1%)	0	0	0.6
Severe	2 (2%)	0	0	0.4
Unknown	4 (4%)	0	1 (2%)	0.3
Prior proximal aortic repair				
Any prior proximal aortic repair	38 (34%)	0	9 (19%)	<0.001
Root replacement	13 (13%)[2]	0	4 (8%)	0.02
Ascending/arch repair/replacement (non-root)	25 (24%)	0	2 (4%)	<0.001
With AV repair/replacement[3]	14 (14%)	0	3 (6%)	0.01
Failure of prior aortic repair[4]	23 (22%)	0	7 (15%)	<0.001
Bioprosthetic AV regurgitation	3 (3%)	0	1 (2%)	0.4
Native AV regurgitation (prior resuspension)	9 (8%)	–	3 (6%)	0.08
Prosthetic aortic valve stenosis	3 (3%)	0	0	0.1
Pseudoaneurysm	8 (7%)	0	4 (8%)	0.047
Infection/endocarditis	1 (1%)	0	2 (4%)	0.1

Values are n (%) or median [Quartile 1–Quartile 3]. [1], congenital or functional bicuspid aortic valve present at the time of repair. [2], includes one prior David II valve-sparing aortic root replacement. [3], AV repair involved valve resuspension. [4], more than 1 type of failure is possible. CVG, composite valve graft; COPD, chronic obstructive pulmonary disease; LV, left ventricular; AV, aortic valve.

Table 2 Operative details stratified by type of aortic root replacement

Variable	Mechanical CVG (n=113)	Valve sparing (n=62)	Bioprosthetic root (n=48)	P value
Characteristics of repair				
1st aortic intervention[1]	69 (61%)	55 (89%)	29 (60%)	<0.001
2nd aortic intervention	27 (24%)	6 (10%)	13 (27%)	0.04
3rd or greater aortic intervention	17 (15%)	1 (2%)	6 (13%)	0.002
Repair before 2005	73 (65%)	14 (23%)	16 (33%)	<0.001
Reoperation (redo sternotomy)	42 (37%)	1 (2%)	11 (23%)	<0.001
Perfusion and ischemia				
CPB time, min	154 [132–186]	164 [146–213]	162 [139–193]	0.5
Hypothermic circulatory arrest	39 (35%)	22 (36%)	26 (54%)	0.052
HCA time, min	28 [20–42]	19 [15–22]	24 [17–32]	0.02
Aortic clamp time, min	89 [80–111]	112 [102–143]	99 [78–124]	<0.001
Cardiac ischemic time, min	104 [83–126]	120 [105–143]	114 [94–140]	0.01
Reattachment technique				
Left coronary artery				
Button	88 (78%)	61 (98%)	43 (90%)	<0.001
Cabrol	21 (19%)	0	2 (4%)	<0.001
Other	2 (2%)	0	1 (2%)	0.6
Right coronary artery				
Button	90 (80%)	58 (94%)	45 (94%)	0.009
Cabrol	15 (13%)	0	2 (4%)	0.004
Other	7 (6%)	5 (8%)	0	0.2
Aortic arch management				
Any aortic arch	34 (30%)	24 (39%)	26 (54%)	0.02
Hemiarch	25 (22%)	22 (36%)	21 (44%)	0.02
Total arch	9 (8%)	2 (3%)	5 (10%)	0.3
Other concomitant procedures				
CABG	6 (5%)	3 (5%)	2 (4%)	0.95
Mitral valve repair/replace	13 (12%)	5 (8%)	7 (15%)	0.6

Values are n (%) or median [Quartile 1–Quartile 3]. [1], aortic intervention captured the sequence of open or endovascular procedures on any aortic segment. The mechanical CVG cohort includes three patients in which a prior mechanical valve was retained during aortic root replacement. The valve-sparing cohort was entirely composed of reimplantation procedures (n=62). The bioprosthetic root cohort included repair using a CVG with a tissue valve (n=6), a porcine bioroot (n=34), a root homograft (n=7), and partial root replacement using a tissue valve but leaving one native sinus intact (n=1). CVG, composite valve graft; CPB, cardiopulmonary bypass; HCA, hypothermic circulatory arrest; CABG, coronary artery bypass graft.

Table 3 Early outcomes stratified by type of aortic root replacement

Variable	Mechanical CVG (n=113)	Valve sparing (n=62)	Bioprosthetic root (n=48)	P value
Operative death	5 (4%)	1 (2%)	4 (8%)	0.2
Persistent stroke	1 (1%)	0	0	0.6
Persistent renal failure[‡]	2 (2%)	1 (2%)	2 (4%)	0.6
Bleeding requiring reoperation	4 (4%)	3 (5%)	3 (6%)	0.7
Cardiac complications	50 (44%)	23 (37%)	22 (46%)	0.6
Arrhythmia	37 (33%)	15 (24%)	15 (31%)	0.5
Cardiac failure	10 (9%)	3 (5%)	4 (8%)	0.6
Pericardial effusion requiring drainage	10 (9%)	3 (5%)	2 (4%)	0.4
Respiratory failure	22 (20%)	6 (10%)	10 (21%)	0.2
Necessitating tracheostomy	8 (7%)	0	3 (6%)	0.1
Survivor ICU LOS, days	3 [2–5]	2 [2–4]	3 [2–5]	0.3
Survivor overall LOS, days	10 [8–13]	7 [6–10]	8 [7–13]	<0.001

Values are n (%) or median [Quartile 1–Quartile 3]. [‡], present at the time of hospital discharge or early death. CVG, composite valve graft; ICU, intensive care unit; LOS, length of stay.

Table 4 Causes of early death (n=10) after aortic root replacement

Case No.	Age, years	Sex	Redo proximal	Type of ARR	POD	Cause of death
Case 1	57	Male	No	Bioroot	43	Cardiac failure and heparin-induced thrombocytopenia leading to sepsis and MSOF
Case 2	52	Female	Yes	Bioroot	19	Unknown
Case 3	34	Male	Yes	CVG-M	13	Respiratory failure, pneumonia and sudden cardiac arrest
Case 4	43	Male	No	Bioroot	10	Cardiopulmonary failure, MSOF, and sepsis
Case 5	39	Female	No	Bioroot	6	Cardiac arrest leading to MSOF
Case 6	42	Male	Yes	CVG-M	5	Intracranial hemorrhage and stroke
Case 7	50	Female	Yes	CVG-M	5	Acute thrombosis of interposition graft to right coronary artery causing heart and respiratory failure leading to MSOF
Case 8	43	Female	No	CVG-M	3	Liver and renal failure leading to MSOF
Case 9	38	Male	Yes	CVG-M	1	Cardiac failure
Case 10	61	Female	No	VS	0	Ventricular fibrillation

Early deaths occurred prior to hospital discharge and included any transfer to another hospital or long-term acute care clinic. ARR, aortic root replacement; POD, postoperative day; MSOF, multisystem organ failure; CVG-M, mechanical composite valve graft; VS, valve sparing.

ranging from 37% to 46% by type of ARR.

Late outcomes

Of 213 early survivors, there were 7 (3%) patients who were lost to follow-up at the time of hospital discharge; these patients were presumed alive and censored at the time of discharge during analysis. All other early survivors [n=206 (97%)] had some measure of follow-up data available. Regarding late echocardiographic data, these were available

Table 5 Late events stratified by type of aortic root replacement

Variable	Mechanical CVG (n=113)	Valve sparing (n=62)	Bioprosthetic root (n=48)	P value
Late adverse event	5 (4%)	11 (18%)	10 (21%)	<0.001
Repair failure	5 (4%)	7 (11%)	8 (17%)	0.03
Involving root	3 (3%)	6 (10%)	7 (15%)	0.02
Pseudoaneurysm	2 (2%)	1 (2%)	2 (4%)	0.6
Infection/endocarditis	2 (2%)	2 (3%)	0	0.5
With reintervention	3 (3%)	7 (11%)	8 (17%)	0.006
Valvular reintervention	0	7 (11%)	8 (17%)	0.003
Valvular-structural deterioration	0	5 (8%)	2 (4%)	0.01
Aortic valve regurgitation > mild	0	5 (8%)	2 (4%)	0.01
Aortic valve stenosis > mild	0	1 (2%)	1 (2%)	0.3
Subsequent repair	23 (20%)	2 (3%)	5 (10%)	0.005
Of proximal aorta	6 (5%)	0	1 (2%)	0.1

Values are n (%). Late adverse event was defined as experiencing a repair failure or aortic valve structural deterioration with or without related reintervention. Repair failure was defined as failure directly involving the index repair (which may have extended into the aortic arch), namely pseudoaneurysm, fistula, or endocarditis, graft infection, and did not include subsequent repair necessitated by progression of aortic disease adjacent to the repair; more than one type of failure was possible. Valvular-structural deterioration was defined as greater than mild aortic valve regurgitation or stenosis; both may occur simultaneously. Subsequent aortic repair was additional aortic repair unrelated to the aortic root that was performed to treat progressive aortic disease. CVG, composite valve graft.

in 138 early survivors (65%); however, patients undergoing VS repair or repair using a bioprosthetic root more commonly had available data [52/61 (85%) and 33/44 (75%), respectively]. The rates of late adverse events varied by type of ARR (*Table 5*), with patients receiving a mechanical CVG experiencing the fewest events. Survival differed by repair type (*Figure 4*) as did rates of reoperation (*Figure 5*). Survival was improved in patients who underwent VS repair, and post-hoc testing determined that these patients had higher rates of reoperation-free survival than did patients undergoing ARR using a bioprosthetic root (P=0.03).

Discussion

We found that repair in patients with MFS undergoing ARR resulted in generally low rates of operative mortality and stroke, despite many patients additionally undergoing aortic arch replacement. Elevated rates of aortic dissection, prior aortic intervention, reoperation, and concomitant repair demonstrate the unique challenges faced in this subset of complex patients. In general, we found that patients undergoing mechanical CVG repair tended to undergo a more complicated repair, with 37% of patients undergoing redo sternotomy.

Compared to the 316 patients described in the early AVOMP experience, (12) our subset of 223 patients had elevated rates of prior aortic surgery (especially prior ascending aortic replacement with aortic valve resuspension and prior ARR), aortic dissection, and concomitant aortic arch repair; in contrast, only 91% of AVOMP repairs were elective. Early outcomes were similar in our work and the AVOMP cohort, with low rates of operative death (4% *vs.* 1%, respectively) and stroke (1% *vs.* <1%, respectively), but substantial rates of cardiac complications (43% *vs.* 23%, respectively) (12). Regarding late findings, our results were similar to those of AVOMP in that patients undergoing VS repair tended to experience greater rates of valvular-structural deterioration, which did not appear to impact late survival (14). This finding is additionally supported by a meta-analysis of outcomes in 2,976 patients with MFS undergoing ARR by a CVG (n=1,624) or a VS (n=1,352) approach that found those undergoing VS had improved late survival (22). Other studies support this finding. The most recent study to describe the overall work of leading VS expert David (23) continues to demonstrate robust survival in patients with MFS undergoing ARR with VS

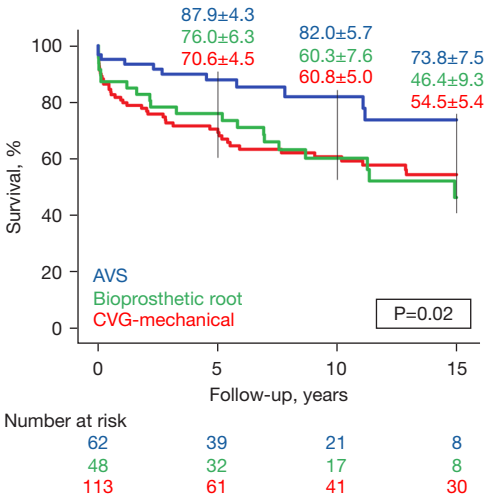

Figure 4 Survival estimates by the Kaplan-Meier method differed by type of aortic root replacement (P=0.02). Survival appears more robust in patients with Marfan syndrome who underwent AVS aortic root replacement, although there are many factors that may influence outcomes in such patients with complex aortic disease. AVS, aortic valve sparing; CVG, composite valve graft.

reimplantation approaches, which was 95% at 10 years.

Importantly, technical aspects of VS repair centering on leaflet repair and coaptation parameters appear to drive durability (23-27). Another recent study summarizing the Washington University experience in a cohort of patients with and without MFS suggests that VS durability (freedom from reoperation and AR >2+) was improved when the coaptation effective height of the aortic valve leaflets following repair exceeded 10 mm (27). Our substantial rate of downstream subsequent aortic repair (ranging as high as 20% in patients undergoing mechanical CVG replacement) is explained by the progressive nature of aortic disease, especially in patients with chronic aortic dissection. The downstream aortic impact after proximal aortic replacement in patients with heritable thoracic aortic disease remains an issue of concern and in need of further evaluation. A study by Lenz and colleagues suggests that ARR itself may enhance rates of aortic dilatation (28). We highlight this finding to raise awareness that ARR is only one element of whole-patient care in those with MFS. In many such patients, progressive disease will necessitate additional repair of the distal aorta, and on occasion, replacement of the entire aorta. We believe such repair should center on open graft replacement (29), which we have demonstrated can be done with good results in most patients (16,18,30).

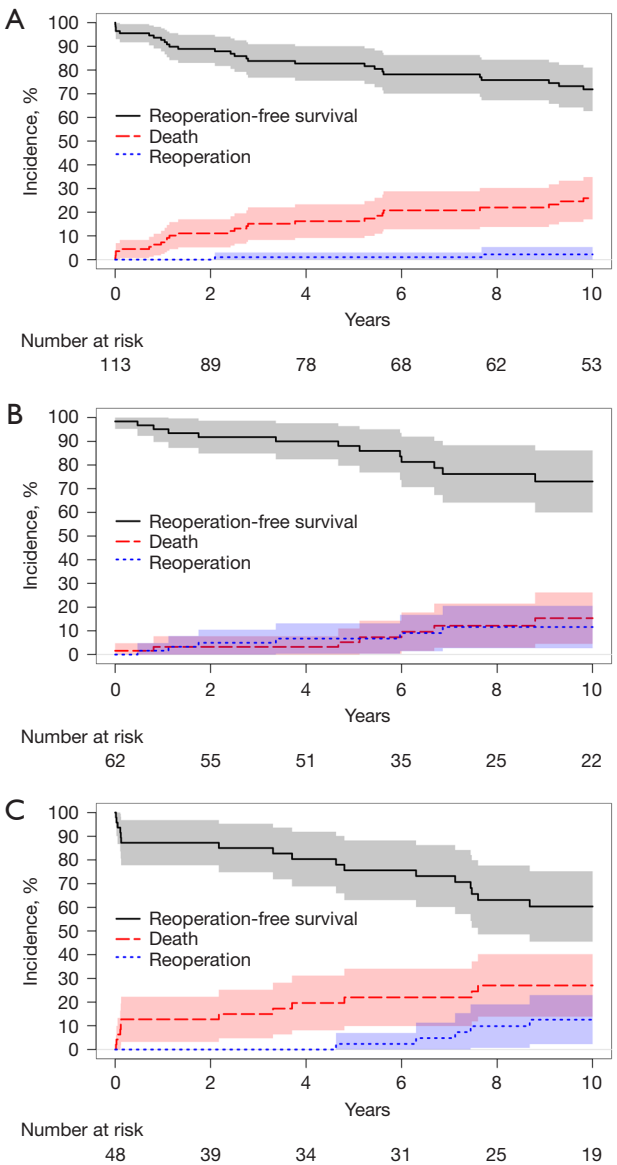

Figure 5 Competing risk analysis for patients with Marfan syndrome undergoing ARR procedures. (A) Patients undergoing ARR using a mechanical composite valve graft had modest rates of reoperation related to their ARR. Patients undergoing AAR with a (B) valve-sparing approach or a (C) bioprosthetic root had increased rates of reoperation. Post hoc testing determined that patients undergoing VS repair had higher rates of reoperation-free survival than did patients undergoing ARR using a bioprosthetic root (P=0.03). ARR, aortic root replacement; VS, valve-sparing.

Limitations of this study include the difficulty in evaluating a heterogeneous study population with a complicated history of aortic disease over a long period of time. Despite

these limitations, we believe it is worthwhile to present our experience, including approaches to repair that are now less frequently used. Here, the complexity of aortic disease frequently necessitated a patient-tailored operative approach. Because of the long study period and the limits of our tertiary-practice service, we were unable to obtain follow-up echo data on all patients (most of whom are followed by a local clinician). Information that we were unable to systematically capture as part of late surveillance included late thrombolytic events, the late onset of aortic dissection, and late rupture events. Additionally, we may have failed to capture late deaths adequately, especially if deaths were unlikely to be recorded in the Social Security Death Index or online.

Conclusions

Aortic repair in patients with Marfan syndrome is complex and necessitates a patient-tailored approach with participation in a life-long surveillance protocol (16). We aimed to describe the scenarios of patient presentation for ARR and to underscore that patients selected for VS repair tend to differ from other patients in that they typically present with less complexity. Evaluating the type of ARR is difficult because of pervasive heterogeneity, the progression of aortic disease that necessities subsequent repair, and unclear late events (e.g., new onset dissection, late rupture, and late complications of multiple prior repairs) that undoubtedly affect long-term survival. What patients should know is that there are multiple approaches in the surgeon's toolkit that can be drawn upon to fit a specific circumstance, including more than one option for a tissue-based repair.

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Footnote

Conflicts of Interest: SAL consults for Terumo Aortic and Cerus and has served as a principal investigator for clinical studies sponsored by Terumo Aortic and CytoSorbents. JSC serves as principal investigator, consults for, and receives royalties and a departmental educational grant from Terumo Aortic; consults and participates in clinical trials for Medtronic, Inc., and W.L. Gore & Associates; and participates in clinical trials for Abbott Laboratories, CytoSorbents, Edwards Lifesciences, and Artivion. MRM advises Medtronic and Edwards Lifesciences. The other authors have no conflicts of interest to declare.

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