Type A Aortic Dissection in Marfan Syndrome
Extent of Initial Surgery Determines Long-Term Outcome

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Background—Data on outcomes after Stanford type A aortic dissection in patients with Marfan syndrome are limited. We investigated the primary surgery and long-term results in patients with Marfan syndrome who suffered aortic dissection.

Methods and Results—Among 1324 consecutive patients with aortic dissection type A, 74 with Marfan syndrome (58% men; median age, 37 years [first and third quartiles, 29 and 48 years]) underwent surgical repair (85% acute dissections; 68% DeBakey I; 55% composite valved graft, 30% supracoronary ascending replacement, 15% valve-sparing aortic root replacement; 12% total arch replacement; 3% in-hospital mortality) at 2 tertiary centers in the United States and Europe over the past 25 years. The rate of aortic reintervention with resternotomy was 24% (18 of 74) and of descending aorta (thoracic-abdominal) intervention was 30% (22 of 74) at a median follow-up of 8.4 years (first and third quartiles, 2.2 and 12.7 years). Freedom from need for aortic root reoperation in patients who underwent primarily a composite valved graft or valve-sparing aortic root replacement procedure was 95±3%, 88±5%, and 79±5% and in patients who underwent supracoronary ascending replacement was 83±9%, 60±13%, 20±16% at 5, 10, and 20 years. Secondary aortic arch surgery was necessary only in patients with initial hemi-arch replacement.

Conclusions—Emergency surgery for type A dissection in patients with Marfan syndrome is associated with low in-hospital mortality. Failure to extend the primary surgery to aortic root or arch repair leads to a highly complex clinical course. Aortic root replacement or repair is highly recommended because supracoronary ascending replacement is associated with a high need (>40%) for root reintervention. (Circulation. 2014;129:1381-1386.)

Key Words: aorta • cardiac imaging techniques • Marfan syndrome • surgery

Marfan syndrome (MFS), an autosomal-dominant disorder with variable penetrance based on fibrillin-1 gene mutations, is an important causative factor for acute Stanford type A aortic dissection in younger patients.1,2 The current American College of Cardiology Foundation guidelines recommend prophylactic aortic root surgery in patients with MFS when a 4.0- to 5.0-cm ascending aortic or aortic root threshold diameter has been reached because this surgery prevents catastrophic proximal aortic events.3 Because of a lack of diagnosis, poor follow-up, and the presence of sporadic mutations with variable phenotypic profile, acute aortic dissection is still a frequent and highly lethal initial presentation of aortic pathology in patients with MFS. Since aortic dissection occurs on average 20 years earlier in patients with MFS compared with peers without MFS,1 ongoing postoperative follow-up and timely, well-planned reinterventions when needed are essential to achieve better life expectancy.

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Clinical Perspective on p 1386

Several groups have described their general aortic surgery experience in patients with MFS,3–7 but to date no large series on Stanford type A aortic dissection in patients with MFS with long-term aortic outcome have been published. Our pooled databases covering 25 years of aortic dissection type A from 2 tertiary cardiac centers in the United States and Europe provide a unique opportunity to analyze clinical data on individuals with MFS. In this study, we sought to present the outcome of primary surgery in patients with MFS who suffered Stanford type A dissection and to investigate the incidence, causes, and results of early and late surgical reinterventions.

Study Population
The institutional review committees at both participating centers approved this study, and the need for informed consent was waived. Researchers at the Hospital of the University of Pennsylvania in Philadelphia and Heart Center Freiburg University in Freiburg and Bad Krozingen reviewed their aortic dissection databases including patients operated on between 1987 and 2013. The cumulative case load at both centers was 1324. Of these, a total of 74 patients (Heart Center Freiburg, 42; University of Pennsylvania, 32; Table) with MFS confirmed according to the revised Ghent criteria9 underwent surgery for Stanford type A aortic dissection. Patients were followed up in the past 25 years at both institutions in MFS clinics in at least 1-year intervals.

Methods
Categorical variables are given as counts and percentages. Survival continuous data are presented as median (first and third quartiles); statistical analysis was performed using an “island” technique or separate reimplantation of the aortic arch surgery after total arch replacement. Freedom from need for aortic root reoperation in patients who underwent primarily a CVG or V-SARR procedure was 95±3%, 88±5%, and 79±5% and in patients who underwent supracoronary ascending replacement was 83±9%, 60±13%, and 20±16% at 5, 10 and 20 years, respectively (Figure 2).

In the CVG group, secondary root repair was indicated in 3 patients because of prosthetic valve thromboembolism. None of V-SARR patients required secondary sternotomy for aortic root reintervention. However, 1 patient developed moderate aortic insufficiency 6 years after primary surgery. We decided to replace his valve and took the chance that he had to undergo a second sternotomy for aortic arch aneurysm repair. In the supracoronary replacement group, the reason for reintervention was aortic insufficiency in 3 patients and root aneurysm in 3 other patients. Three more patients with aortic root aneurysm failed to undergo reintervention: 1 patient died of a ruptured abdominal aortic aneurysm, 1 patient was a Jehovah’s Witness and declined surgery, and 1 patient developed concomitant arch aneurysm and, because of severe aortic arch pathology and high operative risk, underwent only total arch replacement.

Secondary total aortic arch replacement became necessary in 8 of 74 patients (11%) and, together with 5 distal arch reinterventions via lateral thoracotomy, accounted for an 18% overall arch reintervention rate. No patients required secondary arch surgery after total arch replacement. Freedom from aortic arch reoperation in patients who underwent hemi-arch

### Table. Clinical and Operative Data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>n=74</th>
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</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>37 (29, 48)</td>
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<tr>
<td>Male, n (%)</td>
<td>43 (58)</td>
</tr>
<tr>
<td>Height, cm</td>
<td>181 (174, 190)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>74 (69, 84)</td>
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<tr>
<td>Hypertension, n (%)</td>
<td>21 (28)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>BAV, n (%)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Aortic dissection, n (%)</td>
<td>63 (85)</td>
</tr>
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<td>Subacute</td>
<td>4 (5)</td>
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<tr>
<td>Chronic</td>
<td>7 (10)</td>
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<tr>
<td>Distal repair, n (%)</td>
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<tr>
<td>Proximal repair, n (%)</td>
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<tr>
<td>Type I</td>
<td>24 (32)</td>
</tr>
<tr>
<td>Type II</td>
<td>11 (15)</td>
</tr>
<tr>
<td>Supracoronary ascending replacement</td>
<td>22 (30)</td>
</tr>
<tr>
<td>V-SARR</td>
<td>41 (55)</td>
</tr>
<tr>
<td>Distal repair, n (%)</td>
<td>13 (24)</td>
</tr>
<tr>
<td>Hemi-arch replacement</td>
<td>13 (26)</td>
</tr>
<tr>
<td>Total arch replacement</td>
<td>20 (40)</td>
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<tr>
<td>Secondary interventions, n (%)*</td>
<td>5 (10)</td>
</tr>
</tbody>
</table>

Continuous variables are given as median values (first and third quartiles). BAV indicates bicuspid aortic valve; CVG, composite valved graft; and V-SARR, valve-sparing aortic root replacement.

*Percentages are given according to all reinterventions.

### Surgical Techniques

All patients underwent ascending aortic replacement. In those with established MFS and in a condition permitting longer cardiopulmonary bypass times (no visceral or cardiac malperfusion, no neurological deficit), valve-sparing root replacement (V-SARR) in the later era was considered whenever the aortic valve was tricuspid and had symmetrical leaflets and there were no large fenestrations of the leaflets. All other patients underwent composite valve graft (CVG) implantation. In patients with unrecognized MFS at the time of surgery, supracoronary ascending replacement with aortic valve resuspension and eventually aortic root reconstruction applying the “neomedia” concept (in patients operated on in Philadelphia) was performed when the sinus of Valsalva diameter was <4.5 cm, there was no dissection entry proximal to the sinotubular junction, and the aortic valve was reparable. In all other cases, a V-SARR or CVG procedure was performed. Distal aortic procedures included hemi-arch replacement (open distal anastomosis or aggressive hemi-arch with replacement of the aortic-arch concavity), or in case of a dissection entry located in the convexity of the aortic arch, total arch replacement was performed using an “island” technique or separate reimplantation of the supra-aortic branches via a trifurcated vascular graft.

### Statistical Analysis

Continuous data are presented as median (first and third quartiles); categorical variables are given as counts and percentages. Survival and freedom from reinterventions were analyzed with the Kaplan-Meier method. All statistical calculations were performed with SigmaPlot 12 (Systat Software, San Jose, CA).

### Results

A total of 74 patients were included. Clinical and operative data are shown in the Table. At the primary surgery, among patients who received a V-SARR operation, 9 underwent aortic valve reimplantation and 2 had root remodeling procedures. Among 22 patients who underwent supracoronary ascending replacement, all underwent aortic valve resuspension and 12 also received aortic root neomedia repair. Nine patients (12%) underwent total aortic arch replacement. In-hospital mortality was 3% (2 of 74 patients): 1 patient died in the operating room of right heart failure and another patient died 6 days after surgery of sepsis and multiorgan failure. Stroke occurred in 4 of 74 patients (5%). One patient suffered paraparesis. During follow-up, 48 aortic reinterventions were performed on 33 of 72 patients (46%). The pattern of replaced aortic segments is shown in Figure 1.

### Reinterventions With Secondary Sternotomy

Eighteen patients underwent 23 resternotomies for aortic root or arch reinterventions. The median interval between the initial operation and the first reintervention was 8.4 years (first and third quartiles, 2.2 and 12.7 years). Reoperation rates on the aortic root were associated with the extent of primary aortic surgery. Freedom from need for aortic root reoperation in patients who underwent primarily a CVG or V-SARR procedure was 95±3%, 88±5%, and 79±5% and in patients who underwent supracoronary ascending replacement was 83±9%, 60±13%, and 20±16% at 5, 10 and 20 years, respectively (Figure 2).

In the CVG group, secondary root repair was indicated in 3 patients because of a pseudoaneurysm (in 1 patient at the right coronary anastomosis, which required a second and third reintervention, and in 2 patients at the aortic annulus-graft anastomosis), in 1 because of endocarditis, and in another patient because of prosthetic valve thromboembolism. None of V-SARR patients required secondary sternotomy for aortic root reintervention. However, 1 patient developed moderate aortic insufficiency 6 years after primary surgery. We decided to replace his valve and took the chance that he had to undergo a second sternotomy for aortic arch aneurysm repair. In the supracoronary replacement group, the reason for reintervention was aortic insufficiency in 3 patients and root aneurysm in 3 other patients. Three more patients with aortic root aneurysm failed to undergo reintervention: 1 patient died of a ruptured abdominal aortic aneurysm, 1 patient was a Jehovah’s Witness and declined surgery, and 1 patient developed concomitant arch aneurysm and, because of severe aortic arch pathology and high operative risk, underwent only total arch replacement.

Secondary total aortic arch replacement became necessary in 8 of 74 patients (11%) and, together with 5 distal arch reinterventions via lateral thoracotomy, accounted for an 18% overall arch reintervention rate. No patients required secondary arch surgery after total arch replacement. Freedom from aortic arch reoperation in patients who underwent hemi-arch
replacement was 91±4%, 86±5%, and 64±10% at 5, 10, and 20 years (Figure 3).

The in-hospital mortality rates were 22% (2 of 9 patients) and 8% (1 of 13) for elective aortic root and arch reinterventions, respectively.

**Interventions on the Descending Aorta**

Twenty-two patients underwent 25 procedures on downstream aortic segments during the follow-up period. The most common indication was thoracic aortic aneurysm in 17 patients (including distal arch pseudoaneurysms or true aneurysms in 5 patients), followed by abdominal aortic aneurysm in 5 patients, thoracoabdominal aneurysm in 2 patients, and acute aortic dissection type B in 1 patient. One patient died after emergency thoracic aortic replacement, and a second patient died after elective thoracoabdominal repair, accounting for 5% (1 of 20 patients) in-hospital mortality in elective cases.

Aortic dissection extension beyond the aortic arch at the time of initial surgery was associated with higher reoperation rates on the descending aorta. Nineteen of 50 patients (38%) with a DeBakey type I and only 3 of 24 patients (13%) with a DeBakey type II dissection required distal reoperation. Freedom from descending aortic reoperation in patients with a DeBakey type I dissection was 78±7%, 65±8%, and 55±9% and in patients with a DeBakey type II dissection was 96±4%, 96±4%, and 80±10% at 5, 10, and 20 years, respectively (Figure 4).

**Survival**

Overall survival was similar in patients who did and did not undergo aortic reinterventions. Survival in patients who required secondary aortic procedure was 87±6%, 73±8%, and 62±10% and in patients who did not need aortic reintervention

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**Figure 1.** Pattern of primarily and secondarily replaced aortic segments in patients with Marfan syndrome who underwent surgery for Stanford type A aortic dissection. Each vertical column represents 1 patient. CVG indicates composite valved graft; and V-SARR, valve-sparing aortic root replacement.

**Figure 2.** Freedom from need for aortic root reoperation in patients who underwent initially supracoronary ascending replacement vs those with initial aortic root replacement (composite valved graft [CVG]) or repair (valve-sparing aortic root replacement [V-SARR]).

**Figure 3.** Freedom from aortic arch reoperation in patients who underwent primary total aortic arch vs hemi-arch replacement.
was 88±6%, 72±9%, and 63±11% at 5, 10, and 20 years, respectively (Figure 5). Survival in patients with a DeBakey type I dissection was 84±6%, 67±7%, and 60±10% and in patients with a DeBakey type II dissection was 100%, 82±9%, and 66±12% at 5, 10, and 20 years (Figure 6).

**Discussion**

Wide availability of screening modalities and a general awareness of connective tissue disease have not yet completely eliminated the risk of aortic dissection, the most catastrophic and often lethal event in the MFS population. Several major cardiac centers recently reported their general experience in aortic surgery on patients with MFS. One of their main conclusions was that the current rate of acute type A dissection surgery in patients with MFS remains very high, ranging between 16% and 35% of all aortic procedures performed in this cohort.4–7 Here, we report 25 years of international MFS clinical experience in 2 large cardiac centers with primary surgery for Stanford type A dissection and the management of later aortic complications. Our main observations are the following: (1) Although surgical treatment for type A dissection in patients with MFS has a very low in-hospital mortality risk (3%), it is associated with the high risk of later aortic reinterventions (45%); (2) supracoronary ascending replacement at the time of aortic dissection type A is associated with a high need for root reintervention compared with patients receiving CVG or V-SARR, and leaving the diseased root tissue behind at the time of initial operation leads to high aortic root complication rates; and (3) patients with dissection extending beyond the aortic arch at the initial surgery carry an increased risk of later reinterventions on the descending thoracic aorta.

**Relationship to Previous Studies**

Surgical repair of the aorta outcomes have improved dramatically in the past 25 years. In the most recently published MFS cohorts, Schoenhoff et al4 and Cameron et al6 reported series of 86 and 372 patients, respectively, with no in-hospital mortality after elective aortic root surgery. However, there are very few data on outcome after emergency surgery for type A dissection in patients with MFS. In the same series from Johns Hopkins Hospital, Cameron et al reported 4.4% (2 of 45 patients) 30-day mortality in patients with MFS who underwent urgent or emergent ascending aortic repair. In a survey of the International Registry of Aortic Dissection, Januzzi et al10 described 23% perioperative mortality in a series of 46 patients <40 years of age, of whom 50% had MFS. In our composite series, in-hospital mortality is relatively low (3%) and compares favorably with the mortality currently reported for the overall aortic dissection population, which ranges between 8% and 20% in high-volume centers.11–13 The low mortality in patients with MFS, 85% of whom underwent emergency surgery, may be attributed to the facts that they are on average 20 years younger than non-MFS aortic dissection patients and that they usually do not have the comorbidities typical of older patients.

**Extent of Initial Surgery Determines the Need for Aortic Root and Arch Reinterventions**

There is growing consensus that MFS patients with type A dissection who are being operated on should undergo aortic
root replacement during the emergency surgery on the proximal aorta. However, this was a rather intuitive recommendation made according to experiences with nondissected patients with MFS because the number of patients with MFS with aortic dissection at even high-volume centers is very low, ranging from 3% to 5% of the entire dissection population. Until now, no aortic root preservation outcomes in patients with MFS suffering acute dissection have been published. In our cohort, 22 patients underwent supracoronal ascending aortic replacement in the emergency setting of acute type A dissection because the MFS diagnosis was not known at the time of surgery and their aortic root was nondilated. The greater need for reoperation on this group’s aortic root (41%) compared with CVG or V-SARR patients (10%) confirms what we and many other groups dealing with MFS patients have intuitively thought, namely that aortic root replacement or repair is highly recommended in patients with MFS with a dissected ascending aorta. This statement is additionally supported by the fact that in-hospital mortality for root replacement or repair at the initial surgery was very low (1.9%). Interestingly, in the root neomedia reconstruction group, we noted only 1 sinus-segment aneurysm requiring reintervention. Reinforcing the sinus segment with a Teflon felt placed inside the aortic wall may also prevent root dilatation in patients with MFS. However, our patient numbers are insufficient to make a definitive statement.

Several groups reported outstanding durability of the elective David reimplantation operation in patients with connective tissue disorders. Although both V-SARR techniques (valve reimplantation and root remodeling) are feasible in type A aortic dissection patients, they are usually done infrequently because both require long cardiopulmonary bypass times, which can lead to irreversible complications in patients who already present with myocardial or visceral malperfusion or neurological impairment at the time of admission. Some investigators found that the root remodeling technique is associated with an increased risk of premature failure in patients with MFS. In our patients, we performed 11 V-SARR (9 reimplantations and 2 remodelings) procedures: 9 in acute, 1 in subacute, and 1 in chronic dissection. We observed no perioperative mortality, and only 1 patient developed moderate aortic insufficiency 6 years after primary surgery. We decided to replace his valve in a second sternotomy for aortic valve insufficiency. We believe that V-SARR should be considered in patients with MFS with acute type A dissection, especially those who present with uncomplicated dissection without malperfusion. V-SARR not only is superior to the CVG procedure because it preserves the native valve (avoiding the serious risks of mechanical valves) but also appears to circumvent the risk of later proximal pseudoaneurysm development, a factor we observed in 2 CVG patients and in no patients in the V-SARR group. However, because of the small patient numbers, definitive conclusions on the outcomes of V-SARR versus CVG procedures are not possible.

There is a growing consensus that replacing the aortic arch during the initial surgery for type A dissection is unnecessary, although it reduces the rate of further arch reoperations. Our study confirmed this hypothesis. Although aortic arch reintervention was necessary only in patients with initial hemi-arch replacement, elective arch reintervention carried an only moderate risk.

Extension of the Aortic Dissection Is Associated With Descending Aortic Reinterventions

In a recently published cohort of patients with MFS undergoing root repair, the Bern group found that the need for distal aortic reinterventions is precipitated by an initial presentation with Stanford type A dissection. Our data suggest more specific conclusions, namely that the need for reintervention in primarily nontreated aortic segments is determined by the initial extent of type A aortic dissection because most reinterventions on the descending aorta were performed on patients with DeBakey type I dissection. Notably, survival was similar in patients with DeBakey types I and II and in patients with and without secondary aortic intervention, suggesting that elective secondary surgery is effective in the treatment of late distal adverse aortic events.

Limitations

Patients enrolled in this analysis were operated on within the last 25 years. This might be a limitation of our study because both surgical and medical therapies made substantial progress in this time. Although it is the largest series on Stanford type A aortic dissection in patients with MFS, the number of events in subgroups of patients by type of surgery was too small to provide adequate power for statistical hypothesis testing.

Conclusions

The initial surgical intervention on patients with MFS who present with acute Stanford type A dissection is a low-risk procedure when performed in a cardiac center with extensive aortic surgical experience. Because supracoronal ascending replacement is associated with a high root reintervention rate, aortic root replacement or repair during the initial surgery is highly recommended. Although the CVG procedure carries risks associated with mechanical valves, V-SARR, as long as the aortic valve morphology is adequate and the patient’s condition allows longer cardiopulmonary bypass time, appears preferable. Total aortic arch replacement reduces the number of aortic arch reinterventions. However, if secondary aortic arch surgery is performed electively, it carries an acceptable risk. We therefore suggest that an effective strategy to improve long-term outcome in patients with MFS with acute Stanford type A dissection includes the David reimplantation procedure when it does not raise the overall operative risk, and we propose that arch replacement is not necessary during the initial operation unless there are primary tears in the arch itself.

Acknowledgments

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Disclosures

None.
References


CLINICAL PERSPECTIVE

Patients with Marfan syndrome usually suffer acute type A aortic dissection in the fourth or fifth decade of life. Emergent replacement of their ascending and aortic arch segments does not eliminate the risk of later aortic complications affecting their life expectancy because in fact their aorta is structurally abnormal. Surgery for type A dissection in Marfan syndrome patients has low in-hospital mortality risk. Nevertheless, survivors carry a high risk of aortic complications in the untreated segments and frequent pathologies at the graft–native aorta junction. The extent of the initial surgical aortic repair is associated with the need for reoperations during the patient’s follow-up. Leaving aortic root tissue behind leads to high complication rates, and up to 40% of patients require a second sternotomy for aortic root replacement later in life. Therefore, aortic root replacement or repair should be undertaken in all patients with Marfan syndrome with type A dissection. Total aortic arch replacement reduces the number of aortic arch reinterventions. However, if secondary aortic arch surgery is performed electively, the risk it carries is acceptable. The decision to extend initial aortic repair is considered in all patients on an individual basis. Patients with Marfan syndrome type A dissection seem to benefit from extended aortic root repair, including root or valve-sparing root replacement, whereas total aortic arch replacement is unnecessary unless there are primary tears in the arch itself.
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