Aortic Root Surgery in Marfan Syndrome

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Abstract

Background: As the shortcomings of the Bentall operation and its variants in the Marfan syndrome have become apparent, the recent cusp-sparing techniques (remodeling or reimplantation) bear promise of better mid-term and long-term outcomes.

Objective: To examine the results of aortic root surgery in patients with Marfan syndrome.

Methods: During the period March 1994 to September 2007, 220 patients underwent aortic valve-sparing surgery; 20 were Marfan patients (group 1) who were compared with another 20 Marfan patients undergoing composite aortic root replacement (group 2). Fourteen patients had aortic dissection and 26 had thoracic aortic aneurysm. There were 31 males and 9 females with a mean age of 37.9 ± 13.8 years. In group 1, reimplantation was used in 13 patients, remodeling in 4, and aortic valve repair with sinotubular junction replacement in 3. In group 2, a mechanical valve conduit was used. Mean logistic Euroscore was 12.27 ± 14.6% for the whole group, five of whom were emergent cases

Results: Group 2 had more previous cardiac procedures compared to group 1 (9 vs. 2, $P = 0.03$) and shorter cross-clamp time (122 ± 27.1 vs. 153.9 ± 23.7 minutes, $P = 0.0004$). Overall mortality was 10%. Early mortality was 10% in group 2 and 5% in group 1 (NS). Mean follow-up time was 25 months for group 2 and 53 months for group 1. Three patients were reoperated; all had undergone the remodeling. Five year freedom from reoperation and death was 86% and 90% in group 2 and 70% and 95% in group 1 ($P = 0.6$, $P = 0.6$), respectively.

Conclusions: Late survival of patients with Marfan syndrome was similar in both groups. Root reconstruction tends towards a higher incidence of late reoperations if the remodeling technique is used. We now prefer to use the reimplantation technique.

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Aortic root aneurysms with or without dissection occur classically in patients with connective tissue disorders [1]. A characteristic pathological dilatation of the aortic root, namely anuloaortic ectasia, exists in about 75% to 85% of patients with Marfan syndrome [2]. This includes dilatation of the aortic sinuses and annulus in addition to the ascending aorta, leading to aortic valve insufficiency. If left untreated there is a high risk of death due to dissection or rupture of the aorta or heart failure resulting from severe aortic regurgitation. In a study of 721 patients Davis and colleagues [3] showed that aneurysm size has a profound impact and may lead to rupture, dissection, and death. For aneurysms larger than 6 cm in diameter, rupture occurred in 3.7% per year, rupture or dissection in 6.9% per year, death in 11.8%, and death, rupture, or dissection in 15.6% per year [3].

In 1972 the median life expectancy of patients with Marfan's syndrome was reported to be about 45 years [4]. By 1995, follow-up of 417 patients in a multicenter study [5] revealed that median survival had improved to 72 years. Much of the improvement in overall survival appeared to be due to good outcomes of cardiovascular surgery [6-8].

There is still no agreement with regard to the best method of dealing with malfunction of the aortic valve caused by aneurysm or dissection of the aortic root. Aortic valve regurgitation in combination with dilatation of the ascending aorta and root usually requires a combined procedure to restore valve function and eliminate pathological dilatation of the proximal aorta. Since Bentall and De Bono [9] introduced the surgical technique of composite mechanical valve conduit replacement of a large aortic root aneurysm in 1968, various adaptations of the original concept have become the standard therapy for patients with an aortic root aneurysm. The main disadvantage of the Bentall technique is that the implanted Dacron graft contains a prosthetic aortic valve, mandating a permanent anticoagulation regimen which carries its own risks, especially in Marfan patients who often need to be operated at a young age.

In the last two decades two major techniques for aortic cusp sparing have been proposed, which confer the additional benefit of avoiding anticoagulation while reducing the incidence of thromboembolism [10]. The aortic root may be either remodeled with an especially configured vascular graft or replaced with reimplantation of the native aortic valve within the graft [11-13]. The common goal of these techniques is to retain the functioning of aortic valve leaflets while repairing or stabilizing the other components of the aortic root complex (aortic annulus, aortic sinuses, sinotubular junction, subvalvular region and ascending aorta).

Although still debated in the treatment of aortic root aneurysms in Marfan syndrome, valve-sparing techniques have shown favorable durability in mid-term and long-term studies [13-16]. In their 1999 study of 82 Marfan patients Birks et al. [17] reported that the actuarial survival of patients operated for chronic aneurysm was 94.2%, 94.2% and 94.2% at 1, 5 and 10 years, respectively; for acute dissection it was 72.7%, 63.6% and 63.6%; and for chronic dissection 100%, 85.7% and 75.0%. The probability of needing reoperation was 5.7%, 17.3% and 17.3% at 1, 5 and 10 years. In a recent study de Oliveira [18] and associates showed that freedom from valve-related mortality and morbidity was 65%

after root replacement and 100% after valve-sparing operation ($P = 0.02$). It was suggested that aortic valve-sparing surgery is safe in patients with Marfan syndrome and may provide a better clinical outcome than aortic root replacement.

The purpose of our study was to examine the results of aortic root surgery in patients with Marfan syndrome who needed surgical intervention due to aortic aneurysm or aortic dissection and to compare root replacement with root-sparing surgery.

Patients and Methods

From March 1994 to September 2007 we performed 40 aortic root procedures in Marfan patients. Marfan syndrome was diagnosed according to the revised criteria of De Paepe et al. [19]. A positive family history for Marfan syndrome was documented in four patients (10%). There were 31 males and 9 females, with a mean age of 37.9 ± 13.8 (range 15–68 years) at the time of surgery. Fourteen patients suffered from aortic dissection, 26 patients had thoracic aortic aneurysm, and 5 cases were emergent. Three patients who had aortic dissection underwent surgery while in cardiogenic shock. Table 1 presents the patients' clinical profile and operative techniques.

Operative procedures

The patients were divided into two groups according to two major types of aortic root operations: Group 1 included 20 patients who underwent root-sparing procedures using any of three techniques: group 1a – the reimplantation technique (David I) in 13 patients and group 1b – the remodeling technique (Yacoub or David II) in 4 patients. In group 1c, 3 other patients had elongated free margin of one or more aortic cusps that caused an aortic valve prolapse that was treated by plication of the free margin and resuspension of the valve with replacement of the sinotubular junction. Group 2 included 20 patients who underwent root replacement with composite graft containing a prosthetic aortic valve. Indications for surgery in the cases of aortic aneurysms mandated aortic root diameter of at least 4.5 cm with at least grade 2 aortic regurgitation. Table 2 presents the operative data.

Follow-up

Patients were followed and contacted annually by our outpatient Marfan clinic staff and our research personnel. The follow-up for this study was closed in September 2007. Mean follow-up at that time was 3.3 ± 3.5 years (range 0–12.8 years). It was 2.1 ± 2.6 years for patients undergoing root replacement and 4.4 ± 3.9 years for patients undergoing root sparing. No patient was lost to follow-up.

Statistical analysis

Data are reported as the mean ± SD for continuous variables and as frequencies and percentages for categorical variables. Comparisons between groups were made with unpaired *t*-tests for continuous variables and chi-square or Fisher's exact test for categorical variables. Estimates for long-term survival or freedom from reoperation were done by the Kaplan-Meier method.

Results

As anticipated, more patients with aortic dissection were operated on urgently than those who had aortic aneurysm (57.1% vs. 3.8%, $P = 0.0003$) and there were more emergent cases in this cohort of

Table 1. Clinical profile and operative techniques

	All cases (n=40)	Aortic aneurysm (n=26)	Aortic dissection (n=14)	*P*
Gender				NS
Male	31 (77.5%)	20 (77%)	11 (78.6%)	
Female	9 (22.5%)	6 (23%)	3 (21.4%)	
Age (yrs)				
Mean ± SD	37.9 ± 13.8	36.6 ± 13.7	40.29 ± 14.3	0.432
Range	15–68	15–68	21–63	
Timing of surgery				
Elective	26 (65%)	25 (96.2%)	1 (7.1%)	< 0.0001
Urgent	9 (22.5%)	1 (3.8%)	8 (57.1%)	0.0003
Emergency	5 (12.5%)	0	5 (35.7%)	0.003
Congestive heart failure	3 7.5%)	0	3 (21.4%)	0.03
Previous cardiac surgery	11 (27.5%)	9 (34.6%)	2 (14.3%)	0.26
Aortic valve replacement	2 (5%)	1 (3.8%)	1 (7.1%)	NS
Mitral valve replacement	2 (5%)	2 (7.7%)	0	0.53
CABG	1 (2.5%)	1 (3.8%)	0	NS
PDA closure	2 5%)	2 (7.7%)	0	0.53
Previous aortic root procedure				
Root remodeling	1 (2.5%)	1 (3.8%)	0	NS
Composite	1 (2.5%)	0	1 (7.1%)	NS
Hypertension	6 (15%)	3 (11.5%)	3 (21.4%)	0.64
Hyperlipidemia	6 (15%)	5(19.2%)	1(7.1%)	0.399
COPD	1(2.5%)	1 (3.8%)		NS
Smoking	2 (5%)	1 (38%)	1 (7.1%)	NS
Family history for Marfan syndrome	4 10%)	3 (11.5%)	1 (7.1%)	NS
Aortic regurgitation	25 (57%)	18 69.2%)	8 (57.1%)	0.501
Euroscore				
Standard (mean ± SD)	5.9 ± 2.09	5.9 ± 1.6	5.8 ± 3	0.924
Logistic (mean ± SD, %)	12.27 ± 14.62	10.56 ± 14	15.9 ± 16	0.434
NYHA (mean ± SD)	1.8 ± 0.9	1.86 ± 0.96	1.73 ± 1	0.724
Ejection fraction (mean ± SD, %)	54.55 ± 8.4	53.6 ± 8.7	58.7 ± 6.2	0.281
Preoperative creatinine (mean ± SD, mg/dl)	0.8 ± .17	0.85 ± 0.15	0.87 ± 0.26	0.885
BSA (mean ± SD)	2 ± 0.22	1.9 ± 0.2	2.1 ± 0.2	0.109
Operative techniques				
Root sparing	20 (50%)	15 (57.7%)	5 (35.5%)	.320
Reimplantaiom	13 32.5%)	11 (42.3%)	2 (14.3%)	0.089
Remodeling	4 (10%)	3 11.5%)	1 (7.1%)	NS
Aortic valve repair + STJ replacement	3 (7.5%)	1 (3.8%)	2 (14.3%)	0.276
Root replacement	20 (50%)	11 42.3%)	9 (64.3%)	0.320

STJ = sinotubular junction, CABG = coronary artery bypass grafting, PDA = patent ductus arteriosus, COPD = chronic obstructive pulmonary disease, NYHA = New York Heart Association, BSA = body surface area, NS = non significant.

Table 2. Root replacement vs. root sparing – Patient characteristics, operative data and follow-up

	All (n=40)	Root replacement (n=20)	Root sparing (n=20)	*P*
Patient characteristics				
Age (mean ± SD, yrs)	37.90 ± 13.86	41.10 ± 13.57	34.70 ± 13.7	0.14
Gender				NS
Male	31(77.5%)	16(80%)	15(75%)	
Female	9 (22.5%)	4 (20%)	5 (25%)	
Diagnosis				
Dissection	14 35%)	9 (45%)	5 (25%)	0.32
Aneurysm	26 (65%)	11 (55%)	15 (75%)	0.32
Previous cardiac surgery	11 (27.5%)	9 (45%)	2 (10%)	0.03
Standard Euroscore (mean ± SD)	5.9 ± 2.09	6.2 ± 2.4	5.2 ±0i755	0.08
Logistic Euroscore (mean ± SD)	12.27 ± 14.62	11.87 ± 13.3	12.9 ± 17.5	0.83
Preoperative ejection fraction (mean ± SD, %)	54.55 ± 8.4	55 ± 7.9	54 ± 9.3	0.71
Preoperative creatinine (mean ± SD, mg/dl)	0.85 ± 0.179	0.89 ± 0.18	0.80 ± 0.16	0.1
Timing				
Elective	26 (65%)	10 (50%)	16(80%)	0.09
Urgent	9 (22.5%)	6 (30%)	3 (15%)	0.45
Emergency	5 (12.5%)	4 (20%)	1 (5%)	0.34
Operative data				
Bypass time (mean ± SD, min)	182.5 ± 50.6	173.2 ± 58.4	193.23 ± 39.4	0.21
Cross-clamp time (mean ± SD, min)	136.5 ± 29.7	122.7 ± 27.1	153.9 ± 23.7	0.0004
Circulatory arrest time (mean ± SD, min)	30.125 ± 17.4	32 ± 17.9	27 ± 17.9	0.38
Follow-up				
ICU length of stay (mean ± SD, hrs)	43.6 ± 39.6	47.2 ± 43.5	38.2 ± 34.6	0.47
Time on mechanical ventilation (mean ± SD, hrs)	16.2 ± 27.4	15.4 ± 27.1	17.4 ± 29.6	0.82
Postoperative bleeding (mean ± SD, ml)	418.5 ± 497.5	401.07 ± 351.8	443.00 ± 672.7	0.80
Total hospital stay (mean ± SD, days)	11.08 ± 7.239	11.67 ± 6.6	10.53 ± 7.9	0.62
Mortality				
Overall	4 (10%)			
Operative*	3 7.5%)	2 (10%)	1 (5%)	NS
Late	1 (2.5%)	0	1 (5%)	NS

* Up to 30 days from surgery

ICU = intensive care unit, NS = no significant

patients (35% vs. 0%, *P* = 0.03) [Table 1]. There was no significant difference in age, gender and timing of surgery between group 1 and group 2. Patients undergoing root replacement had more previous cardiac surgery compared to patients undergoing root sparing (9 vs. 2, *P* = 0.03). The mean logistic Euroscore was 12.27 ± 14.6% for the whole group. Mean preoperative ejection fraction and logistic Euroscore were similar in both groups: 55% ± 7.9% vs. 54.7% ± 9.3% (*P* = 0.71), and 11.87 ± 13.3 vs. 12.9 ± 17.5 (*P* = 0.83), respectively [Table 2].

Early results

Patients undergoing root-sparing operations had longer cross-clamp time than those undergoing root replacement (153.9 ± 23.7 vs.122.7 ± 27.1 minutes, *P* = 0.0004). There was no significant difference in postoperative bleeding, duration of mechanical ventilation, mean intensive care unit time, and total hospital stay in both groups.

Overall mortality was 10% (n=4): 2 patients had aortic aneurysm and 2 had aortic dissection (NS). Hospital mortality (up to 30 days after surgery) was 10% (n=2) in group 2 (root replacement) and 5% (n=1) in group 1 (root sparing) (NS). All-hospital mortality occurred in patients who were operated urgently or emergently. The cause of death in all was low cardiac output syndrome. There was no hospital mortality among the 26 patients who were operated on electively [Table 2].

Late results

Freedom from reoperation 5 years post-surgery was 86% in group 2 (root replacement) and 70% in group 1 (root sparing) (*P* = 0.6) [Figure 1]. Three patients from group 1b (root-sparing – remodeling technique) were reoperated: two patients at 3 years after the first operation and one patient after 4 years. All three had symptoms of congestive heart failure due to severe aortic regurgitation. No patient from group 1a (the reimplantation cohort) needed reoperation within this study period.

One patient from group 1 (root sparing) died 9 years after his surgery. The 5 year freedom from death was 95% after root sparing and 90% after root replacement (*P* = 0.6) [Figure 2]. One patient from the root replacement group was reoperated 1 year after his primary operation due to endocarditis.

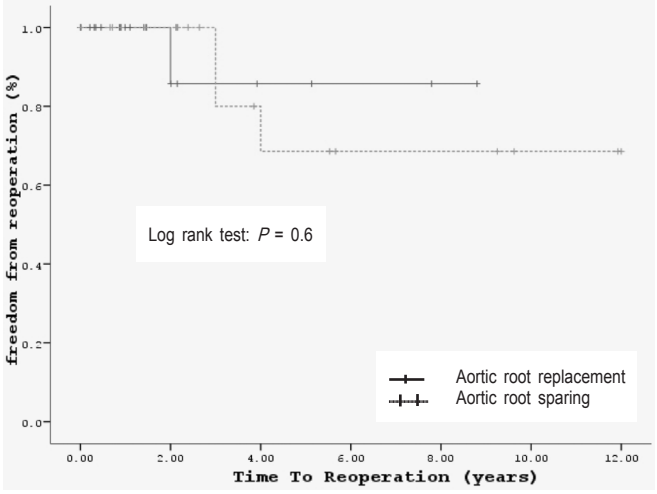

Figure 1. Freedom from reoperation

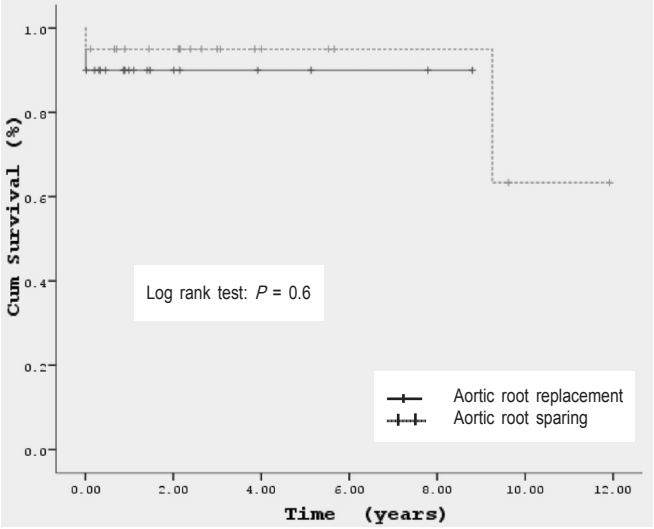

Figure 2. Freedom from death

Discussion

Marfan syndrome is an autosomal dominant connective tissue disorder, with potentially life-threatening cardiovascular manifestations [20]. Dilatation of the aortic root is a well-known cardiovascular manifestation in children and adults with Marfan syndrome. Dilatation of the ascending aorta in Marfan syndrome is extremely rare and may be associated with bicuspid aortic valve. The mechanism causing aortic valve insufficiency is usually the enlargement of one or more components of the aortic root complex (e.g., aortic sinuses and/or annulus), hence the moving of the aortic valve cusps away from their optimal coaptation line. Aortic dissection, on the other hand, occurs in up to 20% of Marfan patients. In this condition, aortic valve incompetence may occur due to dilatation of the sinotubular junction with acute distraction of the valve leaflets, and/or unhinging and prolapse of the leaflets secondary to sinus wall dissection [21].

Broadly speaking, there are two common approaches for repairing the dilated or dissected aortic root that has aortic valve incompetence: a) root replacement using a composite graft containing a prosthetic valve, and b) reconstruction using the reimplantaion, remodeling or other valve-sparing techniques that can be used when there is no leaflet damage [22,23]. Although still under debate for the treatment of aortic root aneurysms in patients with Marfan syndrome, valve-sparing techniques have shown favorable durability in mid-term and long-term studies [13-16]. An alternative approach using a bio-glue (gelatin-resorcine-formaldehyde/glutaraldehyde glue) without graft replacement for localized aortic dissection repair has not been adopted by the mainstream because of the high incidence of reoperation [24]. Similarly, plication aortoplasty and wrap for aortic dilatation have not been favored either.

We have been using the reconstructive approach to the aortic valve since 1994 in almost 60% of the cases of aortic root aneurysms and dissections. In recent years, we extended the reconstructive approach further to the normal aorta and prolapsed leaflets, which in some cases gave rise to pure aortic valve incompetence. In the current study, 50% of the cases were treated by reconstructive techniques.

Of the 105 Marfan patients studied by De Oliveira and coworkers [18], 44 underwent aortic root replacement and 61 had aortic valve-sparing surgery for aortic root aneurysm. Survival at 10 years was 87% in the aortic root replacement group and 96% in the aortic valve-sparing group ($P = 0.3$). Freedom from reoperation at 10 years was 75% in the root replacement group and 100% in the valve-sparing group ($P = 0.1$). Freedom from valve-related mortality and morbidity was 65% after root replacement and 100% after valve-sparing surgery ($P = 0.02$). Freedom from aortic insufficiency (greater than 2+) after aortic valve-sparing surgery was 75% at 10 years and was similar for both types of valve-sparing operations. However, the diameters of the aortic annulus and neoaortic sinuses increased after the remodeling procedure only. De Oliveira et al. [18] concluded that the reimplantation technique may be more appropriate than remodeling the aortic root to prevent dilatation of the aortic annulus; they now use the reimplantation technique exclusively to treat patients with Marfan syndrome.

Although it was not statistically different, the results of aortic root replacement in our series appeared to be superior to the valve-sparing approach in terms of freedom from reoperation after 5 years (86% vs. 70%, $P = 0.6$). This finding might be explained by the fact that all recurrences occurred in patients who underwent remodeling technique and in whom reoperation was needed due to severe aortic valve regurgitation, secondary to subsequent continuous aortic annulus dilatation. Accordingly, the remodeling technique, not the reimplantation technique, may be considered accountable for this higher rate of recurrence.

In a prior work [25] we described our experience, rationale, and development of valve-preserving techniques. In that study of 129 patients undergoing valve-sparing surgery for aortic root and ascending aorta aneurysm or dissection, we found that the reimplantation technique provided a more stable repair with lower rate of recurrence of aortic regurgitation (grade 2+ or more) and higher rate of freedom from reoperation after 5 years than the remodeling technique.

In the present study, all-hospital mortality occurred after urgent or emergent operations and there was no hospital mortality after elective procedures. The 5 year survival was 95% after root sparing and 90% after root replacement ($P = 0.6$). Although a late postoperative echocardiographic follow-up was not completed 100% for all patients, we postulate that this difference in late mortality is due to prosthetic valve-related complications that are anticipated in the replacement group.

Small sample sizes and the lack of a complete postoperative echocardiographic follow-up contributed to the limitations of our study. Efforts are underway to correct these lacunae.

Conclusions

This study indicates that the survival of patients with Marfan syndrome seems to be similar after both approaches: root-sparing surgery and root replacement. However, the former carries a higher incidence of late reoperations, especially when using the

remodeling technique. This observation has been corroborated by similar studies. Aortic valve function appears to deteriorate with time in some patients due to ongoing annular and neosinus dilatation, especially in those undergoing remodeling. Currently we prefer to use reimplantation over the remodeling technique to treat patients with Marfan syndrome.

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