Cardiovascular surgery in children with Marfan syndrome or Loeys-Dietz syndrome

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Objective: This study was undertaken to assess the frequency and outcome of cardiovascular surgery in children with Marfan or Loeys-Dietz syndrome.

Methods: A retrospective review from 2 regional Marfan subspecialty clinics was performed. Between 1997 and 2007, 204 children with Marfan syndrome and 17 children with Loeys-Dietz syndrome were followed serially. Of these patients, 35 were identified who had undergone cardiovascular surgery at 18 years of age or less. Demographic, echocardiographic, and surgical data were collected.

Results: Surgery was performed at a median of 3 years (0–15 years) after diagnosis and a mean age of 11.5 ± 6.2 years. Aortic root replacement was the initial surgery in 30 patients, and mitral valve surgery was the initial surgery in 8 patients, with 3 patients undergoing both. Aortic root replacement was performed using a composite root replacement in 9 patients and valve-sparing techniques in 21 patients (remodeling in 8 patients and reimplantation in 13 patients). Eight patients underwent reoperation at a mean of 4.7 ± 3.0 years after aortic surgery: 3 for aortic insufficiency, 2 for dissection, 2 for valve thrombosis, and 1 for a distal aneurysm. Adverse outcomes included reoperation in 8 patients, aneurysm in 1 patient, and death due to dissection or stroke in 3 patients. Variables associated with an adverse outcome included preoperative aortic insufficiency, valve replacement, and absence of angiotensin-converting enzyme inhibitor therapy.

Conclusion: Patients with Marfan or Loeys-Dietz syndrome requiring surgery during childhood have a favorable long-term outcome. Those undergoing valve-sparing root replacement or mitral valve repair have a low risk for reoperation. Postoperative angiotensin-converting enzyme inhibitor therapy confers clinical benefit.

Marfan syndrome (MFS) is an autosomal dominant disorder marked by the triad of musculoskeletal, aortic, and ocular pathology.¹ The primary cause of morbidity and mortality associated with MFS is aortic dissection.² In 1968, Bentall and de Bono³ described the technique of replacing the ascending aorta and aortic valve in a patient with MFS. Numerous surgical advances followed, including remodeling⁴ and reimplantation⁵ techniques aimed at sparing the patient's own aortic valve, thereby rendering long-term anticoagulation unnecessary. The majority of patients with MFS will not require surgical intervention until their adult years.⁶

Loeys-Dietz syndrome (LDS) is a recently recognized genetic disorder marked by craniofacial and musculoskeletal abnormalities and aggressive aortic pathology.⁷ As in MFS, the disorder is associated with premature morbidity and mortality secondary to aortic dissection.⁷ Indications for surgical replacement of the dilated aorta have been pub-

lished, and in light of the aggressive nature of the disorder, earlier surgical intervention is indicated.⁸

Although cardiovascular surgery in the adult with MFS or related syndromes has been well described, there are little data on the need for cardiovascular surgery in children with these aortopathies.^{8–11} In addition, little is known about the long-term outcome of cardiovascular surgery in these patients. We sought to assess the frequency and long-term outcome of cardiovascular surgery in children with MFS or LDS.

MATERIALS AND METHODS

Patient Population

After institutional review board approval, a retrospective data review was undertaken at the Intermountain West Marfan Cardiology Institute, comprised of 2 pediatric cardiology centers: Primary Children's Medical Center, Salt Lake City, Utah, and The Children's Hospital, Denver, Colorado. The diagnosis of MFS was made in accordance with the Ghent criteria.¹² LDS was diagnosed in those patients with aortic dilation, typical craniofacial features, and a documented *TGFBR1* or *TGFBR2* disease-causing mutation.⁷ The clinical database was reviewed, and patients who underwent surgical intervention in childhood (age < 18 years) were identified. Demographic, echocardiographic, and surgical data were collected on these patients, including age at diagnosis, clinical features, preoperative medical therapy, age at surgery, indication for surgical intervention, type of surgery, presence and type of major postoperative complications (arrhythmia, prolonged ventilation, need for in-hospital reoperation, stroke, death), duration of follow-up, need for reoperation, aortic dissection, and death.

Echocardiography

All patients underwent semiannual echocardiography and echocardiography immediately preoperatively and postoperatively. Data obtained

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Abbreviations and Acronyms

LDS = Loews-Dietz syndrome

MFS = Marfan syndrome

from the echocardiogram at last preoperative visit, first postoperative assessment, and last clinical visit were used for data analysis. Systolic aortic root dimension, obtained from the parasternal long-axis view, was expressed as an absolute value and an indexed score for body surface area (Z-score).¹³ Left ventricular function was expressed as an ejection fraction obtained from volumetric analysis in the apical 4- and 2-chamber views. Mitral insufficiency was assessed in a semiquantitative manner and judged to be trivial, mild, moderate, or severe using regurgitant jet area to left atrial area ratio and mitral insufficiency jet width.

Surgical Techniques

In general, standard hypothermic cardiopulmonary bypass (28°C) and blood potassium cardioplegic arrest were used for all cases. Replacement of the aortic valve and root was performed using a modified Bentall technique.¹⁴ Valve-sparing root replacement was performed using a remodeling technique with annular fixation¹⁵ or a reimplantation technique.^{16,17} Mitral valve surgery consisted of standard repair or replacement techniques.¹⁸

Data Analysis

Data are summarized as frequencies, means $\pm$ standard deviations, or medians with ranges where appropriate. Patients who underwent aortic surgery were divided into 2 groups on the basis of the presence or absence of an adverse clinical outcome, defined as the need for reoperation, new aortic dissection, or death. Patient characteristics for the 2 groups were compared using Fisher's exact test or chi-square analysis for categorical variables and *t* tests and Kruskal-Wallis analysis of variance for continuous variables. Multiple logistic regression analysis was performed on those risk factors found to be significant by univariate analysis.

Patient survival and adverse event-free survival were calculated and presented in Kaplan-Meier format.¹⁹

RESULTS**Patient Population**

Of the 204 children with MFS and 17 children with LDS followed at 2 institutions comprising the Intermountain West Marfan Cardiology clinic, 24 (11% of entire MFS pediatric cohort) and 11 (65% of entire LDS cohort) required surgical intervention in childhood. Patient follow-up and criteria for surgery were uniform across the institutions. Initial surgical intervention was performed at a mean age of 11.5 ± 6.2 years (range, 9 months to 18 years). Sixty-nine percent of the patients were male. Forty percent of the patients had a family history of MFS or LDS. Ten patients (28%) underwent repeat surgical intervention at a mean interval of 4.1 ± 3.0 years.

Of the 35 children, 30 had an aortic procedure performed at the time of initial surgical intervention. The demographics of these 30 patients are displayed in [Tables 1 and 2](#).

Eight patients underwent mitral valve surgery at the time of initial intervention. All carried the diagnosis of MFS. All 6 patients with neonatal MFS required mitral valve surgery, 3 of whom underwent concomitant aortic surgery.

Echocardiography

Patients were followed clinically with echocardiography for a mean of 8.9 ± 5.6 years after initial surgical intervention. Echocardiographic variables are shown in [Table 3](#).

Surgical Intervention

A total of 35 patients underwent first-time surgical intervention. The primary indication for surgery was aortic aneurysm in 30 patients and mitral valve insufficiency in 5 patients.

Aortic surgery. Initial aortic intervention was performed at a mean age of 14.2 ± 4.3 years. Median time to aortic surgery after diagnosis was 3 years (range 0–15 years). Indications for surgical intervention were rapid aortic growth (≥ 1 cm per year) in 1 patient, aortic dissection in 4 patients with LDS, aortic dilation with insufficiency in 5 patients, and attainment of established surgical criteria for aortic root replacement in 15 patients with MFS and in 5 patients with LDS. Criteria included an absolute aortic sinus diameter of 45 to 50 mm or greater for patients with MFS and an aortic sinus diameter indexed to body surface area of 3.5 or greater (Z-score) for patients with LDS. Aortic root replacement was performed in 3 patients at the time of mitral valve surgery because of dissection in 1 patient and aortic aneurysm in 2 patients. In 9 patients, the initial operation consisted of replacement of the aortic valve and ascending aorta using a mechanical prosthesis in 8 patients and a bioprosthesis in 1 patient. One of these patients had a mitral prosthesis placed concomitantly. Aortic valve replacement was performed in all patients with moderate or greater preoperative insufficiency or in the setting of aortic dissection. In 8 patients, a remodeling technique with annular fixation was used. One of these 8 patients with remodeling underwent simultaneous mitral valve repair. Thirteen patients underwent a primary valve-sparing root procedure using a reimplantation technique, with 1 of these patients undergoing simultaneous atrial septal defect closure and another undergoing mitral valve repair.

Eight patients in this cohort underwent reintervention at a mean time from initial surgery of 4.7 ± 3.0 years. Of the 9 patients who underwent aortic valve replacement, 4 required reintervention for the following reasons: valve thrombosis (2), an aneurysm at the distal end of the ascending graft (1), and dissection (1) in a patient with LDS. Reoperation was necessary in 4 of the 21 patients who had a valve-sparing procedure. Of the 8 patients who underwent valve-sparing root replacement using the remodeling technique, 2 required valve replacement 4 and 6 years after the initial procedure because of the development of significant aortic insufficiency. A third patient with LDS underwent reoperation for dissection distal to the ascending graft. One of the 13 patients who underwent valve-sparing root replacement using the reimplantation technique developed significant aortic

TABLE 1. Patient characteristics at diagnosis and initial aortic surgery

Diagnosis	Age at diagnosis (y)	Age at surgery (y)	Aorta at surgery: diameter (mm) (indexed to BSA)	Medication preoperatively; postoperatively	Surgery
LDS	0	3	28 (8)	ACEI; ACEI	Reimplantation
nMFS	0	2	38 (13)	BB; ACEI	Reimplantation
nMFS	2	6	40 (16)	BB; ACEI	Remodeling
LDS	2	2	51 (26)	None; ACEI	Reimplantation
MFS	2	9	50 (8)	BB; BB	AVR
MFS	6	17	50 (7)	BB; BB	Reimplantation
MFS	15	18	49 (11)	BB; ACEI	Reimplantation
LDS	3	3	32 (9)	BB; BB	Remodeling
MFS	18	18	57 (9)	None; ACEI	Reimplantation
LDS	0	1	26 (9)	ACEI; ACEI	Reimplantation
nMFS	0	1	35 (NA)	BB; BB	AVR
LDS	9	9	55 (25)	None	AVR
MFS	7	15	54 (7)	BB; ACEI	Reimplantation
MFS	4	14	50 (7)	BB; ACEI	AVR
LDS	18	18	60 (9)	None; None	AVR
MFS	3	8	48 (13)	BB; BB	Remodeling
MFS	14	14	54 (9)	BB; ACEI	Remodeling
MFS	6	14	53 (11)	BB; None	Remodeling
MFS	17	18	68 (12)	BB; BB	Reimplantation
MFS	14	15	NA	None; None	Reimplantation
MFS	10	17	53 (6)	None; ACEI	Reimplantation
MFS	NA	18	45 (5)	BB; BB	Reimplantation
MFS	19	18	67 (9)	None; ACEI	Remodeling
MFS	10	17	52 (8)	None; BB	AVR
LDS	0	14	43 (7)	BB; ACEI	AVR
LDS	6	16	52 (7)	BB; BB	AVR
LDS	3	18	59 (8)	None; BB	AVR
LDS	10	12	52 (15)	None; BB	Remodeling
LDS	12	17	39 (4)	None; ACEI	Reimplantation
MFS	NA	13	50 (10)	BB; BB	Remodeling

BSA, Body surface area; LDS, Loeys-Dietz syndrome; nMFS, neonatal Marfan syndrome; MFS, Marfan syndrome; NA, not available; ACEI, angiotensin-converting enzyme inhibitor; BB, beta-blocker; AVR, aortic valve replacement.

insufficiency necessitating valve replacement 4 years after the valve-sparing operation. Surgical variables related to initial aortic root procedures are as shown in Table 4. Mean follow-up time of patients surviving initial aortic surgery was 4.6 ± 3.2 years (0.5–13 years). There was 1 early death in the valve replacement cohort and no deaths in the valve-sparing cohort.

Mitral valve surgery. A total of 8 patients underwent mitral valve surgery as their first surgical intervention at a median age of 4 years (range 0–12 years). Median time to mitral valve surgery after diagnosis was 1.5 years (range, 0–11 years). Indications for mitral valve surgery included flail valve with ruptured chordae in 3 patients with neonatal MFS and severe mitral insufficiency with symptoms of congestive heart failure in 5 patients, including 1 patient with left ventricular enlargement and associated ventricular dysrhythmias. Mitral valve repair was the anticipated surgical procedure in all patients, but valve replacement was required in 2 patients: extensive mitral annular and valve calcification

in 1 patient and placement of a mechanical aortic prosthesis for severe aortic insufficiency not amenable to repair in 1 patient. One patient required reintervention at 5 months postoperatively because of severe mitral regurgitation through a hole in the valve leaflet. The valve was amenable to repair with mild regurgitation at last follow-up. Another patient underwent an aortic valve-sparing root replacement for attainment of absolute aortic root dimension of 50 mm 30 months after mitral valve surgery. Mean follow-up time was 4.8 ± 3.0 years. There were no deaths in this group.

Entire surgical cohort. The duration of follow-up for the entire cohort was 8.9 ± 5.6 years. Freedom from reoperation was 94% at 1 year, 89% at 3 years, 73% at 5 years, and 66% at 8 years. Patient survival was 97% at 1 month, 94% at 1 year, 90% at 3 years, and 84% at 5 and 8 years (Figure 1). There were 3 cardiac-related deaths on follow-up, all in patients with a diagnosis of LDS. Two were in-hospital deaths. One in-hospital death occurred in an undiagnosed 9-year-old child who presented with loss of consciousness

TABLE 2. Demographics of patients undergoing initial aortic surgery

Variable	No adverse outcome	Adverse outcome ^a	P
Gender, male	78%	67%	.678
Preoperative height, cm	180	174	.754
Preoperative weight, kg	33	41	.581
Age at diagnosis, y	8.3	6.5	.676
Diagnosis: MFS/LDS	13/ 5	6/ 6	.216
Age at first surgery, y	12.5	11.5	.496
Positive family history	18	12	.880
Preoperative medical therapy			
Duration, y	3.8	4.7	.474
BB vs ACEI ^b	82% vs 18%	100% vs 0	.485
Postoperative medical therapy			
BB vs ACEI ^b	25% vs 75%	100% vs 0	.006

MFS, Marfan syndrome; LDS, Loeys-Dietz syndrome; BB, beta-blocker; ACEI, angiotensin-converting enzyme inhibitor. ^aAdverse outcome is defined as death, dissection, or need for reoperation. ^bPercent of patients with or without an adverse outcome who were receiving beta-blocker therapy versus percent of patients with specified outcome receiving an ACEI.

caused by acute dissection of the ascending aorta with extension into the carotid arteries. Despite successful repair of the dissection, neurologic status remained poor and therapy was withdrawn. The other in-hospital death occurred in a 19-year-old girl who had undergone a Bentall procedure for aortic dissection 7 months earlier; endocarditis with thromboembolism subsequently developed, and the patient died despite successful surgical repair. The third death occurred in a 14-year-old child with LDS 3 years after aortic surgery using the valve-sparing technique. The patient had acute dissection distal to the ascending aortic graft and was dead on arrival

TABLE 3. Echocardiographic variables of patients undergoing initial aortic surgery

Variable	No adverse outcome	Adverse outcome	P
Aortic root			
dimension at diagnosis			
Absolute size, mm	36.9	37.1	.934
Z-score	5.9	10.1	.066
Aortic root			
dimension at surgery			
Absolute size, mm	47.8	49.8	.626
Z-score	9.9	11.9	.397
Aortic insufficiency			
at surgery,			
moderate or more	1 (5%)	8 (67%)	<.001
Preoperative dissection	0	2 (17%)	.142
LV dysfunction,			
ejection fraction < 40%			
Postoperative	2 (11%)	3 (25%)	.364
At last follow-up	2 (12%)	5 (42%)	.092

LV, Left ventricular.

TABLE 4. Surgical variables of patients undergoing initial aortic surgery

Variable	No adverse outcome	Adverse outcome	P
Year of surgery, ≥2002	14 (74%)	6 (50%)	.179
Type of surgery,			.006
Mechanical valve	2 (11%)	7 (58%)	
VSRR	16 (89%)	5 (42%)	
VSRR			.027
Remodeling	4 (25%)	4 (80%)	
Reimplantation	12 (75%)	1 (20%)	
Graft size, mm	25.6	23.6	.881
CPB time, min	185	161	.315
Crossclamp time, min	163	148	.558

VSRR, Valve-sparing root replacement; CPB, cardiopulmonary bypass.

to the hospital. There were no in-hospital deaths in patients undergoing prophylactic root replacement.

Statistical Analysis

Predictors of adverse outcomes after aortic surgery were sought using univariate and multivariate analyses. Adverse outcomes included the need for reoperation in 9 patients and cardiac-related death in 3 patients with LDS.

Univariate analysis. The results from univariate analysis are shown in Tables 2 to 4. Predictors of adverse outcome included the presence of preoperative aortic insufficiency, non–valve-sparing surgical intervention, and lack of angiotensin-converting enzyme inhibitor use postoperatively. Age at surgical intervention and preoperative aortic diameter (absolute or indexed) did not predict adverse outcome. Similarly, underlying diagnosis and presence of preoperative aortic dissection were not related to outcome in this small patient group.

Multiple logistic regression analysis. Because of the small sample size, a full multivariate analysis with stepwise

FIGURE 1. Freedom from reoperation and actual survival.

logistic regression was not performed, but those variables that were found to be significantly associated with adverse outcome by univariate analysis were analyzed by logistic regression. This included the type of aortic surgery, preoperative aortic insufficiency, and the type of postoperative medical therapy. Absence of medical therapy with an angiotensin-converting enzyme inhibitor remained a risk factor for adverse outcome when controlling for the other 2 variables ($P = .04$). The presence of moderate or greater preoperative aortic insufficiency also remained an important variable ($P = .05$). The type of aortic surgery did not (Table 5).

DISCUSSION

Because of earlier diagnosis, more patients with MFS or LDS are undergoing surgical intervention during childhood. We have demonstrated that surgical outcomes in this group of patients are good with low morbidity and mortality rates.

Aortic repair using placement of a mechanical valve was a univariate risk factor associated with adverse long-term outcomes. However, when multivariate analysis was performed, the presence of preoperative aortic insufficiency appeared to confound this finding. This is not surprising because the indication for placement of a mechanical bioprosthesis in most patients was aortic insufficiency not amenable to repair. Notably, 44% of patients in this subset underwent reintervention for valve thrombosis (2 patients), distal dissection (1 patient), and aneurysm (1 patient). Thus, although durability with respect to aortic insufficiency was achieved, the need for relatively early reintervention was not circumvented. The potential complications of bleeding or thrombosis related to anticoagulation for prosthetic valves cannot be overemphasized. Maintenance of appropriate anticoagulation is particularly problematic in younger patients when compliance is an issue.

Outcomes were favorable in those patients with MFS undergoing a valve-sparing operation, specifically, the early and intermediate results of valve-sparing root replacement using the reimplantation technique in this cohort of patients with connective tissue abnormalities were excellent with only 1 patient requiring reintervention for aortic insufficiency 4 years after initial repair. Although advocates of the remodeling technique emphasize the value of recreating the aortic sinuses to minimize stress on the valve leaflets and preserve functioning, the results in this group of pediatric patients do not lend weight to the remodeling technique over that of reimplantation. In fact, patients with aortic aneurysm due to MFS or Marfan-like syndromes may fare better with the reimplantation technique because fixation of the annulus prevents regurgitation caused by annular dilatation. This has been suggested by others who cite a greater risk of late annular dilatation and aortic insufficiency when the remodeling technique is used.²⁰ Statistical analysis beyond the univariate comparison ($P = .03$) was not performed because of the small number of patients undergoing each valve-sparing technique. Nonetheless,

TABLE 5. Multivariate analysis of significant independent variables

Variable	OR	P	95% CI
Preoperative AI	22	.05	(0.92–547)
Type of surgery			
Mechanical valve/VSRR	1.1	.95	(0.04–19)
Postoperative ACEI	0.08	.04	(0.007–0.92)

OR, Odds ratio; CI, confidence interval; AI, aortic insufficiency; VSRR, valve-sparing root replacement; ACEI, angiotensin-converting enzyme inhibitor.

our observation that supports valve-sparing surgery using the reimplantation technique rather than remodeling is in accord with the results of other small studies of valve-sparing surgery in children or young adults with MFS.^{10,21}

Noteworthy in this population is that the need for reintervention in both the valve replacement and valve-sparing groups cannot be solely attributed to the surgical technique but rather in part to the nature of the aortic disease. The outcomes highlight the extent of the aortic pathology and risk of dissection distal to the ascending graft, especially in patients with LDS. Since 2000, all of our patients with MFS or LDS undergo assessment of the entire aorta by magnetic resonance angiography or computed tomographic angiography before and after aortic intervention to identify distal aortic disease not seen preoperatively by echocardiography, to assess the distal anastomosis within 3 months of surgery, and to establish a new baseline for future comparison.

With respect to mitral valve dysfunction in patients with MFS, repair of the valve was achieved in the majority of patients regardless of the mechanism of dysfunction. The long-term results of mitral valve repair were excellent with no patient requiring subsequent valve replacement. Our findings substantiate previous reports that tout the feasibility and durability of mitral valve repair in patients with MFS.^{9,22} Mitral valve repair rather than replacement is especially preferred in children because anticoagulation can be avoided.

During our investigation on the impact of surgical interventions in children with aortopathies, we discovered that postoperative angiotensin-converting enzyme inhibitor therapy confers a long-term clinical benefit over beta-blocker therapy in this cohort of patients. This is not surprising in light of the accumulating data suggesting a beneficial role of angiotensin II blockade in patients with MFS.^{23,24}

The study is limited by its retrospective design with no randomization of patients to the various surgical techniques. In addition, the study includes a relatively small cohort of patients with few adverse outcomes, which precluded more extensive analyses. However, it is one of the larger studies to date focusing on this group of patients, and as such, it adds to the paucity of data on cardiovascular surgery in children with MFS or LDS. Moreover, we differentiated patients with MFS from those with LDS, a potential confounder in studies published before the description of LDS in 2005.

CONCLUSIONS

This study brings to light the success of valve-sparing aortic procedures in patients with aortopathies and highlights the need for further investigation to determine the valve-sparing technique that will afford the best long-term durability. This study also underscores the extent of aortic pathology in patients with these syndromes, especially LDS, and substantiates the importance of continued surveillance for aortic aneurysm and dissection beyond the ascending graft, as well as the need for studies to assess the benefit of medical therapies preoperatively and postoperatively in these patients.

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Discussion

Dr Anees J. Razzouk (Loma Linda, Calif). Congratulations on a nice presentation. Ivan Rebeyka regrets not being here this morning. I will be reading his comments and asking you his questions.

The authors are to be applauded for their initiative in combining the experience from separate centers in Salt Lake City and Denver to provide us with important information in the management of children with Marfan and Marfan-like syndromes. The essence of their data relates to the 30 patients who underwent aortic root surgery at a mean age of 14 years and in whom 21 had a valve-sparing procedure compared to 9 having a composite replacement or a Bentall-type procedure. The two most important surgical decisions required in this group of patients is when to operate and if so what operation to perform. While it is difficult to argue with reasonably well established and accepted indications for surgery based on an aortic size greater than 45 to 50 mm, the decision to operate becomes more challenging when younger and smaller patients present with large ascending aortas relative to their body size but less than 45 mm in diameter. For example, a 2-year-old weighing 15 kg might present with a 30-mm ascending aorta yet only to have a valve annulus size of 16 mm. How do you decide if and when such a patient should be advised to have an operation?

Dr Everitt. I think one of the most important things is to be sure you have the diagnosis correct. In our paper, we did show that there is a difference between patients with Marfan syndrome versus Loeys-Dietz with respect to complications. Those patients, as previously published, were more likely to have dissection and death due to dissection. The published criteria which is what we follow for Loeys-Dietz is Z-score, so if the Z-score is greater than or equal to 3.5, we will operate at an aortic root size less than 45 mm, so based on index to body surface area. There were patients who were identified after 2005 who had an aortic root in the 30s that did undergo the procedure. As far as those with Marfan syndrome, we are still following the criteria of 50 mm unless they have a family history of dissection or the rapid growth. I agree that it is a challenge. I think the literature prior to 2005, much of the literature after 2005, and our experiences have heterogeneous patient population and, like I said, it is important to know what type of aortic pathology you are dealing with, not only to determine the size at which to operate but also the extent of the operation because these patients with Loeys-Dietz syndrome have aortic pathology beyond what we standardly replace in Marfan syndrome. We follow the recommendations to image the entire aorta preoperatively with MRI scan as our method of choice and to follow them yearly with MRI scan to look for further dissection. That was the cause of death. There were four deaths in our paper and three deaths were due to dissection. All three patients had Loeys-Dietz syndrome.

Dr Razzouk. My last question relates to your conclusion supporting the success of valve-sparing techniques over composite

aortic root replacement with mechanical valve in this patient population. More specifically, 4 out of 8 or 50% of patients undergoing the remodeling technique had an adverse outcome defined by you as need for reoperation, new aortic dissection, or death. Conversely, only 1 of 12 or less than 10% of patients having the reimplantation or David procedure experienced one of these issues. Accordingly, I was wondering why you did not include the apparent superiority of reimplantation procedure over remodeling as one of the study's important messages.

Again, congratulations on your superb results and your very nice presentation.

Dr Everitt. I did not want to make that statement too strongly because our numbers were small and we did show a difference in univariate analysis but not in multivariate analysis, so there may be other confounding factors. I do think that it is very suggestive that the reimplantation technique is superior but I think making definitive conclusions are difficult with a small patient population, albeit one of the largest series to be published in children.