Aortic Root Operations for Marfan Syndrome: A Comparison of the Bentall and Valve-Sparing Procedures

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Background. We compared results of the Bentall procedure with valve-sparing aortic root replacement (VSRR) for aortic root aneurysm in Marfan syndrome.

Methods. Marfan syndrome patients who had the Bentall procedure or VSRR at our institution between April 1997 and September 2006 were identified. Follow-up information was obtained from hospital charts and contact with patients or their physicians. Kaplan-Meier survival and propensity score analyses were performed.

Results. One hundred forty Marfan syndrome patients had either the Bentall procedure (n = 56) or VSRR (n = 84; 40 remodeling and 44 reimplantation). Bentall patients were older than VSRR patients (38 versus 29 years; $p = 0.0001$) and had more aortic dissections (16% versus 1%; $p = 0.0012$); more urgent/emergent surgery (20% versus 2%; $p = 0.0008$); larger preoperative sinus diameter (5.7 versus 5.1 cm; $p = 0.0004$); and more preoperative 3+/4+ aortic insufficiency (59% versus 10%; $p < 0.0001$). There were no operative deaths. Postoperatively, 9% Bentall patients (5 of 56) and 1% of VSRR patients (1 of 84) suffered thromboembolic events ($p = 0.03$). Two percent (1 of 56) of Bentall patients required reoperation on the aortic root versus 6% of VSRR patients (5 of 84; $p = 0.40$). Eight-year freedom from aortic valve replacement was 90% for VSRR patients. Eight-year survival was 90% for Bentall and 100% for VSRR patients ($p = 0.01$). Propensity-adjusted regression showed that the Bentall procedure did not predict mortality ($p = 1.00$) and did not protect from reoperation (odds ratio = 0.28; 95% confidence interval: 0.01 to 4.33; $p = 0.36$).

Conclusions. The Bentall procedure and VSRR have similar operative results in Marfan syndrome. The procedures are distinguished by higher rates of thromboembolism among Bentall patients and higher rates of reoperation among VSRR patients. Lower late survival among Bentall patients probably reflects the preferential use of the Bentall procedure for higher risk patients.

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Marfan syndrome (MFS) is a systemic disorder of connective tissue inherited in an autosomal dominant fashion and caused by mutations in the gene encoding fibrillin-1, an extracellular matrix protein that aggregates to form extracellular microfibrils [1]. Rupture of aortic root aneurysm and aortic dissection are the primary causes of premature death in MFS [2], so prophylactic aortic root replacement is often recommended. Traditionally, the Bentall procedure [3] has been the operation of choice for aortic root and valve disease; it has demonstrated excellent long-term outcomes and has dramatically improved life expectancy [4–6]. However, replacing the aortic valve with a mechanical prosthesis necessitates long-term anticoagulation therapy, and bioprosthetic valves degenerate and lead to reoperative aortic valve replacement (AVR).

Many MFS patients have grossly normal aortic valve leaflets that may not need replacement, making valve-sparing aortic root replacement (VSRR), originally described by Sarsan and Yacoub [7] and David and Feindel [8], an attractive option for MFS patients. Although some studies have demonstrated good outcomes after VSRR in MFS patients [9–12], many surgeons remain skeptical about aortic valve preservation in MFS because of fear of late valve failure. We reviewed our results with MFS patients who had the Bentall procedure with those of a group of MFS patients who had VSRR to compare rate of reoperation and late complications between the groups.

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Material and Methods

Study Design, Patient Selection, and Patient Variables

After Institutional Review Board approval, data were collected retrospectively for all patients with clinical or molecular evidence of MFS who underwent the Bentall operation or VSRR between 1997 and 2006 at our institution. Data were obtained from medical and electronic patient records. A waiver for individual consent was granted by our Institutional Review Board.

All VSRR patients had transthoracic echocardiograms to assess preoperative and postoperative aortic valve function. Intraoperative transesophageal echocardiograms were routinely obtained. Echocardiographic data included maximum aortic sinus diameter and the degree of aortic insufficiency (AI [0 to 4+]). Clinical follow-up data, including need for reoperation on the aortic root and bleeding and thromboembolic events, were obtained by telephone interview with the patient, family members, or primary care physicians. For follow-up, all VSRR patients are recommended to have an echocardiogram, computed tomography scan, or magnetic resonance imaging at 6 months, and then annually thereafter.

Some MFS patients were not offered VSRR. Our relative contraindications for VSRR for MFS patients include preoperative annular diameter greater than 34 mm, marked leaflet fenestration and asymmetry, acute aortic dissection in unstable patients, or a giant root with marked leaflet irregularities. For these patients, a Bentall procedure was preferred. We do not perform VSRR on bicuspid valves with calcification, prolapse, thickening, or fenestrations.

Operative Technique

Patients who had the Bentall operation underwent aortic root replacement with composite grafts using standard methods. Our operative technique for VSRR has been described in detail elsewhere [13, 14]. Early in our VSRR experience, we favored the remodeling technique (Yacoub/David II), but in some patients, late AI developed owing to annular dilatation and subsequently required AVR [15]. Since 2002, we have preferred the reimplantation technique using the Valsalva graft, which has prefashioned pseudosinuses, and when used with the reimplantation technique has the advantage of improved annular stabilization and better hemostasis [14].

Postoperative Care

All VSRR patients in this study were maintained on a regimen of aspirin for 1 month and long-term β-blockers indefinitely. A recent finding that losartan, an angiotensin II type I receptor antagonist, slows aneurysmal growth in mouse models of MFS has led to use of this drug in the management of some patients with MFS [16]. Patients who had the Bentall operation were maintained on a life-long regimen of sodium warfarin, as appropriate. We aim for a target international normalized ratio of 2.5 to 3 for all Bentall patients. Many of these patients are taking aspirin; in our experience, a composite graft has a slightly lower annual thromboembolism rate when compared with St. Jude mechanical aortic valves, and thus, the target acceptable international normalized ratio, in our opinion, can be approximately 0.5 less.

Statistical Analyses

Statistical analyses were conducted with Stata, version 9.0 (Stata Corp, College Station, Texas) software package. Preoperative and postoperative variables were compared between Bentall and VSRR patients using Student's *t* test or Fisher's exact test. Survival and freedom from reoperation of the aortic root was estimated using the Kaplan-Meier method and compared between Bentall and VSRR groups with log-rank analysis. We also compared freedom from reoperation for the Bentall, VSRR remodeling, and VSRR reimplantation groups.

In addition, we calculated propensity scores for each patient to control for potential selection bias for the Bentall operation over VSRR. Variables included in the propensity score model were age, sex, preoperative AI, preoperative maximum sinus diameter, bicuspid aortic valve, aortic dissection, and urgent/emergent surgery. We then performed a propensity score adjusted Cox regression analysis to assess whether the Bentall operation predicted mortality and a propensity score adjusted logistic regression analysis to assess whether the Bentall operation protected from the need for reoperation. All continuous variables are presented as mean ± SD, unless otherwise noted.

Results

Preoperative Clinical Characteristics

A total of 140 patients with MFS underwent the Bentall operation or VSRR between April 1997 and September 2006. Fifty-six had the Bentall operation and 84 had VSRR. In the VSRR group, the initial 40 patients under-

Table 1. Baseline Clinical Characteristics

	Bentall n = 56 (%)	VSRR n = 84 (%)	*p* Value
Mean age at operation (years)	38.1 ± 14.1	29.2 ± 12.3	0.0001
Pediatric patients (less than 18 years)	5 (8.9)	19 (22.6)	0.04
Male	35 (62.5)	61 (72.6)	0.26
Indications for VSRR			
Aortic root aneurysm	55 (98.2)	84 (100)	0.40
Aortic dissection	9 (16.1)	7 (12.5)	0.0012
Bicuspid aortic valve	1 (1.2)	1 (1.2)	0.007
Preoperative maximum sinus diameter (cm)	5.7 ± 1.4	5.1 ± 0.5	0.0004
Preoperative 3+/4+ aortic insufficiency	33 (58.9)	8 (9.5)	<0.0001
Emergent/urgent preoperative status	11 (19.6)	2 (2.4)	0.0008

AI = aortic insufficiency; VSRR = valve-sparing aortic root replacement.

Table 2. Operative Data

	Bentall n = 56 (%)	VSRR n = 84 (%)	*p* Value
Mean cross-clamp time (minutes)	115.2 ± 60.4	102.6 ± 14.7	0.06
Mean CPB time (minutes)	161.2 ± 83.0	141.7 ± 22.7	0.04
Concomitant procedures			
PFO closure	13 (23.2)	32 (38.1)	0.06
ASD	2 (3.6)	2 (2.4)	1.00
Mitral valve replacement	7 (12.5)	0 (0)	0.0013
Mitral valve repair	2 (3.6)	3 (3.6)	1.00
CABG	5 (8.9)	0 (0)	0.0092
PDA ligation	0 (0)	2 (2.4)	0.51

ASD = atrial septal defect; CABG = coronary artery bypass graft surgery; CPB = cardiopulmonary bypass; PDA = patent ductus arteriosus; PFO = patent foramen ovale; VSRR = valve-sparing aortic root replacement.

Table 3. Postoperative Complications

	Bentall n = 56 (%)	VSRR n = 84 (%)	*p* Value
In-hospital			
Pneumothorax	1 (1.8)	4 (4.8)	0.64
Pleural effusion	2 (3.6)	2 (2.4)	1.00
Bleeding requiring reoperation	2 (3.6)	0 (0)	0.15
Atrial fibrillation	5 (8.9)	8 (9.5)	1.00
Sternal wound infection	2 (3.6)	1 (1.2)	0.56
Late			
Endocarditis	0 (0)	0 (0)	1.00
Bleeding events	0 (0)	2 (2.4)	0.51
Thromboembolism	5 (8.9)	1 (1.2)	0.03
Reoperation on the aortic root	1 (1.8)	5 (6.0)[a]	0.40

[a] All 5 VSRR patients requiring reoperation on the aortic root underwent aortic valve replacement.

VSRR = valve-sparing aortic root replacement.

went aortic root remodeling procedure (April 1997 to July 2002) whereas the most recent 44 patients underwent the reimplantation procedure using the Valsalva graft (July 2002 to September 2006). Bentall patients were significantly older than VSRR patients at operation and were more likely to have aortic dissection or bicuspid aortic valve (Table 1). Bentall patients were also more likely to have urgent/emergent surgery, larger preoperative maximum sinus diameter, and more preoperative 3+/4+ AI (Table 1).

Operative Data

Operative data are shown in Table 2. Mean cross-clamp time was significantly longer in the Bentall group; significantly more Bentall patients had concomitant mitral valve replacement and coronary artery bypass grafting. Approximately one third of Bentall and VSRR patients had a patent foramen ovale, which was closed concomitantly at the time of operation.

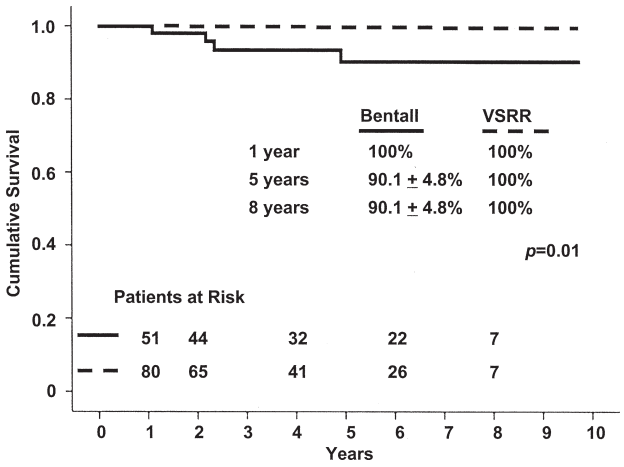

Fig 1. Kaplan-Meier survival for patients with Marfan syndrome who had the Bentall operation (solid line) versus valve-sparing aortic root replacement (VSRR [broken line]).

Survival and Functional Class

There were no operative or in-hospital deaths among elective, emergent, or urgent cases in either the Bentall or VSRR group. Kaplan-Meier survival at 8 years was 90.1% ± 4.8% for Bentall patients and 100% for VSRR patients ($p = 0.01$; Fig 1). There were 4 late deaths in the Bentall group but none in the VSRR group ($p = 0.02$). Cause of death among the 4 Bentall patients was unknown in 3 cases; the fourth late death was a patient who died intraoperatively during a repair of a thoracoabdominal aortic aneurysm 1 year after his Bentall operation. Preoperative maximum sinus diameters for the 4 deaths in the Bentall group were 6 cm, 13 cm, 8.5 cm, and 5.8 cm. All 4 Bentall patients had moderate or severe AI preoperatively, and 2 of the 4 were operated on urgently. Of 52 survivors in the Bentall group, 94.2% (49 of 52) were New York Heart Association (NYHA) functional class I at follow-up, and the remaining 5.8% (3 of 52) were NYHA functional class II. Similarly, 94.0% (79 of 84) of VSRR patients were NYHA functional class I at follow-up; the remaining 6.0% (5 of 84) were NYHA functional class II.

Postoperative Complications

In-hospital complication rates were similar in Bentall and VSRR patients (Table 3). Thromboembolic events were more frequent after the Bentall operation than after VSRR (Table 3). Of the 5 Bentall patients who had thromboembolism, 1 patient suffered a right lower extremity deep vein thrombosis, a second patient's aortic valve prosthesis had a thrombosis and required reoperation, a third had a right renal artery thrombosis, a fourth had a transient cerebral ischemic attack, and a fifth had a right hemisphere stroke. The 1 VSRR patient who shad a thromboembolic event had a brachial artery thrombosis.

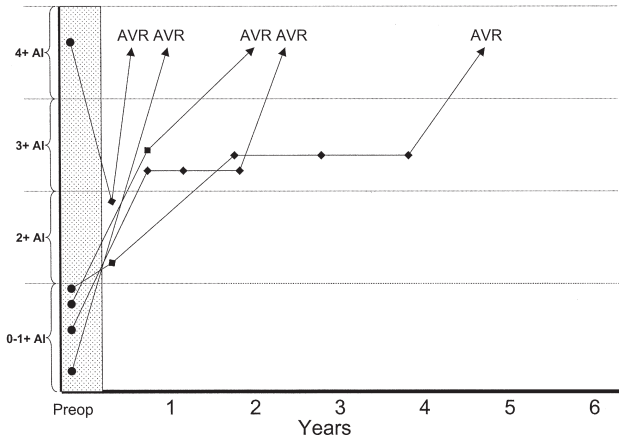

Fig 2. Postoperative echocardiography results in the 5 patients who required aortic valve replacement (AVR) after valve-sparing aortic root replacement using the remodeling technique. No patient who had reimplantation with the Valsalva graft has had AVR. (AI = aortic insufficiency; Preop = preoperative; circles = preoperative echocardiogram; diamonds = postoperative echocardiogram; arrowheads = late AVR; solid = David II remodeling.)

Two Bentall and 2 VSRR patients had postoperative bleeding events (Table 3). The 2 Bentall patients required reoperation for bleeding during their hospital stay, but no Bentall patient had a late postoperative bleeding event. The 2 VSRR patients had bleeding events at late follow-up: the one had a ruptured brain aneurysm that required craniotomy and had no residual neurologic deficits; the other patient had rectal bleeding that resolved spontaneously. No VSRR patient required reoperation for bleeding during hospitalization. There were no episodes of endocarditis or coronary artery anastamotic dehiscence in either group.

Reoperation on the Aortic Root

Reoperation on the aortic root occurred in 1 Bentall patient and 5 VSRR patients (Table 3). The single Bentall patient who underwent reoperation had a thrombosed aortic valve prosthesis owing to poor compliance with anticoagulant therapy. He had a redo sternotomy and had his aortic valve replaced with a bioprosthetic valve. All 5 VSRR patients who had reoperation required late AVR for valvular incompetence owing to annular dilation after the David II remodeling operation. The progression of AI in the 5 remodeling patients who required AVR is illustrated in Figure 2. No patient who had a reimplantation VSRR with the Valsalva graft has required reoperation for valve failure. Freedom from reoperation on the aortic root was 95.8% ± 5.1% for the Bentall group and 90.4% ± 4.3% for the VSRR group at 8 years (Fig 3). When comparing Bentall, reimplantation VSRR, and remodeling VSRR patients, freedom from reoperation on the aortic root was 95.8% ± 5.1% for the Bentall patients at 8 years, 100% for reimplantation VSRR patients at 4.5 years, and 86.1% ± 5.8% for remodeling VSRR patients at 8 years (Fig 4). No MFS patient who had the reimplantation procedure with the Valsalva graft has greater than 2+ AI at follow-up. In addition to the 5 MFS patients who required AVR for valvular incompetence after root remodeling, 3 other remodeling patients have 3+ AI (at 3.7, 4.7, and 7 years after operation), and 1 remodeling patient has 3 to 4+ AI (at 8.2 years after operation) at follow-up; these patients are being closely followed and will likely require AVR.

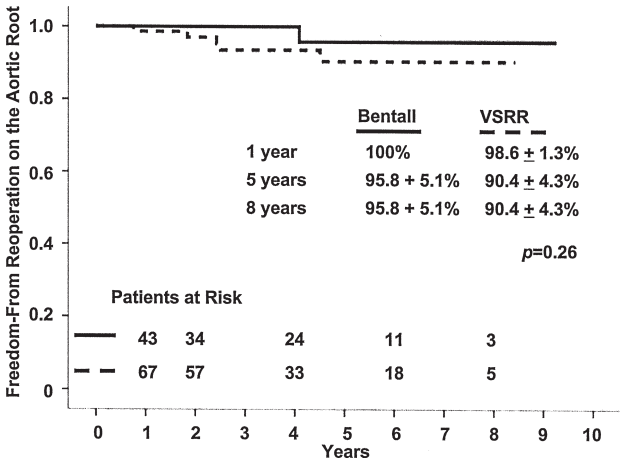

Fig 3. Freedom from reoperation on the aortic root for patients with Marfan syndrome who had the Bentall operation (solid line) versus valve-sparing aortic root replacement (VSRR [broken line]).

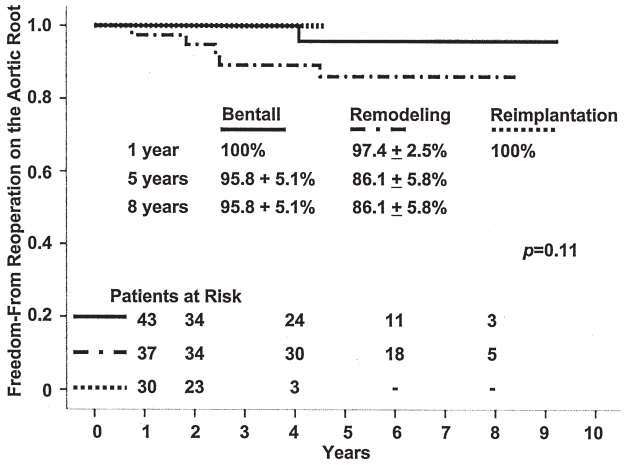

Fig 4. Freedom from reoperation on the aortic root for patients with Marfan syndrome who had the Bentall operation (solid line) versus root remodeling (broken line) versus reimplantation (dotted line) with the Valsalva graft.

Propensity Score Analysis

Propensity scores were significantly different between Bentall and VSRR groups (0.64 versus 0.22; $p < 0.0001$; range, 0.01 to 0.99). Propensity score adjusted Cox regression modeling showed that the Bentall procedure was not a predictor of late mortality ($p = 1.00$). Also, propensity score adjusted logistic regression showed that the Bentall operation did not protect from the need for reoperation (odds ratio = 0.28; 95% confidence interval: 0.01 to 4.33; $p = 0.36$).

Comment

The Bentall operation is the gold standard of surgical treatment for MFS patients with aortic root aneurysm [5]. In a multicenter review by Gott and colleagues [5], 5-year cumulative survival after aortic root replacement was 85%. In that study, operative mortality was 1.5% for elective repair, 2.5% for urgent repair, and 11.7% for emergent repair [5]. Importantly, this study reported a linearized rate of thromboembolism among MFS patients who had composite root replacement of 0.62 events per 100 patient-years, and freedom from thromboembolism was 90% at 20 years. The study also reported freedom from endocarditis of 84% at 20 years. Despite excellent results after the Bentall operation, replacement of the aortic valve with a mechanical prosthesis carries a significant risk of anticoagulant-related morbidity. Valve-sparing aortic root replacement is an attractive alternative for some MFS patients with normal or near-normal aortic valves because it avoids mechanical valve replacement and anticoagulation, but late valvular incompetence remains its Achilles heel.

We recently reported our experience with aortic root replacement in 271 patients with MFS from 1976 to 2000; 232 had composite graft replacement, 15 received a homograft, and 24 had VSRR [6]. We reported no operative mortality among 235 MFS patients undergoing elective aortic root replacement. Survival at 20 years was 67%, and multivariate analysis identified New York Heart Association class and urgent operation as independent predictors of early or late death. Importantly, 15 patients had thromboembolism, 11 had endocarditis, and 3 had coronary dehiscence at late follow-up. Freedom from reoperation on the residual aorta was 74% at 20 years. Because only 24 patients in that study had VSRR, no meaningful comparison between the Bentall and VSRR procedure could be made at that time.

A recent study by Karck and colleagues [12] reported 119 MFS patients who had composite graft replacement or VSRR using the reimplantation technique over a 23-year period. The authors demonstrated similar operative results for each group. Survival at 5 years was 89% after composite root replacement and 96% after reimplantation, an insignificant difference. Five-year freedom-from reoperation was 92% after composite root replacement and 84% after reimplantation VSRR, which was also not significant. Six patients who had composite root replacement required reoperation for problems related to the composite graft. Reoperation was required in 4 patients who had reimplantation owing to aortic cusp prolapse and inadequate primary repair. Importantly, 23% of patients who had composite root replacement versus 2% of patients who had reimplantation suffered thromboembolic or bleeding events. The authors admitted that their study provided limited comparability between groups because of the different lengths of follow-up: mean follow-up was 9.5 years for Bentall patients but only 2.5 years for reimplantation patients.

In this study we, too, compared our results with the Bentall and VSRR operation in patients with MFS. To minimize differential length of follow-up in each group, we limited the review to a recent period (1997 to 2006) when both the Bentall operation and VSRR were offered. Thus, mean follow-up was similar: 4.8 years in the Bentall group and 4.5 years in the VSRR group. Despite limiting the study to 10 years, our collaboration with the Johns Hopkins Marfan Center has allowed us to include a relatively large number of patients, comparable with that of other studies reporting experience over 20 years or more [12, 17, 18].

It was gratifying to observe no operative or in-hospital deaths for the 140 MFS patients who had urgent, emergent, or elective cases in either Bentall or VSRR groups. However, late survival was significantly lower in the Bentall group on log-rank analysis, which we believe is because of our preferential use of this procedure for higher risk patients: the MFS Bentall patients were more likely to have 3+/4+ AI preoperatively, more likely to have aortic dissection, and more frequently had urgent or emergent surgery than VSRR patients. Furthermore, Bentall patients had a higher rate of concomitant coronary artery bypass grafting and mitral valve procedures, which may also contribute to lower survival. The preference for mitral valve repair over replacement among VSRR patients reflects our desire to avoid anticoagulation therapy by repairing the mitral valve when possible. The Bentall group was significantly older and had fewer pediatric patients than the VSRR group, which also reflects our preference to spare the valve and avoid anticoagulation treatment for young patients. Survival was 90% for the Bentall group and 100% for the VSRR group at 8 years; this difference was statistically different and comparable with other studies reporting on composite root replacement or VSRR in Marfan and non-Marfan patients [5, 6, 9–12, 17–21]. However, when adjusting for propensity scores, Cox regression found that the Bentall operation did not predict mortality, highlighting that the differences in mortality more likely reflect patient selection for the Bentall operation over VSRR, rather than the Bentall operation itself.

Although significantly more Bentall patients than VSRR patients had thromboembolism postoperatively, the rates of thromboembolism, endocarditis, bleeding events, and coronary dehiscence were low in both groups. That can be attributed to improvements in operative technique and graft design. Unfortunately, noncompliance with anticoagulants continues to contribute to late thromboembolism. One Bentall patient in this series stopped taking his warfarin for several months and his mechanical aortic valve thrombosed, requiring reoperation and replacement with a bioprosthesis. We demonstrated more frequent aortic root reoperations among VSRR patients, but that was not statistically significant when compared with the Bentall patients. All VSRR patients who required reoperation had AVR for valvular incompetence after initially undergoing a David II/Yacoub root remodeling procedure. Propensity score adjusted logistic regression modeling showed that the Bentall operation did not protect from the need for reoperation over VSRR; we believe that outcome was due

to improvements in valve-sparing surgery from a large experience at our institution.

Valve-sparing root replacement operations have undergone significant technical modification over the years. We began our experience with the remodeling procedure (David II/Yacoub remodeling) [15] because we believed that preservation of sinuses was important for long-term aortic root function. Experimental studies have shown that sinuses are important for optimal aortic root function and minimal leaflet stress [22–25]. In our initial experience with VSRR [15], significant AI developed in 9 remodeling patients and they required late valve replacement; annular dilatation was the culprit in 8 of these patients [15]. The reimplantation technique (David I) stabilizes the annulus better [19–21, 26, 27], but in its original form used straight tube grafts that did not preserve sinuses. Although results after reimplantation with straight tube grafts have been good [19–21], the absence of sinuses may contribute to leaflet stress and valve failure in the long-term. This concern has led to technical modifications of the reimplantation procedure; the David IV operation utilizes oversized grafts and the David V operation utilizes two grafts of different sizes to create billowing neosinuses [26]. Proponents of the David V operation argue that using two different grafts allows the surgeon to tailor the operation for all possible aortic root dimensions, including annular diameter, sinus diameter, sinotubular junction diameter, and sinus and commissure height [26].

After some of our initial remodeling patients developed significant AI, we switched to a modified David I reimplantation procedure using the Valsalva graft, which has prefashioned pseudosinues [28–30]. Our procedure differs from the original David I reimplantation technique in that only three subannular sutures are placed. The subannular sutures serve only to anchor the base of the graft below the annulus, holding the entire aortic valve complex within the graft, and are not hemostatic. We believe that use of the Valsalva graft in a reimplantation procedure provides the "best of both worlds" (annular stabilization and preservation of sinuses); this has been our procedure of choice since 2002. Importantly, the size of the graft is based on the optimal sinotubular junction size determined intraoperatively. Graft size selection is determined once the aorta is divided above the sinotubular junction. We determine the optimal sinotubular junction diameter using valve-sizers and select a graft that is 2 to 3 mm larger as the graft will sit outside the aortic valve complex. Most patients in our experience have had optimal sinotubular junction diameters of 28 to 30 mm, and so most patients receive a 30- to 32-mm graft. We have not found that measurement of leaflet dimension and formulas for graft selection are useful. The Valsalva graft is available in sizes 24 to 34 mm, which can accommodate the majority of MFS aortic roots. Although patients with annular diameter greater than 34 mm may undergo VSRR, in our experience, these patients typically have thin, stretched out leaflets and often have severe AI with marked leaflet abnormalities.

In a study reported by de Oliveira and David [11], the authors reviewed their results with 105 MFS patients who had composite root replacement or VSRR. Survival at 10 years was 86% after composite root replacement and 96% after VSRR. Freedom from reoperation at 10 years was 75% in the root replacement group and 100% in the VSRR group, although 10-year freedom from greater than 2+ AI was 75% for VSRR patients. In a recent study from the same center, the authors reported their results with reimplantation VSRR; 10-year survival was 92%, freedom from moderate or severe AI was 94%, and freedom from AVR was 95% [27]. Forty-seven percent of patients underwent reimplantation with oversized grafts in an effort to create neosinuses. In that study, the authors speculated that the Valsalva graft may lead to poor valve durability because it creates spherical sinuses and alters optimal aortic root geometry.

On the other hand, De Paulis and coworkers [31] assessed opening and closing characteristics of the aortic valve and showed normalization of aortic root structure and physiology after reimplantation with the Valsalva graft. The authors also showed a sufficient gap between the opened aortic leaflet and Dacron wall to avoid leaflet abrasion (a concern with straight tube grafts), and demonstrated preserved slow closing displacement and preserved compliance of the graft, which contributes to decreased mechanical stress on the aortic leaflets and may improve valve durability [31]. Furthermore, in our initial report of 51 patients who had reimplantation with the Valsalva graft, no patient had greater than 2+ AI at midterm [14]. In this current study, no MFS patient who had reimplantation with the Valsalva graft has had greater than 2+ AI, and none has required reoperation or AVR. Similar results with VSRR using the Valsalva graft have also been reported elsewhere [9]. A recent multicenter study of MFS patients who had reimplantation VSRR with the Valsalva graft demonstrated survival was 100% at midterm, but 3 of 35 MFS patients in that study required AVR for significant AI [9]. The authors attributed the late valvular incompetence to an inappropriately undersized prosthesis in 1 patient, endocarditis in a second patient, and abnormally stretched aortic leaflets in a third.

Surgeon experience and patient selection are important factors for good outcomes after VSRR. We recommend the Bentall procedure for patients with severe AI who have marked leaflet asymmetry or leaflet fenestrations, and for patients with bicuspid valves with significant stenosis, thickening, prolapse, or fenestrations. Although 1 MFS patient with a bicuspid aortic valve underwent VSRR with successful postoperative outcomes, most patients in this study who had a bicuspid aortic valve underwent the Bentall operation. In the event that intraoperative echocardiography reveals significant AI after VSRR, we do not hesitate to excise the native valve and replace it with a mechanical prosthesis, which has been a rare event.

Low operative risk and excellent postoperative results after the Bentall operation and VSRR have led to more

aggressive treatment of aortic aneurysm in MFS patients. Our current recommendation for surgery in MFS is to proceed when aortic root diameter greater than 5.0 cm, when sinus diameter increases more than 1.0 cm/year, or when AI is progressive.

Our study has the limitations inherent in a retrospective analysis. We attempted to avoid differences in follow-up periods by reviewing a recent cohort of patients from 1997 to 2006, a period during which both the Bentall operation and VSRR were offered. Although we collected 140 MFS patients in only 10 years, longer follow-up will be necessary to make definitive conclusions. Furthermore, among VSRR patients, our early experience from 1997 to 2002 was with root remodeling; since 2002 we have exclusively used reimplantation with the Valsalva graft. Because of the difference in follow-up time (out to 8 years in the remodeling group versus 4.5 years in the reimplantation group), our ability to make comparisons between remodeling and reimplantation remains limited. Regardless, freedom from AVR at 4.5 years was greater for reimplantation than remodeling. We anticipate long-term valve durability for MFS patients who had reimplantation VSRR with the Valsalva graft, but longer follow-up is needed. Currently, there are no randomized controlled trials evaluating different surgical management of aortic root aneurysm in MFS, and because of surgeon preference, it is unlikely that a trial will take place.

To minimize selection bias between Bentall and VSRR groups in this nonrandomized setting, we calculated propensity scores for each patient. Propensity score analysis is considered a valid statistical method for reducing bias when comparing two nonrandomized groups. We believe we are the first to calculate propensity scores and use propensity adjusted Cox and logistic regression modeling to analyze predictors of mortality and need for reoperation in MFS patients undergoing the Bentall versus VSRR operations. Importantly, mean propensity scores were found to be significantly different between the Bentall and VSRR groups, which demonstrates that our propensity score model adequately adjusted for selection bias in our study.

The Bentall operation and VSRR for aortic root aneurysm in MFS can be performed with low operative risk. Bentall patients had a lower late survival, but the Bentall operation did not predict mortality on propensity score adjusted Cox regression analysis, which likely reflects our preference for the Bentall operation in higher risk patients. Although the incidence of late thromboembolism was significantly higher in the Bentall group, the difference in need for reoperation on the aortic root was not statistically significant on univariate or propensity score adjusted logistic regression analysis. We recommend VSRR for patients with Marfan syndrome when possible to avoid anticoagulation-related complications associated with mechanical valves. Reimplantation with the Valsalva graft seems to offer better aortic valve durability over root remodeling and, in our opinion, is technically simpler than creating neosinuses using oversized or multiple-sized grafts. Nevertheless, the Bentall operation has demonstrated excellent and reproducible outcomes, so longer follow-up is necessary to make definitive conclusions about the durability of valve preservation versus replacement in patients with Marfan syndrome.

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DISCUSSION

DR JOHN S. IKONOMIDIS (Charleston, SC): That was a beautifully presented study. I very much enjoyed watching the evolution of the Hopkins experience with the valve-sparing root and culminating now with this very large and impressive series in Marfan's patients. I have two questions for you. The first one is that your results are very compelling in favor of the reimplantation form of the valve-sparing root over the remodeling procedure. At Hopkins in 2007, is there a situation—clinical, anatomic, or otherwise—in which a remodeling type of valve-sparing root would be considered?

MR PATEL: Thank you, Dr Ikonomidis. At present, we no longer perform the remodeling procedure. However, that is not because we believe it is a poor operation. It is a great operation, and it was successful in approximately 90% of our patients. Nevertheless, we do believe that the reimplantation technique is simpler, provides better hemostasis, and stabilizes the root better.

DR IKONOMIDIS: I also appreciate your sending me your manuscript in advance, and you mention in it that measurement of leaf dimensions and graft selection formulas in your hands is not useful and rather the graft size is based on the optimal sinotubular junction size determined intraoperatively. Would you go over how you evaluate in the operating room what the optimal sinotubular junction would be for these patients?

MR PATEL: Thank you for that important question. We have not used formulas in the operating room to determine the appropriate graft size. It is a judgment call in the operating room after the aorta is divided above the level of the sinotubular junction. We use valve sizers to determine the optimal sinotubular junction diameter for best leaflet apposition and select a graft size that is approximately 2 to 3 mm larger, as the graft will sit outside of the aortic root complex. In most of our patients, the optimal sinotubular junction diameter is 28 to 30 mm, and we choose a graft that is 30 to 32 mm.

DR IKONOMIDIS: Could you elaborate on thromboembolism in the composite graft patients? Also, what is your current practice, and would you do a valve sparing procedure in acute dissection?

MR PATEL: Thank you very much for those important questions. In regard to your first question on the thromboembolic events, most of them were fairly early after their operation. There were 5 patients total who had thromboembolism. One had a deep vein thrombosis, a second had a thrombosed aortic valve due to poor compliance with anticoagulants and actually required a reoperation; the third had a renal artery thrombosis; a fourth, a TIA, and a fifth had a right hemispheric stroke.

With regard to your second question on preference for an elective operation in a Marfan patient, we attempt to spare the valve whenever possible.

And the third question regarding aortic dissection, I think one of the salient points from our experience has been that patient selection is pivotal for getting great results. We do prefer the Bentall operation in patients who have acute aortic dissection and are relatively unstable.

DR CONSTANTINE MAVROUDIS (Chicago, IL): Congratulations on a beautiful presentation. I would also like to thank you and your colleagues for being so responsive to telephone calls about all these issues in your presentation. I have taken advantage of this expertise over the years and I am grateful to you all. How many patients did you have in the inclusion group who had coronary artery anatomy that was not amenable to direct implantation in the graft by the button technique? Did you have to use any prosthetic grafts or other methods to ensure coronary perfusion?

MR PATEL: Thank you, Dr Mavroudis, for your comments. While I do not have those data available, the need for an interposition Gore-Tex graft has been very rare in our experience.

DR ANDREW C. FIORE (St. Louis, MO): The decision as to which operation to perform is an important one and can be difficult. Please correct me if I am wrong, but the variables that would lead you to perform the Bentall operation include a sinus diameter and degree of AI as you defined it, as well as the setting of an urgent or emergent procedure. Are there any other variables? Are there any other anatomic features that would lead you to a Bentall as opposed to a valve repair operation?

MR PATEL: There are other important factors that we did not include in the propensity model because the data weren't readily available in our database, including the presence of any marked leaflet fenestrations, severe prolapse, bicuspid aortic valves with severe calcification or fenestrations, and giant aortic aneurysms with leaflet irregularities. The presence of these abnormalities has led us to favor the Bentall operation. Unfortunately, I don't think I could comment on other features or factors that would lead us to abandon a valve sparing procedure.

DR WILLIAM A. BAUMGARTNER (Baltimore, MD): I think the reason that Nishant can't comment on it is that Nishant is a third-year medical student at Johns Hopkins and has been in our laboratory and working with us for the past several years as an undergraduate and medical student. But the answer to the question is, in acute dissections we will do everything we can to preserve the valve. But particularly in the Marfan patient, if the dissection significantly carries down into the root or, particularly, involves the coronary artery, we will often perform a Bentall. Because of the large Marfan clinic that we have at Hopkins, we follow these patients very closely, and I think you can see that the number of dissections are very minimal in this group of patients.