David I reimplantation procedure for aortic root replacement in Marfan patients: medium-term outcome

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METHODS: Forty-eight Marfan patients (25 males, mean age 33 ± 12 years, range 15–62 years) underwent the original variant of the David V-SARR (David I) between 1997 and 2013. Forty-two operations (88%) were performed as elective procedures for aortic root aneurysms and six for acute dissections (12%). Seventeen had aortic regurgitation (AR) grades ≥2+ preoperatively, and 3 had AR >2+. No patients with severe AR (4+) were selected for V-SARR. Three full or hemi-arch replacements were performed. Patients who were operated on using a variation of the David I or David II procedure were excluded.

RESULTS: Mean prosthesis size was 28 ± 3 mm (18–30 mm). Mean clinical and echocardiographic follow-up (98% complete) was 3.8 ± 3.7 years with a cumulative follow-up of 178 patient-years. The early mortality rate was 2% (one hospital death). The survival rate was 98% (95% confidence 84–99%) at 4 years and 90% (57–98%) at 8 years with 5 patients at risk at 10 years. The rate of freedom from root or valve reoperation was 97% (79–99%) and 97% (79–99%) at 4 and 8 years, respectively. Only one patient required mechanical aortic valve replacement for progression of AR.

CONCLUSIONS: Despite potential theoretical drawbacks of the David I V-SARR technique without neo-sinuses or a neo-sinotubular junction, it results in a favourable mid-term outcome in Marfan patients and compares well with reported results of different modifications of David V-SARR.

Keywords: Marfan syndrome • Aortic aneurysm • Aortic dissection • Aortic valve • Valve-sparing aortic root replacement

BACKGROUND

Patients with Marfan syndrome (MFS) [1] typically present with aneurysm of the aortic root and/or ascending aorta and aortic valve dysfunction, commonly aortic regurgitation (AR). The David valve-sparing aortic root replacement procedure (V-SARR) has been established as a durable treatment alternative to valve replacement or a composite valve graft procedure [2, 3]. Several technical variations of the original David operation (David I) [4, 5] have been introduced [6], mainly aimed at re-creation of the sinuses of Valsalva (SOV), or ‘neo-sinuses’ and a neo-sinotubular junction (STJ) with presumed superior haemodynamics and long-term functional valve outcomes [7]. By contrast, the original David I procedure utilizes a single prosthesis for root and ascending aortic replacement, whereby neither a neo-STJ nor neo-SOV are created. The lack of physiological SOV vortical flow and potential contact of the cusps and the prosthesis in systole after the David I operation, particularly in patients with intrinsic structural valve tissue defects as present in MFS, are thought to result in accelerated cusp degeneration and structural valve deterioration. However, clinical data on mid- and long-term follow-up are limited; published series on Marfan patients report mostly on cohorts after different modifications of the David V-SARR operation. We analysed mid-term clinical outcomes of a consecutive Marfan patient cohort treated exclusively using the original non-modified David I V-SARR procedure. These results are discussed in the light of reported series of patients treated using modifications of the David procedure with hypothetically superior haemodynamics.

METHODS

Patients and procedures

Patients (mean age 33 ± 12 years, range 15–62 years) with confirmed MFS (total cohort under surveillance n = 205, n = 48 David I
procedure) were operated on for acute Type A dissection or root aneurysm between 1997 and 2013 at our institution. All underwent the David I V-SARR procedure as described previously [4, 5, 8, 9]. This procedure uses a single vascular graft to replace both the aortic root and ascending aorta without creating neo-sinuses or a neo-STJ [10]. Procedures were performed using standard aortic cannulation in n = 43 patients (90%) and cannulation of the axillary or femoral artery in five patients (10%). Baseline clinical and procedural characteristics are listed in Tables 1 and 2. Operations were performed for ascending/aortic root aneurysm in 42 patients (87%) and for acute type A dissection in 6 patients (13%). Seventeen patients had 2+ AR or higher (35%), 11 patients presented without any AR preoperatively (Table 1). No patients with severe AR or structurally degenerated, thickened or calcified cusps were selected for David V-SARR. A subgroup of 6 patients, which was excluded from this analysis, was treated using a modified David II procedure, in which only the non-coronary sinus or all three sinuses were replaced, whereas the rest of the aortic root, commissures and annulus was left untreated.

### Table 1: Baseline clinical patient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td>33 ± 12</td>
</tr>
<tr>
<td>Male gender</td>
<td>25 (52)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>182 ± 13</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>74 ± 18</td>
</tr>
<tr>
<td>BMI</td>
<td>22 ± 5</td>
</tr>
<tr>
<td>BSA (cm²)</td>
<td>2</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>12 (25)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1 (2)</td>
</tr>
<tr>
<td>LVEF &lt;50%</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Urgency</td>
<td>6 (12.5)</td>
</tr>
<tr>
<td>NYHA &gt;I</td>
<td>2 (4)</td>
</tr>
<tr>
<td>β-Blocker</td>
<td>35 (73)</td>
</tr>
<tr>
<td>Losartan</td>
<td>5 (10)</td>
</tr>
<tr>
<td>BAV</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Preoperative AR grade ≥2+</td>
<td>17 (35%)</td>
</tr>
<tr>
<td>Aneurysm</td>
<td>42 (85%)</td>
</tr>
<tr>
<td>Dissection</td>
<td>6 (13%)</td>
</tr>
</tbody>
</table>

Continuous variables are given as mean ± 1 standard deviation. Categorical variables are given as n (%). BMI: body mass index; BSA: body surface area; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; BAV: bicuspid aortic valve; AR: aortic regurgitation.

### Table 2: Procedure details

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>Cardiopulmonary bypass time (min)</td>
<td>171 ± 31</td>
</tr>
<tr>
<td>Aortic cross-clamp time (min)</td>
<td>139 ± 22</td>
</tr>
<tr>
<td>Arch replacement</td>
<td>4 (7)</td>
</tr>
<tr>
<td>Femoral cannulation</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Auxillary cannulation</td>
<td>4 (7)</td>
</tr>
<tr>
<td>Aortic cannulation</td>
<td>47 (87%)</td>
</tr>
<tr>
<td>Graft size (mm)</td>
<td>28 ± 3</td>
</tr>
<tr>
<td>David I</td>
<td>48 (89%)</td>
</tr>
<tr>
<td>David II (excluded from analysis)</td>
<td>6 (11)</td>
</tr>
</tbody>
</table>

Clinical and echocardiographic follow-up

The mean clinical follow-up was 3.8 ± 3.7 years (range 0.3–15 years) and the cumulative clinical follow-up comprised 178 patient-years. Patients were followed up on an annual basis at our institution’s dedicated Marfan clinic: evaluation included an annual transthoracic echocardiogram (TTE), physical and MR or CT aortic imaging. TTE assessment and grading of AR were performed by an experienced cardiologist. AR grading was 0 for none or trace AR, 1+ for mild AR, 2+ for moderate AR, 3+ for moderate to severe AR and 4+ for severe AR. The mean duration to the latest TTE assessment was 3.2 ± 3 years (range 0.02–13 years). For this analysis, retrospective chart review was performed, and clinical follow-up data were collected prospectively (consisting of regular Marfan Clinic visits, and partially of telephone follow-up). Written informed consent was waived for this retrospective clinical investigation. The local institutional review board of the University of Freiburg approved this study.

### Statistical analysis

Data are given as mean and one standard deviation if numerical; categorical data are given as median and confidence intervals (70%), if not otherwise stated. Kaplan–Meier and log-rank calculations were performed to describe parametric actuarial event-free survival and to compare the different groups. The Cox model and multiple logistic regression analyses were performed to identify independent variables associated with adverse outcomes. In addition, ANOVA, t-test and Mann–Whitney rank-sum test were performed to compare groups. Study end-points were survival, central nervous system deficit, including transient ischaemic attack (TIA), stroke, infection, AR development or progression during the course of the follow-up, as well as the need for reoperation.

### RESULTS

#### Survival

The 30-day mortality rate was 1.8%, with one death resulting from sepsis and multiorgan failure 1 week after the procedure for acute type A dissection. The overall survival rate was 97% (84–99%) and 90% (60–97%) at 4 and 8 years, respectively, with 9 patients remaining at risk at 8 years. There were two late deaths resulting from sepsis and multiorgan failure and one late death because of unknown causes. Overall survival Kaplan–Meier curve is illustrated in Fig. 1. Log-rank calculations revealed that total arch or hemi-arch replacement (P = 0.049) was associated with decreased survival. Freedom from reoperation in patients after total arch or hemi-arch replacement was 74% (13–96%). Emergent surgery for acute aortic dissection was linked to decreased survival (P = 0.034).

#### Aortic reoperation, valve replacement and echocardiography

In the complete cohort, including patients treated using the David II remodelling procedure, 3 patients underwent a second procedure for thoracic aorta or aortic valve pathology 2, 5 and 1.5 years after initial V-SARR procedure, respectively; these
included one composite valve graft for an ascending anastomotic aneurysm and two mechanical aortic valve replacement procedures for severe AR. Only one of these patients was initially treated with a David I procedure, and parametric freedom from reoperation is depicted in Fig. 1. One patient required replacement of the aortic arch subsequently after David I for aneurysm progression. Progression of AR was observed in the two aforementioned patients. Kaplan–Meier curves for overall freedom from reoperation on the aortic valve or thoracic aorta are depicted in Fig. 1.

Initial total arch or hemi-arch replacement was not linked to higher reoperation rates (100 vs 92% at 4 years and 100 vs 83% at 8 years, \( P = 0.65 \), log-rank). Also, operation for initial acute aortic dissection was not linked to higher reoperation rates, with only 8 patients after type A dissection and overall only one event as described earlier, and three events in the entire cohort (100 vs 94% at 4 years and 100 vs 86% at 8 years, \( P = 0.461 \)).

Distribution of baseline AR grades before surgery as well as echocardiographic follow-up data are depicted in Fig. 2. No patients with severe AR (4+) underwent V-SARR. The median AR was 1+ before operation (range 0–3+, Table 1) with a mean of 1.2. At the most recent follow-up, the median AR grade was 1+, including patients who needed a reoperation, and the mean 0.8; most patients had no or mild AR (Fig. 2). AR progressed in 5 patients, of whom 2 required reoperation as described below.

### Other adverse events

Of the patients treated for acute type A dissection, 5 patients had a remaining chronic dissection of the aortic arch and/or descending thoracic or thoracoabdominal aorta. Of patients treated for aneurysmal or valvular disease only, no patient suffered acute late distal Type B aortic dissection. In the entire study cohort, one distal aortic reintervention was performed (full arch replacement in a patient operated for root/ascending aortic aneurysm who subsequently demonstrated aortic arch aneurysm progression). Freedom from haemorrhagic or ischaemic stroke or TIA including completely reversible neurological events such as amaurosis fugax was 90% (75–99%) at 4 years and 73% (42–90%) at 8 years. Initial arch replacement was linked to an increased incidence of stroke or TIA early after the procedure \( (P<0.001) \). Right axillary cannulation was preferably used in the setting of acute dissection, which was linked to a higher incidence of stroke or TIA \( (P = 0.01) \). The rate of freedom from infectious complications overall was 98% (84–99%) at 4 years and 90% (58–95%) at 8 years.

### DISCUSSION

This study demonstrates good functional and clinical outcome of a cohort of MFS patients who were treated with the David I
procedure exclusively. Although many reports on results after V-SARR for syndromic and non-syndromic patients are available, as described below, literature on homogeneous groups of syndromic patients is sparse. Given the proposed theoretical disadvantages of the David I, especially in syndromic patients with potentially intrinsic structural cusp tissue weakness, including structural valve deterioration resulting from lack of neo-sinuses, we analysed the results of this cohort.

The original David I V-SARR technique uses a single graft, corresponding to the size of the aortic neo-annulus [4, 5, 8, 11]. This graft is used to replace all sinus tissue and the ascending aorta; therefore, no neo-STJ or neo-sinuses are created, unless performed using a Valsalva graft as reported by El Khoury et al. [12–14]. Exposure of the commissures and sinus tissue might be problematic, resulting in a higher risk of technical mistakes during reimplantation, such as inadequate bites on the graft, incomplete reimplantation of proximal aortic rim and subsequent bleeding or even distortion of the valve apparatus. Theoretically, this can lead to higher early and mid-term failure rates after V-SARR. Besides these technical challenges, the lack of neo-sinuses of Valsava and of a neo-STJ has theoretical haemodynamic and functional adverse consequences, potentially leading to faster structural valve deterioration and a higher need of reoperation when compared with modifications of the David V-SARR operation. The cusps might touch the vascular graft in peak systole, although this has been shown not to be the case in many patients as reported by the Hannover group [10]. Opening and closing dynamics of the cusps might be faster than in the setting of preserved sinuses of Valsava [6]. A decreased or even impeded coronary blood flow is theoretically possible, as well as an unphysiologically fast cusp closure phase. The lack of a neo-STJ could lead to unphysiological ascending aortic and aortic root flow patterns and different wall stress distribution. This might theoretically be linked to higher rates of distal aortic growth or even late distal aortic complications like acute type B dissection. The majority of these theoretical disadvantages have so far not been evaluated in comparative studies on different modifications of the David V-SARR operation. However, in the setting of a connective tissue disorder, they might be of greater importance given intrinsic tissue abnormalities and younger cohort age necessitating longer durability.

**Results of modifications of David valve-sparing aortic root replacement in Marfan syndrome**

A modified David V-SARR technique was introduced by the Stanford group using a relatively large proximal graft for replacement of sinus tissue, which is necked down over a valve-sizer before reimplantation [6]. This creates an individual neo-annulus and neo-sinuses. By replacing the ascending aorta using a separate smaller graft in a second step and anastomosing this graft to the proximal larger graft right on top of the commissures, a neo-STJ is generated. In 2013, Miller et al. reported their mid-term results of 233 patients after David V Smod (Stanford modification), including n = 93 MFS patients and representing a cumulative follow-up of 1102 patient-years, the largest reported experience with the David V technique [15]. In this cohort, the survival rate was 99 and 94% at 5 and 10 years, respectively, freedom from reoperation was 92% at 10 years with only three reoperations, all valve replacements for structural valve deterioration, without any differences in outcome between syndromic and non-syndromic patients, or between patients with tricuspid and bicuspid aortic valves (BAVs). Freedom from AR >2+ at 10 years was 95% in this series [15]. This report demonstrates the outstanding results that are possible with this technique.

Svensson et al. from the Cleveland Clinic reported on 144 patients treated with a modified David reinplantation or remodelling procedure [16]. Thirty-day and 5-, 10- and 15-year survivals were 98, 86, 74 and 58%, respectively. The rate of freedom from reoperation at 30 days and 5 and 10 years was 99, 92 and 89%, respectively, and was similar across procedures. The rate of survival of MFS patients alone was 100% at the 10-year follow-up [16].

An extensive experience with a modified David technique, now using a Valvalsa graft for their reimplantation procedures, has been built up by the El Khoury group in Brussels [17, 18]. The latest report from 2013 on a series of a total of 475 patients after any kind of V-SARR and/or aortic valve repair included an overall survival rate of 73% at 10 years, a rate of freedom from cardiac death of 81% and a rate of freedom from valve-related death of 90% at 10 years. The rate of freedom from more than mild AR was 84% and a total of 28 patients needed early (seven) or late (n = 21) aortic reoperations [19]. The incidence of MFS was not reported in this particular series.
Cameron’s group in 2009 [20] reported the evolution of aortic root procedures in 372 MFS patients operated on over a long time period at Johns Hopkins University in Baltimore. Eighty-five patients underwent a V-SARR procedure; 40 had root remodelling (David II or Yacoub procedure) and 1 patient was treated using a David I procedure and a straight tube graft. Forty-four patients underwent the David I procedure using a Valsalva graft. Late aortic valve replacement was needed by one patient after David I with a straight tube graft, by 5 patients after remodelling and by none of the patients treated with David I using a Valsalva graft. Eight patients (7 after remodelling, 1 after David I with straight tube graft) had 3 or 4+ AR at the time of follow-up [20]. Schaefer’s group, in a series from 2010, reported on 640 patients after any type of aortic valve repair followed up over a 12-year period out of which 208 were treated with a combination of root and cusp repair [21]. The hospital mortality rate was reported to be 3.4% in the total patient cohort and 0.8% for isolated aortic valve repair. The rate of freedom from valve replacement was 95 and 90% in bicuspid and 97 and 94% in tricuspid aortic valves (P = 0.36). The rate of freedom from all valve-related complications at 10 years was 88%. Marfan patients were reported to have been treated with a David I technique, but no stratified results for this subgroup of patients were reported [21].

Results of David I type of valve-sparing aortic root replacement in Marfan syndrome

David et al. [9] reported in 2010 long-term results of a total of 296 patients operated on between 1989 and December 2010 with a mean age of 45 years. These patients underwent reimplantation of the aortic valve mostly using the David I technique. Thirty-six percent of the total cohort (n = 106) had confirmed MFS and none were operated on for acute dissection. The mean follow-up was 6.9 ± 4.5 and, at 15 years, the rate of freedom from reoperation of the entire cohort was reported to be as high as 98%. Moderate AR developed in 9 patients, with MFS a protective factor against AR progression after the procedure [9].

Shrestha et al., from Hannover [10], reported on the largest series of David I, with 450 patients, including 26 with confirmed MFS and a median age of 57 years. The hospital mortality rate was reported to be 4.8%, and 6 MFS patients required a reoperation during follow-up. However, cusp degeneration because of touching of the cusps and prosthesis was not observed over a cumulative follow-up of 790 patient-years and there was no stroke or bleeding. The rate of survival was overall 93, 85 and 70% at 1, 5 and 10 years, and the rate of freedom from valve replacement 96, 91 and 87% [10], respectively.

Kallenbach et al. [3] in 2007 summarized a decade’s experience with V-SARR (David I) for MFS performed from 1993 to 2005. Fifty-nine patients had confirmed MFS in this series and were 30 ± 12 years old (range 9–62 years). Additional procedures included arch replacement in 4 patients. The hospital mortality rate was 0%, and five late deaths (8.5%) occurred during the follow-up. Reoperation of the reconstructed valve was required in 7 patients. The rate of freedom from reoperation was 88 ± 5% at 5 years and 80 ± 9% at 10 years and the mean grade of aortic insufficiency was 1.81 preoperatively compared with 0.20 early postoperatively (P < 0.001). At the last investigation, the mean grade of aortic insufficiency increased slightly to 0.22 (P = 0.16).

Liebrich et al. [22] recently reported their experience with 236 David I procedures; mean age was 56 years with a cumulative follow-up of 896 patient-years. The rate of freedom from valve replacement was 94 and 87% at 5 and 10 years, respectively. Twenty-six patients had MFS and the rates of freedom from valve replacement and from AR >2+ were 100% [22]. Hanke et al. from Sievers’ group reported on 191 V-SARR procedures including David II remodelling and David I procedures, with 13 and 20% of patients having MFS [23]. Factors associated with the development of a significant increase in AR were MFS and preoperative aortic annulus dimension, among others. In MFS, the mean annual progression rate of AR was marginally higher in the group treated with a remodelling David II technique [23].

In conclusion, the original David I procedure has been shown to result in favourable clinical outcomes with a low rate of reoperation, in concordance with other studies. Our results further support these findings. The coexistence of a connective tissue disorder such as MFS and a BAV has not been studied extensively so far. However, the incidence of BAV might be somewhat higher in the MFS cohort, although this has not been substantiated so far. Our results indicate that an MFS patient’s BAV might be better treated using either one of the David modifications or, in many cases, probably a composite valve graft procedure, but this is still subject to further investigation.

LIMITATIONS

This manuscript reports on a single-centre retrospective analysis. The most important limitations are the limited number of patients within the specific group of individuals treated with the David I procedure and especially the limited number of events, possibly rendering risk factor analysis underpowered.

Conflict of interest: none declared.

REFERENCES


I read with great interest the paper by Kari et al. who reported their results of a Marfan cohort that was treated with the non-modified David I procedure. The early mortality rate was 2%. The survival rates at 4 years and 8 years were 98% and 90%, respectively. The rate of freedom from root or valve reoperation at 4 years was 97% and at 8 years it was 97%. One patient required mechanical aortic valve replacement (AVR) because of progression to aortic regurgitation. The authors showed that the original David I procedure resulted in favourable mid-term outcome [1]. I would like to add some thoughts about the creation or not of neo-sinuses. Grande-Allen et al. in their finite element study showed that valve-sparing techniques which allowed the potential for sinus space formation (the tailored cylindrical graft, the pseudosinus graft) resulted in simulated leaflet stresses that were closer to normal than the cylindrical technique [2]. David et al. noticed that the creation of neoaortic sinuses remains a controversial issue with aortic valve sparing (AVS) operations. They have never used the Valsalva graft as the aortic annulus will be placed inside a spherical structure instead of a cylindrical structure, such as nature created the semilunar valves. They have created neoaortic sinuses by placing darts in a tubular Dacron graft in the spaces between the commissures [3, 4]. This manoeuvre reduces the diameter of the sinotubular junction at a rate of 1 mm for each 3 mm of plication. But they have been unable to show that the neo-sinuses improve the durability of the AVS procedure. So, they finally plicate the spaces in between commissures if they notice, after the implantation of the aortic valve, that the intercommisural distance of a specific cusp prevents the cusp from coapting with others [4]. It is also interesting that Schmidtko et al. showed their first encouraging short-term results with the new prosthesis with three separate sinuses of Valsalva that was used for AVS operations. The creation or not of aortic sinuses for AVS operations is an important issue and it remains to be proven.

Conflict of interest: none declared.

References